



A CASE OF ACUTE EXTENSIVE VIRAL SINUSITIS SECONDARY TO ACUTE EPSTEIN BARR VIRUS

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ABSTRACT

Infectious mononucleosis (IM), the most common presentation of acute Epstein Barr virus (EBV) infection, typically presents with fever, pharyngitis and lymphadenopathy. We describe an unusual case of IM presenting as acute sinusitis. A 25 year-old male presented to the emergency department with worsening right frontal sinus pain along with fever, chills, and greenish nasal discharge for 3 weeks. Laboratory workup showed leukocytosis with high lymphocyte counts as well as transaminitis. Facial computerized tomography (CT) showed extensive right frontal, ethmoidal and maxillary sinusitis and antrochoanal polyp. The patient underwent endoscopy with drainage of purulent material and polyp removal. Unfortunately, cultures of the sample were not sent and bacterial infection could not be ruled out. Broad spectrum antibiotics were continued. Pathology of redundant tissue revealed large atypical lymphocytes with positive EBV-encoded RNA and lack of evidence of extranodal natural killer/T-cell (NK/T-cell) type lymphoma (ENKTCL). Tests for serum EBV IgM antibodies and EBV early Antigen antibodies were positive, indicating acute EBV infection. Lymphocytosis resolved along with significant clinical improvement at the 10-day follow up visit. Even though patient did receive antibiotics, multiple factors including isolated lymphocytosis, pathology positive for EBV with no neutrophilia were more suggestive of sinusitis caused by viral infection, EBV in this case. Lymphocytosis with fever and sore throat should prompt physicians to consider IM. There are no known reports in the literature of EBV as a causal organism for acute viral sinusitis. There are some studies relating EBV with ENKTCL. It is unknown whether this particular patient with a history of EBV sinusitis will be at high risk for nasal type lymphoma in the future. Further studies should be conducted to understand the pathogenesis and relationship between EBV and ENKTCL.

KEYWORDS

Epstein Barr Infection, infectious mononucleosis, lymphocytosis, viral sinusitis

LEARNING POINTS

- Infectious mononucleosis (IM) can present with various atypical presentations. Consideration of IM should not be limited to people presenting with a triad of fever, lymphadenopathy and sore throat. Lymphocytosis with atypical symptoms should raise suspicion of infectious mononucleosis.
- No case has been reported of EBV as a causal organism for acute sinusitis. Association with EBV infection and chronic sinusitis or nasal polyp or extranodal NK/T cell lymphoma has been demonstrated but pathogenesis is poorly understood.
- Studies should be done on whether acute sinusitis secondary to EBV poses a risk for nasal type lymphoma.



BACKGROUND

Epstein-Barr virus (EBV) is a highly prevalent member of the herpes virus family; approximately 90-95% of adults worldwide have tested positive for EBV^[1]. Most EBV infections remain latent. Infectious mononucleosis (IM) is the most common presentation of acute EBV infection. Typical features of IM include fever, pharyngitis, cervical lymphadenopathy, and atypical lymphocytosis^[2]. IM has also been associated with splenomegaly, splenic rupture, and maculopapular rash. EBV is reported to affect multiple organ systems, and can lead to Guillain-Barré Syndrome, facial and cranial nerve palsies^[3], aseptic meningitis, encephalomyelitis^[4], cholestatic hepatitis, pancreatitis, and acute renal failure. The link between EBV and certain lymphomas, including nasopharyngeal carcinoma, is well known. To date, sinusitis has not been described as an initial presentation of acute EBV infection. Below, we present a rare case of acute right-sided extensive sinusitis and polyp, which was found to be positive for EBV in an endoscopic drainage biopsy, with initial suspicion of lymphoma.

