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Sarcoidosis of the urogenital tract

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Blurb

Kidney involvement is stated to be a clinically relevant organ manifestation of sarcoidosis which does tend to lead to the development of increased morbidity and complications. Even though the exact incidence of sarcoidosis of the kidney is not known it is believed that sarcoidosis of the kidney is likely to occur in up to one third of all sarcoidosis patients. It has been advised that every patient who has a newly diagnosed sarcoidosis should undergo a renal assessment work-up and screening for disrupted calcium metabolism. Among various forms of kidney disease that tend to be found in sarcoidosis of the kidney glomerulonephritis, granulomatous interstitial nephritis is stated to be the most common affliction, but this rarely leads to renal function impairment. Most often, in cases of sarcoidosis of the kidney, pathology examination of the kidney lesion does tend to demonstrate non-caseous granulomas. However, in some cases of sarcoidosis of the kidney, it has been iterated that histologically, granulomas could be absent or not seen upon pathology examination. It has been pointed out that nephrocalcinosis and nephrolithiasis tend to be identified as frequent forms of sarcoidosis of the kidney in the presence of hypercalcaemia and hypercalciuria. It has been pointed out that medications that are used for treatment of systemic sarcoidosis could also cause damage to the kidney. It has been iterated that in view of its high heterogeneity, sarcoidosis of the kidney could be difficult to diagnose as well as treat. Diagnosis of sarcoidosis of the kidney is established based upon the pathology examination features of the kidney lesion. Steroids and various immunosuppressive medicaments had been proven to be effective based on case series, but it has been pointed out that clinical trials on the treatment of sarcoidosis of the kidney are few as well as that a treatment guideline for sarcoidosis of the kidney is urgently required. A high-index of suspicion is required in order to diagnose sarcoidosis of the kidney in view of the fact that sarcoidosis of the kidney does manifest with non-specific symptoms that simulate the manifestations of more common diseases of the kidney. It has been pointed out that a better understanding of the pathogenesis of sarcoidosis is the key for the development of more specific, targeted treatment options.

Abstract

Sarcoidosis is a terminology that is used for systemic inflammatory disease of unknown aetiology. The pathogenesis of sarcoidosis is iterated to rest upon an aberrant T cell response to unidentified antigens in individuals, who are predisposed by genetic and environmental factors. It has been iterated that the increased expression of polarized macrophages and disequilibrium between effector and regulator T cells do contribute to the formation of non-caseating granulomas, which are frequently found within the afflicted organs. The main kidney abnormalities in sarcoidosis are iterated to be granulomatous interstitial nephritis (GIN) and

hypercalcemia-related disorders. It has been pointed out that the clinical diagnosis of sarcoidosis has tended to be difficult. The outcome of sarcoidosis has been iterated to be variable, ranging from spontaneous remission to end-stage kidney disease (ESKD). It has been pointed out that early diagnosis of sarcoidosis and prompt treatment with corticosteroids could improve the prognosis sarcoidosis. The diagnosis of sarcoidosis of the kidney is usually confirmed based upon the histopathology examination features of most biopsy specimens which demonstrate non-caseating granulomas in the biopsy specimens. It has been pointed out that in cases of sarcoidosis of the kidney, hypercalcemia may be responsible for the development of acute kidney injury (AKI) which is caused by vasoconstriction of afferent arterioles. Some of the complications of persistent hypercalcemia in cases of sarcoidosis of the kidney had been iterated to include nephrocalcinosis and renal stones. It has been iterated that in patients with ESKD, dialysis and renal-transplantation could offer results that are comparable to those that are observed in patients with other causes of kidney failure.
Key Words
Sarcoidosis of the kidney; renal sarcoidosis; acute kidney injury; renal biopsy; histopathology; steroids; immunosuppressants; Rare.

Introduction

Sarcoidosis is a chronic granulomatous inflammatory disorder which afflicts various systems of the body. Amongst the organs that tend to be damaged by this inflammatory disorder, the lungs are the most commonly affected. Kidneys even though they tend to be protected from sarcoidosis, it has been iterated that the kidney can be damaged by sarcoidosis in very rare cases. [1] It has been stated that sarcoidosis of the kidney is not very often seen in routine clinical practice. [1] It has been pointed out that the manifestation of sarcoidosis of the kidney could be vague and could vary according to the underlying pathological mechanism and that the diagnosis of sarcoidosis considering its rarity could be very challenging at times. [1] Considering that sarcoidosis of the kidney is not that common, it would be envisaged that the majority of clinicians in the world would tend not to be familiar with the diagnostic features and management of sarcoidosis of the kidney. The ensuing update on sarcoidosis of the kidney is divided into two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to sarcoidosis of the kidney.

Aim

To provide an update on sarcoidosis of the kidney.

Method

Internet databases were searched including: Google, google scholar; yahoo; and PUBMED. The search words that were used included: Sarcoidosis of the kidney; and renal sarcoidosis. Forty-six (46) references were identified which were used to write the chapter which has been divided into two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to sarcoidosis of the kidney.

Results

[a] overview

Definition / general statement [2]

- Sarcoidosis is stated to be a terminology that is used for a multisystem granulomatous disease of unknown cause, which is histologically characterized by epithelioid noncaseating granulomas. [2]
- It has been iterated that the classic pathological lesion of sarcoidosis of the kidney is granulomatous interstitial nephritis but there are other forms of renal involvement in sarcoidosis. [2]

Essential features

The essential features of sarcoidosis of the kidney had been summated as follows: [2]

- Kidney disease in sarcoidosis could present as follows: [2]
  - Granulomatous interstitial nephritis. [2]
  - Non-granulomatous interstitial nephritis. [2]
  - Nephrocalcinosis of the calcium phosphate and oxalate type. [2]
  - Nephrolithiasis. [2]
  - Sarcoidosis associated glomerular diseases. [2]

Terminology

- With regard to terminology, it has been iterated that sarcoidosis is also known as Besnier-Boeck-Schaumann disease. [2]

Epidemiology

The epidemiology of sarcoidosis of the kidney has been summated as follows: [2]

- It has been iterated that kidney manifestations of sarcoidosis could present in patients who have a diagnosis of sarcoidosis of other systems of the human body; notably, hilar adenopathy or pulmonary infiltrates upon chest radiographs, or be an initial or sole manifestation of the sarcoidosis disease. [2]
- It has been iterated that the best-known kidney manifestation of sarcoidosis, which is granulomatous interstitial nephritis, is observed in 7% to 23% or 30% to 79% of native kidney biopsies from patients with sarcoidosis. [3] [4]
- In contrast to the female predominance in patients with pulmonary sarcoidosis, 63.8% of patients with granulomatous interstitial nephritis are stated to be men [5]
- It has been iterated that the mean age at initial manifestation of granulomatous interstitial nephritis is 46.9 years with an age range of between 11years and 80 years or is reported at 59 years, plus or minus 18 years [5] [6]
- It has been documented that 74% of patients with granulomatous interstitial nephritis are White individuals [5]
- It has been iterated that non-granulomatous interstitial nephritis is found in 14 - 44% of native kidney biopsies from patients with sarcoidosis. [2] [3] [4]
- It has been iterated that in some studies, glomerular disease was found in between 4% to 26% or up to 42% of native kidney biopsies in patients with sarcoidosis but is generally believed to be a rare occurrence. [3] [4] [7]
- It had been pointed out that sarcoidosis associated glomerular disorders might precede the diagnosis of sarcoidosis. [2] [7]
- It has been iterated that dysfunctional vitamin D and calcium metabolism leading to hypercalcemia, hypercalciuria, nephrolithiasis and nephrocalcinosis are common problems that tend to be found in patients with sarcoidosis [2] [5]
- It has been iterated that nephrocalcinosis is seen in 10% to 11% of sarcoidosis patients presenting with kidney disease. [2] [3] [4]

- It has been documented that nephrolithiasis is found in about 10% of patients with sarcoidosis. [2] [8]
- It has been iterated that Blau syndrome, which is a terminology that is used for: early sarcoidosis, a familial granulomatous inflammatory disease; presents in early childhood, usually in the first year of life. [2] [9]

Sites

The sites most commonly afflicted by sarcoidosis had been summated as follows: [2]

- It has been stated that sarcoid granulomatous lesions preferentially involve the lower respiratory tract but they may afflict any extrapulmonary site, such as the heart, the thyroid gland, the parathyroid gland, the skin, and the eye. [2]
- The kidney involvement in sarcoidosis also occurs. [2]

Pathophysiology

The pathophysiology of sarcoidosis has been summated as follows: [2]

- Sarcoidosis is stated to be associated with chronic hypercalcemia and increased levels of 1,25 dihydroxy vitamin D (calcitriol) [2] [8]
- It has been stated that in sarcoidosis, altered level of vitamin D and hypercalcemia suppress the parathyroid hormone. [2] [8]
- In sarcoidosis increased calcium filtration at the glomerulus and suppression of parathyroid hormone secretion by calcitriol (diminished tubular reabsorption of calcium) lead to hypercalciuria and thus to nephrocalcinosis and nephrolithiasis. [2] [8]
- In sarcoidosis of the kidney, hypercalcemia is stated to cause afferent arteriole vasoconstriction, decreasing blood flow and the glomerular filtration rate. [2] [8]
- It has been iterated that glomerular diseases that are found in patients with sarcoidosis are conjectured to be caused by functional disorders of the immune system. [2]
    - It has also been stated that in sarcoidosis of the kidney, cytokines that produced locally by granulomas may contribute to alterations in the glomerular filtration barrier. [2] [7]

Aetiology

- It has been iterated that the aetiology of sarcoidosis is incompletely understood. [2] [10]

Clinical features

The clinical features of sarcoidosis had been summated as follows: [2]

