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Case Report

Severe choreoathetosis with neuropsychiartic illness as a rare presentation of systemic lupus erythematosus : A case report and a brief review of literature

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ABSTRACT:
We report a case of severe generalised choreoathetosis associated with psychiatric systemic lupus erythematosus in a female patient who presented with involuntary movements of hand and footwithout any other manifestation of SLE. The patient was started on aspirin and hydroxychloroquine and her chorea resolved after three weeks of follow up. This is one of the extremely rare case reports of Neuropsychiatric systemic lupus erythematosus (NSLE) where chorea is presented as manifestation of SLE.Neuropsychiatric systemic lupus erythematosus (NPSLE) is the least understood and the most prevalent manifestation of lupus. This review focuses on the pathophysiology, treatment, and new potential therapies for neuropsychiatric manifestations of systemic lupus erythematosus associated with generalised choreoathetosis.

Keywords: System lupus erythematosus (SLE), Neuropsychiatric lupus, Chorea.

INTRODUCTION:

SLE is a chronic idiopathic autoimmune disorder with a broad spectrum of clinical and immunologic manifestations affecting multiple organ systems. A challenging problem in SLE is the diagnosis and management of NP involvement. Central nervous system (CNS) lupus is a serious but potentially treatable illness, which still presents a very difficult diagnostic challenge. The frequency of neuropsychiatric manifestations in SLE varies widely, depending on the type of manifestations and the method used for evaluation[1]. However, neurologic and psychiatric symptoms are reported to occur in 14 to 80 percent of patients either prior to the diagnosis of SLE, or during the course of their illness[2]. Chorea is a relatively uncommon manifestation of SLE and moreover, chorea as the first and sole manifestation of SLE is extremely rare[3].Neuropsychiatric lupus (NPSLE) is the least understood yet perhaps the most prevalent manifestations of lupus. It affects 14% to over 80% in adults[4] and 22% to 95% in children[5] and can occur independently of activesystemic disease and without serologic activity[6]. NSPLE is associated with increased morbidity and mortality[7].

CASE REPORT:

A 16-year-old girl presented to OPD withinvoluntary movements of her arms, lips, neck, face and legs.There were smacking movements and drooling of saliva. There was no history of fever, headache, or any visual abnormality. These movements had started 3 years earlier and gradually became worse, involving the body; she had difficulty in holding things, worked and difficulty in walking. The movements disabled her normal life. There was no history of rash, photosensitivity, hair loss, oral ulcer, Raynaud's phenomenon, dryness of mouth or eyes, oral contraceptive intake, weight loss, headache, loss of consciousness, or seizure. She had no family history of rheumatic or neurological diseases and her past medical history was unremarkable. She did not smoke or drunk alcohol.

On examination, she was conscious, and well oriented with continuous choreoathetotic movements of limbs. Physical examination revealed choreic movements. They were jerky, purposeless, intermittent, and irregular movements. Examination showed her cardiorespiratory and gastrointestinal systems to be normal. Initial investigations showed a normal complete blood count, blood chemistry, and liver function tests. Her coagulation profile was normal. Urine examination was normal. Her family members

reported frequent mood swings. Antinuclear antibody (ANA) was 1 : 1280, and antidsDNA was 70.5IU (<25 IU) was also positive. Her C3 was low and C4 complement was normal. Lupus anticoagulant was positive and anticardiolipin IgG was borderline positive-18.5 GPL (<15 GPL), but anticardiolipin IgM antibody and anti-beta 2 glycoprotein-1 were negative. Anti-streptolysin O (ASO) titre was 157 IU/mL (<200 IU/mL) and thyroid function tests were normal. The electrocardiogram (ECG), 2DECHO, chest x ray, and cardiac evaluations were all normal. Her electroencephalogram (EEG) showed only non-specific slowing, and computed tomographic (CT) brain scan was normal. Magnetic resonance imaging (MRI) of brain showed tiny foci of high-intensity signal in FLAIR and T2-weighted image in bilateral basal ganglia and occipital periventricular white matter (Figures 1(a) and 1(b)). Magnetic resonance angiography (MRA) showed normal cerebral arterial caliber with no area of stenosis or occlusion, or aneurysmal dilatation.

