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Case Reports

Epistein-Barr Virus Infection with Concurrent Pancreatitis and Hepatitis: A Rare Disease Entity

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Abstract: Concurrent acute hepatitis and acute pancreatitis is a rare disease entity. Most commonly it can be attributed to infectious etiologies such as hepatitis A, Hepatitis B and Hepatitis E. Although not as common, Epstein Barr Virus (EBV) should be considered in the differential diagnosis in patients with combined hepatitis and pancreatitis. We report a case of a 25 year-old male admitted with 2-day history of abdominal pain, nausea and dark stools. Laboratory findings were significant for mixed hepatocellular and cholestatic liver injury. Abdominal imaging showed evidence of acute pancreatitis, without biliary obstruction. Serologic tests and radiologic imaging excluded common infectious, autoimmune and/or structural etiologies. The diagnosis of EBV infection was made by a positive IgM antibody to the viral capsid antigen and Epstein-Barr nuclear antigen. The patient had a prolonged hospitalization for persistent abdominal pain and lag in improvement in his cholestatic liver injury. This disease process has been described in 6 children and no cases in adults have been reported to our knowledge.

Keywords: EBV, Hepatitis, Pancreatitis

Case Report

A 25-year-old healthy male was admitted with a 2-day history of severe right upper quadrant and epigastric abdominal pain with radiation to the back. Symptoms were associated with nausea, but no fevers, vomiting, or diarrhea. Patient denied prodromal viral symptoms, sick contacts, or recent international travel. He reported no skin rash, arthralgias, medication use, or ingestion of herbal supplements.

On examination, our patient had a low grade fever (temperature 100.4), pulse 100, blood pressure 138/60 with orthostasis and respiratory rate of 22. He was clinically dehydrated and in distress. He had mild scleral icterus. There was no cervical lymphadenopathy. No skin rashes or eschars were observed. Cardiovascular examination was significant for tachycardia. Pulmonary examination was unremarkable. His abdomen was mildly distended without ecchymosis. There was no gross ascites. On palpation, the abdomen was soft, but tender to gentle palpation, greatest in the periumbilical region and without peritoneal signs. No palpable masses and the liver and spleen were not palpable. The remainder of the physical exam was unremarkable.

Comprehensive laboratory evaluation was significant for the following abnormalities. Initial Complete Blood Count (CBC) was remarkable for white blood cell count of 6,900 (monocytosis of 14%) and platelet count of 126,000. Chemistry evaluation showed lipase of 429, Aspartate Aminotransferase (AST) 729, Alanine Transaminase (ALT) 657, Alkaline Phosphatase (ALP) 209, total bilirubin 3.8 and direct bilirubin of 2.3. Serologies for acute hepatitis were sent, including: EBV IgG, EBV IgM, Herpes Simplex Virus (HSV); Cytomegalovirus Virus (CMV); parvovirus B19; Hepatitis A, Hepatitis B DNA PCR, Hepatitis C Ab, Hepatitis E; Antinuclear Antibody (ANA); anti-smooth muscle antibody, antimitochondrial antibody, ceruloplasmin, ferritin/iron studies.

Abdominal ultrasound was obtained on admission, which showed a normal Common Bile Duct (CBD), no gallstones and no evidence of acute cholecystitis. Computed Tomography (CT) was significant for a few nonspecific prominent porta hepatis lymph nodes, 0.4 cm CBD with a distended gall bladder and an edematous pancreas with fat stranding and ill-defined fluid (see Fig. 1). One day after admission, magnetic resonance cholangiopancreatography was obtained, which showed severe acute pancreatitis with marked progression in edema and fluid retention and mildly distended gallbladder without evidence of acute cholecystitis (see Fig. 2).

