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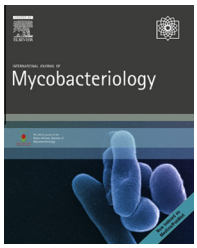

Case Report

Selective immunoglobulin M deficiency in an adult with miliary tuberculosis: A clinically interesting coexistence. A case report and review of the literature

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ABSTRACT

Selective immunoglobulin M (SIgM) deficiency is a rare form of dysgammaglobulinemia. Here we are reporting a 31 year old man with multiple cervical and testicular abscesses who was investigated and found to have miliary tuberculosis (MTB) with primary SIgM deficiency (Serum IgM: 17.4 mg/dL) and was treated aggressively with anti-tuberculous treatment.

Case report

A 31-year-old previously healthy man with an unremarkable clinical history presented with predominant symptoms of fatigue fevers, chills, malaise, anorexia and weight loss 1 year duration. 3 months later, the patient developed painful scrotal swelling on the left side of the scrotum which was drained by a doctor associated with greenish foul discharge and patient was empirically started on broad-spectrum intravenous (IV) antibiotics. The patient was admitted to the Fever Hospital in February 2015 for evaluation of history fever and recurrent scrotal swellings, he was found to have multiple testicular abscesses, which were treated with multiple courses of antibiotics. Despite the medical treatment, the

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patient had another painful swelling on the right side of the neck, so he was subsequently referred to our hospital in April 2015 as a case of recurrent mucocutaneous abscess formation in order to create a diagnosis and treatment plan. He did not have any significant past medical history or surgical history or any risk factors for HIV. There was no history of childhood infections, relatives with opportunistic infections or immunodeficiencies.

Physical examination of the patient on admission was normal except his body temperature was ranging between 38.2 and 39.4 °C and pallor. Cystic tender swelling (4 × 3 cm) was located in the subclavian triangle area, in the supraclavicular region expanding to the occipital triangle. The skin over the swelling was lividly discolored with signs of necrosis associated with generalized small lymphadenopathy. There was scrotal sinus on the left side of the scrotum with signs of necrosis.

At that moment, laboratory tests revealed normal blood sugar, urine analysis and serum biochemistry except mild hypoalbuminemia, mild elevation in liver enzymes and ESR 70 mm/h. There were no abnormalities in WBCs and platelets count except mild lymphocytopenia and microcytic anemia. Serum iron, ferritin were within normal limits.

In routine work up chest X-ray revealed radiologic evidence of MTB and this was confirmed with a positive culture for acid alcohol fast bacilli from a laryngeal swab and blood culture revealed *Mycobacterium tuberculosis*. The BCG scar was present and normal, with negative results of tuberculin test. Neck U/S revealed a bilocular cystic lesion each of them about 2.5 × 3 cm with markedly turbid fluid content. Pus is seen at lower deep cervical to suprasternal notch with multiple enlarged variable size lymph nodes with no abnormal vascularity. Abdominal U/S was normal except mild hepatomegaly. Scrotal U/S and Doppler revealed an abscess about (3 × 1 cm) at the left scrotal neck with hypo echoic area about (3 × 1 cm) is seen at the parenchyma of the testis and another abscess about (5 × 3 cm) is seen at the left thigh (intra muscular). Rt testis showed multiple hypoechoic focal lesions. Screening for malignancy revealed negative results for testicular tumors such as alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), lactate dehydrogenase (LDH). Serological viral studies revealed negative results of HIV, hepatitis C virus antibodies and hepatitis B surface antigen. Most clinically relevant autoantibodies were checked, but all of them were found to be negative. Laboratory work-up of immunodeficiency was performed (Table 1). The blood cell count, T cells, T cell subsets, B cells, and natural killer cells were within normal limits. Also, we examined the performance of delayed-type hypersensitivity (DTH) antigens using a tetanus toxoid. Our patient was of middle aged. Therefore, our patient is unlikely to have a partial deficiency of adenosine deaminase (ADA). Therefore, no ADA analysis was performed. Interferon y secretion and IFN-yR expression could not be done due to financial causes.

Once the diagnosis of symptomatic sIgMD with miliary tuberculosis was recognized, the patient was treated aggressively with the courses of Isoniazide, Rifampicin, Pyrazinamide, Ethambutol and Clarithromycine to covering for disseminated TB or severe atypical mycobacterial infection. He showed dramatic improvement after antimycobacterial therapy and the patient was discharged after 1 month of hospitalization on Isoniazide, Rifampicin and Pyrazinamide. Subsequently, chest X-ray normalized. But sputum smears still positive for AFB after 4 months of treatments. Within 5 months, most of patient symptoms disappeared and scrotal, Abdominal and neck U/S normalized and sputum smears for AFB became negative.

Discussion

SIgM deficiency is a rare form of dysgammaglobulinemia which was described first in 2 children with fulminant meningococcal septicemia, more than 45 years ago [1] and characterized by an isolated low level of serum immunoglobulin M (IgM). There have been a few cases reported in the literature, with a reported prevalence of 0.03–3% [2–4]. Adults with primary sIgM deficiency usually associated with autoimmune diseases and malignant neoplasm [3,4] whereas children may present with severe life-threatening infections, a few cases of possible primary sIgM deficiency in adults with no evidence of autoimmunity or malignant neoplasm have been reported [5]. Adult patients usually present with mild infections. Our patient, who was previously healthy with no evidence of autoimmunity or neoplasm, represents a possible case of primary sIgM deficiency in adults with severe life-threatening and unusual infections (Miliary tuberculosis). We reviewed and compared previously reported 43 patients with sIgMID from 1967 to 2015, including our patient, and their characteristics are summarized in Table 2.

IgM provides the initial response to foreign antigen and plays a regulatory role in the subsequent immune response development, accelerating the production of high-affinity IgG [6]. SIgM deficiency can be asymptomatic or may symptomatically present with infections from encapsulated bacteria and viruses, some of which can be serious and even life threatening infections varying from pneumonia to septicemia and meningitis. A few cases of sIgMD with mycobacterium avium complex (MAC) infection or *M. tuberculosis*, but none of them presented with MTB without T-cell disorders [7].

In primary sIgM deficiency, B cells, T cells and T cell subsets, and NK cells are normal [2,8]. T cell functions are normal [2]. Innate immune functions are normal [2]. Specific antibody response to pneumococci is impaired in 50% of symptomatic cases [2] as in our case. However, several patients with selective IgM deficiency and T cell and NK cell defects with MAC intracellulare infections have been reported [7]. In a subset of patients with sIgM deficiency circulating IgM + B cells are decreased or completely lacking. Specific IgG antibody responses against pneumococcus polysaccharides are impaired in a subset of patients with selective IgM deficiency who appear to respond to immunoglobulin therapy [6]. Furthermore, immunologic investigation neglected any possibility of an immune defect associated with tuberculosis, In our case the innate immunity is intact. T cells, T cell subsets, and T cell functions and phagocytic responses, serum IgA,