- It has been pointed out that granulomatous interstitial nephritis in sarcoidosis is usually clinically silent but in less than one percent (< 1%) of causes acute kidney injury emanates. [2] [3]
- It has been iterated that according to other studies, granulomatous interstitial nephritis accounts for 7% to 27% of clinically significant renal failure in patients with sarcoidosis. [2] [3] [4] [5]
- It has been iterated that acute kidney injury, when it develops, does appear to be more severe in patients with granulomatous interstitial nephritis versus patients with non-granulomatous interstitial nephritis. [2] [3] [4]
- It has been documented that acute kidney injury in patients with hypercalcemia is milder in comparison with in patients without hypercalcemia. [2] [4]
- It has been iterated that granulomatous kidney masses (so called pseudo-tumoral renal sarcoidosis) are usually found to be associated with normal renal function. [2] [11]
- It has been pointed out that Blau syndrome presents as a triad of granulomatous dermatitis, arthritis and uveitis. [2] [9]

Diagnosis

The diagnosis of sarcoidosis has been summated as follows: [2]

- Diagnosis of sarcoidosis has been stated to be based upon 3 major criteria: a compatible clinical presentation, the finding of non-necrotizing granulomatous inflammation in 1 or more tissue samples and the exclusion of alternative causes of granulomatous disease. [2] [12]
- It has been iterated that the undertaking of kidney biopsy is the key instrument in diagnosis of kidney involvement in sarcoidosis. [2]

Laboratory

Summations which had been made regarding laboratory tests that tend to be undertaken or which should be undertaken in sarcoidosis include the ensuing: [2]

- For patients with sarcoidosis who have neither kidney symptoms nor established renal sarcoidosis, baseline serum creatinine testing is suggested for screening
    - Diagnosis and detection of sarcoidosis
    - Official American Thoracic Society Clinical Practice Guideline
- Disordered calcium metabolism is stated to be found in a significant number of patients. [2] [5] [13]
- It has been stated that the levels of serum angiotensin converting enzyme, interleukin 2 receptor (IL2R), C reactive protein (CRP), serum amyloid A (SAA) and chitotriosidase might be helpful in establishing the diagnosis. [2] [3]

Radiology description

The radiology-imaging in cases of sarcoidosis of the kidney had been summated as follows: [2]

- It has been iterated that contrast-enhanced computer tomography scan may demonstrate signs of interstitial nephritis or less frequently multiple hypoattenuating nodules that resemble lymphoma or metastases. [2]
- It has been iterated that upon MRI scan, granulomatous kidney masses tend to be poorly circumscribed and infiltrative and slightly hypointense to surrounding renal cortex; the zone of transition between the mass and normal renal parenchyma is ill defined and consistent with interstitial infiltration. [2] [14]
- It has been iterated that attenuation corrected whole body positron emission tomography (PET) scan demonstrates intense radiotracer uptake in the kidney and lymph nodes; this can be misconstrued as indicative of malignancy. [2] [14]

Prognostic factors

Factors of prognostication associated with sarcoidosis of the kidney had been summated as follows: [2]

- Severe interstitial infiltrates within the kidney are stated to tend to predict a worse prognosis. [2] [3])
- Interstitial fibrosis, severe interstitial infiltration and the presence of giant cells are associated with a worse outcome. [3] [6]

Treatment

The treatment of sarcoidosis of the kidney had been summated as follows: [2]

- It has been iterated that corticosteroids are the standard of care in sarcoidosis of the kidney. [2]
- It has been iterated that the majority of cases of sarcoidosis of the kidney respond to steroid therapy. [2] [6]

- It has been iterated that in steroid resistant sarcoidosis of kidney patients, other immunosuppressive reagents (azathioprine, mycophenolate mofetil or TNF inhibitors) are used. [2] [15]
- Steroid responsiveness of sarcoidosis is stated to be associated glomerular diseases does not correlate with that of the main disease, suggesting that both diseases require a more aggressive therapy. [2] [7]

Microscopic (histologic) description

The pathology microscopy examination features of sarcoidosis of the kidney had been summated as follows: [2]

- It has been iterated that microscopy pathology examination of specimens of the sarcoidosis of kidney lesions show granulomas that are well formed concentrically arranged layers of immune cells with a central core of macrophages, epithelioid cells and multinucleated giant cells and an outer layer of loosely organized lymphocytes (mostly T cells) and interposed dendritic cells, sometimes surrounded by collections of B lymphocytes. [2]
- It has been iterated that epithelioid cells (epithelioid histiocytes) of sarcoidosis lesions of the kidney are derivatives of activated macrophages resembling epithelial cells. [2]
- It has been stated that caseous necrosis in sarcoidosis of the kidney is the grossly visible, cheese-like appearance of the granulomas, and that this terminology has no microscopy counterpart and hence, the terminology necrotizing is preferable. [2] [16]
- It has been pointed out that sarcoidosis granulomas are most often non-necrotic. [2] [12]
- It has been iterated that epithelioid cells are elongated, with pale eosinophilic cytoplasm and central, ovoid nuclei, which are less dense than that of a lymphocyte. [2]
- It has been stated that presence of numerous non-caseating (non-necrotizing) granulomas upon microscopy examination of the kidney lesion favours sarcoidosis. [2] [12]
- It has been stated that upon microscopy pathology examination of specimens of sarcoidosis of the demonstrate that the sarcoid granulomas feature compact, tightly formed collections of large epithelioid histiocytes and multinucleated giant cells. [2] [12]
- These granulomas are stated to be confined to the renal cortex and stay discrete; interstitial inflammatory infiltration is observed in all cases. [2] [12]
- Blau syndrome [2]
- It has been iterated that in sarcoidosis of the kidney, non-granulomatous interstitial nephritis may demonstrate numerous eosinophils in the interstitial infiltrate. [2] [12]
- It has been iterated that in specimens of sarcoidosis of the kidney, nephrocalcinosis does manifest as calcium phosphate or oxalate tubulointerstitial deposits. [2]
    - Such deposits are also said to be found in patients who have granulomatous and non-granulomatous interstitial nephritis. [2] [4]
- It had been iterated that the most frequent glomerular disease that occurs in sarcoidosis is membranous glomerulonephritis.[2] [7]
- It has also been stated that other glomerular diseases that tend to be found in patients with sarcoidosis include IgA nephropathy, focal segmental glomerulosclerosis, minimal change disease, and lupus nephritis. [2] [7]

- It had also been stated that in sarcoidosis of the kidney focal segmental glomerulosclerosis and hypertensive nephrosclerosis might be found in sarcoidosis patients with interstitial nephritis. [2] [6]

Immunofluorescence description

- It has been stated that in cases of sarcoidosis of the kidney, immunofluorescence staining for IgG, IgA, IgM, C3, C1q, kappa and lambda light chains is usually negative within all kidney compartments. [2]
- It has been stated that in sarcoidosis of the kidney, rare cases of nonspecific deposits of IgM or deposits of C3 had been reported. [2] [3]
- It has been iterated that sarcoidosis associated glomerular diseases are diagnosed with the use of the appropriate immunofluorescence features. [2]

Positive stains

- It has been stated that CD68 immunohistochemical staining is used to highlight histiocytes and multinucleated giant cells in order to facilitate findings of granulomas. [2] [17]

Negative stains

- It has been iterated that: specimens of sarcoidosis of the kidney, upon immunohistochemistry staining studies exhibit negative staining for bacterial and fungal stains, such as:
  - Acid fast Ziehl-Neelsen stain. [2]
  - GMS (Grocott-Gomori methenamine silver) stain. [2]
  - PAS (periodic acid-Schiff) stain. [2]

Electron microscopy description

- It has been iterated that no specific electron microscopy findings are associated with granulomatous or non-granulomatous interstitial nephritis, nephrolithiasis or nephrocalcinosis. [2]
- It has been stated that electron microscopy is undertaken to diagnose sarcoidosis associated glomerular pathology and to exclude other aetiologies. [2]

Genetics

- It has been iterated that genetic studies do confirm the very strong genetic heterogeneity in sarcoidosis. [2] [18]
- It has been pointed out that familial as well as sporadic forms of sarcoidosis do exist. [2] [18]
- It has been iterated that familial sarcoidosis might be associated with variants in mTOR gene and its regulator, a GTPase Rac 1. [2] [18]
- It has been stated that mTOR pathway regulates autophagy and might be involved in the clearance of pathogens. [2] [18]
- It had been pointed out that genomic associations of sarcoidosis renal lesions had not been explored. [2]
- It has been iterated that Blau syndrome, a monogenic autoinflammatory disease, is due to NOD2 (nucleotide binding oligomerization domain containing 2) gene gain of function mutations. [2] [9]
- It has been iterated that NOD2 protein is primarily expressed in the peripheral blood leukocytes and plays a role in the immune response to intracellular bacterial lipopolysaccharides. [2]

Differential diagnoses

The differential diagnoses of sarcoidosis of the kidney had been summated to include the ensuing: [2]

- Mycobacterial infections which exhibit the following features:
  - History of exposure.
  - Diagnosis of extrarenal mycobacterial infection.
  - Mycobacterial DNA fragments may be identified by polymerase chain reaction (PCR).
  - Present with necrotizing granulomas.
  - Positive acid-fast stain.
- Fungal infections which exhibit the following features:
  - History of exposure.
  - Positive GMS stain and fungal culture.
- Adenoviral infection which exhibits the following features:
  - Seen in renal allografts.
  - Tubulo-centric polymorphonuclear neutrophil (PMN) rich inflammation and acute tubular necrosis. [2]
  - Ground glass tubular epithelial cells with viral inclusions.
  - Serum, urine and kidney tissue PCR positive for adenovirus.
  - Positive immunohistochemical stain for adenovirus.
- Intravesical Bacillus Calmette-Guérin (BCG) therapy which exhibits the following features:
  - History of bladder carcinoma and BCG treatment.
- Granulomatous inflammation associated with extra-tubal Tamm-Horsfall protein which exhibits the following features:
  - Glassy PAS+ acellular material.
  - Associated with interstitial kidney disease.
  - Positive stain with anti-Tamm-Horsfall protein antibody.
- Allergic acute interstitial nephritis. Medication related which exhibit the following features:
  - History of medications known to cause granulomatous interstitial nephritis.
  - Predilection for the corticomedullary junction involvement
  - Poorly formed granulomas. [2] [19]
- Berylliosis (occupational exposure) which exhibit the following features:
  - History of inhalation of beryllium dust.
  - Granulomas are poorly formed. [2] [16]
- Tubulointerstitial nephritis with uveitis which exhibit the following features:
  - Affects mainly children and young women.
  - Uveitis.
  - Rare non-necrotizing granulomas.
- Crohn’s disease which exhibits the following feature:
  - History of inflammatory bowel disease.
- Granulomatosis with polyangiitis which exhibit the following features:
  - Antineutrophilic cytoplasmic antibody (ANCA) positivity.
  - Presents as necrotizing and crescentic glomerulonephritis.
  - In very rare cases, may present with granulomatous acute interstitial nephritis in the absence of glomerulonephritis. [2] [20]

- Vessel associated granuloma may be seen.

