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Case Report

A case of Epstein-Barr virus presenting as spondyloarthritis

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ABSTRACT

Viral arthritis can be caused by various viruses such as parvovirus, alphavirus, rubella, hepatitis B, C and flavivirus. High titre of antibodies to Epstein-Barr virus (EBV) is present in rheumatoid arthritis (RA) patients. EBV, a member of the herpes virus family, is one among the most common human viruses. Vitamin D deficiency can worsen the prognosis in such patients. Abnormalities in innate and adaptive immune reactions in response to EBV infection were one of the complications observed in RA patients. It was a self-limiting infection with a 90% lifetime prevalence. On the other hand, spondyloarthritis was rarely associated with viral infections. A 35 year old male patient who had a history of TB, admitted through OP, with complaints of intermittent fever, joint pain, pain radiating from back to lower limbs. On investigation, the patient was found to be vitamin D deficient. Differential diagnosis such as TB with reactive arthritis, lymphoma and CMV infection were ruled out. MRI of the spine and pelvis confirmed spondylarthritis. The serology for EBV showed that the EBV IgM levels had increased by two-fold. The on-going inflammatory status was well-managed with NSAIDS, as there was low evidence for antiviral therapy. EBV infection presenting as spondyloarthritis is a very rare presentation and here we are discussing a case of spondylarthritis in a patient with infectious mononucleosis. The patients with fever, polyarthritis, lymphadenopathy and spondylarthritis are to be investigated for EBV infection along with the other cause of polyarthritis.

Keywords: Cytomegalovirus, Epstein-Barr virus, Rheumatoid arthritis, Spondyloarthritis

INTRODUCTION

EBV, also known as human herpesvirus 4 and a member of the herpes virus family. This virus is one of the most common human viruses and is found across the globe with a good number of people getting infected. It spreads most commonly through body fluids, primarily saliva and causes infectious mononucleosis and is associated with B-cell, T-cell, Hodgkin's lymphomas and nasopharyngeal carcinomas. Arthralgia and monoarthritis of the knee with infectious mononucleosis are reported frequently.[1]

During primary EBV infection, an innate and adaptive immune response occurs. Although it controls infection, does not eliminate it and the virus persists for the lifetime of the infected individual.[2] The observed abnormalities in EBV-directed immune responses and it's viral loads are a cause or complications of RA which remains controversial.[3] It is a self-limiting infection with a 90% lifetime prevalence.

Many viruses could be the reason for causing viral arthritis, the most common being parvovirus, alphavirus, rubella, hepatitis B, C and flavivirus. Certain other viruses can also cause arthritis/arthralgia rarely.[4] High titers of antibodies to EBV antigens have been shown in patients with RA.[5] Posterior cervical or generalized adenopathy or hepatosplenomegaly suggests infectious mononucleosis.[6] Recent report demonstrated that vitamin D deficiency compromises the patient's immune response and makes

them more vulnerable to viral infections and perhaps worsen disease prognosis.[7,8] Spondylarthritis on the contrary to RA was usually seen in association with a gastrointestinal and genitourinary bacterial infection. Here we presented a case of spondylarthritis which was seen in association with active EBV infection.

CASE REPORT

A 35 year old male came with complaints of joint pain, low backache radiating down to both lower limbs, generalized body ache associated with muscle pain and fever for 2 months. The patient developed intermittent fever and joint pain simultaneously. There were no complaints of chills or rigor, dysuria, loose stools, upper respiratory symptoms, headaches, weight loss or cough. No history of evening rise of temperature and no diurnal variation. The joint pain was also present in small as well as large joints including the back. The pain which started in the left ankle with associated early morning stiffness of more than 30 mins, later advanced and involved the right ankle. It was also associated with low backache, which was predominantly in the late night and early morning hours. The pain was relieved with exercise and aggravated post rest. The patient had a past history of pulmonary tuberculosis in 2003 which was treated with the full course of ATT.

General examination

O/E conscious and oriented, BP=120/80 mm Hg, HR=66 per min, RR=20 per min, SpO_2=97% in room air, CVS=S1S2 (+), RS=normal vesicular sounds, PA=soft and nontender, no palpable lymphadenopathy. Upon evaluation, he was detected to have left axillary lymphadenopathy and other general physical examinations were non-contributory. The musculoskeletal examinations revealed a tender left ankle and the FABER test was positive for sacroiliac joint involvement. The straight leg raising test was negative and there wasn't any tender spine on palpation. All other system evaluation was found to be normal.

