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Case Report

Disseminated Mycobacterium Bovis

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Abstract

Intravesical Bacillus Chalmette- Guerin (BCG) still a popular medication for non-invasive bladder cancer in the low-income country, one of the uncommon side effects is disseminated Mycobacterium Bovis
we present a patient who presented with haematuria, diagnosed as urothelial superficial bladder cancer, treated with incomplete resection and intravesical BCG, 6 months after treatment, he presented with increasing shortness of breath, headache and abdominal pain, diagnosed as tuberculous, meningitis, massive pleural effusion, granulomatous hepatitis he responded very well to anti tuberculous treatment.

Keywords: intravesical bacillus chalmette- guerin; haematuria; bladder cancer

Case report

50-year-old man presented to ED with frank total haematuria for three weeks and fever, His past medical history was unremarkable, he was up-to-date with vaccination including Double dose Fizer vaccine, he lives in Kuala Lumper and works as a truck driver, He smokes for the last three years 15 cigarette a day and drinks two glass of wine in the weekend and public holidays, he does not suffer from any medical condition and does not take any medication.

He is married and was in monogamous relationship and has had two healthy children, On examination, he had a low grade fever 37.8, Blood Pressure 130/80, normal oxygen saturation on room air, systemic examination was unremarkable with no rash or arthritis, Urine deep stick showed frank haematuria, no nitrates, the following investigation were done and were either normal or negative, FBC, Urea, electrolytes, immunoglobulin, PANCA, CANCA, Anti GBM, serum IGA, Albumin creatinine ratio (from urine), ANA, DNA, ACCP, complements,

LFT, corrected serum Calcium, patient had cystoscopy and multiple biopsies from the bladder mass,

Pathology confirmed high grade Urothelial tumour, immunohistochemistry confirmed the diagnosis, patient treated with transurethral resection, six months later, patient developed total haematuria,

Cystoscopy confirmed recurrence of the tumour, whole body scan excluded any metastasis,

Patient treated with surgery and intravesical BCG (live attenuated Bacille Chalmette –Guerin)

6 months later patient presented to his GP with headache, low grade fever , abdominal pain and increasing shortness of breath, patient transferred to hospital for investigation and management,

In ED patient was unwell with fever, neck pain, tachypnoea,

On examination he had neck stiffness, fever 38, respiratory rate of 28/min, heart rate 110/minute,

No rash, generalised arthralgia but no arthritis, congested sclera, examination of the chest showed stony dullness in the right hemithorax with decreased chest expansion and vocal resonance, normal cardiac sounds, abdominal examination showed a palpable spleen and tender liver, results of blood test in the hospital HB 9 grams, neutrophils 8000, and platelets 600000, normal urea and creatinine,

Normal transaminases, ALK 400, Gam GGT 500, INR 1, Aptt 30, corrected serum calcium 3 momol/L,

ESR 100 CRP 200, parathyroid hormone assay marginally low, serum phosphate normal, 25 hydroxy vitamin D low (30), 1-25 hydroxyl vitamin

D elevated, parathyroid related protein negative, urinary calcium elevated, CXR massive right pleural effusion, echocardiogram normal myocardium, valves, and no coronary calcification, normal, systolic and diastolic function of right and left ventricles, and normal pressure,

CSF study Normal including opening pressure, CSF sugar 2,5 mmol/L (corresponding serum sugar 6 mmol/L)

Cells 300 all mononuclear, Protein elevated, CSF saved for viral and bacterial cultures, including Acid fast bacilli, Cryptococcus, listeria monocytogenes, patient started om cephalosporin, ampicillin, gentamycin and dexamethasone, Pleural cavity was punctured and one litter of fluid f withdrawn, fluid sent for cells, culture, lactic acid dehydrogenase, albumin, and deaminase, sugar, PH, ProBNP, culture and PCR for tuberculosis, Listeria, Cryptococcus, and Toxoplasmosis, Pleural fluid examination was consistent with exsudative, pleural fluid deaminase level was 219u/ml(less than 40u/ml), and pleural biopsy was performed and sent for culture.