[B] Miscellaneous Narrations and Discussions from Some Case Reports, Case Series, And Studies Related To Sarcoidosis Of The Kidney

Klaus et al. [21] stated that paediatric sarcoidosis is a complex inflammatory disorder with multisystemic presentations, and that sarcoidosis kidney involvement in children is not common as well as that the prognostic factors are not known. Klaus et al. [21] reported the case of a 16-year-old girl who had multi-organ sarcoidosis and kidney involvement. Klaus et al. [21] reported that the patient manifested with tubulointerstitial nephritis, acute kidney injury (AKI), chest CT disseminated noduli, granulomatous iridocyclitis, giant-cell sialadenitis, and arthralgia. She underwent biopsy of her kidney lesion, and pathology examination of the kidney biopsy specimen demonstrated non-granulomatous interstitial nephritis. Her treatment consisted of initial high-dose methylprednisolone pulse, which was ensued by oral prednisolone and methotrexate. Full remission was achieved. In addition, Klaus et al. [21] undertook a literature review using PubMed and they analysed data on paediatric renal sarcoidosis cases. Klaus et al. [21] summated the results as follows:

- They had identified 36 cases of paediatric sarcoidosis with renal involvement on presentation and data on the end-of-follow-up glomerular filtration rate (GFR).
- The data from the literature review had demonstrated that renal involvement was slightly more prevalent in males (60%).
- AKI was present in majority of the reported patients (84%).
- Oral prednisolone was utilised in 35 of 36 cases; in more severe cases, other immunosuppressants were utilised.
- They had newly identified renal concentration impairment and granulomatous interstitial nephritis as factors with a clear trend toward GFR loss at the end of follow-up, emphasizing the importance of kidney biopsy in symptomatic patients.
- In contrast, higher GFR at manifestation and hypercalcemia were rather favourable factors.
- According to the identified predictive factors, their patient had a good prognosis and was in remission.

Klaus et al. [21] concluded that the factors indicating a trend toward an unfavourable renal outcome in paediatric sarcoidosis include: renal concentration impairment and granulomatous interstitial nephritis at presentation, while a higher GFR is beneficial.

De la Hoz et al. [22] made the ensuing iterations:

- Sarcoidosis manifest in a variety of ways, but historically, kidney involvement had been considered rare with an incidence of 0.7% and is seldom the manifesting feature of the illness.
- Concomitant renal involvement and bone marrow is very rare.
- Atypical forms of manifestation, such as in their reported case, may pose a true diagnostic challenge.

De la Hoz et al. [22] reported a 20-year-old African-American male, who presented to the emergency department with vague symptoms including fatigue, malaise, anorexia, right-sided lower back pain, and nausea. Acute kidney injury was clearly evident, in that his serum creatinine was 19.78 mg/dL (normal range 0.60-1.20 mg/dL), and BUN was 124.0 mg/dL (normal range 5.0-25.0 mg/dL). His laboratory test results were also remarkable for leukopenia, microcytic anaemia, hyperkalaemia, anion gap metabolic acidosis, and non-PTH dependent

hypercalcemia. Interestingly, his urinalysis was equivocal and both his chest x-ray (CXR) and computed tomography (CT) scan of his abdomen and pelvis did not demonstrate any abnormality. He was admitted to the hospital and required renal replacement therapy in order to stabilize his clinical condition while planning for a renal biopsy that was subsequently undertaken. While awaiting pathological results, he developed pancytopenia, and a bone marrow biopsy was then undertaken. On further investigation, his angiotensin-converting enzyme (ACE) turned out to be significantly raised, which had suggested sarcoidosis. He had biopsy of his renal lesion and pathology examination of the kidney biopsy specimen demonstrated moderate acute tubular injury, tubulitis, extensive interstitial oedema, and infiltration by many non-caseating granulomas, which had confirmed the diagnosis of sarcoidosis. Histopathology examination of his bone marrow specimen demonstrated hypocellularity but no granulomatous infiltration. The patient remained largely asymptomatic throughout his hospital stay, with no signs or symptoms suggesting the involvement of other organs. High-dose corticosteroids were commenced and this was continued on outpatient basis after his discharge back home while still on haemodialysis. His pancytopenia resolved while on glucocorticoids and improvement in his renal function was such that after roughly two months of steroids medication, renal replacement therapy was no longer necessary. De la Hoz et al. [22] made the ensuing discussions and conclusions:

- Overall, kidney injury severe enough to require haemodialysis associated with pancytopenia in a previously healthy 20-year-old constitutes a rather rare sarcoidosis presentation.
- This has highlighted the importance of considering sarcoidosis as a possible cause of kidney and bone marrow dysfunction as well as has emphasized the need for timely biopsy to facilitate accurate diagnosis and early initiation of appropriate therapy to avoid delayed or inadequate care, especially considering that even severe damage is potentially reversible when identified early and treated promptly.

Zia et al. [1] made the ensuing iterations:

- Sarcoidosis is a multisystem granulomatous disorder, which is typified by non-caseating granulomas in multiple organs.
- Sarcoidosis most commonly involves the lungs and it is very rare to find isolated cases affecting other organ systems with no associated pulmonary findings.

Zia et al. [1] reported a case of a young 30-year-old male who was referred to the hospital by his primary medical doctor due to right eye pain secondary to iritis and acute kidney injury (AKI). His initial laboratory test results had demonstrated anaemia, AKI, mild hypercalcemia, and the urinary analysis revealed proteinuria. He underwent radiology-imaging studies, which were negative and a kidney biopsy was undertaken and pathology examination of the kidney biopsy specimens showed diffuse tubulointerstitial disease with early fibrosis, widespread moderate inflammation, multifocal tubulitis, and focal aggregate of epithelioid cells suggestive of granuloma consistent with sarcoidosis. The patient was treated with prednisone. Zia et al. [1] made the ensuing discussions:

- Renal involvement of sarcoidosis is very rare (around 0.7%).
- Renal involvement of sarcoidosis has a wide spectrum of presentations including: abnormal calcium metabolism, nephrolithiasis, nephrocalcinosis, and acute tubulointerstitial nephritis with or without granulomas.
- Their reported case was a unique case as it showed renal sarcoidosis without coexisting pulmonary finding of hilar lymphadenopathy on chest X-ray.

- There are very few reported cases of renal sarcoidosis in the literature and their case had been added to the pool of those cases.
- Their reported case had also emphasized the need for urgent renal biopsy in the settings of AKI associated with mild to moderate proteinuria.
- Lack of availability of comprehensive research on the disease may lead to misdiagnosis and delay in treatment.

RØMER [23] reported forty-two patients with sarcoidosis, who were studied with special attention to renal disease and disturbance of calcium metabolism. RØMER [23] reported the results as follows:

- Abnormal calcium metabolism was found in 19 patients and prednisone had corrected hypercalcaemia in those affected within two weeks, except in one patient who had concomitant primary hyperparathyroidism.
- Renal failure was found in 19 patients, 15 of whom had hypercalcaemia.
- Prednisone had a beneficial effect upon kidney function within four weeks in all of the patients except in one with co-existing glomerulonephritis.
- Arterial hypertension was found in six patients, proteinuria in six patients, and calcinosis in six patients.
- Among 14 patients who had undergone kidney biopsy, granulomas were found in five. In only one of these was granulomatosis extensive bringing out renal failure and death within two years after temporary remission with prednisone.
- Co-existent non-sarcoid diseases affecting the kidneys or calcium metabolism had occurred in ten out of 23 patients with sarcoidosis and kidney disease/calcium abnormality. In the majority of the cases these conditions had contributed more to the prognosis than did sarcoidosis.

RØMER [23] concluded that from the reported case series and review of the literature it did appear that young males within the first two years of diagnosis are at the greatest risk of hypercalcaemia or kidney disease.

Menezes et al. [24] stated that sarcoidosis is a multisystemic granulomatous disease with rare renal involvement. Menezes et al. [24] reported a case of a 45-year-old female patient who was admitted to the hospital with severe acute kidney injury and uveitis. After clinical investigation, sarcoidosis with renal, hepatic and ocular involvement was diagnosed. Pathology examination of her kidney biopsy showed acute granulomatous interstitial nephritis and treatment with systemic corticosteroids was commenced with marked improvement in her renal function.

Casella et al. [25] made the ensuing iterations:

- Sarcoidosis had been associated with a wide spectrum of renal manifestations, including disordered calcium metabolism, nephrocalcinosis, nephrolithiasis, granulomatous interstitial nephritis, and glomerulonephritis.
- In some patients, two or more manifestations of sarcoidosis of the kidney may coexist.

Casella et al. [25] reported the case of a young patient with sarcoidosis who presented with hypercalcemia and acute renal failure. Despite normalization of the serum calcium with intravenous fluids and corticosteroids, his renal insufficiency persisted. A diagnostic renal biopsy was undertaken to determine the aetiology of his renal failure and was helpful in the selection of optimal medical therapy.

Calatroni et al. [26] made the ensuing iterations:

- Sarcoidosis is a systemic inflammatory disease of unknown aetiology.