In view of these findings, the patient was diagnosed with neuropsychiatric systemic lupus erythematosus (SLE) with choreoathetosis and was treated with steroids, Benzodiazepines, aspirin and hydroxychloroquine. After three weeks of followup, her choreoathetosis resolved completely. She has followed up for the past 6 months without any recurrence.

DISCUSSION:

Systemic lupus erythematosus (SLE) is a disease that can affect persons of all ages and ethnic groups and both sexes, but more than 90% of new patients presenting with SLE are women in the childbearing years. SLE is a disease that affects multiple systems[8]. SLE symptoms vary widely. SLE is an autoimmune disorder characterized by multisystem microvascular inflammation with the generation of numerous auto antibodies, particularly antinuclear antibodies (ANA). In 1872, Moric Kaposi first recognized the systemic nature of the disease[9]. SLE affects the immune system, thus reducing the body's ability to prevent and fight infection. SLE is associated with neuropsychiatric symptoms, which occurs in 30 to 60% of patients. Chorea is associated with a large number of hereditary or systemic diseases. Chorea consists of involuntary, irregular movements that may either take on a " worm-like " appearance called athetosis. Chorea is a well recognised but rare manifestation of SLE[10]. The incidence of chorea in SLE varies in different studies. It ranges from 1% to 8%[11], and it is strongly associated with antiphospholipid (aPL) antibodies, especially anticardiolipin and lupus anticoagulant[12]. Although chorea usually occurs during the course of SLE, it may also be, the presenting feature of the illness, sometimes preceding other symptoms by several years. In NPSLE, cognitive impairment is one of the most common manifestations, with a varying prevalence of 15% to 66% due to the differences in definition in the studies of mainly adult lupus patients[13]. It is estimated that 28% to 40% of adult NPSLE manifestations develop before or around the time of the diagnosis ofSLE and 63% occur within the first year after diagnosis[14]. The pathogenesis of NPSLE is multifactorial and can involve various inflammatory cytokines, autoantibodies, and immune complexes resulting in vasculopathic, cytotoxic and autoantibody-mediated neuronal injury. The most common microscopic brain finding in SLE seems to be microvasculopathy although not specific, which may due to complement activation and antiphospholipid antibodies[15]. Although the pathophysiology of chorea in SLE is unknown[16], an association with aPL antibodies has recently been suggested[17]. Because anti-cardiolipin antibodies are known to cross react with other phospholipids it has been suggested that direct antibody mediated damage to phospholipid containing structures in the basal ganglia may play a part in the pathogenesis of these disorders[10]. There are many explanations regarding pathophysiology of chorea in SLE, one such explanation is that it is immune-mediated mechanism secondary to aPL antibodies mainly anti-cardiolipin- IgG as in our case[18]. Another potential pathogenic mechanism for lupus chorea is ischemia affecting the basal ganglia or the tracts connecting the basal ganglia, thalamus, and cerebral cortex.Disruption of the blood-brain barrier is integral to the neuropathology of SLE[19]. Additionally, damage to the blood-brain barrier may be implicatedin corticosteroid-induced psychiatric disorders[20].The patients with SLE may present with various systemic manifestations. The general symptoms include: fever, malaise, arthralgias, myalgias, headache, and loss of appetite and weight. Nonspecific fatigue, fever, arthralgia, and weight changes are the most commonsymptomsin new cases or recurrent active SLE flares. Neurological manifestations of lupus are reported in 25 to 75% of patients and can involveall parts of the nervous system. Cognitive disorders may be variably apparent in patients with SLE[21]. Formal neuropsychiatric testing reveals deficits in 21-67% of patients with SLE. Whether this represents true encephalopathy, neurological damage, medication effects, depression, or some other process is unclear[22]. Localizing the areas of the CNS associated with neuropsychiatric symptoms in SLE continues to be elucidated withbrain imaging studies, though these modalities are not without limitations. While focal neurologic symptoms of NPSLE correlate with conventional structural magnetic resonance imaging (MRI) abnormalities, abnormalities reflecting altered perfusion or neuro-metabolite changes in NPSLE can be demonstrated by functional Imaging techniques even in the absence of morphological lesions detectable by conventional MRI[23]. Metabolic neuroimaging (positron emission tomography/PET,

MR spectroscopy) and perfusion imaging (single photon emission computer tomography/SPECT) can detect abnormalities in patients who present exclusively with psychiatric manifestations, but otherwise have normal MRI studies[24].Functional MRI (fMRI) is another neuroimaging technique that has been used to assess for cognitive function in SLE. Neuroimaging modalities have greatly advanced the understanding of NPSLE, which appears to be caused by acute and chronic brain injury caused by SLE and are promising approaches to elucidate the areas and mechanisms involved in NPSLE andspecific manifestation as in cognitive dysfunction.The differential diagnosis of chorea includes cerebrovascular accidents, drug intoxication, hyperthyroidism, Huntington'sdisease, Sydenham's chorea, and collagen vasculardiseases like SLE.