While patient in the hospital he started to have continuous fever and testicular pain, patient seen by surgeon who diagnosed epedidmoorchitis, testicular ultrasound supported the diagnosis of epedidmoorchitis, patient taken to theatre and had testicular biopsy and sent for microbiology and culture.

Metronidazole was added to his antibiotics, patient seen by infectious disease specialist who added interferon gamma assay to pleural fluid and serum trsting, and advised to start on rifampicin, INH, Ethambutol, Pyrazinamide and dexamethasone, after two weeks, result of pleural biopsy confirmed mycobacterium tuberculosis, resistant to pyrazinamide and sensitive to refamcin, INH and Ethambutol , interferon gamma assay was strongly positive, patient was started on Reamfin, INH , Ethambutol and levofloxacin for 12 months, patient started to improve after 4 month of quadruple therapy, repeated induced sputum for mycobacterium was negative, Patient was diagnosed as TB meningitis, epididmoorchitis and pulmonary TB due to disseminated TB related BCG.

Discussion

BCG is an attenuated live strain of mycobacterium bovis which is used as a vaccine to prevent tuberculosis in low-income country, [1]

People vaccinated with BCG develop positive tuberculin skin test (Monteux test), BCG was part of Australian vaccination rejmn till 1989, because of decreased incidence of TB in Australia, it was removed, BCG is currently recommended for people of high risk of TB [2.3]

BCG had shown good efficacy to prevent fulminant TB in young children, BCG still used as a diagnostic tool to exclude latent TB in some countries where the exposure risk is low, BCG had been replaced by interferon gamma release assay (IGRA) as it is more specific for latent TB, it is also a common screening test for ptients to do for patients starting on rituximab and other immunotherapy in patient at risk to develop TB while they are on chemotherpay

Intravesical BCG had proven efficacy as an adjacent treatment for intermediate and high grade non muscle invasive bladder cancer, despite its proven efficacy, it can cause disseminated Tuberculosis, [4,5] clinicians should have a low threshold to treat for disseminated TB, in patients treated with intravesical BCG in the past especially if they developed pulmonary, meningeal or disseminated symptoms

Until metastasis related primary disease (urothelial bladder cancer) are ruled out all symptoms of BCG include hepatitis and pancytopenia, carditis, pneumonitis, epididymitis, meningitis should be treated as disseminted Tuberclosis till proved potherwise

The mode of dissemination could be due to haematogenous dissemination from the bladder and type 1V hypersensitivity reaction, the response to steroid treatment had supported the notion of delayed allergic reaction, there is no established measures to avoid disseminated TB related BCG, but

Patients who had the injection close to the site of surgery and those who had repeated catherization or had multiple bladder biopsies are at increased risk of infection, disseminated non-caseating granuloma detected by histology, positive acid-fast bacilli and mycobacterium bovis by molecular biology almost confirm the diagnosis, dissemination can happen six months to few years after intravesical instillation of BCG,

The incidence of systemic complications ranged from 3% to 4.3%, common organs to develop granuloma are liver and lung, corticosteroids had been reported to ameliorate the systemic symptoms in most patients, [6,7,8]

BCG should only be used as an adjacent therapy to TURP in high grade non-invasive cancer due to unfavraboule risk of disseminated Tuberculosis [9,10].

The optimum dose of BCG, optimal frequency and duration differs among urologists,

The standard of care is 6 weekly injections as an induction dose followed by a maintance dose of one injection every three months for one year,

Most of the BCG tested vaccine strains are susceptible to all antituberculosis drugs apart from Pyrazinamide and this should be taken into consideration when starting empirical treatment, There is in vitro evidence that BCG vaccine strains that have lost region of deletion 2(RD2) are susceptible to macrolides whereas those retained RD2 are resistant,

Different strains are used in BCG and this might have impact on the choice of empirical antituberculosis treatment, [11,12,13].

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