A rare case of infectious mononucleosis complicated by Guillain-Barre syndrome

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Abstract

Infectious mononucleosis is a clinical syndrome characterized by fever, lymphadenopathy and pharyngitis. Neurologic complications of infectious mononucleosis, such as the development of Guillain-Barre syndrome, have been rarely reported and usually present late in the course of the disease. We describe a case of a 29 year old male with no significant past medical history who was diagnosed with Guillain-Barre syndrome following an infection with Epstein-Barr virus associated infectious mononucleosis. Supportive treatment resulted in full recovery.

Case Report

A 29 year old white male with an unremarkable past medical history was evaluated at an outpatient setting for sore throat, cough productive of whitish sputum and pink eye. Physical examination at the time revealed several 1 cm mobile, non-tender cervical lymph nodes. Mild diffuse wheezing was audible on chest auscultation. Chest X-ray showed thickened bronchi and a small calcified nodule in the right lower lobe. No further studies were performed and the patient was sent home with a follow-up visit. Three weeks later the patient reported tingling in his fingertips, toes and lips. The following day his lower extremity tingling sensation had spread to his calves and he was soon accompanied by lower extremity weakness. The patient’s condition deteriorated to the extent that he was unable to ambulate. He was admitted to the intensive care unit. Upon admission, the patient’s temperature was 98.3 F, blood pressure 170/80 mmHg, pulse 82 beats/min and respirations 24 breaths/min. He appeared to be in mild respiratory distress. On physical exam his pupils were equal and reactive to light, sclera were anicteric. Examination of the oropharynx was normal and his thyroid gland was non palpable. Neck was supple and cervical lymphadenopathy was appreciated. Auscultation of the lungs was within normal limits, but he was noted to have shallow breathing. Pulses were palpable throughout. There was no edema, cyanosis or clubbing of the extremities. The skin was dry and no rashes were noted. The spleen and liver were not palpable. On neurological examination the motor power of his upper and lower extremities had decreased significantly, estimated Grade 2 according to the Medical Research Council muscle strength grading system. Deep tendon reflexes were absent throughout. He had mild parasthesia with a symmetric distribution. Based on the history and initial physical exam Guillain-Barre syndrome was strongly suspected.

Initial chemistries were within normal limits. Liver function tests showed albumin of 3.7 g/dL, total bilirubin of 2.3 mg/dL, alkaline phosphatase of 179 U/L and aspartate aminotransferase of 89 U/L. Prothrombin time and activated partial thromboplastin time were within normal limits. CBC revealed white count 10,400/mm3, hemoglobin 15.1 g/dL, platelets 136,000/mm3. White cell differential was notable for 38% neutrophils, 7% lymphocytes, 51% atypical lymphocytes, 4% monocytes. Lyme titers were within normal limits. HIV antibody test was negative. Serum antibody titers for cytomegalovirus (CMV), toxoplasma, Hepatitis B and C were also negative. Peripheral blood smear showed large atypical lymphocytes–a hallmark finding of infectious mononucleosis. This was followed by heterophile antibody test, which was positive. Immunofluorescence assays of antibody titers to EBV antigens showed absence of EBNA IgG antibodies, Viral Capsid Antigen (VCA) (IgM) of 317 units (normal between 0-90 units), VCA (IgG) of 5 units, suggestive of an acute primary Epstein-Barr virus (EBV) infection. Lumbar puncture was performed and cerebrospinal fluid revealed white cell count 0 cells/dL, red cell count 4 cells/mm3, glucose 60 mg/dL and protein 56 mg/dL. The findings of the CSF analysis further supported the diagnosis of Guillain-Barre syndrome.

Results from motor and sensory nerve conduction studies on day 5 showed slowing of nerve conduction velocity and prolongation of F-wave latencies, a pattern consistent with demyelinating polyneuropathy. Over the course of the next ten days the patient was treated supportively and received a total of five plasmapheresis treatments, one treatment every other day.