- The pathogenesis of sarcoidosis rests upon an aberrant T cell response to unidentified antigens in individuals predisposed by genetic and environmental factors.
- Increased expression of polarized macrophages and disequilibrium between effector and regulator T cells contribute to the formation of noncaseating granulomas, which are often found in sarcoidosis affected organs.
- The main kidney abnormalities in sarcoidosis are granulomatous interstitial nephritis (GIN) and hypercalcemia-related disorders.
- The clinical diagnosis of sarcoidosis of the kidney is difficult.
- The outcome is variable, and the outcome ranges from spontaneous remission to end-stage kidney disease (ESKD).
- Early diagnosis and prompt treatment with corticosteroids could improve the prognosis of sarcoidosis of the kidney.
- Hypercalcemia may be responsible for acute kidney injury (AKI) which is caused by vasoconstriction of afferent arterioles.
- Complications of persistent hypercalcemia in cases of sarcoidosis of the kidney include nephrocalcinosis and renal stones.
- In patients with ESKD, dialysis and transplantation could offer results comparable to those observed in patients with other causes of kidney failure

Bergner et al. [27] made the ensuing iterations:

- The purpose of their article was to provide understanding of renal sarcoidosis, the different types of renal sarcoidosis, disease burden of renal involvement, and treatment options.
- The frequency of sarcoidosis renal involvement seems to be underestimated, but sarcoidosis of the kidney represents a relevant group of organ manifestations and significantly adds to the patient's morbidity.
- In view of the fact that histopathological analysis of renal biopsy specimens could demonstrate various entities, a diagnostic workup is necessary in every patient with sarcoidosis.
- If systematically screened for renal manifestations are likely to occur in up to 25–30% of all sarcoidosis patients.
- The most common histological form of sarcoidosis the kidney is the granulomatous interstitial nephritis; nevertheless, granulomas could be absent.
- Furthermore, one could find various forms of secondary glomerulonephritis.
- In cases with dysregulated calcium homeostasis, nephrocalcinosis and nephrolithiasis are commonly detectable kidney diseases.
- AA amyloidosis or kidney masses because of granuloma formation are considered to be rare manifestations.
- In addition to glucocorticoids various immunosuppressive treatments such as tumour necrosis factor alpha inhibitors had been proven to be effective based upon case series.

Vender et al. [28] made the ensuing iterations:

- PET scan has emerged as method to determine the location and extent of disease activity in sarcoidosis.
- As the majority of clinicians do not routinely use PET in the management of sarcoidosis, an understanding of the imaging technique is necessary to comprehend the impact that PET abnormalities have on diagnosis, prognosis, and treatment.

- Even though PET can detect inflammation because of sarcoidosis throughout the body, it is most often used for the diagnosis of cardiac sarcoidosis for which it might provide information about prognosis and adverse events.
- Whenever PET is combined with cardiac magnetic resonance (CMR), clinicians may be able to increase the diagnostic yield of imaging. Furthermore, PET abnormalities have the potential to be utilized in the reduction or augmentation of therapy based on an individual's response to treatment.
- Even though various biomarkers are used to monitor disease activity in sarcoidosis, an established and reproducible relationship between PET and biomarkers does not exist.
- PET has the potential to improve the diagnosis of sarcoidosis and alter treatment decisions but prospective trials are required to define the role of PET while also standardizing the performance and interpretation of the imaging modality.

Bonella et al. [29] made the ensuing iterations:

- Kidney involvement is a clinically relevant organ manifestation of sarcoidosis, leading to increased morbidity and complications.
- Even though the exact incidence remains unknown, renal disease is likely to occur in up to one third of all sarcoidosis patients.
- Every patient with newly diagnosed sarcoidosis should receive a renal work-up and screening for disrupted calcium metabolism.
- Amid various forms of glomerulonephritis, granulomatous interstitial nephritis is the most common one, however, it rarely leads to renal impairment.
- Histologically, granulomas could be absent is sarcoidosis of the kidney.
- Nephrocalcinosis and nephrolithiasis are frequent forms when hypercalcaemia or hypercalciuria do occur in sarcoidosis of the kidney.
- Medications that are used for the treatment of systemic sarcoidosis could also cause renal damage.
- In view of its high heterogeneity, sarcoidosis of the kidney could be difficult to treat.
- Glucocorticoids and various immunosuppressive treatments had been proven to be effective based upon case series, but clinical trials are lacking.
- A treatment guideline for sarcoidosis of the kidney is urgently required.
- A better understanding regarding the pathogenesis of sarcoidosis is the key for the development of more specific, targeted treatments for sarcoidosis of the kidney.

Bergner et al. [30] made the ensuing iterations:

- Sarcoidosis is an immune-mediated disease of unknown cause, which is characterized by noncaseating epithelioid granulomas, affecting multiple organs.
- Clinically apparent renal involvement is rare and had been documented mostly as case reports.
- The incidence of sarcoidosis kidney involvement ranges from 3% to 23% with a wide spectrum of abnormalities.

Bergner et al. [30] investigated the renal involvement in patients who have sarcoidosis. Bergner et al. [30] summarised the results as follows:

- From 1995 to 2002 they had diagnosed 46 patients with sarcoidosis.
- Fifteen patients had suffered from acute sarcoidosis with arthritis, mediastinal adenopathy and erythema nodosum (Löfgren's-syndrome).

- Thirty-one patients had chronic sarcoidosis with organ involvement, such as granulomatous hepatitis, uveitis and pulmonary sarcoidosis.
- In 15 patients they found renal abnormalities, 10 patients underwent kidney biopsy. Six patients had nephrocalcinosis, 2 patients, had granulomatous interstitial nephritis, one patient had interstitial nephritis without granuloma, and 1 patient suffered from IgA-glomerulonephritis. In 2 patients they found a combination of granulomatous interstitial nephritis either with nephrocalcinosis or with IgA-glomerulonephritis.
- In all patients the serum creatinine decreased after treatment with corticosteroids.

Bergner et al. [30] made the ensuing conclusions:

- In their retrospective analysis they found renal abnormalities in about 48% of patients with chronic sarcoidosis, but never in patients with acute sarcoidosis (Löfgren's syndrome).
- They had concluded that kidney involvement in chronic sarcoidosis is more frequent than was previously reported.

Bagnasco et al. [31] made the ensuing iterations:

- Kidney involvement by sarcoidosis in native and transplanted kidneys classically presents as non-caseating granulomatous interstitial nephritis.
- Nevertheless, the incidence of sarcoidosis in native and transplant kidney biopsies, its frequency as a cause of end stage renal disease and its recurrence in renal allograft are not well defined, which prompted this study.
- The electronic medical records and the pathology findings in native and transplant kidney biopsies reviewed at the Johns Hopkins Hospital from 1/1/2000 to 6/30/2011 were searched.
- A total of 51 patients with a diagnosis of sarcoidosis and renal abnormalities that required a native kidney biopsy were identified.
- Granulomatous interstitial nephritis, consistent with renal sarcoidosis was identified in kidney biopsies from 19 of these subjects (37%). This was equivalent to a frequency of 0.18% of this diagnosis in a total of 10,023 biopsies from native kidney reviewed at our institution.
- Follow-up information was available in 10 patients with biopsy-proven renal sarcoidosis: 6 responded to treatment with prednisone, one progressed to end stage renal disease. Renal sarcoidosis was the primary cause of end stage renal disease in only 2 out of 2,331 transplants performed. Only one biopsy-proven recurrence of sarcoidosis granulomatous interstitial nephritis was identified.

Bagnasco et al. [31] made the ensuing conclusions:

- Renal involvement by sarcoidosis in the form of granulomatous interstitial nephritis was a rare finding in biopsies from native kidneys reviewed within their centre, and was found to be a rare cause of end stage renal disease.
- However, their observations had indicated that recurrence of sarcoid granulomatous inflammation may occur in the transplanted kidney of patients with sarcoidosis as the original kidney disease.

Berliner et al. [5] made the ensuing iterations:

- Sarcoidosis is an idiopathic multisystem illness of granulomatous inflammation that is postulated to be an autoimmune response to either an infection, possibly caused by Mycobacteria or Propionibacteria species, or an unknown environmental agent.
- In addition, more than 30 cases were associated with interferon-α use.

- Sarcoidosis is diagnosed most often by 40 years of age worldwide and across all ethnicities, even though in the United States, African Americans have a 10-fold greater incidence than whites.
- Sarcoidosis may wax and wane chronically and require long-term corticosteroid therapy, or the diagnosis may be incidental when hilar lymphadenopathy is found on routine chest radiography followed by transbronchial lymph node biopsy.

Shah et al. [32] made the ensuing iterations:

- Sarcoidosis is an idiopathic multisystem disease, which is typified by noncaseating granulomatous inflammation.
- Renal biopsy is often undertaken to evaluate the patient with sarcoidosis and acute kidney injury (AKI).
- Diagnosis rests upon the demonstration of non-caseating granulomas and exclusion of other causes of granulomatous inflammation.
- They had reported a patient with pulmonary sarcoidosis and AKI whose renal function improved after prednisone therapy despite the absence of kidney biopsy findings characteristic of sarcoidosis.