The patient was medically managed for acute hepatitis and acute pancreatitis of unknown etiology. He was treated with aggressive hydration (normal saline at 300 mL/hr), Nil Per Os (NPO) and pain

management with intravenous Dilaudid. On day 2, Hepatitis A IgM, HbsAb, HbcAb IgM, HbsAb, HBV DNA PCR, HCV Ab, ANA, AMA, Anti-smooth muscle were negative. The patient continued to have fevers, progressive abdominal pain and increasing cholestatic liver injury on day 2-5 of hospitalization. Repeat imaging was obtained on day 3 due to concern of pancreatic necrosis and/or hemorrhage. CT abdomen showed worsening of acute pancreatitis with moderate ascites, moderate bilateral pleural effusions, anasarca, but no fluid collections or necrosis identified (See Fig. 3). Conservative management was continued.

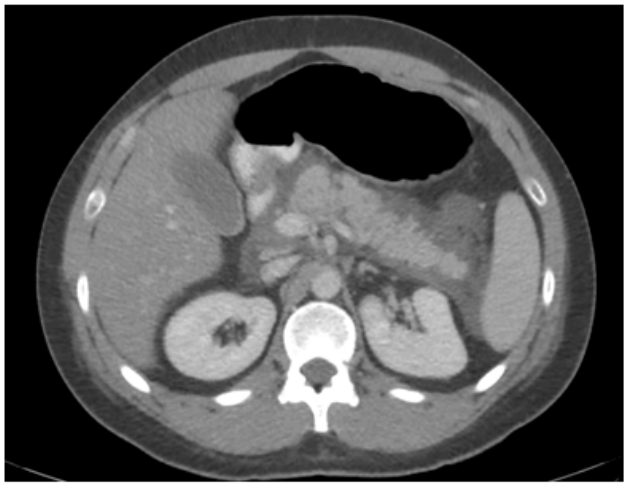

Fig. 1. Day 1 hospitalization. CT abdomen/pelvis w/contrast showing acute pancreatitis

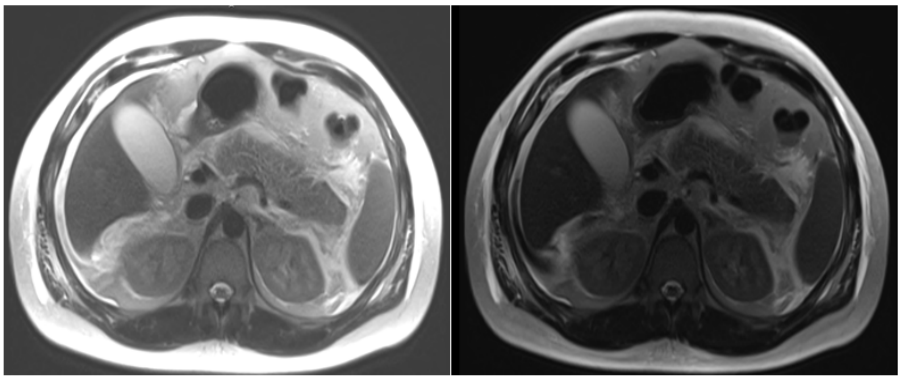

Fig. 2. Day 2 hospitalization. T1 and T2 weighted images of MRCP w/o contrast showing severe acute pancreatitis with marked progression in edema and fluid retention

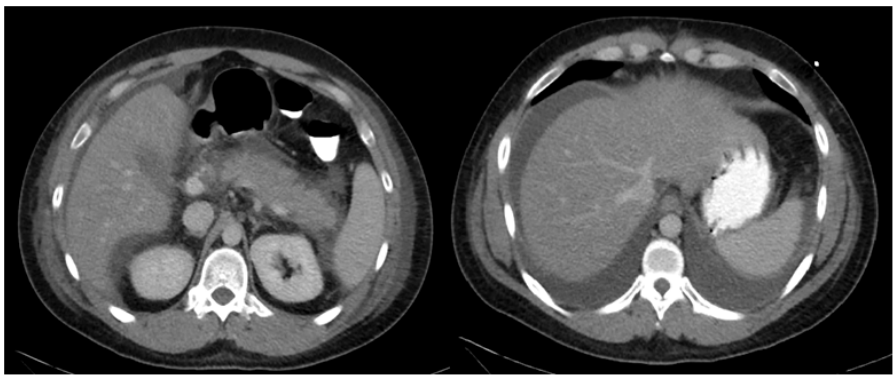

Fig. 3. Day 5 Hospitalization. CT abdomen/pelvis w/o contrast showing worsening acute pancreatitis, new bilateral moderate pleural effusions, increased amount of moderate ascites and new anasarca