Despite initial deterioration in the patient’s respiratory condition, he subsequently improved and did not require mechanical ventilation. He demonstrated progressive recovery of function of his upper extremities. On day eight of his hospital stay he was transferred to the medical service. On day nine he developed a new left facial nerve palsy, from which he later fully recovered. His upper extremities function returned back to baseline and he demonstrated marked improvement of the motor and sensory function of his lower extremities. The rest of his hospitalization was uneventful, and he was discharged to a rehabilitation facility on day eighteen.

Discussion

The present case illustrates all the classical features of infectious mononucleosis (IM) including clinical presentation, findings on peripheral blood smear and heterophile antibody positivity. More than half of the patients diagnosed with IM present with a triad of fever, lymphadenopathy and pharyngitis.1 Laboratory studies often reveal thrombocytopenia, leukocytosis, elevated aminotransferases and the presence of heterophile antibodies.1 A hallmark finding of acute IM is the expansion of lymphoid cells, collectively termed the atypical lymphocyte population.2 The lymphocytes seen represent mostly T lymphocytes produced in order to target EBV-infected B lymphocytes.1,3 The presence of 10% atypical lymphocytes on peripheral smear corresponds to 75% sensitivity and 92% specificity for the diagnosis of IM.4 This case highlights the importance of obtaining a peripheral blood smear in a patient with a history of cervical lymphadenopathy and neurological symptoms consistent with the diagnosis of Guillain-Barre syndrome (GBS). Our patient was initially diagnosed with GBS and it was not until the finding of atypical lymphocytes on peripheral smear that a suspicion for the diagnosis of an

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It stimulates polyclonal B cell activation, which in turn results in increased immunoglobulin production. EBV associated infection leads to the development of the demyelinating subtype GBS, while C. jejuni associated infection is associated with the axonal subtype GBS. The axonal subtype GBS results from the development of auto antibodies due to molecular mimicry between the bacterial and peripheral nerve components.

Since the identification of EBV as the cause of classic, heterophile positive infectious mononucleosis it has become possible to confirm the disease by specific serologic tests. Due to the fact that EBV like all herpetic viruses causes persistent, lifelong infection, it is important to recognize the patterns seen at different stages of the infection. The first antibodies generated during the course of primary EBV infection are against the VCA complex. The IgM antibodies are transient and the IgG antibodies persist for life. Later in the course of primary EBV infection, antibodies against the early antigen (EA) complex are generated. These are present transiently and usually disappear after 3 months. Antibodies against the EBV nuclear antigen (EBNA) complex appear more slowly. In contrast to the kinetics of the antibody responses against VCA and EA, antibodies to EBNA rise during convalescence and then level off. Due to the distinctive kinetics of the different EBV antibody responses, one can often diagnose EBV infection based on a single serum sample. Thus, the presence of IgM and IgG antibodies against VCA and the absence of antibodies to EBNA are diagnostic of a acute EBV infection.

In our case immunofluorescence assays of antibody titers to EBV antigens showed absence of EBNA IgG antibodies, VCA IgM of 317 units and VCA IgG of 5 units, suggestive of the presence of primary EBV infection.

Although the association of GBS with facial nerve palsy has been described as a complication of IM, this relationship is not well recognized by clinicians in primary care setting. Bell’s palsy following serologically documented IM has been described by Grose et al. who reported 3 cases without other neurological deficits. However, results from both can be negative in the early stages of the disease. In our case the diagnosis of GBS was supported by the presence of ascending upper and lower extremity symmetric polyneuropathy, conduction studies and CSF findings.

Conclusions

The present case describes the development of two rare neurologic complications of IM in the same patient. The occurrence of both GBS and Bell’s palsy within a short time span from the development of EBV associated IM supports the theory that these entities are variants of the same pathologic process. However, this relationship is not well recognized by physicians in the primary care setting or the emergency department. Increased awareness will aid in the timely recognition of the disease complex and the initiation of prompt supportive care. Randomized controlled trials have confirmed the efficacy of plasmapheresis and gamma globulin in the treatment of GBS. Moreover, conducting clinical trials of treatment modalities under development are vital in the effort to improve outcomes in patients with GBS.

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