Shah et al. [32] reported a 63-year-old Caucasian male who had a history of hypertension and who was treated for pulmonary sarcoidosis with a 6-month course of prednisone. His creatinine was 1.6 mg/dL during the course. Two months after completing his treatment, he manifested with creatinine of 4 mg/dL. A kidney biopsy was undertaken and pathology examination of the kidney biopsy specimen showed non-specific changes without evidence of granuloma or active interstitial inflammation. He was empirically commenced on prednisone for a presumed sarcoidosis of the kidney, even with a non-diagnostic kidney biopsy finding. Within a month of treatment, his serum creatinine had improved to 2 mg/dL, even though not to the baseline. He continued to be stable on low-dose prednisone. With this case as a background, Shah et al. [32] aimed to determine the incidence of inconclusive kidney biopsies in patients with sarcoidosis presenting with AKI and to identify the various histological findings seen in this group of patients. Shah et al. [32] therefore, undertook a retrospective study, which involved all patients who had native renal biopsies read at The Ohio State University over the period of 6 years they had identified. Those patients with a diagnosis of sarcoidosis, presenting with AKI, were included for further review. Shah et al. [32] summarised the results as follows:

- Out of 21 kidney biopsies undertaken in patients with sarcoidosis over a period of 6 years, only four (19%) had shown granulomatous interstitial nephritis (GIN).
- An equal number of patients (4 [19%]) had presence of membranous nephropathy.
- Nephrocalcinosis was found in three patients (14%).
- Almost half of the biopsies had findings, which was indicative of diabetic nephropathy or other non-specific changes not characteristic of sarcoidosis of the kidney (48%).

Shah et al. [32] made the ensuing conclusions:

- Sarcoidosis of the kidney could be focal in nature and characteristic lesions could be missed in a small-needle core biopsy.
- Inconclusive kidney biopsies with only non-specific findings are frequent in patients with sarcoidosis and AKI.
- The presence of GIN on kidney biopsy, even though classic, is not common.

- Sarcoidosis of the kidney remains a presumptive clinical diagnosis and empiric treatment with steroids may be commenced in cases with a strong clinical suspicion even in the absence of characteristic kidney biopsy findings.

Agrawal et al. [33] stated that among the various kidney manifestations of sarcoidosis, granulomatous inflammation, which is confined to the tubulointerstitial compartment is the most commonly reported finding. Agrawal et al. [33] reported the case of a 66-year-old man with acute kidney injury, hypercalcemia, mild restrictive pulmonary disease, and neurological signs of parietal lobe dysfunction. Pathology examination of his kidney biopsy specimen demonstrated diffuse interstitial inflammation with non-caseating granulomas which had exhibited the unusual feature of infiltrating the walls of small arteries with destruction of the elastic lamina, consistent with granulomatous vasculitis. The findings of granulomatous interstitial nephritis on kidney biopsy, hypercalcemia, and possible cerebral and pulmonary involvement in the absence of other infectious, drug-induced, or autoimmune causes of granulomatous disease had helped the authors to establish the diagnosis of sarcoidosis. Pulse methylprednisolone followed by maintenance prednisone therapy had led to improvement in the patient's kidney function, hypercalcemia, and neurologic symptoms. Agrawal et al. [33] concluded that:

- Vasculo-centric granulomatous interstitial nephritis with granulomatous vasculitis is a rare and under-recognized manifestation of sarcoidosis of the kidney.

Rastelli et al. [3] made the ensuing iterations:

Granulomatous interstitial nephritis in sarcoidosis (sGIN) is generally clinically silent; however, less than one percent (<1%) causes acute kidney injury (AKI). Rastelli et al. [3] undertook an Italian multicentric retrospective study, which included 39 sarcoidosis-patients with kidney involvement at renal biopsy: 31 sGIN-AKI, 5 with other patterns (No-sGIN-AKI), 3 with nephrotic proteinuria. Rastelli et al. [3] investigated the predictive value of clinical features, laboratory, radiological parameters and histological patterns regarding steroid response. Primary endpoint: incident chronic kidney disease (CKD) beyond the 1°follow-up (FU) year; secondary endpoint: response at 1°line steroid therapy; combined endpoint: the association of initial steroid response and outcome at the end of FU. Rastelli et al. [3] summated the results as follows:

- Complete recovery was found in all 5 No-sGIN-AKI-patients, only in 45% (13/29) sGIN-AKI-patients (p=0.046) (one lost in follow-up, for another not available renal function after steroids). Nobody had not response.
- Primary endpoint of 22 sGIN-AKI subjects included: 65% (13/20) commencing with normal renal function developed CKD (2/22 had basal CKD; median FU 77 months, 15-300).
- Combined endpoint included the ensuing: 29% (6/21) had complete recovery and final normal renal function (one with renal relapse), 48% (10/21) had partial recovery and final CKD (3 with renal relapse, of whom one with basal CKD) (p=0.024).
- Acute onset and hypercalcaemia were noted to be associated to milder AKI and better recovery than subacute onset and patients without hypercalcaemia, women had better endpoints than men.
- Giant cells, severe interstitial infiltrate and interstitial fibrosis seemed to be negative predictors in terms of endpoints.

Rastelli et al. [3] concluded that: sGIN-AKI-patients with no complete recovery at 1°line steroid should be treated with other immunosuppressive in order to avoid CKD, in particular if males who have sub-acute onset and III stage-not hypercalcaemic AKI.
Horino et al. [34] reported a case of acute kidney injury, which was caused by granulomatous interstitial nephritis as a renal manifestation of sarcoidosis proven by renal biopsy, which could be confirmed by ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography. Horino et al. [34] also reported that Glucocorticoid therapy was helpful for improving and maintaining her renal function over a 6-year period.
Francesco Bonella et al. [35] made the ensuing iterations:

- Kidney involvement is a clinically relevant organ manifestation of sarcoidosis, which leads to increased morbidity and complications.
- Even though the exact incidence had remained unknown, kidney disease is likely to occur in up to one third of all sarcoidosis patients.
- Every patient who has a newly diagnosed sarcoidosis should receive a renal work-up and screening for disrupted calcium metabolism.
- Among the various forms of glomerulonephritis, granulomatous interstitial nephritis is the most common one, but it rarely leads to kidney impairment.
- Histologically, granulomas could be absent in sarcoidosis of the kidney.
- Nephrocalcinosis and nephrolithiasis are frequent forms when hypercalcaemia or hypercalciuria do occur.
- Medications that are used for treatment of systemic sarcoidosis could also cause renal damage.
- In view of its high heterogeneity, sarcoidosis of the kidney could be difficult to treat.
- Glucocorticoids and various immunosuppressive treatments had been proven to be effective based upon the results of case series, but clinical trials are lacking.
- A treatment guideline for renal sarcoidosis is urgently required.
- A better understanding regarding the pathogenesis of sarcoidosis is the key for the development of more specific, targeted therapies.

Hilderson et al. [15] made the ensuing iterations:

- Sarcoidosis is a multisystem granulomatous disease of unknown aetiology characterized by the presence of noncaseating granulomas.
- Sarcoidosis may afflict any organ including the kidney.
- A disordered calcium metabolism is most often responsible for the development of kidney failure.
- Granulomatous interstitial nephritis is the most typical histopathology finding in sarcoidosis of the kidney, but it rarely leads to renal insufficiency.
- In view of the fact that the development of renal insufficiency in sarcoidosis is uncommon, clinicians lack large (randomized) trials concerning the treatment of this disorder.
- Clinicians gather most information from case reports and small series. Clinicians' knowledge of pulmonary sarcoidosis is more comprehensive. It is, however, impossible to treat renal manifestations identically because some of the medications that are used in pulmonary sarcoidosis are nephrotoxic. Moreover, renal sarcoidosis is a specific entity with its own characteristics and response to therapy.
- A guideline for the treatment of sarcoidosis of the kidney is lacking.

- Based upon a review of the literature, they had provided an overview of the different treatment options to promote a more uniform and scrutinized approach of this disease.
- Hypercalcaemia and hypercalciuria could be treated with corticosteroids, (hydroxy)chloroquine or ketoconazole.
- Preventive measures play a supportive role.
- In granulomatous interstitial nephritis, glucocorticoids are the standard of care of treatment.
- In patients who have failure of or a contraindication to corticosteroids or in those patients who require a high maintenance dose of corticosteroids, azathioprine or mycophenolate mofetil could be used.
- TNF-alpha inhibitors are useful in case of steroid-resistant sarcoidosis or in patients who develop severe steroid toxicity.
- With increasing insight into the pathogenesis of sarcoidosis, other immunosuppressive drugs had been proposed, but more research is needed before their routine use can be advocated.

Wang et al [36] made the ensuing iterations:

- Sarcoidosis is a chronic non-caseating granulomatous disease which has an unknown aetiology that can affect multiple organs.
- Sarcoidosis kidney involvement in paediatric-onset adult-type is rare, and only a few cases had been reported.
- They had reported a case of a Chinese patient with paediatric-onset adult-type sarcoidosis with renal involvement, and a literature review was performed.

The PubMed database was searched by Wang et al [36] for publications, and relevant clinical data were extracted and presented by them as follows:

- They had identified 22 paediatric-onset adult-type sarcoidosis cases kidney involvement.
- Acute kidney injury was found to be the major clinical presentation.
- Granulomatous interstitial nephritis was the predominant histopathology examination feature.
- All of the patients were treated with corticosteroids and immunosuppressive agents, and most of the patients had achieved improved outcome.

Wang et al [36] made the ensuing concluding iterations:

- Sarcoidosis should be considered in children with acute kidney injury of an unknown aetiology.
- A final diagnosis is established via a combination of the clinical and laboratory characteristics, radiology-image presentation, and histopathology examination features of non-caseating granulomas.
- A treatment schedule should be decided following a systemic assessment.

Harzallah, Amel et al. [37] reported a case who presented an acute kidney failure and had sarcoidosis with vasculitis and nodular splenic involvement. Harzallah, Amel et al. [37] reported a 35-year-old woman, who manifested with a Lofgren syndrome, who was hospitalized for acute renal failure with cervical lymphadenopathy without other clinical findings. Her laboratory data revealed elevated angiotensin converting enzyme serum level. She had ultrasound scan of her abdomen which demonstrated a multinodular spleen. Pathology examination of her renal biopsy specimen demonstrated granulomatous interstitial nephritis

with necrotizing vasculitis. Her outcome was favourable pursuant to the institution of high dose corticosteroids along with cyclophosphamide. Harzallah, Amel et al. [37] made the ensuing concluding iterations:

- Kidney involvement is rare in sarcoidosis.
- Nevertheless, the diagnostic delay should be avoided in order to improve the outcome.

