A Rare Acute Lymphoblastic Leukemia in a Patient Infected with Epstein-Barr Virus: A Case Report

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Abstract

We present an 18-year-old male suffering from myalgia, cough, and anorexia with symptoms of jaundice and lymphadenopathy. He was infected with the Epstein-Barr virus which leads to acute lymphoblastic leukemia in this patient.

Introduction

Epstein-Barr virus was first discovered 50 years ago through its association with Burkitt's lymphoma, and as seen, the virus encodes a set of products that have been found to have an interaction or similarity between them and a wide range of Anti-apoptotic molecules, cytokines may promote immortalization in cells and transformation.[1-3] The delayed infection hypothesis proposed by Greaves also suggests that late exposure to infectious agents, as opposed to early exposure, can lead to an abnormal immune response that by an indirect mechanism can increase leukogenesis and acute lymphocytic leukemia.[4]

Lymphoma is divided into two categories: Hodgkin's and non-Hodgkin's. The most common site of NHL lymph node proliferation is the gastrointestinal tract, which accounts for 15 to 20 percent of all cases.[5]

Obstructive jaundice is one of the manifestations of malignancies that is usually caused by external compression of the common bile duct, but many cases of malignant infiltration of the internal bile duct have not been reported. Acute lymphoblastic leukemia (ALL), which is a clonal hematologic disorder and is known as non-Hodgkin's lymphoma, also has symptoms such as fever and fatigue and thrombocytopenia and hepatomegaly. However, there are limited reports of liver failure and jaundice as early manifestations of the disease.[6-10]

Here we look at a case that presents with symptoms of jaundice and lymphadenopathy and is known in tests for Epstein-Barr virus to cause acute lymphoblastic leukemia in this patient.

Case report

An 18-year-old man who has been suffering from myalgia, cough, and anorexia for about 11 days has been referred to our hospital with severe abdominal pain, yellowing of the eyes, and myalgia. The onset of persistent abdominal pain 6 days ago was sudden in the epigastric and pre-embolic areas, which were non-radical and non-positional and did not improve with eating. The patient then reports three episodes of anemic vomiting containing food in the last 6 days. During the last 3 days, the patient's abdominal pain intensified and spread to LUQ, and he developed jaundice and red lesions on the chest and abdomen. The night before going to the hospital, he also mentioned fever and chills. Symptoms included cough, dry mouth, skin rash on the chest and abdomen, petechiae in the abdominal area above the navel and chest, icteric sclera, dry nose, flank pain, and facial edema. The patient does not report symptoms of shortness of breath, orthopnea, and PND. Erythema of the pharynx and tonsils and bilateral submandibular lymphadenopathy was also observed, and the thyroid gland was normal to the touch and lacked tenderness and nodularity.

Other examinations of the body system were also normal and had no significant results. The patient also mentions an unknown weight loss history during the last 3 months. There is no significant medical history, except for the history of COVID-19 3 months ago, which was treated at home and without hospitalization, and the onset of cold symptoms a week ago, which was accompanied by runny nose and cough. The history of taking a particular drug is not mentioned. Examinations of the patient showed dry mouth and red rashes on the chest and abdomen with fever and chills. On examination of the patient's abdomen, the intestinal sounds were normal and about 8-9 cm was measured liver span and the spleen was 3 cm below the edge of the rib and despite the tenderness observed in the epigastrium and periumbilical region and LUQ, no mass was touched on superficial and deep touch.

