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Case Report

Hepatitis B Virus-Associated Polyarteritis Nodosa: A Case Report

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Abstract

Polyarteritis nodosa (PAN) is a medium-sized artery necrotizing vasculitis that is mostly idiopathic. However, hepatitis B virus was found to be one of the triggers for the activation of PAN. The disease affects multiple systems, including the heart, kidneys, GI tract, skin, and nervous system, among others, but usually spares the lungs. We report a case of a 43-year-old male patient with hepatitis B-induced PAN showing multi-systemic manifestations such as terminal renal failure, gastrointestinal bleeding, and congestive heart failure. The patient was treated with glucocorticoids and hemodialysis, and after 3 months, his cardiac function was found to be normal again.

Key Words: hepatitis b virus, polyarteritis nodosa, cardiac manifestations, glucocorticoids, hemodialysis, LVEF, ED, heart rate

Introduction

Polyarteritis nodosa (PAN) is a form of systemic necrotizing vasculitis affecting mostly the medium-sized arteries. Although the etiology is mostly idiopathic, hepatitis B was found to be a trigger for PAN through an immune complex-induced mechanism. Being a systemic disease, PAN has numerous manifestations involving the nervous system, skin, kidneys, gastrointestinal tract, and heart [4] As per B. Petar et al, PAN's cardiac manifestations could present as congestive heart failure caused by nephropathy or by direct coronary involvement and myocardial ischemia [3]. The medical approach to hepatitis B-induced PAN is a triad of corticosteroids, anti-viral treatment, and plasma exchange therapy [13]. We report a case of a 43-year-old male with hepatitis B-induced PAN showing multi-systemic symptoms including congestive heart failure with Left Ventricular Ejection Fraction (LVEF) of 25-30%. The patient was treated with steroids and anti-virals. The patient was not treated with the standard medications for heart failure with reduced ejection fractions (e.g. ace inhibitors, angiotensin-receptor blockers, mineralocorticoid receptor antagonists) due to his condition of renal failure and persistent hyperkalemia. Instead, the patient was only managed with systemic glucocorticoids, and later on his cardiac function improved towards a normal LVEF.

Case presentation

A 43-year-old male patient presented to the Emergency Department (ED) with remarkable nausea but without vomiting. The patient denied headache, fever, dyspnea, cough, abdominal pain, bowel movement abnormalities, or any urinary symptoms at the time of presentation. He reported that the nausea started 1 month before the presentation and gradually became so severe that he could not tolerate eating or drinking. He mentioned having a flu-like illness 3 weeks before the presentation with fever, myalgia, arthralgia, and dyspnea. He sought medical assistance and was diagnosed with heart failure with reduced ejection fraction at that time, so he was discharged on loop diuretics. No further cardiac or laboratory workup was done since the patient was lost to follow-up.

Physical examination:

On admission, the patient was afebrile, with a heart rate of 70 beats per minute, blood pressure of 180/96, and oxygen saturation of 96% on room air.

He had grey, metallic-colored skin with no identifiable lesions, left eye ptosis of several years duration, clear lungs on auscultation, regular S1 and S2 heart sounds without any audible murmurs on auscultation, normal abdominal exam, and normal lower limbs exam.

Laboratory test	Patient's value	Normal range
Hemoglobin	9.9 g/dL	12-16 g/dL
Blood Urea Nitrogen	126 mg/dL	6-20 mg/dL
Creatinine	12 mg/dL	0.5-0.9 mg/dL
Sodium	135 mmol/L	136-245 mmol/L
Potassium	5.2 mmol/L	3.7-5.3 mmol/L
Bicarbonate	18 mmol/L	23-28 mmol/L

Table 1: Relevant ED laboratory results

An urgent Uroscan without intravenous (IV) contrast done in the emergency department showed bilateral atrophic kidneys with normal ureters and bladder. The patient was then admitted to the nephrology service for investigation and management of renal failure and was planned for hemodialysis due to uremic symptoms.

Serology and other laboratory investigations were done.