Akiyama et al. [38] reported a case of renal sarcoidosis manifesting as acute kidney injury (AKI) during treatment with etanercept for rheumatoid arthritis. The patient's blood test results showed a high level of angiotensin-converting enzyme and a renal biopsy was undertaken following which pathology examination of the biopsy specimen, demonstrated non-caseating granulomatous tubulointerstitial nephritis. The administration of high-dose steroid treatment (1 mg/kg) and discontinuation of etanercept resulted in an improvement in the patient's renal function. Akiyama et al. [38] concluded that:

- Even though sarcoidosis of the kidney which is induced by anti-tumour necrosis factor (TNF) therapy is an extremely rare manifestation, this case had indicated that sarcoidosis of the kidney should be considered in the differential diagnosis of AKI in patients receiving anti-TNF therapy, as providing an early diagnosis and treatment is important for preventing irreversible renal impairment.

Kikuchi, et al. [39] made the ensuing iterations:

- Granulomatous interstitial nephritis (GIN) is one of the renal pathological presentations of sarcoidosis.
- It is usually clinically silent; however, , it may present occasionally as acute kidney injury (AKI).
- AKI which is caused by sarcoid GIN without extrarenal manifestations is extremely rare.

Kikuchi, et al. [39] reported a case of a 70-year-old man, who had a history of type 2 diabetes mellitus, who was admitted with progressively worsening kidney function. The patient also had exhibited anorexia, malaise and weight loss. His laboratory test results showed an elevated serum lysozyme level, but the serum angiotensin-converting enzyme (ACE) and his serum calcium levels were normal. Increased uptake was evident only in kidney on gallium 67 scintigraphy. Even though typical organ involvement of sarcoidosis was not evident, a renal biopsy was undertaken and pathology examination of the biopsy specimen demonstrated granulomatous interstitial nephritis with non-caseating granulomas. No medications had been added in the 3 years preceding his renal function deterioration. Following a bronchoalveolar lavage that demonstrated a high CD4:CD8 ratio, and a skin test that showed negative result for tuberculin, a diagnosis of sarcoidosis of the kidney was established. On diagnosis, oral prednisolone was commenced and his renal function improved. His anorexia and malaise also disappeared. Kikuchi, et al. [39] concluded that their reported case was an extremely rare case of AKI, which was caused by sarcoid GIN without extra-renal manifestations or elevated serum ACE level.

Rajkumar et al. [40] reported a case series of patients whose diagnosis of sarcoidosis was only brought to light by the development of renal impairment. Concurrent hypercalcaemia was identified which prompted further investigation. The patients subsequently discussed having experienced a significant and rapid improvement in their both renal function and hypercalcaemia in response to treatment with prednisolone. Rajkumar et al. [40] stated that this was out of keeping with previous reports of sarcoidosis-induced renal impairment. Rajkumar et al. [40] made the ensuing conclusions:

- Their case series had highlighted the importance of testing for hypercalcaemia in the context of acute kidney injury.
- Sarcoidosis is primarily a disease of the lungs and reticuloendothelial system; nevertheless, the prevalence of kidney involvement with sarcoidosis might be under-recognized.
- They had postulated that in the context of sarcoidosis-induced renal injury, concurrent hypercalcaemia might present prior to the development of chronic renal injury and therefore these patients might be more likely to recover renal function.

Mahévas et al. [41] collected a retrospective data were by the French Sarcoidosis Group. Mahévas et al. [41] assessed forty-seven adult patients (30 male/17 female, M/F ratio: 1.76). Mahévas et al. [41] summarised the results as follows:

- The median estimated glomerular filtration rate (eGFR) was 20.5 mL/min per 1.73 m^2 (range, 4-93 mL/min per 1.73 m^2).
- Moderate proteinuria was identified in 31 (66%) patients (median, 0.7 g/24 h; range, 0-2.7 g/24 h), non-visible haematuria in 11 (21.7%) patients, aseptic leukocyturia in 13 (28.7%) patients.
- Fifteen of 47 (32%) patients had hypercalcemia (>2.75 mmol/L).
- Eleven of the 22 (50%) patients, who were diagnosed between June and September had hypercalcemia in comparison with only 4 of the 25 (16%) cases, who were diagnosed during the other months ($p < 0.001$).
- Thirty-seven patients had manifested with non-caseating granulomatous interstitial nephritis (GIN), and 10 with interstitial nephritis without granulomas.
- Apart from hypercalcemia, the clinical phenotype was also remarkable for the high frequency of fever at presentation.
- All of the patients had initially received prednisone (median duration, 18 months), 10 received intravenous pulse methylprednisolone. eGFR increased from 20 ± 19 to 44 ± 24.7 mL/min per 1.73 m^2 at 1 month ($p < 0.001$, $n = 38$), to 47 ± 19.9 mL/min per 1.73 m^2 at 1 year ($p < 0.001$, $n = 46$), to 49.13 ± 25 mL/min per 1.73 m^2 at last follow-up ($p < 0.001$, $n = 47$).
- A complete response to treatment at 1 year and at last follow-up was found to be strongly correlated with complete response at 1 month ($p < 0.01$).
- Renal function improvement was found to be inversely related to the initial histopathology fibrosis score.
- A complete response to treatment at 1 year was found to be strongly correlated with hypercalcemia at presentation ($p = 0.003$).
- Relapses were noted to be purely renal ($n = 3$) and purely extrarenal ($n = 10$) or both ($n = 4$), often a long time after presentation, with in some cases severe cardiac or central nervous system involvement.

Mahévas et al. [41] made the ensuing conclusions:

- Hypercalcemia and fever at initial manifestation are often associated with RS.
- RS is most often and permanently responsive to corticosteroid treatment, but some degree of persistent renal failure is highly frequent and its degree of severity in the long run is well predicted from both histopathology fibrotic renal score and response obtained at 1 month.

Mocanu et al. [42] reported the case of a 10-year-old boy who presented with advanced renal failure with nephrocalcinosis and important hepatosplenomegaly. The diagnosis was

established by histopathology examination, with consequent cortisone treatment and haemodialysis. Mocanu et al. [42] made the ensuing conclusions:

- Their review had emphasized that sarcoidosis should be considered in the differential diagnosis of paediatric patients who develop acute kidney insufficiency or chronic kidney disease of an unknown aetiology.
- As far as they knew, their reported case was the first study regarding extra-pulmonary sarcoidosis in children from Romania.

Sharma et al. [43] reported a case of a 61-year-old woman, who had presented with substernal chest pain. She was found to have elevated calcium levels, anaemia, and acute kidney injury. Her hypercalcemia had persisted despite treatment with fluids and bisphosphonates. She was found to have non-parathyroid hormone (PTH) mediated hypercalcemia. She had chest X-ray, which did not demonstrate any pathology. The authors' initial impression was likely an underlying haematological malignancy such as lymphoma or multiple myeloma. A bone marrow biopsy was undertaken and pathology examination of the specimen demonstrated non-necrotizing granulomatous inflammation. Her further assessment revealed elevated vitamin 1,25 dihydroxy level, beta-two micro-globulin level, and ACE levels. She had non-contrast computed tomography (CT) scan of chest, which demonstrated bilateral apical bronchiectasis, but did not demonstrate any lymphadenopathy or evidence of malignancy. Subsequently, she had a bronchoscopy with trans-bronchial biopsy, and pathology examination of the biopsy specimen demonstrated non-necrotizing granulomatous inflammation, which was consistent with sarcoidosis. After commencing glucocorticoid treatment, the patient's hypercalcemia improved and her kidney function returned to baseline.

Charkviani et al. [44] made the ensuing iterations:

- Sarcoid-like granulomas could be a manifestation of immune-related adverse events associated with immune checkpoint inhibitor (ICI) treatment.
- To their knowledge, kidney biopsy–proven sarcoid-like granulomas had not been described in the context of a sarcoid-like reaction associated with ICI treatment.

Charkviani et al. [44] reported a man in his early 60s with renal cell carcinoma who was undergoing treatment with the ICIs nivolumab and ipilimumab, and who was hospitalized for treatment of acute kidney injury stage 3, hypercalcemia, and hyponatremia 10 weeks after commencing ICI treatment. Charkviani et al. [44] summated the results as follows: Results from his workup showed parathyroid hormone–independent hypercalcemia (ionized calcium, 3.3 mEq/L) with an elevated 1,25-dihydroxyvitamin D level. Pathology examination of his kidney biopsy specimen showed sarcoid-like noncaseating granulomas. The patient commenced a corticosteroid regimen with a 500 mg bolus dose of methylprednisolone and he continued treatment with prednisone, 80 mg once daily for the first week and then a taper for 8 weeks. His kidney function gradually improved as his hypercalcemia resolved. After 2 weeks of treatment, his creatinine values returned to the baseline. Charkviani et al. [44] made the ensuing conclusions:

- The reported case had shown that ICI treatment could be associated with sarcoidosis of the kidney.
- In view of the fact that ICIs are increasingly used to treat cancer, physicians should be aware of this possible inflammatory complication so that they could use appropriate diagnostic and treatment approaches.

Singh et al. [45] reported the case of a 55-year-old female patient, who had renal limited sarcoidosis, who manifested with worsening sensorium and acute kidney injury. Results of her investigation demonstrated elevated levels of serum calcium and angiotensinogen converting enzyme; and radiology imaging study of her chest was normal. She had kidney biopsy undertaken for non-resolving acute kidney injury and pathology examination of the biopsy specimen demonstrated non-caseating granulomatous interstitial nephritis and the presence of concurrent Immunoglobulin A (IgA)nephropathy. She responded to a treatment which comprised of fluid resuscitation, hemodialysis, and oral steroids.