Laboratory tests showed a decrease in platelet count (19000 per microliter) and amylase (25 U/L) and a sharp increase in white blood cells (14,400 per microliter), 80% of which were lymphocytes, and atypical lymphocytes were also observed. Alkaline phosphatase (ALP) 686 IU/L, Aspartate aminotransferase 93 U/L, ALT 75 U/L and Lactate Dehydrogenase (LDH) 4280 U/L were observed along with bilirubin total 12.6 mg/dL, bilirubin direct 8 mg/dL and hemoglobin 15 g/dL. An ultrasound was performed for the patient and in it the gallbladder with increased thickness (about 10 mm) and splenomegaly and lymph nodes with dimensions of 14.5 * 11 and 8 mm were seen at the site of gastrohepatic ligament and Porta Hepatis, respectively. Due to fever, jaundice, abdominal pain and thrombocytopenia, and cervical lymphadenopathy, possible diagnoses including acute viral hepatitis and AIH and Wilson and hemochromatosis and viral infection with EBV, CMV, and HSV as well as lymphoma were proposed. Related tests were requested based on these differential diagnoses, and according to the submandibular lymphadenopathy observed on the second day of cervical lymph node ultrasound, in which a number of lymph nodes with a reactive view with a maximum short-axis diameter of 6.6 and 6 mm, respectively, in the right-side zone and with A maximum of 10 mm was seen in the submandibular region and a maximum of 5.5 in the left of zone 2.

During the hospitalization process, the AST and ALT levels increased to 93 and 75, respectively, the white blood cell count also reached 7900, and the platelet count decreased to 14,000 after an increase. On the third day of hospitalization, jaundice and abdominal pain improved, but the patient developed joint pain and tenderness in the joints, but no active arthritis was seen, which led to the possibility of infectious processes such as hepatitis and lupus. ANA and viral marker tests were performed to check them. The results of the patient tests showed that the patient was infected with Epstein-Barr virus due to a positive VCA test and a high EBV IgM antibody titer, and the results of other patient tests were negative. Abdominal and pelvic CT performed on the fourth day of mild pleural effusion hospitalization with lung collapse in the right hemithorax as well as splenomegaly, hepatomegaly, and multiple lymphadenopathies in the mesenteric area of the celiac region and with maximum size were observed, which are cases of non-Hodgkin's lymphoma, and due to this possibility and the decrease in the patient's platelets from 65,000 to 14,000, a BMA patient was performed, which was a dry tap, followed by a biopsy, which was based on the biopsy result and the observation of fragmented and crushed bone trabeculae with the scattered and small crushed nest of marrow cells on the fibrotic background, which appeared to be mainly small lymphocytes that make the possibility of lymphoma increased and a request for immunohistochemistry was made, but unfortunately, the patient was expired. (Figure 1)

(Figure 1)

Discussion

Acute lymphoblastic leukemia, although the most common hematologic neoplasm in children, is less common in adolescents and adults and has a survival rate of 20% to 40.[11-13] Symptoms of the disease are nonspecific and often include fever, fatigue, bruising and bleeding due to thrombocytopenia and infection due to neutropenia, but other symptoms include hepatomegaly and splenomegaly and joint pain. However, the occurrence of cholestatic jaundice in this disease and as one of the early manifestations is very rare.[9, 10, 14, 15] Acute lymphoblastic leukemia is a type of non-Hodgkin's lymphoma and among the types of lymphomas that are divided into two categories: Hodgkin's and non-Hodgkin's, non-Hodgkin's lymphomas, unlike Hodgkin's lymphomas, often spread to the lymphatic tissues and especially spread to the Gastrointestinal tract.[5, 16]

ALL, due to over-proliferation and abnormalities in the differentiation of leukemic blasts following inadequate normal hematopoiesis, usually has a rare extra-medullary shape, but if it does occur, it will affect most of the bones and then the soft tissue, skin and lymph nodes, and hepatic manifestations are rare in leukemia patients.[14, 15, 17] There are limited reports in this regard, one of which mentions malignant infiltration of the internal bile duct in a girl with leukemia with jaundice and cervical lymphadenopathy at the beginning of the visit and also Intrahepatic cholestasis has been observed in two other children with leukemia.[6, 18]

The development of liver failure during malignancies can also be challenging for the patient's treatment process, as it can reduce the patient's tolerance to intensified chemotherapy. Therefore, some recommend a short course of prednisolone before starting full-dose chemotherapy until the treatment reduces bilirubin levels so that chemotherapy can be continued with greater vigor.[8, 19, 20] Drainage methods may also be useful in patients with biliary obstruction, but in the case of diffuse infiltration of the liver parenchyma, this procedure is not beneficial.[21]