CASE DESCRIPTION

The patient is a 25-year-old caucasian male with a past medical history of asthma, who presented to the emergency department (ED) with worsening right frontal sinus pressure and pain for 3 weeks. Symptoms included headache, ear fullness, sore throat, and yellow/green nasal discharge which did not improve with outpatient antibiotics. Symptoms persisted for 3 weeks, and the patient started developing fever and chills, prompting him to go to the ED for further care. On admission, he had a temperature of 38.8 °C, right periorbital swelling and right frontal sinus tenderness on examination. No hepatosplenomegaly was noted. Laboratory workups were remarkable for leukocytosis of 24.7 k/ μ l, absolute lymphocyte count 17.3 k/ μ l, 70% lymphocyte, 23% neutrophils, as well as transaminitis with alanine aminotransferase (ALT) 150 U/l, aspartate aminotransferase (AST) 64 U/l, alkaline phosphatase (ALP) 382 U/l. Respiratory pathogen panel for coronavirus, influenza, and respiratory syncytial virus (RSV) was negative. Facial Computed Tomography (CT) showed extensive sinusitis primarily involving the right frontal, ethmoid, and maxillary sinuses (Fig. 1) with a widening of the right ostiomeatal unit suggestive of possible antrochoanal polyp. The patient was started on IV empiric antibiotics and eventually underwent a sinus endoscopy. The endoscopy showed significant hyperemia of inferior and medial turbinate on the right side as well as right maxillary sinus. The patient was taken to the operating room for drainage. A large amount of purulent material was expressed, a polyp in the medial meatus was removed and redundant tissue was biopsied. Culture of the sample however was not done. Pathology testing revealed nasal mucosa with zonal necrosis surrounded by polymorphous infiltrate of large atypical lymphocytes, immunoblasts, small lymphocytes and plasma cells (Fig. 2, 3). In situ hybridization was positive for EBV-encoded ribonucleic acid (RNA).

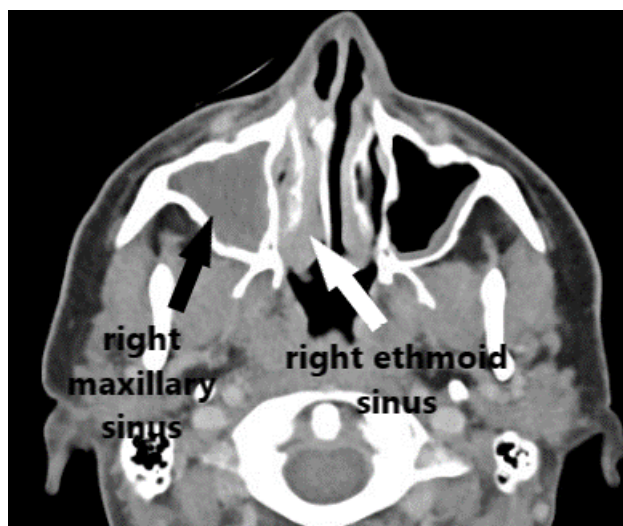


Figure 1. Computerized tomography (CT) of the facial bone with contrast (axial view) showing extensive sinusitis primarily involving the right frontal, ethmoid and maxillary sinus with possible antrochoanal polyp

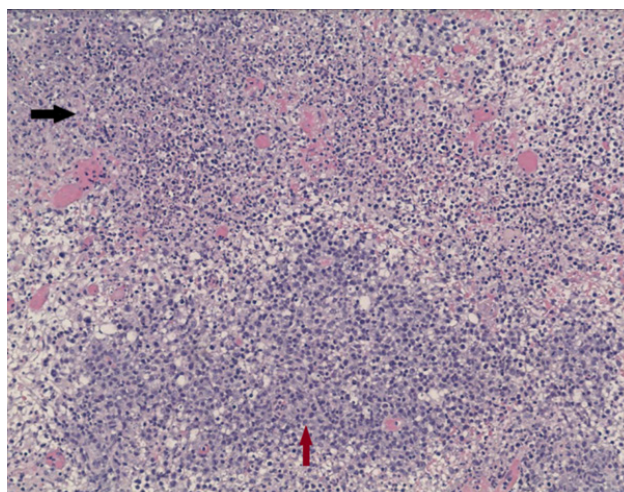


Figure 2. Low power hematoxylin and eosin-stained slide at 100x with the upper portion showing zonal necrosis (black) and the lower portion of the picture showing large atypical cells (red)

