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Boom of Resilience: Unleashing the ANCA Positive Power after TB Infection – A Remarkable Case Report

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Abstract

Tuberculosis may mimic systemic autoimmune diseases like ANCA associated vasculitis (AAV). Microscopic polyangiitis (MPA) is the most common subtype and often positive for anti- MPO antibodies with a P-ANCA pattern. Case report A 36-years-old woman presented with haemoptysis, chronic cough with constitutional symptoms and acute kidney impairment. She had a history of smear positive tuberculosis (TB). Her TB workout was negative, and she was treated as Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV), likely Microscopic polyangiitis (MPA). This case illustrates the difficulty in distinguishing between tuberculosis and AAV due to similar clinical, and radiological features, with previous history of pulmonary tuberculosis.

Keywords: ANCA associated vasculitis (AAV), Microscopic polyangiitis (MPA), Tuberculosis

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1. Introduction

Tuberculosis is known to have diverse clinical presentations, some of which may mimic systemic autoimmune diseases like ANCA associated vasculitis (AAV). The association between TB and vasculitis has been described, but generally uncommon. Microscopic poly angiitis (MPA) is the most common subtype in AAV and kidneys are the most affected organs. The serology is often positive for anti-MPO antibodies with a P-ANCA pattern.

2. Case Report

A 36-years-old woman with history of previous smear positive TB presented hemoptysis for 4 days duration. She had chronic cough and significant weight loss for past 3 months. She had intermittent fever and was short of breath. Upon examination, her temperature was 37 °C, blood pressure of 130/80mmHg, pulse rate of 101beat/minute and oxygen saturation was 90% under room air. Auscultation of the lungs revealed bilateral crepitations. The initial blood test showed urea of 10.8 mmol/L, creatinine 374 mmol/L, CRP 118 mg/L, procalcitonin 0.18 ng/mL (normal <0.05 ng/mL) and urine FEME RBC 3+. Chest radiograph (**Figure 1**) showed pulmonary infiltrates bilaterally. Sputum culture, AFB smear, Gene-Xpert and TB PCR were negative. The patient was initially treated for pneumonia with antibiotics and hydration, however she got worsen. Further workout showed Antinuclear antibody (ANA) titters were detected (1:80), with negative for anti-double-stranded DNA (dsDNA), ENA (extractable nuclear antigen) and complement levels were normal. Specific antibody positive test for MPO antibodies and a positive p-ANCA, and negative PR3 and GBM antibodies. She was planning for renal biopsy however she declines. The patient was given IV methylprednisolone 160 mg OD for 3 days followed by a tapering dose of oral prednisolone. Her condition fortunately improved significantly.

3. Discussions

Pulmonary–renal syndrome (PRS) is characterized by the combination of pathological features present in Diffuse alveolar Haemorrhage (DAH) and rapidly progressive glomerulonephritis (RPGN) (1). The underlying pathology is a small vessel vasculitis involving arterioles and alveolar capillaries. Small vessel vasculitis is divided into ANCA-associated vasculitis (AAV), including microscopic polyangiitis (MPA), granulomatosis with polyangiitis (Wegener's) (GPA) and eosinophilic GPA (Churg-Strauss) and immune complex small vessel vasculitis, which comprises anti-GBM disease (Goodpasture's disease), IgA vasculitis (Henoch-Schönlein) (IgA) and hypocomplementemic urticarial vasculitis (anti-C1q vasculitis) (2).

In AAV, only a few or no immune deposits are found in small vessels, contrasting with immune complex, where it occurs moderately to mark deposition of immunoglobulin or complement. Renal vasculitis is the most common severe manifestation of AAV typically presented with rapidly progressive glomerulonephritis (GN) (3). A rapid decline in kidney function, which is defined as a drop of at least fifty percent in glomerular filtration rates over a short period of time, is a hallmark of RPGN. Thus, a renal biopsy needs to be taken into consideration whenever there is a suspicion of an autoimmune etiology of pulmonary renal syndrome (4,5). The differential diagnosis in the case of pulmonary-renal syndrome is very important. This case illustrates the difficulty in distinguishing between tuberculosis and AAV due to similar presentation and previous history of pulmonary tuberculosis. The prognosis for the recovery of kidney function depends on early vigorous therapy, such as corticosteroids, cyclophosphamide, and plasmapheresis, thus early detection of the illness is essential.

The diagnostic approach includes careful and thorough clinical evaluation of the patient's medical history, physical examination, radiological imaging with CT to detect lung involvement, biochemical evaluation including serum urea and creatinine levels, and urine analysis to detect proteinuria, haematuria, or active urine sediment including white cell or red cell casts and targeted laboratory exams including immunological assays. The use of GeneXpert as a means of ruling out tuberculosis infection is one of the excellent clinical tool for detection of Mycobacterium Tuberculosis in early stage where the direct smear is negative as well as in early detection of Rifampicin resistance (6). The Xpert MTB/RIF assay is a revolutionary test that contributes to the rapid diagnosis of tuberculosis disease as well as medication resistance (7). This is helping to revolutionize the way that tuberculosis (TB) is controlled. In less than 2 hours, the test may identify both Mycobacterium tuberculosis complex (MTBC) and rifampin resistance.

