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Case Report

A rare case of mixed connective tissue disease presenting with central nervous system glioma, vasculitis and polymyositis

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ABSTRACT

Mixed connective tissue disease (MCTD) was first recognized by Sharp and Colleagues in 1972 among a group of patients with overlapping clinical features of systemic lupus erythematosis (SLE), scleroderma and myositis, with the presence of distinctive antibodies against, what now is known to be U1-ribonucleoprotein (RNP). We report an unusual case of a 23-year old female with MCTD characterized by the coexistence of signs, symptoms and immunological features of 3 defined autoimmune diseases SLE, systemic sclerosis (SSc), polymyositis (PM) and an unusual presence of central nervous system (CNS) Glioma.

Keywords: Mixed connective tissue disease, CNS glioma, Vasculitis, Polymyositis

INTRODUCTION

Glioma is a broad category of brain and spinal cord tumors that come from glial cells, brain cells, which can develop into tumors. These tumors grow and infiltrate into the normal brain tissue, which makes them very difficult to approach and remove hence complicating the treatment. Some genetic disorders also increase the risk of development of these tumors in children but rarely in adults. Vasculitis is an autoimmune condition that involves inflammation in the blood vessels. This may happen following an immune reaction secondary to infection, certain medications or any other disease or condition.

The term polymyositis refers to group of patients with demonstrable evidence of muscle necrosis with perivascular cell infiltration, following symptoms of muscle pain and severe tenderness. The presence of erythematous skin rash in few such cases makes the term dermatomyositis more appropriate. This constellation of symptoms is more often referred to polymyositis-dermatomyositis complex (PM-DM Complex).[2] All such conditions presenting together with SLE and SSc is a rare presentation of MCTD which is reported in the following case.

CASE REPORT

A 23 year old unmarried female, right handed person, student by profession, hailing from Navi Mumbai (India) was brought to the Emergency Department (ED) with 2 episodes of generalized tonic clonic convulsions half an hour before presenting to the ED. The patient was at home when she suddenly got generalized tonic clonic convulsions at around 11 am as witnessed by her mother. The convulsions lasted for around 2-3 minutes and were associated with up rolling of eyeballs and frothing of mouth. The patient was unconscious for about 10 minutes after convulsions as per informed by the accompaniers. The patient was drowsy on presentation. Patient had a history of fever, intermittent and high grade for past 12 days. She also complained about pain in both thighs on squatting. She was immediately shifted to the intensive care for further management.

Clinically, she was febrile (103°F). The blood pressure was 144/90 mm Hg, the pulse 124 beats per minute, and was tachypnoeic with oxygen saturation 98% while she was breathing ambient air. On general examination she was pale. She had thickening of skin and loss of wrinkles over her forehead. Sclerodactyl was present .Periungual telangiectasia and healed ulcers over fingers were seen with stellate scars. Multiple well defined hypo pigmented patches with hyper pigmented periphery over the chest, hands, back and knees were seen. On enquiry she also had history of photosensitivity and bluish discoloration of the fingers on exposure to cold.

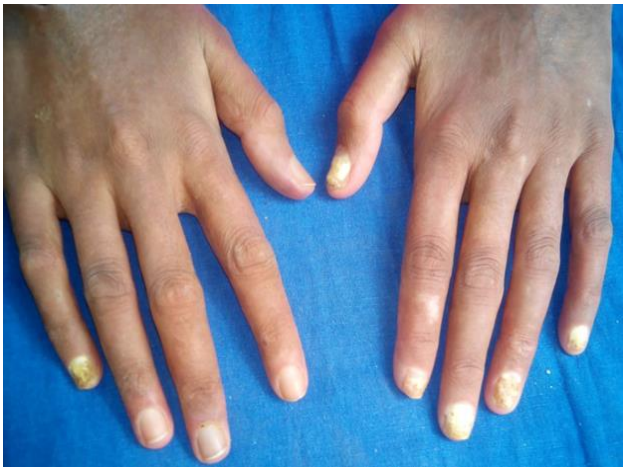

Figure 1: Calcinosis cutis universalis.

Her basic investigations were sent and the blood reports showed pancytopenia with Hb-6.7g/dl, TLC-2.9x10^3/ul, Plt -74x10^3/ul which was suggestive of active SLE status. Electrolytes, RFT and urine routine report was normal. LFT showed mildy raised enzymes. Sr. Calcium and Magnesium was normal. ESR and CRP were highly raised. ECG showed normal sinus rhythm with low QRS voltage and 2Decho was suggestive of a normal LV function with minimal pericardial effusion, mild tricuspid regurgitation with mildy elevated pulmonary artery pressure of 39mmHg. Thyroid profile was within normal limits. Abdominal sonography showed mild hepatosplenomegaly. CNS manifestations of lupus were also considered and the following investigations were done. Lumbar puncture was done, total proteins were 68.5mg/dl, sugars were 48.7mg/dl, and total leucocyte count was 5 cells with 100% lymphocytes without any cobweb formation which ruled out any infective etiology in the patient. HIV 1 & 2 were both negative by ELISA & PCR.

Certain special investigations were sent which were found to be in the abnormal range and are as follows: LDH – 985.5 IU/L (230-460) and CPK – 2064.4 IU/L (24-170).

The immunological profile revealed a positive ANA titre with a speckled pattern. ANA Blot was send. Anti-nRNP, AntiSm, AntiRO/SSA, AntiScl70 and Anti-rib P protein were all positive.

MRI Brain following the convulsions was suggestive of a non enhancing lesion in the left posterior temporal sub cortical white matter measuring approximately 4.1x3.0cm which was suggestive of a low grade glioma most likely.

