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Acute uveitis and myositis secondary to EBV infection

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Abstract
Infectious myositis is quite common and usually occurs in the context of Influenza viruses. Recently there has been a surge of reports of myositis in the setting of Covid-19 infection. A 34 year old man presented to us with fever, uveitis and myositis. Myositis was diagnosed with clinical and electrophysiological features. Confirmation was obtained by muscle MRI. Extensive testing revealed a convalescent phase of Epstein Barr viral [EBV] infection. This report reiterates the importance of acute EBV in the differential diagnosis of acute viral myositis and the dramatic changes on muscle MRI.

Keywords: acute uveitis, myositis secondary, EBV infection

Introduction

Infectious myositis can be caused by viruses, bacteria, or fungi. Clinical features of an infectious myositis include fever and systemic symptoms in the context of a monophasic spontaneously remitting illness. Furthermore, patients may complain of generalised myalgias, elevated muscle enzymes and develop concurrent myocarditis. Usually, the diagnosis of a viral myositis is confirmed by serologic studies rather than by muscle biopsies. Most patients improve spontaneously or with short courses of steroids. Muscle MRI is useful in detecting subtle changes of myositis and non-invasively confirming myositis. We have demonstrated the utility of MRI in viral myositis earlier [1, 2]. In the ongoing Covid-19 pandemic, myalgias and myositis have been described in 6-10% of patients [3].

Case Report

A 34-year-old man presented to with fever of 7 days duration. He had high grade fever (102F) with chills, myalgia, joint pains, and generalised weakness. He also developed conjunctival congestion and blurring of vision over the past 5 days. There was no significant travel history or contact with patients with COVID-19. On examination, he was febrile [38 ^{0}C] and had calf and thigh muscle tenderness. There was mild proximal muscle weakness [MRC grade 4/5] in the hip flexors. Deep tendon reflexes and sensory system examination were normal. Ophthalmological evaluation revealed an unaided vision of 6/6 bilaterally with circumcorneal congestion, anterior chamber [4+] with a normal vitreous, optic disc and retinal vessels. The findings were suggestive of a bilateral severe non granulomatous anterior uveitis. Both eyes showed cells [4+] and flare [3+] in the anterior chamber (Graded as per the standardisation of uveitis nomenclature]. Pigments and fibrin material were seen on the anterior lens surface. CPK levels were 92 U/L. Leptospira, Dengue, Malaria rapid testing and SARS CoV-2 testing were negative. ESR was 92 mm/Hr, CRP was 97. He was empirically started on intravenous Ceftriaxone. Blood and urine cultures were also negative. ANA immunofluorescence, ACE, ANCA, VDRL, serum calcium, chest xray and Mantoux test were also negative. A nerve conduction study was normal. EMG showed features of acute denervation [fibrillations, positive sharp waves] in both tibialis anterior muscles. MRI -STIR imaging of lower limbs showed muscle hyperintensities in proximal and distal muscles of both lower limbs as well as in the gluteus maximus

Differential Diagnosis

The differential diagnosis included a viral syndrome, sarcoidosis or an inflammatory rheumatological disorder like Behçet's disease.

Course

Blood cultures were negative, and antibiotics were stopped. He was subsequently treated only with antipyretics. His fever subsided and on the day 15, an EBV & CMV quantitative DNA PCR, HIV, HBsAg and HCV serology were negative. EBV Viral Capsid Antigen Antibody (VCA) IgG and EBV Nuclear Antigen Antibody EBNA by IFA were positive. EBV VCA IgM and EA [early antigen] were negative suggesting convalescing EBV infection. He recovered completely without steroids or other immunomodulatory therapies.

Discussion

Fever with myalgia is a common accompaniment of many viral, bacterial or parasitic infections. Due to the self-limiting nature of most viral infections, this is not investigated further, unless the illness worsens. Hence viral myositis is underdiagnosed in many instances, although this entity is well known. The commonest 'viral myositis' occurs in the context of Influenza A & B

infections. Many other viruses including SARS-CoV2, and other respiratory viruses are also associated with a myositis. Chronic active Epstein-Barr virus infection (CAEBV) is associated with a chronic generalized myositis mimicking a refractory polymyositis [4, 5]. Acute EBV infection is infrequently associated with an acute myositis [6]. In contrast to CAEBV which is progressive even with immunotherapy, acute EBV myositis [AEBV] is a self-limited illness.