On 3 June 2021, CT chest showed multiple enlarged mediastinal lymph nodes. No evidence of necrosis/calcification. No significant lung parenchymal pathology. MRI pelvis showed, bilateral SI joint edema was noted. Both hip joints appeared normal. The acetabulum and the visualized pelvic bone appeared grossly normal. The head, neck, trochanter and upper part of the shaft of the femur appeared normal. Surrounding muscle planes appeared normal with no evidence of any fluid collection. Impression was bilateral sacroiliitis (Figure 1). On 2 June 2021 MRI whole spine showed mediastinal lymphadenopathy. C5-6: posterior bulge cord and nerve roots were not compressed. Endoscopic USG guided FNAC on 08 June 2021: Right paratracheal lymph node, EUS FNB: non-caseating granulomatous lymphadenitis. On 8 June 2021, USG soft tissue both axillae and neck showed lymph nodes with maintained fatty hilum on both sides, largest measuring 1.4 cm on right and 1.8 cm on left. No significant cervical lymphadenopathy. Left axillary node biopsy on 14 June 2021, left axillary lymph node, biopsy: reactive lymphadenitis. AFB stain on 07 June 2021: AFB was not seen in the fluid aspirated from the mediastinal node by USG guided transoesophageal. GeneXpert: XPERT MTB-RIF assay G4 on 21 June 2021: MTB not detected. PET scan on 16 June 2021: moderate to intensely FDG concentring mediastinal lymph nodes, metabolically active lymph nodes. No definite pet evidence of any metabolically active disease elsewhere in the body (Figure 2).

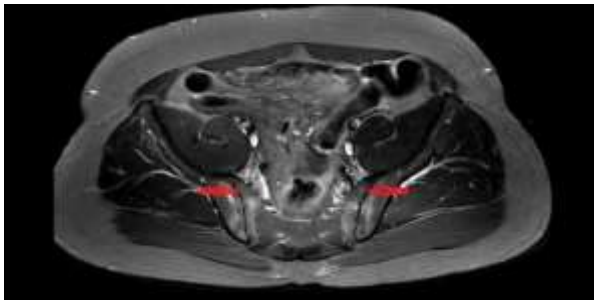

Figure 1: MRI-pelvis.

Figure 2: PET scan on 16 June 2021.

The initial blood workup showed elevated inflammatory markers (ESR=70/1st hour and CRP=58 mg/l). The initial possibilities considered were the reactivation of tuberculosis with reactive arthritis, spondyloarthropathy and other causes of reactive arthritis. A rheumatology consultation was sought for the same and a plane X-ray of the chest, lumbosacral spine, pelvis with hip and ankle were taken and showed normal appearance. An MRI pelvis and spine was done to see any evidence of active spondyloarthritis as he was fulfilling the ASAS classification criteria. The MRI revealed active sacroiliitis with a Romanus sign in the lower lumbar spine. Incidentally, a mediastinal lymph node was detected on the MRI and hence a CT chest and abdomen were done. It showed multiple lymph nodes in the mediastinum and mild hepatosplenomegaly. As there was a possibility of TB reactivation the patient was subjected to Mantoux test, quantiferon TB gold and EUS guided mediastinal lymph node biopsy. The lymph node was sent for histopathologic evaluation and tissue PCR for TB. The histopathology evaluation showed the presence of non-caseating granuloma, with PCR and AFB staining negative for TB.

There was the presence of double-nucleated lymphocytes in the histopathological evaluation. A possibility of lymphoma was considered and hence a search for the same was conducted.

USG showed that the axillary lymph node was enlarged and a surgical excision biopsy was done. However, the histopathology was showing only reactive changes. As there was a strong suspicion of lymphoma on a PET scan done which showed moderate to intensely FDG-concentring mediastinal-metabolically active lymph nodes, but there wasn't any other organ or lymph node enlargement. In search of an alternate possibility the serology for EBV and CMV was done which showed 2 times elevation in the EBV IgM, confirming the possibility of an acute EBV infection.

As there was ongoing inflammatory status, NSAIDs were initiated to which he responded well. As there is low evidence on the management of EBV with antiviral therapy, it was not initiated at the moment. He was planned to be kept under regular follow up given the risk of hematologic malignancies in the future.

DISCUSSION

Despite the high incidence of EBV infection worldwide, the studies on EBV-associated viral arthritis were very rare.[1,10] The present case report described the rare incidence of spondyloarthritis with EBV infection. EBV infection was characterised by infectious mononucleosis-like symptoms.[6,11] Through the current case we emphasised the need for considering EBV as a differential diagnosis in spondyloarthritis patients. The maintenance of vitamin D level had also been emphasised for prevention of such infections.

The pathogenic mechanism by which EBV virus induced rheumatologic and musculoskeletal diseases have been well documented by Roberts et al 1996, in which EBV binded to the complement receptor type 2 (CR2/CD21) via the viral envelope glycoprotein primarily seen on the B lymphocyte. It also can transfer to the CD21 negative epithelial cells which acted as an enhancer for transferring the virus to other cells causing latency in B cells.[12] Both latent and lytic EBV were potent immunogens causing high-intensity B and T cell response which can also induce a cross-reaction with cellular self-antigen triggers that perpetuate the rheumatologic and musculoskeletal complications.

Treatment of infectious mononucleosis was managed by supportive care and corticosteroids may be helpful for severe disease. This patient was managed with NSAID and sulfasalazine for joint pain and paracetamol for fever. Currently, the patient was undergoing treatment and close follow up with the treating physician for the resolution of the disease. There have been multiple reports on RA associated with EBV infection, but case reports on spondyloarthritis was a very rare entity.[12,13]

CONCLUSION

This patient had presented with extremely rare manifestations of spondyloarthritis and infectious mononucleosis. Such an entity is rarely seen and reported. This patient is also having vitamin D deficiency and hence is more prone to viral infections. The patients with fever, polyarthritis, lymphadenopathy and spondylarthritis are to be investigated for EBV infection along with the other cause of polyarthritis.

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