Laboratory test	Patient's value	Normal range
Hepatitis B surface antigen (HBsAg)	34	Negative < 1
HIV antibodies	0.23	Negative < 1
Hepatitis C antibodies	0.10	Negative < 1
Erythrocyte Sedimentation Rate	43 mm/hr	0-15 mm/hr
Proteins in urine over 24 hours	327 mg/ 24 hours	<150 mg/ 24 hours
Anti neutrophil cytoplasmic antibodies (ANCA)	Negative	Negative
Anti nuclear antibodies (ANA)	Negative	Negative
Anti glomerular basement membrane antibodies (anti-GBM)	Negative	Negative

Table 2: Relevant laboratory results

An echocardiogram was done; it revealed mid-range systolic function, with moderate concentric hypertrophy of the left ventricle with global hypokinesia and grade III diastolic dysfunction. During the hospital stay, the patient had a drop in hemoglobin level from 9.9 g/dL to 7.9 g/dL with melena. Gastroscopy was done, which showed erosive gastritis. In the context of advanced renal failure, congestive heart failure, GI bleeding, and hepatitis B seropositivity, the diagnosis of polyarteritis nodosa was suspected.

An abdominal angio-scan was done (images 1 and 2). It revealed the following:

- Distal right artery aneurysm (10 x 7 mm) (the red arrow)
- Filiform aspect of bilateral renal arteries (the green arrows)
- Significant narrowing of the left renal artery distally (the yellow arrow).

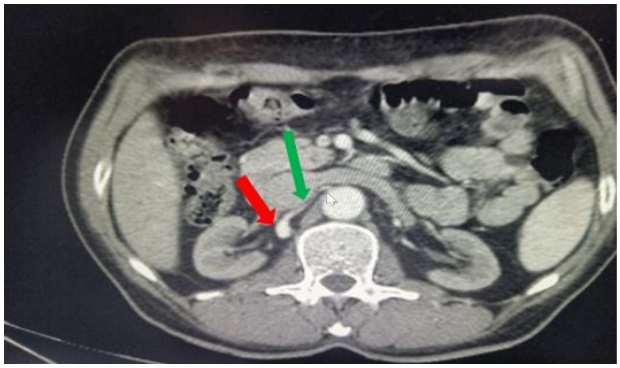

Image 1

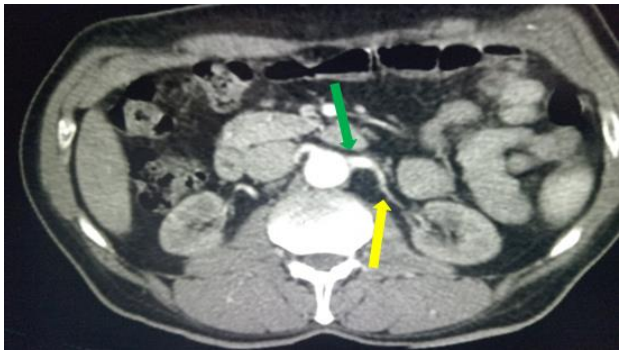

Image 2

The above findings confirmed our diagnosis of PAN.

Renal-wise, the patient was maintained on thrice weekly hemodialysis.

Being hepatitis B positive, the patient was initially started on Tenofovir 25 mg once daily. The initiation of immunosuppressive treatment was delayed until 2 weeks after antiviral treatment initiation to avoid the possibility of HBV flare-up causing fulminant hepatitis.

After 2 weeks of Tenofovir, our patient was started on Prednisone 1mg/kg, which was then gradually tapered down by 5 mg every week after one month until we reached a maintenance dose of 10 mg daily.

Follow-up echocardiography at 3 months following Prednisone initiation showed total resolution of the aforementioned cardiac abnormalities and a return of the ejection fraction and diastolic function back to normal.

Discussion

Polyarteritis nodosa is a rare multi-system necrotizing vasculitis, that primarily targets medium-sized and to a lesser extent small-sized arteries [5].

