Parvovirus İnfection in a Child Complicated With Diabetic Ketoacidosis and Acute Fulminant Hepatitis: A Case Report

Parvovirus Enfeksiyonu Olan Bir Çocukta Diyabetik Ketoasidoz ve Akut Fulminan Hepatit Birlikteliği: Olgu Sunumu

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) results from the destruction of pancreatic beta cells, genetic and environmental factors are believed to be major component for the development of disease. Viruses have been suspected to contribute to the onset of T1DM.

Case report: We describe here a patient who had diabetic ketoacidosis with acute fulminant hepatitis following asymptomatic infection with parvovirus B19 virus (PB19).

Discussion: To our knowledge this is the first report of diabetic ketoacidosis (DKA) and acute fulminan hepatitis due to PB19. We suggest close monitoring the liver functions in DKA and giving attention when the liver functions worsens.

Key words: acute fulminan hepatitis, parvovirus, diabetic ketoacidosis, hypoglicemia

ÖZET

Giriş: T1DM pankreatik beta hücrelerinin harabiyeti ile ortaya çıkmaktadır.Genetik ve çevresel faktörlerin hastalığın gelişimindeki ana faktörler olduğu düşünülmektedir. Virusların hastalığın başlangıcında etkili olduğu düşünülmektedir.

Olgu: Bu olguda asemptomatik parvovirus b19 enfeksiyonunu takiben ortaya çıkan diyabetik ketoasidoz ve akut fulminan hepatit birlikteliğinin olduğu bir vaka sunulmuştur.

Tartışma: Diyabetik ketoasidozda karciğer enzimlerinin de yakın izlenmesini ve kötüleşme olduğunda dikkat edilmesini önermekteyiz.

Anahtar Kelimeler: Akut fulminan hepatit, parvovirus, diyabetik ketoasidoz, hipoglisemi

Abbreviations:

T1DM: Type 1 diabetes mellitus

DKA: Diabetic ketoacidosis

Introduction:

Infection with parvovirus is very common and occurs worldwide. Acquisition is often during childhood and continues at lower rates throughout adulthood. Infectivity is more common in winter and spring. The clinical spectrum of disorders were variable. Beside known outcomes, hepatitis and acute liver failure could be developed <1>. Diabetic ketoacidosis (DKA) is a rare complication of diabetes mellitus. There is an increase of ketone bodies due to lipolysis. Ketone body accumulation leads to acidosis. The acidosis state of DKA could cause multiple organ failure and a threat to human life <2> . Here, we describe a patient with type 1 diabetes mellitus (T1DM) and DKA who also had fulminant acute hepatitis triggered by PB19. Close clinical and biochemical monitoring is necessary for successful management.

Case Presentation

The patient who was 9 years 9 months old boy was admitted to the hospital with complaints of polyuria, polydipsia, decreased appetite, hyperglicemia for two days. His medical history was normal. There was no record of transfusion. He had also hypoglicemia episodes as well as hyperglicemia for one week. He has been followed with T1DM for 3 years. In physical examination vital signs were normal. The patient's weight was 24,5 kg (-1,48 SDS) and his height was 133,2 cm (-0,56SDS). Body mass index was 13,81kg/m2 (-1,95SDS). He had second degree dehydratation signs. The liver was palpable 4 cm in the right hypochondrium, but it was smooth and non-tender. There was 3 cm splenomegaly. Other systemic examination findings were normal. Blood gas analysis showed a pH 7,29 and HCO_3 11 mmol/L, blood ketone was 2+. The diagnosis of DKA was made, and appropriate fluid-electrolyte and insulin therapy was started. Complete blood count showed white blood cell (WBC) : 3331/ mm^3 , neutrophil: 756/ mm^3, lymphocytes: 2240/ mm^3, Hb: 11 g/dl, platelets : 200000/ mm^3. Biochemical findings revealed increased hepatic enzyme levels [aspartate transaminase (AST) 274 IU/L, alanine transaminase (ALT) 206 IU/L] and kept rising later [AST 5653 U/L,

ALT 1523 U/ L, gamma glutamyl transferase (GGT) 183 U/L]. In coagulation profile Internasyonel normalized ratio (INR) was 3.46, prothrombin time (PT) was 34.4 sn and activated partial thromboplastin time (aPTT) was 40 sn. He had no hyperbilirubinemia and ammonia was 79 mcg/dl (31-123 mcg/dl). He had hypoglisemia episodes beside hepatic enzyme increase. One week before hospitalization he developed general fatigue and nausea. The patient did not exhibit autoantibodies, including antinuclear antibodies and antineutrophilic cytoplasmic antibodies. Seruloplasmin was normal. Serology was negative for; hepatitis A, B, C, E, viruses, cytomegalovirus, Epstein–Barr virus, rubella virus, herpes virus, chlamydia, syphilis, mycoplasma, brucella, toxoplasma or human immunodeficiency virus but the PB19 IgM was positive. The patient was diagnosed as acute hepatitis secondary to PB19 infection beside DKA. Insulin treatment, vitamin K, ursodeoxycholic acid and acetyl cysteine were administrated. The patient's liver chemistry values gradually improved. On the 15th day of hospitalization his liver function was normalized, hypoglisemia episodes were corrected and he was discharged.

