Case report

Meningitis as the initial manifestation of systemic lupus erythematosus

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A B S T R A C T

Systemic Lupus Erythematosus (SLE) is an idiopathic chronic autoimmune disease that can affect multiple organs including the Central Nervous System (CNS). CNS involvement is seen in many SLE patients; however, usually it is preceded by/or in conjunction with other organ-system involvement. The spectrum of CNS involvement is wide and includes numerous neuro-psychiatric syndromes but rarely meningitis. Even when meningitis occurs it is almost never the presenting manifestation of SLE. Our case had chronic aseptic meningitis as the initial and seemingly sole manifestation of SLE, which was erroneously, treated as tuberculous (TB) meningitis.

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Introduction

The incidence rates of SLE vary by region, race, age group and gender. It is generally estimated to affect as many as 25 per 100,000, mostly in females between the age of 16 and 55 [1]. The etiology of SLE is unknown but evidence implicates genetic, hormonal, and environmental factors amongst others. SLE is a multisystem autoimmune disease characterized by a heterogeneous constellation of organ involvement. Neuropsychiatric ailments are common in SLE; including aseptic meningitis, cerebrovascular disease, demyelinating syndrome, cognitive dysfunction, mood disorder and psychosis [2]. Despite that meningitis is an uncommon feature of SLE and is only observed in less than 2.0 % of patients with SLE [2].

Case report

The patient is a 40-year-old housewife, native of India, resident of the UAE for several years, who had been at her normal state of health up until a month before she presented to a local hospital with complaints of intermittent low grade fever, myalgia, headache, lethargy and behavioral changes in the form of increasing social withdrawal and self-neglect. There had been no known TB exposure or recent travel (her last trip was 5 months prior to presentation to Oman). She denied any personal or family history of autoimmune diseases or TB. On presentation, she was hemodynamically stable with a low-grade temperature (37.8°C). She had a Glasgow Coma Score of 11/15. There were no meningeal signs and the remainder of the exam was unremarkable. Initial workup including metabolic profile, CBC and CXR were negative, and a lumbar puncture was performed due to abnormal GCS in the absence of other explanations.

The initial cerebrospinal fluid analysis revealed pleocytosis (WBCs 88 cells/µL, lymphocytes 100 %), glucose 63.61 mg/dL (3.53 mmol/L), and elevated protein (404 mg/dL). Neither Gram stain nor acid-fast stain reveal any bacteria. Brain MRI showed diffuse leptomeningeal enhancement. At the time, given her 1 month history of intermittent low grade fevers, associated with headaches and her due to her being from a high risk area, anti-TB therapy was initiated (rifampin, isoniazid, pyrazinamide, ethambutol and dexamethasone 4 mg intravenous twice daily). After 14 days she had slight improvement in the level of consciousness but developed a severe drug eruption and all medications were discontinued. Her mental status declined over the ensuing days and was transferred to our facility for further care as a case of TB meningitis.

She was admitted to our ICU as a case of meningitis/encephalitis, she was awake, lying curled on the bed with generalized rigidity. Her temp was 39°C and she was saturating at 100 % on room air with normal other vital signs. Repeat investigations were done which included CT head and MRI brain.

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which were normal, as well as 24 h EEG monitoring which showed no epileptiform discharges. Repeat CSF analysis revealed normal glucose of 68.65 mg/dL (3.81 mmol/L), elevated protein (183 mg/ dl), pleocytosis (11 cells/μL, 99 % lymphocytes). The Meningitis/ Encephalitis cerebrospinal fluid (CSF) panel was negative (Polymerase Chain Reaction (PCR) was done for: Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae (Group B), Streptococcus pneumoniae, Cryptococcus gattii and neoformans, Cytomegalovirus, Herpes simplex virus 1 and 2, Human herpesvirus 6, Enterovirus, Human parechovirus, and Varicella zoster virus). Additional CSF studies included VDRL, mycobacterial PCR, Gram stain, and culture. Blood serology tested for human immunodeficiency virus (HIV), Brucella, syphilis and Lyme disease were all negative.