Reis Santos et al. [46] reported a 59-year-old woman, who was autonomous in her activities of daily living, and who was admitted to the Multipurpose Emergency Service (MES) with nausea, generalized tremors, and a week-long notion of decreased urine output. She denied having any fever, eye, skin, respiratory, gastrointestinal, or osteoarticular complaints. Her medical history included: hypertension, scleroderma affecting the skin, and hepatic sarcoidosis, with a recent histopathology diagnosis of granulomatous hepatitis after years of follow-up due to altered liver function tests and the exclusion of toxic and infectious aetiology (brucellosis, hepatitis A/B/C, human immunodeficiency virus, syphilis, cytomegalovirus, toxoplasma, and Epstein-Barr virus). She had a poor adherence to sarcoidosis treatment due to her apparent intolerance/skin reactions to previous treatment with corticosteroids, azathioprine, ursodeoxycholic acid, and hydroxychloroquine. Upon clinical examination, she was found to be apyretic and hemodynamically stable, with no alterations on cardiopulmonary auscultation and brief neurological examination. Plaque lesions were identified in her sub-mammary, abdominal, and lower limb regions. There were no signs of inflammation or joint swelling found during her examination. The study which was undertaken on the MES demonstrated normocytic and normochromic anaemia (hemoglobin 11.5mg/dL), acute kidney injury (new-onset creatinine 2.3mg/dL, baseline creatinine 0.8mg/dL and urea 61mg/dL), hypercalcemia (ionized calcium 1.6mEq/L), and high SACE level (serum angiotensin-converting enzyme) of 157U/L. She had ultrasound scan of the renal tract which demonstrated her kidneys to have normal morphology and topography, with a good preservation of sinus-parenchyma differentiation and no alterations to the excretory cavities or obvious images of lithiasis. She was therefore admitted to the Nephrology Ward under medical team for her treatment to correct the hypercalcemia and for monitoring and studying the acute kidney injury in a patient with a history of systemic disease. Her hypercalcemia persisted despite the measures that were instituted, and there was no improvement in her renal function (creatinine 2.4mg/dL and ionized calcium 1.72 mmol/L). Her complementary study was inconclusive (see tables 1 and 2), and a renal biopsy was then undertaken. Faced with the most likely diagnostic hypotheses of acute kidney injury secondary to hypercalcemia and/or intrinsic kidney involvement due to sarcoidosis, after a multidisciplinary discussion with rheumatology, empirical corticosteroid therapy was proposed and she was commenced on methylprednisolone 0.5mg/kg/day. At the time of her discharge, her kidney function and hypercalcemia were stable, and she was referred to the nephrology and systemic autoimmune disease departments of Internal Medicine (given the absence of clinical/systemic and osteoarticular complications) under deflazacort 45mg/day, pantoprazole 20mg, and vitamin D supplementation (addressing her deficiency values), awaiting the results of the renal biopsy. Pathology examination of her renal biopsy specimen demonstrated pathology examination features which confirmed the hypothesized aetiologies. On light microscopy, an interstitial infiltrate of mononuclear cells was evident, which was adjudged to be compatible with acute interstitial nephritis (see figure 2). Acute tubular necrosis

was present in 50% of the cortex that was observed, and tubular calcium phosphate crystals were also visualised. Her glomerulus and blood vessels were found to be normal, and the immunofluorescence study was negative. The instituted therapy was maintained.

Analytical parameter		Laboratory results	Reference ranges
Urea		59 mg/dL	19–49 mg/dL
Creatinine		2.4 mg/dL	0.5–1.2 mg/dL
Sodium		137 mEq/L	135–145 mEq/L
Potassium		4.5 mEq/L	3.5–5.0 mEq/L
Chlorine		100.5 mEq/L	95.0–110.0 mEq/L
Total calcium		6.2 mg/dL	4.2–5.1 mg/dL
Ionized calcium		1.72 mmol/L	1.16–1.31 mmol/L
Phosphorus		3.3 mEq/L	2.8–4.1 mEq/L
Albumin		3.8 g/dL	3.5–5.0 g/dL
Parathormone		6.00 pg/mL	18.50–88.00 pg/mL
Proteinuria (urine sample)		13.6 mg/dL	1.0–14.0 mg/dL
Urine sediment	Leukocyturia	23/µL	1.0–10.0/µL
	Erythrocyturia	9/µL	1.0–24.0/µL
Anti-glomerular basement membrane antibody		0.9 U/mL	0–10 U/mL
Anti-dsDNA Ac.		12.0	0.0–15.0

Table 1: Initial analytical evaluation of acute kidney injury in the nephrology ward

Anti-dsDNA Ac, anti-double stranded DNA antibodies. Reproduced from: [46] under the Creative Commons Attribution License.

Analytical parameter	Results
Gamma interferon (QuantiFERON)	Negative
Wright's reaction	Negative
ANA	Positive (1/320) in a homogeneous pattern
ENA screen	Negative
C3, C4	Normal
Serum electrophoretic proteinogram and immunofixation	Exclusion of monoclonal pathology with evident polyclonal hypergammaglobulinemia

Table 2: Complementary study carried out during the diagnostic process

ANA, antinuclear antibodies; ENA, extractable nuclear antigen antibodies; C, complement
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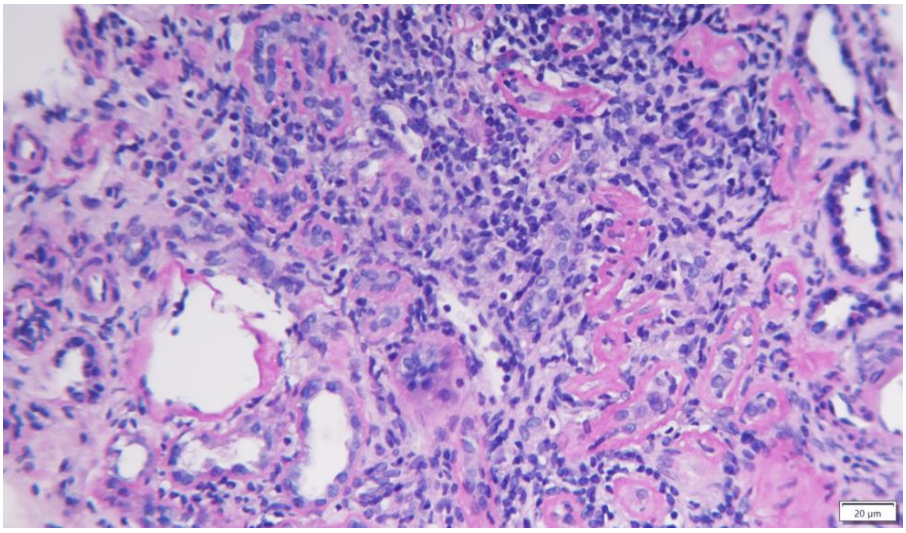

Figure 1: Kidney biopsy

Interstitial infiltrate of mononuclear cells, compatible with acute interstitial nephritis. Reproduced from: [46] under the Creative Commons Attribution License.

Two months pursuant to her discharge from the hospital, the patient's renal function, calcium levels, and anaemia had normalized (creatinine 0.9mg/dL, total calcium 4.9mEq/L with albumin 4.4g/dL, and hemoglobin 12.4g/dL), SACE (serum angiotensin-converting enzyme) was normal, and albuminuria was absent. Her corticosteroid treatment was weaned after eight weeks when the disease became stable and after the introduction of azathioprine 75mg twice daily. She maintained her follow-up in both specialties with stabilization of the disease activity and renal function at two years' follow-up under prednisolone 2.5mg and azathioprine 75mg bid, with no record of new organ systems being affected. Her intercurrences included the development of diabetes secondary to corticosteroid therapy, requiring insulin treatment, and the occurrence of osteoporotic fractures requiring vertebroplasty.

Reis Santos et al. [46] made the ensuing conclusions:

- Despite the rarity of renal involvement in sarcoidosis, it is clinically significant and probably underdiagnosed in this multisystemic disease.
- Considering the risk of organ dysfunction with the perpetuation of untreated sarcoidosis disease, it is essential to screen for renal involvement when diagnosing and following up on patients with sarcoidosis by assessing urinary sediment, quantifying proteinuria, and monitoring renal function.
- With the report of the case, the authors wanted to emphasize the importance of sarcoidosis as a multi-organ disease and to recommend that clinicians need to be aware of the systems involved in sarcoidosis disease when making the initial diagnosis, as the earlier the diagnosis is made and the commencement of appropriate treatment, the greater the likelihood of successful treatment interventions.

Conclusions

- Kidney involvement in sarcoidosis does tend to occur in about one third of patients and could be ensued by the development of significant morbidity.
- Various forms of sarcoidosis of the kidney exist, but most frequently granulomatous interstitial nephritis is what has been found in sarcoidosis of the kidney.
- It has been pointed out that a complete diagnostic assessment for renal involvement is mandatory in all patients who are diagnosed as having newly diagnosed sarcoidosis.

- Diagnosis of sarcoidosis of the kidney can be established by undertaking biopsy of the kidney lesion for pathology examination in cases of suspected sarcoidosis of the kidney.
- It has been iterated that steroids are considered to be the first-line treatment for sarcoidosis of the kidney and further immunosuppressants could be added in case of relapse of sarcoidosis of the kidney.
- It has been iterated that the undertaking of haemodialysis and kidney transplantation are valid options when end stage disease occurs in sarcoidosis of the kidney.