Omar et al. described GeneXpert test is accurate in diagnosing pulmonary TB with 95.9% sensitivity and 94.4% specificity and overall diagnostic accuracy of 95.5% (8). ANCA autoantibodies may be present in both diseases. There are other conditions besides AAV have the capability to induce ANCAs include infections such as tuberculosis (TB), respiratory tract infections, endocarditis, malaria and leprosy; and drugs such as isoniazid (9,10,11,12,13). Many studies have been done before in addressing this issue. Examples of study that showed a significant number of positive ANCA antibodies in Tuberculosis patients are Flores-Suárez and Cabiedes (14). This study revealed ANCA antibodies are present in 20 (44.4%) of 45 tuberculosis patients by IIF (16 c-ANCA, four p-ANCA) and in 18 (40%) patients by ELISA (15 PR3-ANCA, three MPO-ANCA) (14). Other than that, Badakere SS et al. noted that ANCA was detected in 30% cases, with 52.4% showed perinuclear pattern (p-ANCA), 38.1% cytoplasmic (c-ANCA) and 9.5% showed an 'atypical' pattern (15). In opposition to that however, there are also study in Brazil that found no Tuberculosis patient exhibited positive ANCA (16). Almost similar to that, a study in China display pANCA was only detected in 4.8% (5/103) of patients, and c-ANCA was not observed in any patients (17). Due to these conflicting results, more studies are needed to investigate the role of ANCA autoantibodies in differentiating Tuberculosis patient and ANCA associated vasculitis patient.

Immunosuppression is the mainstay of treatment for Goodpasture's disease and ANCA-associated pulmonary-renal syndrome (18). Often used to induce remission, high-dose intravenous steroids for 3–5 days are occasionally coupled with oral or intravenous cyclophosphamide as remission is achieved, steroid dosage is gradually reduced over 3–5 months. Plasmapheresis may be useful in acute situations but are currently a subject of debate (19). The function of plasma exchange in ANCA vasculitis is unclear, however it is believed to be beneficial in certain circumstances due to the existence of unexplained serum antibodies in these patients.

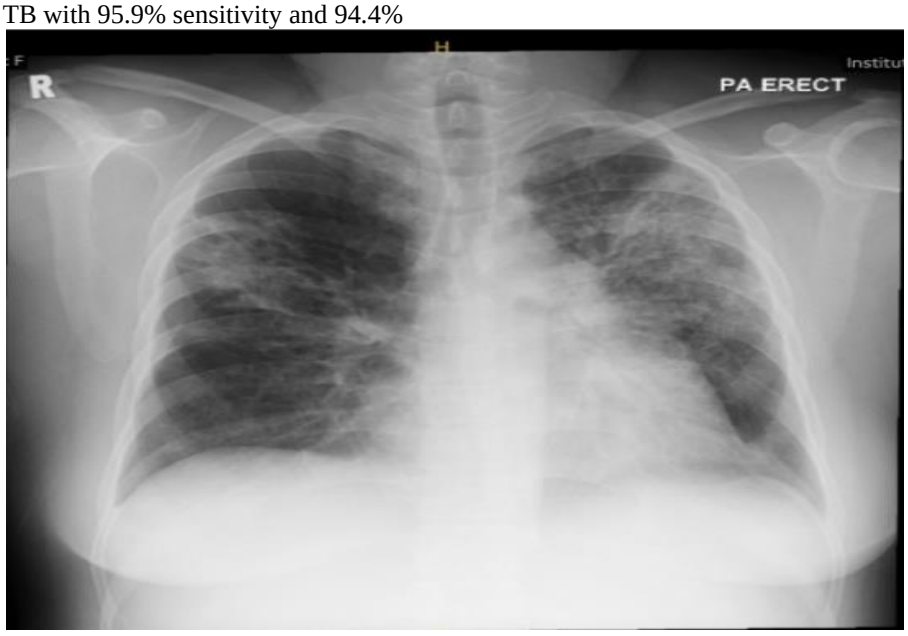

Figure 1. Chest radiograph

4. Conclusions

In conclusion, pulmonary TB and AAV might present with overlapping symptoms, making it difficult to differentiate between the two clinically. Here we review the diagnostic considerations between differentiating AAV and tuberculosis in patients from endemic regions. Preemptive tuberculosis screening for ANCA-positive individuals prior to high-dose immunosuppression is important to avoid further complications.

References

[1] S.C. West, N. Arulkumaran, P.W. Ind, & C.C. Pusey. (2013) Pulmonary-renal syndrome: a life threatening but treatable condition. Postgrad Med J. 89 (1051): 274–83.

[2] D. Geetha, & J.A. Jefferson. (2020). ANCA-associated vasculitis: Core curriculum American Journal of Kidney Diseases. 75 (1): 124–137.