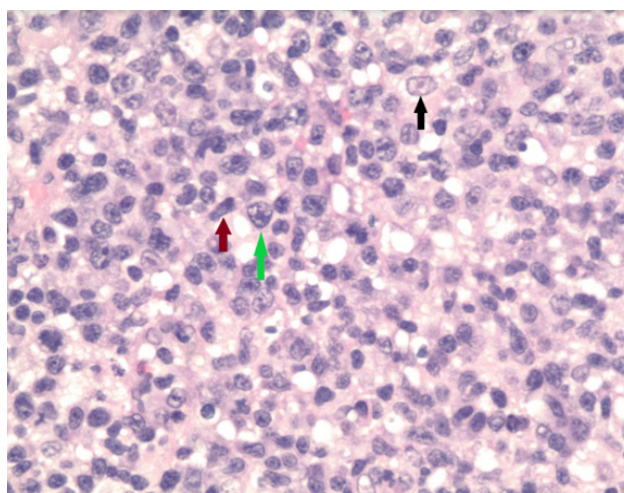


Figure 3. High power hematoxylin and eosin-stained slides at 400x showing polymorphous infiltrate of the large atypical lymphocytes (red), immunoblasts (black), small lymphocytes, and plasma cells (green)

Differential diagnoses included acute EBV infection and extranodal NK/T cell type lymphoma. Natural Killer (NK) cell marker, CD56, was negative. Lack of NK cell markers and T cell aberrancy in the biopsy are more consistent with acute EBV infection than with extranodal NK/T cell type lymphoma. Additional tests were done to confirm EBV infection. Monospot testing revealed reactive heterophile antibodies with EBV viral capsid antigen (VCA) IgM >160 U/ml, VCA IgG 29.6 U/ml, Epstein Barr early Ag-Ab 15.2 U/ml, which is consistent with acute infection. Flow cytometry showed a polytypic mixture of T cells (83%) and B cells (5%) with no evidence of clonal or immunophenotypically abnormal proliferation. During the follow-up visit 10 days later, symptoms including fever had resolved with markedly improved lymphocytosis and transaminitis.

DISCUSSION

Epstein Barr virus is a widely disseminated virus. Most adults have evidence of prior infection. It is a primary agent for infectious mononucleosis. Typically, mononucleosis presents with fever, lymphadenopathy and pharyngitis. However, there are also several variants and atypical presentations of acute EBV infection which pose a diagnostic challenge. One study showed decreased likelihood of infectious mononucleosis with absence of any type of lymphadenopathy and increased likelihood with presence of enlarged posterior cervical lymph nodes^[5]. One meta-analysis revealed that more than 40 % of atypical lymphocytes, and a combination of lymphocytosis greater than 50% and atypical lymphocytes greater than 10%, significantly increased the probability of infectious mononucleosis^[6].

In our case, the patient only has two of the three classic symptoms which were sore throat and fever. Presence of enlarged posterior cervical lymph nodes would decrease the likelihood of IM. Moreover, the patient presented with significant sinus symptoms which were suggestive of bacterial sinusitis. Unfortunately, culture of the secretions collected during sinus drainage was not performed, so bacterial infection could not be ruled out. The patient however had significant lymphocytosis which prompted us to do more workup in addition to management of sinusitis. Sinus drainage secretions were later found to have atypical lymphocytes which was more suggestive of viral than bacterial causes. Further serological workup for antibodies of EBV and heterophile test confirmed the acute nature of EBV infection. Resolution of lymphocytosis and transaminitis on 2-week follow up further indicated that sinusitis was due to EBV and not to bacteria. Even in cases with atypical symptoms of IM, lymphocytosis should alert physicians to consider IM as a differential diagnosis.

Sinusitis is a very common medical condition in outpatient or inpatient settings. Most viral sinusitis have been associated with rhinovirus, influenza and parainfluenza virus^[7]. Literature so far has not associated acute sinusitis with EBV and alternatively sinus symptoms have rarely been documented as one of the presenting symptoms

for acute infectious mononucleosis. EBV however has been related to chronic sinusitis secondary to extranodal natural killer NK/T cell lymphoma (ENKTCL)^[8]. NK/TCL is an aggressive malignancy commonly seen in Asian and Latin American populations and several studies have consistently associated the specified disease with EBV^[9]. Despite the genome of EBV being found in tumor cells, pathogenesis is unclear. A study proposed that it could be related to genetic alteration following the infection^[10]. In our patient, there was no evidence of ENKTCL on biopsy but the question arose whether his EBV sinusitis would put him at risk for development of EBV related lymphoma, especially the nasal type. We believe that further studies on this aspect would help to identify the at-risk populations for this aggressive nasal type lymphoma.

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