Second-line regimen for TB was initiated (moxifloxacin, linezolid, amoxicillin/clavulanate, meropenem, and amikacin IV). Isoniazid was reintroduced slowly after obtaining verbal consent from the next of kin. Additionally, dexamethasone 0.3 mg/kg/day intravenously (IV) for 2 weeks, then the dose was tapered (0.2 mg/kg/day IV for a week, 0.1 mg/kg/day IV for the 4th week, then 4 mg per day orally and further tapered by 1 mg off the daily dose each week (total 8 weeks). However, the diagnosis of CNS tuberculosis came into question due to the lack of evidence from microbiology and failure of empiric treatment. Other investigations that were done included a quantiferon gold assay which was negative, a repeat CT head and MRI brain, which were normal, as well as CT of the chest, abdomen and pelvis which showed no evidence of related TB findings. The possibility of autoimmune disease was then considered. Laboratory tests results are displayed in Table 1.

Based on the 2019 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria for SLE, our patient’s clinical and biochemical picture fits with the diagnosis of SLE. The classification for SLE requires the presence of a positive antinuclear antibodies (ANA) as an entry criterion. Additive criteria consist of seven clinical (ie, constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal) and three immunologic (ie, antiphospholipid antibodies, complement proteins, SLE-specific antibodies) categories, each of which are weighted from 2 to 10. Patients are classified as having SLE with a score of 10 or more points.

Our patient had positive ANA titers, which made her eligible for the 2019 EULAR/ACR criteria. She presented with a one-month history of intermittent fevers (two points) associated with neuropsychiatric symptoms (three points). She had low C3 and C4 levels (four points), and positive anti-smith antibodies (six points). This gave her a total score of 15, consisted with SLE. Once her final AFB cultures came out and her rheumatology work up came highly suspicious for SLE. We discontinued her TB medications and started her on a tapering dose of Prednisolone starting at 40 mg daily with a 10 mg taper each week. She followed up with a rheumatologist at an outside hospital, which confirmed our diagnosis of SLE and stared her on hydroxychloroquine 200 mg per day and prednisone 5 mg daily. She is doing well and has returned to her baseline.

Discussion

Meningitis can be seen in patients with established SLE. It can be autoimmune because of the disease itself or infectious due to treatment adverse effect on immunity resulting in reactivation of latent infections or predisposing patients to opportunistic infections [3,4]. Nonsteroidal anti-inflammatory drugs used to ameliorate some of the symptoms of SLE can cause aseptic meningitis and monoclonal antibodies have also been associated with meningeoencephalitis [4]. Many of the chronic aseptic meningitides are caused by TB. In one case series more than half of the patient with chronic aseptic meningitis were confirmed tuberculous meningitis or improved on empiric TB treatment [5]. Therefore, it is appropriate to suspect TB in chronic meningitis and begin empiric treatment while awaiting test results. However, it is important to consider other causes for chronic meningitis especially when the preponderance of evidence argues against TB and/or when empiric TB treatment is not effective.

Chronic meningitis can result from Borrelia burgdorferi, Treponema pallidum, Brucella, Listeria, Nocardia, HIV, Cytomegalovirus, Epstein-Barr virus, Cryptococcus, Taenia solium (cysticercosis), Toxoplasma, sarcoidosis, SLE and Bechet’s disease [6]. In our case, the autoimmune diseases were not suspected due to the absence of the typical features associated with SLE (cutaneous, musculoskeletal, mucosal, hematologic,). SLE has a spectrum of organ involvement ranging from mild localized inflammation to life-threatening organ dysfunction. The subtle symptoms of the disease often delay its diagnosis (6–8).

In conclusion, aseptic meningitis is rarely seen in SLE, however, it should be considered in patients with or without known diagnosis of SLE who present with chronic meningeval symptoms. It can be directly caused by SLE or indirectly due to treatment complications. Autoimmune diseases, epically SLE should be considered in patients with aseptic meningitis after careful evaluation and exclusion of infectious etiologies.

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Declaration of Competing Interest

Nothing to declare to any of the authors

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