Epidemiologic studies did not reveal an ethnic predilection for PAN, but it has been demonstrated that it more typically affects older adults, aged 40-60 years old, with a 1.5:1 male preponderance [6]. PAN is estimated to have a prevalence ranging from 2 to 33 per million [7]. with an annual incidence rate of 0.9–8.0 per million in European countries [8]. Most cases of polyarteritis nodosa occur idiopathically, yet some occur secondary to drugs (e.g., minocycline), infections (e.g., hepatitis B and C virus (HBV, HCV), Klebsiella, Toxoplasma, Pseudomonas, parvovirus B-19, Yersinia), and hairy-cell leukemia [5,9,10]. Additionally, PAN has been linked to autoimmune diseases (e.g., Sjogren syndrome, rheumatoid arthritis) [5]. and Familial Mediterranean Fever (FMF) [11]. Hepatitis B-associated polyarteritis nodosa (HBV-PAN) is a well-recognized entity as HBV infection used to account for up to 30% of PAN cases [12]. Due to the widespread vaccination against hepatitis B, the incidence has dropped to less than 8% [2]. PAN usually occurs within the first 6 months of HBV infection [5]. The exact pathophysiology of HBV-PAN remains unknown. However, there has been some evidence related to immune complex (IC)-mediated inflammation of vessels, which is not the case in non-HBV-associated cases [5,14]. ICs induce segmental transmural inflammation of medium-sized arteries, sparing arterioles, capillaries, and veins. Affected vessels become thickened due to intimal proliferation secondary to infiltration by polymorphonuclear and mononuclear cells [5]. Consequently, this leads to luminal narrowing, reduced perfusion, and eventually a higher risk of thrombosis and infarction of the perfused organs. The inflammatory process also results in vessel weakening due to elastic lamina destruction, predisposing to aneurysm formation and rupture [15]. PAN displays varied clinical manifestations depending on the involved organ (skin, neurologic, cardiac, gastrointestinal, muscular, renal). The lungs are usually spared [5]. The kidneys, on the other hand, are the most commonly affected, where PAN can result in glomerular ischemia, activation of the renin-angiotensin-aldosterone system (RAAS), and thus hypertension [16]. Patients with PAN also typically present with systemic symptoms of fever, fatigue, arthralgia, and weight loss [17]. The diagnosis of PAN is suspected upon the presence of characteristic clinical findings and compatible laboratory results, that mainly help assess organ involvement. Basic laboratory tests include complete blood count, serum creatinine and urinalysis to assess renal function, liver function tests, creatinine kinase, and hepatitis B and C serologies to rule out secondary disease [5]. Elevation of acute phase reactants including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), although neither sensitive nor specific, may suggest PAN [18]. Additional tests can be made to narrow the differential diagnosis, such as anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), complement components (C3 and C4), rheumatoid factor, cryoglobulins, serum and urine protein electrophoresis (SPEP and UPEP), and human immunodeficiency virus serology. To confirm the diagnosis, a biopsy of the affected organ is performed [19], or mesenteric or renal arteriography can be done alternatively [20]. PAN is usually treated with glucocorticoids and cyclophosphamide, and, in cases of HBV-PAN, antivirals and plasmapheresis are indicated. In this presented case, the combination of renal failure, hypertension, positive hepatitis B serology, gastrointestinal bleeding, and heart failure, with elevated ESR, raised the suspicion of a systemic disease. Polyarteritis nodosa was later confirmed by abdominal CT angiography, revealing renal arterial involvement (narrowing and aneurysm). Thus, putting all the pieces together, hepatitis B infection has predisposed the patient to the development of PAN, which targeted renal vessels resulting in renal failure and hypertension. The improvement in left ventricle ejection fraction following the initiation of PAN treatment suggests that heart failure could be attributed to intramural vasculitis, replicating findings of other studies [21,22]. Polyarteritis nodosa is a systemic disease that can target many organs in the body, resulting in organ injury and, in severe cases, failure. For this, proper assessment is crucial to establish the diagnosis and commence with the proper treatment to prevent exacerbation and reverse the complications.

Conclusion

Polyarteritis Nodosa is a systemic disease with multi-organ involvement. The diagnosis of PAN should be thought of in a patient presenting with multi-organ dysfunction including the kidneys, GI tract, skin, heart, and the peripheral nervous system. The main pathology is due to vascular inflammation and ischemia of the affected organs. The diagnosis often requires a high index of suspicion in the appropriate clinical setting and is confirmed angiographically. PAN should be promptly recognized and treated since if left untreated, it's almost fatal. The association between PAN and HBV infection remains a therapeutic challenge. The initiation of antiviral treatment is crucial to avoid immunosuppression-related HBV replication and flare-up.