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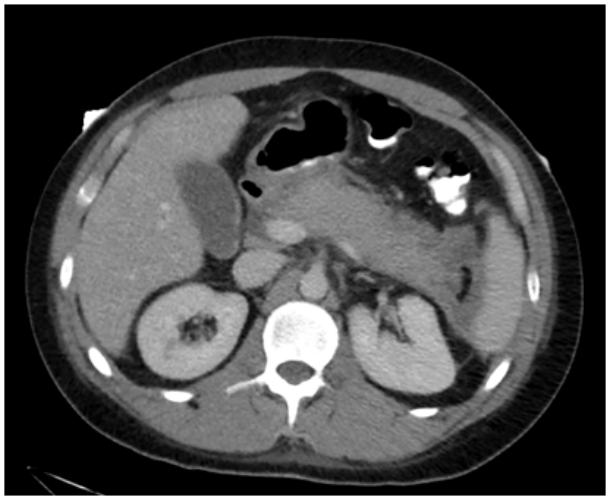

Fig. 4. Day 10 Hospitalization. CT abdomen/pelvis w/o contrast showing evidence of interstitial edematous pancreatitis, with a walled off early pseudocyst formation

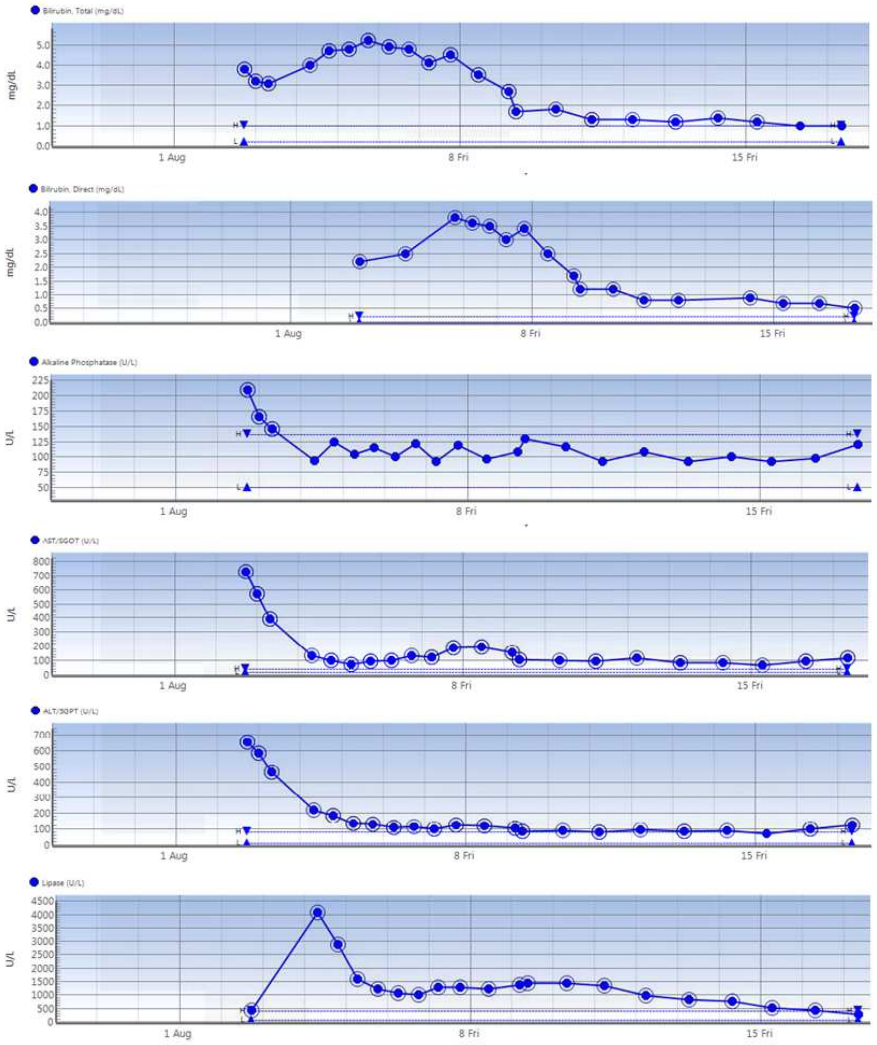

Fig. 5. Trend of AST, ALT, alk phos, total bilirubin and direct bilirubin during hospitalization