[3] A. Salmela, T. Törnroth, T. Poussa, & A. Ekstrand. (2018). Prognostic factors for survival and relapse in ANCA-associated vasculitis with renal involvement: A clinical long-term follow-up study. Int J Nephrol. 2018: 6369814.

[4] M.S. Parmar, & K Bashir. Crescentic Glomerulonephritis. (2023). In: StatPearls, Treasure Island (FL): StatPearls Publishing.

[5] M. Yates, R.A. Watts, I.M. Bajema, M.C. Cid, B. Crestani, T. Hauser, B. Hellmich, J.U. Holle, M. Laudien, M.A. Little, R.A. Luqmani, A. Mahr, P.A. Merkel, J. Mills, J. Mooney, M. Segelmark, V. Tesar, K. Westman, A. Vaglio, N. Yalçındağ, D.R. Jayne, & C. Mukhtyar. (2016). EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis. 75(9): 1583–1594.

[6] A.K. Prakash, B. Datta, P. Goyal, P. Chatterjee, & G. Gupta. (2016). GENE-XPERT gives early diagnosis in early tuberculosis. In: 102 Tuberculosis. European Respiratory Society; PA, USA.

[7] World Health Organization. (2018). Global tuberculosis report 265.

[8] A. Omar, A.E. Abo Elfadl, Y. Ahmed, & M. Hosny. (2019). Valuing the use of GeneXpert test as an unconventional approach to diagnose pulmonary tuberculosis. Egyptian J. Bronchol. 13:403–407.

[9] A.D. Mahr, T. Neogi, & P.A. Merkel. (2006). S-82 [Internet]. Clin Exp Rheumatol., 24, Available from: www.rarediseasesnetwork.org/vcrc

[10] E. Houben, W.A. Bax, B. van Dam, W.A.T. Slieker, G. Verhave, F.C.P. Frerichs, I.C. an Eijk, W.G. Boersma, G.T.M. de Kuyper, & E.L. Penne. (2016). Diagnosing ANCA-associated vasculitis in ANCA positive patients. Medicine. 95 (40): e5096.

[11] L.F. Flores-Suarez. (2003). Prevalence of antineutrophil cytoplasmic autoantibodies in patients with tuberculosis. Rheumatology. 42(2): 223–229.

[12] G.S. Hoffman, G.S. Kerr, R.Y. Leavitt, C.W. Hallahan, R.S. Lebovics, W.D. Travis, M. Rottem, & A.S. Fauci. (1992). Wegener Granulomatosis: An analysis of 158 patients. Ann Intern Med. 116 (6): 488–498.

[13] J.C. Jennette, R.J. Falk, P.A. Bacon, N. Basu, M.C. Cid, F. Ferrario, L.F. Flores-Suarez, W.L. Gross, L. Guillevin, E.C. Hagen, G.S. Hoffman, D.R. Jayne, C.G. Kallenberg, P. Lamprecht, C.A. Langford, R.A. Luqmani, A.D. Mahr, E.L. Matteson, P.A. Merkel, S. Ozen, C.D. Pusey, N. Rasmussen, A.J. Rees, D.G. Scott, U. Specks, J.H. Stone, K. Takahashi, & R.A. Watts (2013). Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 65 (1):1–11.

[14] L.F. Flores-Suárez, J. Cabiedes, A.R. Villa, F.J. Van Der Woude, & J. Alcocer-Varela. (2022). Prevalence of antineutrophil cytoplasmic autoantibodies in patients with tuberculosis. [cited 2022 Nov 5]; Available from: https://academic.oup.com/rheumatology/article/42/2/223/1788364

[15] V.D. Pradhan, S.S. Badakere, K. Ghosh, & A.R. Pawar. (2004). Spectrum of anti-neutrophil cytoplasmic antibodies in patients with pulmonary tuberculosis overlaps with that of Wegener's granulomatosis. J Med Sci. 58 (7): 283-288.

[16] I. Lima, R.C. Oliveira, M.S. Cabral, A. Atta, S. Marchi, E. Reis, M.G. Reis, L. Barbosa, & M.B. Santiago. (2014). Anti-PR3 and anti-MPO antibodies are not present in sera of patients with pulmonary tuberculosis. Rheumatol Int. 34 (9): 1231–1234.

[17] G. Huan, G. Yang, Q. Xiao-Yu, X. Jiancheng, S. Yan-Qing. (2018). Antineutrophil cytoplasmic antibodies in Chinese patients with tuberculosis. Rev Soc Bras Med Trop. 51 (4): 475–478.

[18] S.R. Henderson, & A.D. Salama. (2018). Diagnostic and management challenges in Goodpasture's (anti-glomerular basement membrane) disease. Nephrology Dialysis Transplantation. 33 (2): 196–202.

[19] S. Tsiakas, S. Marinaki, S. Lionaki, & J. Boletis. (2021). Plasma exchange in ANCA-associated vasculitis: A narrative review. J Clin Med. 10 (21): 5154.