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Case Study

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TUBERCULOSIS-ASSOCIATED IGA NEPHROPATHY: A NEW CASE

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ABSRACT

Introduction: Tunisia is a country of intermediate endemicity for tuberculosis. Immunoglobulin A nephropathy (IgAN) is the most frequent pathological diagnosis of tuberculosis-associated glomerulonephritis. It's challenging owing to atypical presentations. Few cases of tuberculosis-associated IgAN have been reported since 1983. **Case Report:** A 47 year-old white woman presented asthenia, chest pain and fever for a month. Biological tests found an inflammatory syndrome, aminotranferases elevation, proteinuria and hematuria. Imaging showed pleural and pericardial effusion with multiple lymphadenopathies. Further tests and biopsies revealed multifocal tuberculosis. Renal biopsy showed the aspect of IgA nephritis. Clinical, biological and radiological abnormalities disappeared under anti-tuberculosis therapy and high doses of corticosteroids. **Conclusion:** IgAN is a rare complication of tuberculosis with frequent misdiagnosis. We report the first Tunisian case.

KEYWORDS: Tuberculosis – IgA glomerulonephritis – Exsudates – Lymphadenopathy.

INTRODUCTION

Tuberculosis is an infection caused by bacteria of *Mycobacterium tuberculosis* (*MT*) complex that can be prevented and cured. Still, it represents a public health issue due to its increasing importance and its high morbi-mortality around the world. According to the World Health Organization (WHO), almost a quarter of the population has latent infection with (*MT*).[1] Tunisia is a country of intermediate endemicity with an incidence of 29/100 000 habitants in 2017.[2] In the same year, the national surveillance system counted 38% of pulmonary tuberculosis and 62% of extra-pulmonary tuberculosis with a high prevalence of the lymph nodes form (18/100 000 habitants).[2] Urinary tuberculosis is rare. It typically results in cystitis but it can also affect kidneys causing a latent glomerular disease. Immunoglobulin A nephropathy (IgAN) is the most frequent pathological diagnosis of tuberculosis-associated glomerulonephritis.[3] Nevertheless, its diagnosis remains challenging owing to atypical presentations. Few cases of tuberculosis-associated IgAN have been reported since 1983. To our knowledge, there is no similar case of this rare association reported from Tunisia.

CASE REPORT

A 47 year-old white tunisian woman, non-smoker, under treatment for iron deficiency, presented with asthenia, weight loss, moderate fever and chest pain evolving for one month. Physical examination was normal except for pulmonary auscultation where a decreased murmur was noted in the right lung field. Chest radiography showed right pleural effusion and cardiomegaly (Fig.1). Biologically, hemoglobin was at 8.1 g/dL, mean corpuscular volume = 75 fl, white cells were normal (8920/mm3), platelets were high (622000/mm3), sedimentation rate was elevated (90 mm in the first hour), C-reactive protein was high (150mg/L), proteins' rate was normal (75g/L), albumin was low (30g/L) and alpha2-globulins were high (14.2g/L), ASAT = 117UI/L and ALAT = 188UI/L. Urine test strip indicated hematuria (+++) and proteinuria (+++), which was confirmed by the 24-hour urine protein test (1.97g/24h). Other biological parameters were normal (renal function, hepatic function and calcemia). Echocardiography showed a pericardial effusion and the integrity of the other cardiac elements. Two computed tomography (CT) scans of the thorax, abdomen and pelvis revealed moderate pleural and pericardial effusion with multiple thoracic and abdominal lymphadenopathies (Fig.2). No tumoral lesion was found. Renal morphology was normal.

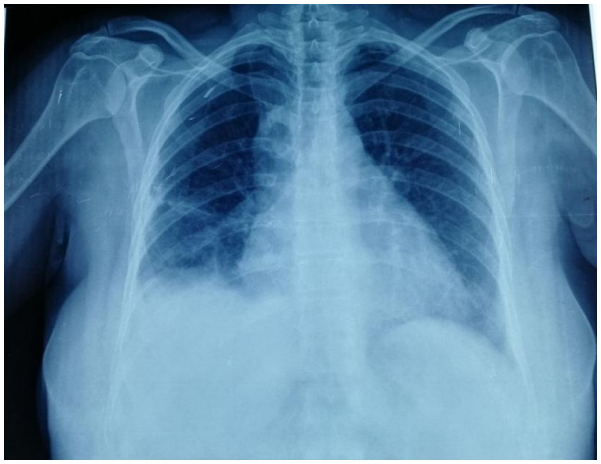

Figure 1: Chest radiography showing right-side pleural effusion and cardiomegaly.