On day 4 of hospitalization, acute EBV was diagnosed by finding of positive IgM antibodies to the viral capsid antigen and Epstein-Barr nuclear antigen. HSV, CMV and parvovirus B19 antibodies were negative. On day 7, the patient was started on Total Parenteral Nutrition (TPN). CT scan on day 10 showed severe interstitial edematous pancreatitis without necrosis, new pseudocyst formation and mild improvement in bilateral pleural effusions (see Fig. 4). Day 11, the patient showed clinical signs of defervescence, TPN was discontinued and he was started on a liquid diet. Days 6-15, the patients laboratory investigation showed slowly improving hepatocellular liver injury/cholestatis (see Fig. 5). Day 15, the patient was discharged from the hospital.

Discussion

Epstein-Barr Virus is a double helix DNA virus from the Herpesviridae family, which infects B cells and epithelial cells. It is most commonly implicated in Infectious Mononucleosis and Burkitt's lymphoma, however, other rare presentations have been reported. In developing countries, EBV tends to infect children at an early age and most often with absent or subclinical symptoms. By adulthood, more than 90% of individuals have been exposed with development of IgG antibodies. However, in higher socioeconomic areas, infection is often delayed until early adulthood and may have more profound clinical presentations, such as in our case.

Acute hepatitis concomitant with acute pancreatitis is often caused by infectious etiologies such as Hepatitis A, B and E (Javid *et al*., 2012; Mishra *et al*., 1999). EBV associated acute cholestatic hepatitis and acute pancreatitis is a rare disease entity and even more rarely described in the adult population. Most of the previously reported cases have been in the pediatric population, ranging from age 8-23 (Koutras, 1983; Mor *et al*., 1982; Everett *et al*., 1969; Wislocki, 1966; Narchi *et al*., 2014; Khawcharoenporn *et al*., 2008; Kang *et al*., 2013). Only two cases reported by Kang *et al*. (2013) and Narchi (2014) have shown patients with signs of EBV related acute pancreatitis and mixed cholestatic/hepatocellular hepatitis, similar to our patient, which also could not be attributed to other etiologies. However, these patients are aged eight and eleven, in comparison to our patient who is twenty-five. Also, in the prior reported cases, the patients noted prodromal symptoms, which our patient did not have (Khawcharoenporn *et al*., 2008).

The mechanism of injury is not clearly understood, but is likely multifactorial. Postulated mechanisms are direct destruction and inflammation of pancreatic acinar cells by the virus and/or possible development of edema of the ampulla of vater with obstruction to the outflow of pancreatic fluid. Regardless of the etiology, the treatment remains supportive.

The diagnosis of EBV pancreatitis and hepatitis combined is rare in itself and the length of time that our patient required hospitalization, nutritional support and prolonged time from presentation to defervescence was interesting. In one case, an eleven year old female took eleven days to recover based on pancreatic enzymes, transaminases and symptoms, however, the patient was able to tolerate an oral diet on the fourth day of admission (Kang *et al*., 2013). This patient also required TPN, however, was able to tolerate a regular diet earlier than our patient and may indicate a difference in recovery time between pediatric and adult populations with associated EBV hepatitis and pancreatitis.

EBV associated hepatitis with concomitant acute pancreatitis is a rare condition, primarily seen in the pediatric population when it does occur. However, this reports shows that it is an important differential diagnosis that must be included when assessing the adult population as well.

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Authors Contribution

All authors have equal contribution to this manuscript.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues involved.

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