"The Girl who Grew Horns": Temporal Swelling as an Atypical Presenting Symptom of Epstein-Barr Virus Infection

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KEY WORDS: Epstein-Barr virus (EBV) infection, temporal swelling, presenting symptom, infectious mononucleosis

IMAJ 2016; 18: 761–762

Primary Epstein-Barr virus (EBV) infections in children are common and frequently asymptomatic. When symptoms do occur, a variety of symptoms may be observed. Infectious mononucleosis is the best known clinical syndrome caused by EBV but it should be remembered that EBV can affect virtually any organ system and has been associated with a variety of manifestations. Typical features of infectious mononucleosis include lymphadenopathy, fever, pharyngitis, fatigue, splenomegaly and hepatomegaly.

Atypical presenting symptoms of EBV infection have been also extensively described, such as pneumonitis, pleural effusion, cholestasis, ascites, carditis, encephalitis, pancreatitis and renal failure. We present the case of a girl with bitemporal swelling as a unique presenting symptom of primary EBV infection. Moreover, during the illness the patient also developed severe myositis, another uncommon manifestation of EBV infection.

PATIENT DESCRIPTION

An otherwise healthy 8 year old girl presented to our department with acute onset of bitemporal painful swelling [Figure 1A]. She denied trauma or having been stung in the head area. She also complained of bilateral pain at her popliteal. Two weeks earlier, she had had pharyngitis and completed a 10 day course of penicillin V. A throat swab was not taken.

On admission she was febrile (39.8°C). Physical examination showed bilateral temporal swelling without tenderness or redness, and bilateral popliteal tenderness without any swelling, redness, edema or local warmth. She could barely walk. Laboratory studies on admission showed normal white blood cell (WBC) count, hemoglobulin 11.8 g/dl, and thrombocytes 132 K/μl. Blood smear was normal, kidney and liver function were normal, amylase level was 95 IU/L (normal level < 90), and creatine phospokinase (CPK) was slightly elevated (200 IU/L, normal level < 170). C-reactive protein (CRP) was 8 mg/L (normal level < 0.08–5) and erythrocyte sedimentation rate (ESR) 25 mm/hour. Blood culture was negative. On her second day in our department the following tests were taken: blood test for complement level, antinuclear antibody (ANA), anti-DNA antibody, thyroid function, and serology for EBV and cytomegalovirus.

Temporal ultrasound demonstrated bilateral soft tissue hyperplasia with normal blood flow and no signs of collection, mass or periosteal reaction. Clinically, the temporal swelling was stable, but the popliteal tenderness worsened and we began treatment with naproxen, a non-steroidal anti-inflammatory drug.

In the following days fever of up to 39°C persisted, and the popliteal pain exacerbated to the point that she could hardly stand. Repeated blood tests showed a trend of increasing CRP level reaching 158 mg/L and CPK level 1770 IU/L. Liver enzymes showed a slight increase: aspartate aminotransferase 131 IU/L (normal < 60) and alanine aminotransferase 53 IU/L (normal < 45). Due to the fever and increasing inflammatory markers we began empiric treatment with cefuroxime.

The serology tests that had been taken earlier were positive for IgM and IgG viral capsid antigen (VCA) of EBV and negative for Epstein-Barr nuclear antigen (EBNA). These were suggestive of acute EBV infection and the antibiotic treatment was stopped. Because of her non-specific complaints and

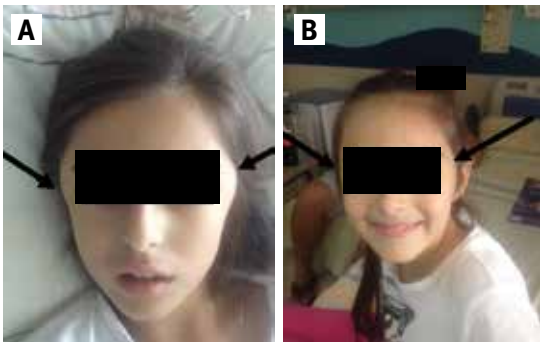

Figure 1. [A] Patient on her first day of hospitalization: the arrows indicate the temporal swelling. **[B]** Patient on her discharge day: the arrows indicate the complete resolution of the temporal swelling

elevated inflammatory markers a thorough workup was performed. Thyroid function was normal, complement level was normal, ANA and anti-DNA antibodies were negative, and there were no signs of uveitis or any other eye involvement. Bone marrow aspiration and biopsy, VMA level and bone scan were normal. Chest X-ray was normal and the abdominal ultrasonography showed only splenomegaly with mild hepatomegaly. Popliteal ultrasound showed mild swelling with fat infiltration bilaterally with a 5 mm lymph node at the left side. Since the initial workup was suggestive of EBV infection, we quantified EBV copies by PCR and the results were positive (1.042 x 10^3 cp/ml). Repeated EBV serology 10 days after her admission was negative for VCA IgM and positive for VCA IgG; the EBNA result was still negative. These results confirmed that the patient had a recent EBV infection.

On her tenth day of hospitalization, the fever and the temporal swelling resolved [Figure 1B], the popliteal pain and tenderness were significantly reduced, CRP and liver enzymes returned to normal, and she was discharged.

Two months later, at the follow-up visit, she was asymptomatic, her physical examination was normal, laboratory studies were normal and serology tests for EBV were positive for both IgG ENBA and IgG VCA.

COMMENT

EBV infection in children is common and usually has a typical clinical presentation. Here we report a case of bitemporal swelling as an unusual presentation of EBV infection in a child. EBV infection, in our case, was confirmed by specific serology tests and PCR and by excluding other etiologies. While the majority of EBV-infected cases remain clinically asymptomatic, some present with a typical IMN phenotype. A variety of manifestations have been described in EBV. Facial edema is a known sign of EBV infection that has been described in 10% of cases [1]. This sign of periorbital edema or puffiness on physical examination can give the physician a significant clue about the possibility of EBV infection. Surprisingly, in our case, the girl presented with bitemporal edema. Differential diagnosis of bitemporal swelling has been rarely described and includes acute myeloid leukemia [2], an unusual presentation of primary extrapulmonary tuberculosis infection [3], idiopathic benign masticatory muscle hypertrophy [4] and "chewer's cheeks" – most probably due to excessive use of mastication muscles [5]. None of these etiologies fit the clinical picture presented here.

The combination of tonsillitis as a prodrome and the diverse manifestations of EBV infection raised the suspicion of EBV infection, and serology tests had been taken early during her hospitalization. The clinical course that followed her hospitalization, with the appearance of fever, myositis and splenomegaly with mild hepatomegaly, are all symptoms that have been described as part of an EBV infection. Fever and organomegaly are common and present during the acute illness. Myositis, however, can appear as an atypical sign of infectious mononucleosis or as a major presentation of chronic active EBV (CAEBV) infection. Due to the unique presentation and the clinical course and despite the initial serology results of EBV, it was essential to rule out other possibilities and to verify the diagnosis of EBV by PCR analysis. During the outpatient follow-up, EBV serology was repeated to verify that indeed the symptoms were part of an acute EBV infection.

In summary, we present an unusual case of EBV infection in a child. As far as we know this is the first documented description of temporal swelling as a symptom of EBV infection, a fortiori, as a presenting symptom of the disease. We believe this case will help pediatricians by adding EBV infection to their differential diagnosis when encountering such a symptom.

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