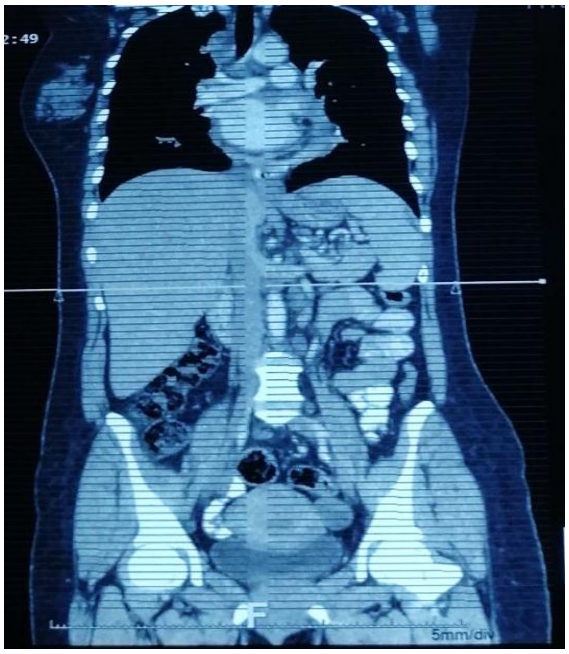

Figure 2: Computed tomography axial reconstruction showing diffuse lymphadenopathies.

Pleural puncture brought back an exsudative fluid rich in lymphocytes. No MT were detected. Screening for infectious diseases was negative (urine bacteriological examination, HIV, HVB, HVC, EBV, CMV, Parvovirus B19, brucellosis, rickettsiosis and Q fever serologies, gamma interferon assay, tuberculin dermal reaction and sputum tests for *MT*). Antinuclear antibodies were negative and serum complement was in a normal range. Converting enzyme was normal. A lymphadenopathy biopsy realized by mediastinoscopy revealed epitheloid and giganto-cellular granulomatous lymphadenitis with positive polymerase chain reaction for *MT*. Thus, the diagnosis of multifocal tuberculosis was confirmed. Regarding the persistent proteinuria, we proceeded to renal biopsy which revealed the aspect of IgA nephritis with focal endo and extracapillary proliferation and IgA (++) and IgG (+) mesangial deposits in direct immunofluorescence study.

The patient received initial anti-tuberculosis treatment with adapted doses of Isoniazide, Rifampicine, Ethambutol and Pyrazinamide along with pleural physiotherapy. Echocardiography control after five days revealed no change in effusion abundance. High dose of oral corticosteroids (1mg/Kg/day of equivalent Prednisone) was added to the therapy. After two months, all symptoms disappeared, biological parameters have normalized, effusion regressed, lymphadenopathies decreased in size and proteinuria became negative. Anti-tuberculosis treatment was conducted for six months in total and corticosteroids were maintained for a total duration of four months.

DISCUSSION

IgAN represents the most frequent cause of primary renal diseases. Its aetiology remains unclear in most of the cases. This nephropathy is mostly found in patients with liver disease or mucosal inflammation.[4] Some observations suggest that IgAN pathogenesis might be related to microbial antigens. In tuberculosis-associated IgAN, the exact pathological mechanisms are still under study. Humoral immunity has been incriminated. In fact, the humoral immune response in active tuberculosis would generate high serum levels of specific IgA aimed at certain mycobacterial antigen.[5] Furthermore, gamma-delta-T-cells are activated and proliferate on the mucosal surface inducing the secretion of a large amount of TGF- 1 which stimulates B-cells resulting in the production of defective IgA1.[6] Accordingly, circulating immune complexes with IgA and mycobacterial antigens deposit in the mesangial area of the kidneys, then activate the alternative complement and the lectin pathways causing IgAN. Another hypothesis has been advanced by Gao and *al*.[7] in tuberculosis-associated renal injury. A T-cell antigen associated with the virulence and the pathogenicity of MT and having a role in the disseminated forms has been identified. It's the early secreted antigenic target of 6kDa (ESAT-6). It has a role in innate and adaptative immune responses[8] and it may be involved in the development and progression of IgAN. Also, it can be used in the early diagnosis of this nephropathy.[9] In fact, tuberculosis-associated IgAN diagnosis is difficult because of nonspecific presentation, atypical symptoms and insidious onset, as was the case with our patient. Thus, it must be suspected in patients with glomerulonephritis along with a history of tuberculosis, a strong positive result on a tuberculin protein purified derivate skin test, a positive result with a tuberculosis antigen assay, and a pathological diagnosis of IgAN.[3] Sun L and *al*.[10] proposed clinical, biological and histological criteria for this condition. Renal biopsy must be conducted in case of tuberculosis with renal manifestations. It is important for the diagnosis although no pathogenic features are observed.

To alleviate kidney damage, anti-tuberculosis therapy must be introduced. Manifestations improvement can be seen at variable degrees and delays.[11,12] The use of glucocorticoids and/or immunosuppressive therapies is

not consensual.[3] It can be considered in case of non-response to anti-tuberculosis therapy. In our case, the combination of antibiotics with corticosteroids permitted the regression of all clinical and biological manifestations within two months.

CONCLUSION

IgAN is a rare complication of tuberculosis. Nonspecific manifestations can lead to a misdiagnosis or a delay in the adequate treatment initiation. A greater understanding of the clinical characteristics of tuberculosis-associated IgAN is necessary to raise awareness and improve disease treatment.

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