References

1. José Hernández-Rodríguez, Marco A. Alba, Sergio Prieto-González, Maria C. Cid, (2014). Diagnosis and classification of polyarteritis nodosa, *Journal of Autoimmunity*, Vol48-49, Pages 84-89.
2. Guillevin, Loïc M.D, Lhote, François M.D, Cohen, et. al., (1995) Polyarteritis Nodosa Related to Hepatitis B Virus a Prospective Study with Long-Term Observation of 41 Patients. *Medicine* 74(5): p 238-253.
3. Peters B, von Spiczak J, Ruschitzka F, Distler O, Manka R, et. al., (2018). Cardiac manifestation of polyarteritis nodosa. *Eur Heart J*. 39(27): 2603.
4. Guillevin L, Lhote F, Sauvaget F, Deblois P, Rossi F, et. al., (1994). Treatment of polyarteritis nodosa related to hepatitis B virus with interferon-alpha and plasma exchanges. *Ann Rheum Dis*. 53(5):334-337.
5. Stanton M, Tiwari V. (2024). Polyarteritis Nodosa. 2023 In: StatPearls [Internet]. Treasure Island (FL): *StatPearls Publishing*

6. Mahr, A., Guillevin L., Poissonnet M. & Aymé S. (2004). Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome in a French urban multiethnic population in 2000: a capture-recapture estimate. *Arthritis Rheum*. 51, 92-99.
7. Watts RA, Lane SE, Scott DG, Koldingsnes W, Nossent H, et. al., (2001). Epidemiology of vasculitis in Europe. *Ann Rheum Dis*. 60(12):1156-1157.
8. Mohammad A. J., Jacobsson L. T. H., Westman K. W. A., Sturfelt G. & Segelmark, M. (2009). Incidence and survival rates in Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome and polyarteritis nodosa. *Rheumatology* 48, 1560–1565.
9. Kermani TA, Ham EK, Camilleri MJ, Warrington KJ. (2012). Polyarteritis nodosa-like vasculitis in association with minocycline use: a single-center case series. *Semin Arthritis Rheum*. 42(2):213-221.
10. Hasler P, Kistler H, Gerber H. (1995). Vasculitides in hairy cell leukemia. *Semin Arthritis Rheum*. 25(2):134-142.
11. Balcı-Peynircioğlu B, Kaya-Akça Ü, Arıcı ZS, Avcı E, Akkaya-Ulum ZY, et. al., (2020). Comorbidities in familial Mediterranean fever: analysis of 2000 genetically confirmed patients. *Rheumatology* (Oxford). 59(6):1372-1380.
12. Mahr A, Guillevin L, Poissonnet M, Aymé S. (2004). Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome in a French urban multiethnic population in 2000: a capture-recapture estimate. *Arthritis Rheum*. 51(1):92-99.
13. Guillevin L, Lhote F, Cohen P, Sauvaget F, Jarrousse B, et. al., (1995). Polyarteritis nodosa related to hepatitis B virus. A prospective study with long-term observation of 41 patients. Medicine (Baltimore). 74(5):238-253.
14. Stone JH. (2002). Polyarteritis nodosa. *JAMA*. Oct 2;288(13):1632-1639.
15. Levin S, Graber J, Ehrenwald E, Skeik N. (2015). Polyarteritis nodosa-induced pancreaticoduodenal artery aneurysmal rupture. *Int J Angiol*. 24(1):63-66.
16. Stockigt JR, Topliss DJ, Hewett MJ. (1979). High-renin hypertension in necrotizing vasculitis. *N Engl J Med*. 300(21):1218.
17. Wolff L, Horisberger A, Moi L, Karampetsou MP, Comte D. (2023). Polyarteritis Nodosa: Old Disease, New Etiologies. Int *J Mol Sci*. 24(23):16668.
18. Howard T, Ahmad K, Swanson JA, Misra S. (2014). Polyarteritis nodosa. *Tech Vasc Interv Radiol*. 17(4) :247-251.
19. Pagnoux C, Mahr A, Cohen P, Guillevin L. (2005). Presentation and outcome of gastrointestinal involvement in systemic necrotizing vasculitides : analysis of 62 patients with polyarteritis nodosa, microscopic polyangiitis, Wegener granulomatosis, Churg-Strauss syndrome, or rheumatoid arthritis-associated vasculitis. Medicine (Baltimore). 84(2) :115-128.
20. Balow JE. Renal vasculitis. *Curr Opin Nephrol Hypertens*. 2(2) : 231-237.
21. Chimenti C, Alfarano M, Toto F, Fanisio F, Verardo R, et. al., (2020). Myocarditis and intramural coronary vasculitis in polyarteritis nodosa : an unusual treatable form of heart failure. *ESC Heart Fail*. 7(6):4357-4360.
22. Watanabe Y, Sakamoto K, Matsukage S, Ogimoto A. (2020). Heart failure in a patient with polyarteritis nodosa. *Eur Heart J Case Rep*. 4(5):1-2.

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