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Case Report

Mixed connective tissue disease with secondary immune thrombocytopenic purpura - A case report

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Introduction

Mixed connective tissue disease [MCTD] is a systemic autoimmune disease with features of systemic lupus erythematosis [SLE], systemic sclerosis and polymyositis/dermatomyositis along with positive anti-U1 ribonucleoprotein [RNP] antibodies [1].

Here we report a case of an 18-year-old female presenting with menorrhagia and symptomatic anaemia, along with small joint pain, Raynaud's phenomenon, alopecia with thrombocytopenia and positive anti-U1RNP antibodies which led to a diagnosis of MCTD with secondary ITP. Even though secondary ITP is associated with autoimmune diseases, cases of MCTD with secondary ITP are rare [1,2].

Case presentation

An 18-year-old, previously healthy schoolgirl presented with menorrhagia of 3 months duration, along with exertional dyspnoea, palpitations and fatiguability. She complained of bilateral small joint pain and skin thickening of hands for 3 weeks associated with early morning stiffness. She had alopecia and complained of bluish discoloration, pain and numbness of fingers when exposed to cold water. She did not have other symptoms of autoimmune disease. She denied any family history of haematological diseases, autoimmune diseases or malignancy.

On examination, her body mass index was 16kg/m^2. She was pale and had alopecia and sclerodactyly. Pulse rate was 104bpm and blood pressure was 120/80mmHg. There was a loud second heart sound in the pulmonary area. There was no lymphadenopathy or hepatosplenomegaly. Digital rectal examination was normal. Lung bases were clear.

Full blood count revealed a total white cell count of 7.9x 10^9 /L [neutrophils-62.7%, lymphocytes-25.7%], haemoglobin of 7.1 g/dl [13.6-17.2], mean corpuscular volume of 85 fL[80-96] and a platelet count of 24 x 10^9 /L [150-400].Blood picture was reported as

inflammation/ infection, anaemia of chronic disease with mild thrombocytopenia. Erythrocyte sedimentation rate was 78mm/hr. Serum ferritin was 400 ng/mL (12-300) while the other iron studies were low. Anti-nuclear antibodies were positive with a titre of >1/100. Anti-double stranded deoxyribonucleic acid antibodies, anti-Scl70 antibodies, rheumatoid factor and screening for anti-phospholipid syndrome were negative. Anti U1 RNP antibodies were positive. Haemolytic screening and clotting profile were negative. Thyroid profile and renal and liver function tests were normal. Ultrasound scan abdomen and pelvis was normal. Serological screening for infections including retroviral infection and hepatitis B/C were negative. Electrocardiogram revealed p pulmonale and the 2D-echo reported the presence of a pericardial effusion and moderate pulmonary hypertension with an ejection fraction >60%. High-resolution computed tomography was normal. Bone marrow biopsy revealed megaloblastic anaemia with immune thrombocytopenic purpura [ITP].

She was diagnosed to have MCTD complicated by pulmonary hypertension and secondary ITP. She was started on high dose prednisolone along with methotrexate and hydroxychloroquine. Sildenafil, nifidipine and iron supplements were added. Menorrhagia settled following treatment and she achieved remission in 6 months.

Discussion

MCTD, which was first described in 1972, is a syndrome with overlapping clinical features of SLE, systemic sclerosis and polymyositis/dermatomyositis along with a positive anti-U1RNP antibody. The characteristic presenting symptoms include Raynaud's phenomenon, sclerodactyly, interstitial lung disease, pulmonary hypertension, arthritis, swollen hands and proximal muscle weakness [3]. In contrast to SLE, renal and central nervous system (CNS) involvement is not seen in MCTD [4]. Information about the incidence and prevalence of MCTD is limited. A population-based study done in Norway revealed that MCTD is rare, occurring at a rate of 0.21 per 100,000 adults and more common in females than in males [5].

Approximately 75% of patients have low-grade anaemia while some patients have leucopaenia, but thrombocytopenia is seen very rarely [6] and cases of MCTD presenting with bleeding manifestations are rare. We encountered a case of fatal gastrointestinal haemorrhage in MCTD, due to diffuse arteritis with fibrinoid necrosis involving the blood vessels of intestinal wall [7].

Even though secondary ITP has been reported in a wide variety of autoimmune disorders, ITP secondary to MCTD is rare [3,4]. A study done among ITP patients at King Abdulaziz University Hospital (KAUH) between September 2002 and August 2010 revealed that 29 (43.3%) of 67 patients were having secondary ITP. Among those, autoimmune diseases were observed in 22 (75.9%) patients. Underlying conditions were 9 (31.0%) having SLE, 7 (24.1%) having anti-phospholipid syndrome, 2 (6.9%) having Evan syndrome and 2 (6.9%) having Hodgkin lymphoma while the remaining patients had renal cell carcinoma, sarcoidosis, T-cell lymphoma and positive ANA [8]. Ecchymosis and purpura were observed in 4 (13.8%) patients with secondary ITP. The pathogenesis of secondary ITP remains unclear.

Treatment options for MCTD with secondary ITP include corticosteroids and anti-malarials such as hydroxychloroquine. Immunosuppressants are used in refractory synovitis [9]. MCTD is considered as a connective tissue disorder with a relatively benign prognosis. A cohort study

of 280 patients with MCTD reported favourable prognosis with 5, 10, and 15-year survival following diagnosis as 98%, 96% and 88%, respectively [**Error! Reference source not found.**]. Another study reported 5 deaths among 440 patients, with a standardized mortality ratio of 1.1 which was not significantly different from the normal population [11]. Prognosis and mortality of cases of secondary ITP associated with MCTD are not available in literature since this association is very rare.

Conclusion

This case highlights the importance of considering MCTD with secondary ITP as a differential diagnosis in a patient presenting with bleeding manifestations along with symptoms of connective tissue disease. Early recognition and prompt treatment is mandatory in order to reduce morbidity and mortality.

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