Discussion:

The clinical spectrum of disorders that are associated with PB19 infection is wide. Erythema infectiosum, arthralgias and arthritis, transient aplastic crisis, also associations based on organ system. Hepatitis and fulminant liver failure could be developed <1>. Patients with impaired humoral immunity are at risk for chronic infections with parvovirus. Chronic anemia is the most common manifestation.Sometimes complete marrow supression was occured. Also chronic infections are seen in cytotoxic chemotherapy , congenital immun deficiency on immun supressive therapy and with IgG

production defects <3>. Temporary suppression of erythropoiesis during the viremic phase is usually well tolerated owing to the long life span of erythrocytes, and hemoglobin levels remain fairly stable. <4>. Our patient had leukopenia and slightly low hemoglobin level and after one week leukopenia was corrected.

Multiple factors are believed to involved in the development of T1DM. Virus may trigger beta cell-specific autoimmunity leading to diabetes, or may directly infect and destroy insulin-producing pancreatic beta cells, resulting in clinical T1DM <5>. There is evidence associating T1DM with enterovirus infection in humans. This virus promote a T-cell-mediated lymphoproliferative response that is dependent upon its presentation to CD4 cells by HLA class II antigens and could generate T-cell-mediated autoimmunity <6> Additionally prenatal rubella infection which is associated with beta-cell autoimmunity in up to 70%, and diabetes in up to 40% of infected children. Also intrauterine exposure to enteroviral infection is thought to be associated with beta-cell autoimmunity. Patients with autoimmunity may be more prone to enteroviral infection, may have a stronger humoral response to infection because of their particular HLA genotype, or may be in a nonspecific hyperimmune state marked by elevation of antibody levels to various exogenous antigens. Islet related autoantibodies have been found after various viral infections <7>. In patients with T1DM, plasma insulin concentrations are determined by the rate of insulin delivery and the rate of insulin clearance. The liver has a major role in insulin clearance as well as other aspects of glucose homeostasis. Patients with acute viral hepatitis have marked impairment of hepatic glycogen synthesis and a defect in gluconeogenesis. Such problems might have contributed to the hypoglicemia in this patient <8>. Despite the insufficient data in literature, PB19 could be one of the triggers for DKA as well as acute hepatitis. Similarity of PB19 proteins and human proteins thought to be related to the pathogenesis of autoimmune disorders triggered by this virus. Immunologic processes triggered by viral infection considered as a cause in the pathophysiology of fulminant T1DM <9>.

The mechanism by which PB19 infection may result in hepatic injury is not clear. Hepatic manifestations of PB19 infection range from abnormal liver function tests to fulminan hepatic failure, especially in young children. Sokal et al. showed PB19 infection with fulminant hepatitis of unexplained etiology <10>. The main distinctive features are low bilirubin levels, high ALT and/or AST activity, and favorable outcome with rapid return to normal liver function without orthotopic liver transplantation. Rash, arthropathy and hematologic disturbances did not necessarily accompany fulminan hepatic failure <11>.Acute hepatitis in association with PB19 infection has only rarely been reported in the literature <10>. Díaz et al. described 2 patients with acute hepatitis. Both patients were positive for PB19 IgM. Two additional cases of PB19 associated hepatitis were reported by Hillings et. al. Also Sun and Zhang reported hepatic dysfunction in an adult due to parvovirus <12>. In this case, acute hepatitis was complicated with DKA. Our patient had an established biological diagnosis of PB19 primary infection with IgM positivity. Our patient's clinical course was appropiate with the findings in the literature. Although our patient had acute fulminan hepatitis due to PB19, the outcome returned to normal liver function rapidly. The notion of PB19 virus as a causative agent of hepatic dysfunction has not been fully accepted. The associations have been proposed on the basis of the temporal association of symptoms in the context of serologic documentation of recent infection or detection of PB19 in peripheral blood or affected tissue <4>.

We considered that acute deterioration of liver functions by PB19 infection diminished insulin clerance and resulted in both hyperinsulinemia and hypoglicemia. PB19 infection can cause acute hepatitis, the role of parvovirus infection as a trigger of both hepatitis and DKA with hypoglicemia episodes has not been defined. To our knowledge this is the first report of DKA and acute fulminan hepatitis due to

PB19. We suggest close monitoring the liver functions in DKA and giving attention when the liver functions worsens.

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