The patient was also infected with Epstein-Barr virus (EBV) according to tests performed, which is asymptomatic in more than 90% of patients, and only some patients develop infectious mononucleosis and usually resolve on their own.[1, 22, 23] EBV is an oncogenic lymphotropic DNA virus belonging to the herpes virus family and can play a role in the development of leukemia and lymphoma by cloning B memory cells.[24-26] It is estimated that 15 to 20 percent of all tumors are associated with infection by a direct tumorigenic agent, and EBV has been shown to cause Burkitt's lymphoma and some other types of neoplasms, and one of the malignancies associated with infection in childhood is acute lymphoblastic leukemia.[27-30]Maternal infection with EBV has been shown to be associated with an increased risk of ALL in children[31], In two studies, the high serum prevalence of EBV in children with ALL has been observed, which, along with the transcription activity of the latent membrane protein gene 1 (LMP1) of EBV, in a significant proportion of patients with ALL, supports its role in this disease.[32-34]

Finally, bone marrow sampling of this patient showed the presence of non-Hodgkin's lymphoma and in the final diagnosis was known as ALL case, which along with the rare symptoms of jaundice and the possible role of Epstein-Barr virus in its development was very significant.

Acknowledgment

None.

Conflict of interests

The authors declare no conflict of interest.

Authors' contributions

Mohammad Heidary decided to present this patient as a case report and designed the concept of study. Mohammad Heidary, Mostafa Majidi Moghaddam, Maryam Zahedi, and Hani AziziKia drafted and revised the manuscript. Mostafa Majidi Moghaddam, Maryam Zahedi, and Hani AziziKia followed up the patient and acquisition of data. Mohammad Heidary had reviewed and edited the final version. All authors have read and approved the final manuscript.

Ethical approval

Authors state that consent for publication in print and electronically has been obtained from the patient.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Data availability statement

The case report data is not publicly available, but it could be available from the corresponding author with a reasonable request.

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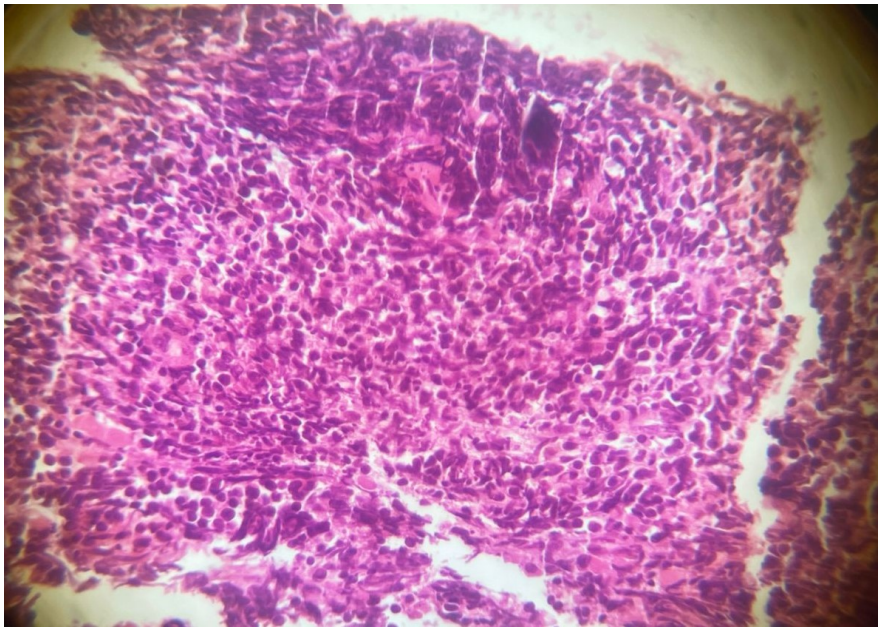
Figure legend:

Figure 1. A view of the bone marrow biopsy of this patient has shown the fragmented and crushed bone trabeculae with the scattered and small crushed nest of marrow cells on the fibrotic background.



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