MRI B/L Thigh was done in view of diagnosis of polymyositis and showed diffuse STIR hyperintensity involving vastuslateralis, medialis and intermedius, pectineus, obturatorexternus muscles on right side and vastuslateralis and intermedius on left side suggestive of inflammatory etiology.

Skin biopsy was also done from the finger lesions and the right thigh which revealed typical aspects of vasculitis and characteristic lesions of myositis.

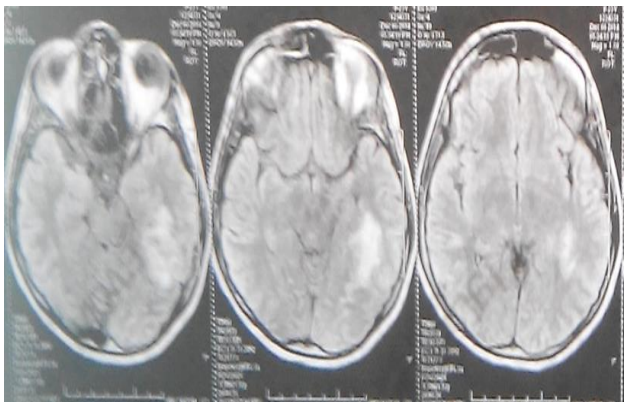

Figure 2: MRI brain showing glioma in left posterior temporal sub-cortical white matter.

Patient was treated with anti-consultants and corticosteroids along with immunosuppressant. The patient was given antibiotics. After about 1 month of intensive treatment, the evolution was excellent with significance remission of subjective clinical complaints and an improved general status. An improvement of laboratory parameters was also seen.

The long term prognosis is uncertain due to involvement of multi organic dysfunction. A close follows up of the patients' clinical condition, evolution and therapeutic adjustments are necessary.

DISCUSSION

The prevalence for MCTD it is probably around10/100000. The female:male ratio is about 9:1. The term "connective tissue disease" (CTD) includes a large group of conditions characterized by considerable clinical diversity, heterogeneity and complexity.

Although MCTDs can generally be clinically and serologically defined as distinct and separate entities, many patients diagnosed with autoimmune rheumatic

disease cannot be categorized easily into one of the established conditions.[3] The existence of patients with signs, symptoms and certain laboratory test results suggestive of a systemic autoimmune disease but fulfilling more than one classification criteria for well-defined CTDs is a more and more common experience in clinical practice. As opposed to some early stages of CTDs that might be undefined, unclassifiable or perhaps incomplete, with clinical elements and laboratory results suggestive of a systemic disease but not fulfilling criteria for well-defined CTDs, overlap syndromes define patients exhibiting enough features to meet the diagnosis of several CTDs at the same time. Thus, they "overlap" two or more diseases. Any CTD can be a partner in an overlap disorder.[4] Mixed connective tissue disease (MCTD) is the prototype of an overlap syndrome. Since its original description by Sharp and collaborators in 1972, as an apparently unique syndrome combining clinical elements of SSc, SLE and PM, associated with antibodies to RNAse sensitive extractable nuclear antigen, many clinical, serologic, and genetic studies have analysed the different aspects of this entity.[5] The relevance of defining MCTD as a separate disease entity has been challenged, some authors considering it just a subset of SLE.[6] Over the past 30 years there has been a continuing debate as to whether MCTD constitutes a "distinct clinical entity" and it still remains a controversial diagnosis.[7] Most authors agree that MCTD is a distinctive entity rather than a haphazard association of clinical and serological features and that the presence of high titres of autoantibodies to U1RNP influences the expression of connective tissue disease in ways that are relevant to prognosis and treatment.[8]

In our patient, the clinical examination and the data obtained by investigations did not permit us to include this case in one of the typical, well established CTDs. MRI Brain was which was done for the convulsions revealed a low grade glioma incidentally. The diagnosis of vasculitis was confirmed with the biopsy from the thigh muscles. Autoimmune condition was then suspected on the basis of detailed clinical examination and the basic laboratory investigations which were done. A high level of suspicion in such cases can usually lead to prompt diagnosis of any CTD. Therefore after reviewing our case we found that our patient is suffering from a MCTD which presented with a CNS glioma, vasculitis and polymyositis. In a study on 118 patients, Caramaschi and collaborators evaluated the coexistence of additional autoimmune disease in a population of patients suffering from SSc. Their findings showed that approximately one third of patients affected by SSc developed one or more additional autoimmune diseases.[9] Hence such patients must be carefully evaluated, both at the onset as well as during follow up for the possible co-existence of multiple autoimmune disorders. We intend to undergo a close follow-up of the patient's clinical status and to monitor repeatedly, the titers of the autoantibodies in order to obtain an overview of their dynamics.

In practice, the exact immunologic diagnosis makes a big difference because the detection of an autoantibody may help the clinician to anticipate particular complications and to evaluate the outcome of the patient. The identification of overlapping features in a given patient is also important because treatment needs to be directed specifically at some of these features.

Overall, the picture of overlap syndromes with respect to CTDs is complex and heterogeneous. Observer bias might play a role in disease classification, so the presence of specific autoantibody profiles is certainly a useful tool in the diagnosis evaluation of such patients.[10]

CONCLUSION

Our patient presented with a CNS glioma with vasculitis and polymyositis and was furthermore diagnosed to have MCTD which is a very rare incidence in itself and such a presentation has not been reported as of yet .Early diagnosis and appropriate treatment forms the key for the management of this rare disabling condition.

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