The eye is often involved in systemic illnesses. The anterior chamber of the eye is normally cell free and transparent due to its low protein content [<1% of serum levels]. With uveitis, the anterior chamber is flooded with cells and proteins due to a breakdown of the blood–aqueous barrier (BAB). This aqueous humor is thus opacified and demonstrates a 'flare' of opacification. Fibrin material deposited on the lens surface leads to visual blur or cloudy vision. When uveitis occurs along with fever and myositis, the differential diagnosis is greatly narrowed. [Table 1]

Ocular manifestations described in dermatomyositis included conjunctival edema, nystagmus, extraocular muscle imbalance, iritis, cotton wool spots, optic atrophy, and conjunctival pseudopolyposi. In this case there were no cutaneous manifestations of dermatomysositis. Sarcoidosis typically produces granulomatous uveitis along with myositis, unlike our case. This patient did not have any recurrent oral or genital ulcers to suggest Bechet's disease. The commonest cause of recurrent anterior uveitis in rheumatological practice is spondylarthritis. However myositis and fever are uncommon in the spondylarthritides. In this case we ruled out all the other differential diagnosis given the table 1

MR muscle imaging adds an additional perspective in the evaluation of fever with myalgia. It can easily detect subtle or widespread muscle involvement in myositis and helps to differentiate between bacterial 'pyomyositis' and viral myositis. Even though serum CPK levels may be normal, the combination of clinical examination, electrophysiological investigation and MR muscle imaging can confirm a myositis.

This case highlights the necessity of considering viral myositis in the appropriate clinical scenario, to avoid the unnecessary use of steroids and other immunomodulation.

Table 1: Differential diagnosis of uveitis with myositis [11–19]

Sarcoidosis
Dermatomyositis
Behçet's disease
Spondyloarthritis
Autoimmune paraneoplastic disorders with NK/T-cell lymphomas
Anti-TNF drugs [tumor necrosis factor]
HIV infection
EBV infection
HTLV-1 infection
Hepatitis A infection
Tropical myositis
Tropical myositis
Whipple's disease
Granulomatosis-associated myositis
Inflammatory bowel disease
Immune checkpoint inhibitor therapy
Etanercept therapy

Figure Legend

Panel A; Coronal STIR MRI images of the legs show patchy hyperintensities in the thigh and calf muscles. Panel B- Axial MRI images through the thigh show involvement of selected muscles [VL-Vastus lateralis, Vi,m- Vastus intermedius and medius, AM- Adductor magnus, BF-Biceps femoris]. Panel C- Axial MRI images through the calf show selective muscle hyperintensities [TA- Tibialis anterior, TP- Tibialis posterior, FDL- Flexion digitorum longus, EDL- extensor digitorum longus]. Panel D- Slit lamp exam of right eye shows 'flare' [green arrow] and iris pigment stuck onto the anterior lens surface [yellow arrow]. Panel E- Broken early posterior synechiae at 5 o'clock position [blue arrow]. The pupil has been pharmacologically dilated.

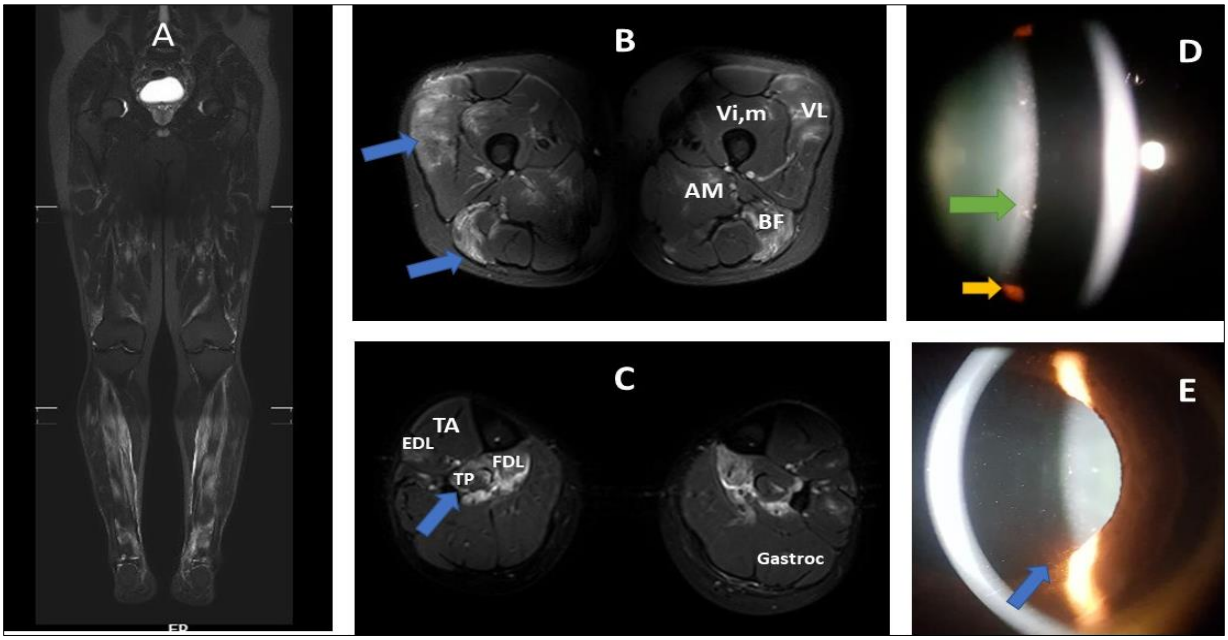

Fig 1

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