The management of patients with NPSLE is multimodal and continues to be a major therapeutic challenge due to thebroad spectrum of the NPSLE manifestations and limitationsin diagnostic testing. Currently, only three medications areFDA-approved for treatment of SLE in the United States:

glucocorticoids, aspirin, and hydroxychloroquine. Glucocorticoids are one of the primary therapeutics in the management of NPSLE[25].Medication use can range from non-steroidal anti-inflammatory drugs for symptomatic relief, anticoagulation for thrombotic diseases, to the immune-suppressives for inflammation such as cyclophosphamide, azathioprine, mycophenolate mofetil, and methotrexate[26]. Mild NPSLE may only need symptomatic treatment. Treatment strategies should include identification and treatment of any secondary causes of CNS dysfunction such as infection, increased intracranial pressure, medication side effects, or primary psychiatric disorders. Glucocorticoids (e.g. prednisone, methylprednisolone) are one of the three FDA-approved drugs for the treatment of SLE; currently in the United States, as many as 90% of SLE patients are treated with glucocorticoids. The treatment with glucocorticoids is widely used in the management of seizures, refractory headache, chorea, transverse myelitis and other CNS manifestations of SLE. Glucocorticoids are used in high doses orally (1-2 mg/kg by mouth daily), or intravenously (usually 1 gram daily for 3 days, followed by daily high-dose oral glucocorticoids) for acute and severe flares. Antimalarial drugs, specifically hydroxychloroquine,have immune-modulatory properties that may also provide lipid-lowering and antiplatelet effects, thus preventing thromboembolic events[27]. Hydroxychloroquine can be used as maintenance therapy to prevent disease flare and may also improve fatigue and possibly cognitive dysfunction.Anticoagulation is the mainstay of therapy with or without immunosuppressive in NPSLE related to thrombosis and the presence of aPL antibodies.

Cyclophosphamide is an immunosuppressive and cytotoxic alkylating agent used in organ-threatening disease in SLE and other autoimmune disorders. Severe NPSLE manifestations, mainly CNS involvement like cerebrovascular disease due to inflammation and transverse myelitis, has been treated with cyclophosphamide[28]. Cyclophosphamide can be given as monthly intravenous (500–1000 mg/m2) doses for a 6-month induction period followed by quarterly maintenance doses for a period of 2 years; however, studies have shown that immunosuppressives with less toxicity can be used for maintenance[29]. Other agents such as azathioprine and methotrexate have been used in systemic lupus erythematosus to treat a variety of manifestations or have been used as glucocorticoid sparing agents, but controlled trials are lacking[30].

Intravenous immunoglobulin (IVIG), plasmapheresis, and rituximab have been used in central nervous system manifestations unresponsive to glucocorticoid therapy and/or cytotoxic therapy. Non pharmacological approaches, like cognitive rehabilitation programs or psychological group intervention may be important in SLE patients with psychiatric disorders such as depression, anxiety or cognitive dysfunction with impaired attention, concentration and memory[31].

Most of the patients with chorea secondary to SLE improve without any treatment and there is no role for anticoagulation in the treatment of chorea in the absence of a thromboembolic event. Alternatively, prednisone, dopamine antagonists, and antiplatelet agents appear to be effective to treat chorea in SLE patients with anti-phospholipid antibodies[32].

CONCLUSION:

We report a very rare case of SLE related severe choreoathetosis with choreoathetosis as the sole presenting feature slight mood swings. The occurrence of chorea is a rare in SLE and chorea as the sole manifestation of SLE is a very rare[3]. The incidence of chorea in SLE is estimated to be as low as 1%[11]. The management strategies in neuropsychiatric SLE are not very clear and hence have to depend and vary with individual case.

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