Conflict Of Interest - None

Acknowledgements

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References

1. Zia Z, Iqbal QZ, Ruggiero RA, Pervaiz S, Chalhoub M. (2021). A Rare Case of Renal Sarcoidosis. *Cureus.* Jun 7;13(6):e15494.
2. Jankowski K, Mikhailov A. Sarcoidosis. PathologyOutlines.com website.
3. Rastelli F, Baragetti I, Buzzi L, Ferrario F, Benozzi L, et. all., (2021). Renal involvement in sarcoidosis: histological patterns and prognosis, an Italian survey. *Sarcoidosis Vasc Diffuse Lung Dis*;38(3):e2021017.
4. Naderi S, Amann K, Janssen U. Renal involvement in sarcoidosis: Histologic findings and clinical course. Nephrology @ Point of Care. 2019;5.
5. Berliner AR, Haas M, Choi MJ. (2006). Sarcoidosis: the nephrologist's perspective. *Am J Kidney Dis.* Nov;48(5):856-870.
6. Kamata Y, Sato H, Joh K, Tsuchiya Y, Kunugi S, ET ALL., (2018). Clinical characteristics of biopsy-proven renal sarcoidosis in Japan. *Sarcoidosis Vasc Diffuse Lung Dis;35*(3):252-260.
7. Stehlé T, Joly D, Vanhille P, Boffa JJ, Rémy P, ET ALL., (2013). Clinicopathological study of glomerular diseases associated with sarcoidosis: a multicenter study. *Orphanet J Rare Dis.* Apr 30; 8:65.
8. Correia FASC, Marchini GS, Torricelli FC, Danilovic A, Vicentini FC, et all., (2020). Renal manifestations of sarcoidosis: from accurate diagnosis to specific treatment. *Int Braz J Urol.* Jan-Feb;46(1):15-25.
9. Wouters CH, Maes A, Foley KP, Bertin J, Rose CD. (2014). Blau syndrome, the prototypic auto-inflammatory granulomatous disease. *Pediatr Rheumatol Online J.* Aug 6; 12:33.
10. Lee S, Birnie D, Dwivedi G. (2020). Current perspectives on the immunopathogenesis of sarcoidosis. *Respir Med*. Nov; 173:106161
11. Duveau A, Sayegh J, Beloncle F, Moreau A, Subra JF, ET ALL., (2013) Pseudotumours: an atypical presentation of renal sarcoidosis. *QJM.* Oct;106(10):947-949.
12. Crouser ED, Maier LA, Wilson KC, Bonham CA, Morgenthau AS, et all., (2020). Diagnosis and Detection of Sarcoidosis. An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med.* Apr 15;201(8): e26-e51.

13. Dahl K, Canetta PA, D'Agati VD, Radhakrishnan J. (2008). A 56-year-old woman with sarcoidosis and acute renal failure. *Kidney Int.* Sep;74(6):817-821.
14. Heldmann M, Behm W, Reddy MP, Bozeman C, Welman G, et. all., (2005). Pseudotumoral renal sarcoid: MRI, PET, and MDCT appearance with pathologic correlation. *AJR Am J Roentgenol*. Sep;185(3):697-699.
15. Hilderson I, Van Laecke S, Wauters A, Donck J. (2014). Treatment of renal sarcoidosis: is there a guideline? Overview of the different treatment options. Nephrol Dial Transplant. Oct;29(10):1841-1847.
16. Rosen Y. (2022). Pathology of Granulomatous Pulmonary Diseases. Arch Pathol Lab Med. Jan 2;146(2):233-251.
17. Ueda S, Murakami T, Ogino H, Matsuura M, Tamaki M, et. all., (2019). Systemic Sarcoidosis Presenting with Renal Involvement Caused by Various Sarcoidosis-associated Pathophysiological Conditions. *Intern Med.* Mar 1;58(5):679-684.
18. Calender A, Weichhart T, Valeyre D, Pacheco Y. (2020). Current Insights in Genetics of Sarcoidosis: Functional and Clinical Impacts. *J Clin Med.* Aug 13;9(8):2633.
19. Shah S, Carter-Monroe N, Atta MG. (2015). Granulomatous interstitial nephritis. Clin Kidney J. Oct;8(5):516-23.
20. Guo W, Woo KT, Choo JC, Tan PH, Lim CC. (2020). Granulomatosis with Polyangiitis and Acute Tubulointerstitial Nephritis in the Absence of Glomerulonephritis. *Am J Med.* Nov;133(11): e679-e680.
21. Klaus R, Jansson AF, Griese M, Seeman T, Amann K, ET ALL., (2021). Case Report: Pediatric Renal Sarcoidosis and Prognostic Factors in Reviewed Cases. *Front Pediatr. Sep* 13; 9:724728.
22. De la Hoz I, Osman A, Ryad R, Li W, Shah S, ET ALL., (2023). A Rare Presentation of Sarcoidosis in a Young Male with Acute Renal Failure: A Case Report and Literature Review. *Cureus.* Nov 27;15(11): e49512.
23. FRODE K. (1980). RØMER, Renal Manifestations and Abnormal Calcium Metabolism in Sarcoidosis, *QJM: An International Journal of Medicine*, Volume 49, Issue 3, SUMMER,
24. Menezes M, Patarata E. (2018). Renal sarcoidosis: a rare case. *BMJ Case Rep.* Dec 14;11(1): e227023.
25. Casella FJ, Allon M. (1993). The kidney in sarcoidosis. *Journal of the American Society of Nephrology.* Mar 1;3(9):1555-1562.
26. Calatroni M, Moroni G, Reggiani F, Ponticelli C. (2023). Renal sarcoidosis. *Journal of Nephrology.* Jan;36(1):5-15.
27. Bergner R, Löffler C. (2018). Renal sarcoidosis: approach to diagnosis and management. Current opinion in pulmonary medicine. Sep 1;24(5):513-520.
28. Vender, Robert J.[a]; Aldahham, Hamad[c]; Gupta, Rohit[b]. (2022). The role of PET in the management of sarcoidosis. *Current Opinion in Pulmonary Medicine* 28(5): p 485-491, September.
29. Bonella F, Vorselaars AD, Wilde B. (2024). Kidney manifestations of sarcoidosis. Journal of Autoimmunity. Mar 22:103207.
30. Bergner R, Hoffmann M, Waldherr R, Uppenkamp M. (2003). Frequency of kidney disease in chronic sarcoidosis. Sarcoidosis, vasculitis, and diffuse lung diseases: official journal of WASOG. Jun 1;20(2):126-132.

31. Bagnasco SM, Gottipati S, Kraus E, Alachkar N, Montgomery RA, Racusen LC, Arend LJ. Sarcoidosis in native and transplanted kidneys: incidence, pathologic findings, and clinical course. PLoS One. 2014 Oct 20;9(10): e110778.
32. Shah R, Shidham G, Agarwal A, Albawardi A, Nadasdy T. (2011). Diagnostic utility of kidney biopsy in patients with sarcoidosis and acute kidney injury. International journal of nephrology and renovascular disease. Sep 26:131-136.
33. Agrawal V, Crisi GM, D'Agati VD, Freda BJ. (2012). Renal sarcoidosis presenting as acute kidney injury with granulomatous interstitial nephritis and vasculitis. American Journal of Kidney Diseases. Feb 1;59(2):303-308. ISSN 0272-6386,
34. Horino, T., Matsumoto, T., Inoue, K. et al. (2018). A case of acute kidney injury caused by granulomatous interstitial nephritis associated with sarcoidosis. *CEN Case Rep* **7**, 34–38.
35. Francesco Bonella, Adriane DM (2024). Vorselaars, Benjamin Wilde. Kidney manifestations of sarcoidosis. *Journal of Autoimmunity.,* 103207,
36. Wang C, Liu H, Zhang T, Xu H, Shen J, ET ALL., (2019). Acute kidney injury as a rare manifestation of pediatric sarcoidosis: a case report and systematic literature review. *Clinica Chimica Acta.* Feb 1; 489:68-74.
37. Harzallah Amel, Kaaroud, Hayet, Boubaker, Karima, Barbouch, Samia, Goucha, Rim Hamida Fethi Ben, Abdallah Taieb Ben. Acute Kidney Injury with Granulomatous Interstitial Nephritis and Vasculitis Revealing Sarcoidosis. *Saudi Journal of Kidney Diseases and Transplantation* 28(5): p 1157-1161.
38. Akiyama M, Kaneko Y, Hanaoka H, Kuwana M, ET ALL., (2015). Acute kidney injury due to renal sarcoidosis during etanercept therapy: a case report and literature review. *Internal Medicine*;54(9):1131-1134.
39. Kikuchi, H., Mori, T., Rai, T. et al. (2015). Acute kidney injury caused by sarcoid granulomatous interstitial nephritis without extrarenal manifestations. *CEN Case Rep* **4**, 212–217.
40. Rajkumar T, Lea-Henry T, Chacko B. Acute kidney injury as the presenting manifestation of sarcoidosis: A case series and review of literature. Nephrology. 2018 Jun;23(6):597-600.
41. Mahévas M, Lescure FX, Boffa JJ, Delastour V, Belenfant X, Chapelon C, Cordonnier C, Makdassi R, Piette JC, Naccache JM, Cadranel J. Renal sarcoidosis: clinical, laboratory, and histologic presentation and outcome in 47 patients. Medicine. 2009 Mar 1;88(2):98-106.
42. Mocanu A, Bogos RA, Trandafir LM, Cojocaru E, Ioniuc I, Alecsa M, Lupu VV, Miron L, Lazaruc TI, Lupu A, Miron IC. The Overlap of Kidney Failure in Extrapulmonary Sarcoidosis in Children—Case Report and Review of Literature. International Journal of Molecular Sciences. 2023 Apr 15;24(8):7327.
43. Sharma N, Tariq H, Uday K, Skaradinskiy Y, Niazi M, Chilimuri S. Hypercalcemia, anemia, and acute kidney injury: a rare presentation of sarcoidosis. Case Reports in Medicine.;2015(1):565243.
44. Charkviani M, Herrmann SM. Immune Checkpoint Inhibitor–Associated Sarcoidosis Reaction in the Kidney: Case Report. Kidney Medicine. 2023 May 1;5(5):100626.
45. Vishal Singh, Pavitra Manu Dogra, Pulkit Singh, Indranil Ghosh, Gaurav Singhal, (2023). Renal limited sarcoidosis presenting with acute kidney injury, Medical Journal Armed Forces India, , ISSN 0377-1237,

46. Reis Santos S, Cunha Rodrigues A, Melo Pereira J, et al. (August 11, 2024) An Infrequent Histopathological Diagnosis in a Prevalent Systemic Disease: A Case of Renal Sarcoidosis. Cureus 16(8): e66633.