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Chronic Pyogenic Meningitis and Leukemia – Case Report of Chronic Meningitis in Acute Lymphoblastic Leukemia

Case Report

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Abstract

Chronic meningitis is rare but morbid condition in patients with hematological malignancy who have impaired cellular and humoral immunity. It is seen in less than 10% of patients who developed meningitis. Though it is less common in patients with acute leukemia ,repeated lumbar puncture as well as overall immunocompromised status make them susceptible to meningeal infection. We report a case of young boy with Acute lymphoblastic leukemia who developed chronic pyogenic meningitis during chemotherapy. He was treated and discharged successfully after prolonged course of antibiotics.

Keywords: Immunocompromised; Meningitis; Fever

Introduction

Pyogenic Meningitis is usually manifested as an acute illness, predominantly affecting children and young adults. In most cases it presents with neck stiffness, high grade fever and an altered sensorium. In Chronic meningitis, inflammatory cerebrospinal fluid (CSF) profile persists for more than four weeks. The clinical presentation includes headache, vomiting, and persistent fever. In addition to this clinical symptoms of elevated intracranial pressure or focal neurologic deficits may be appreciated in most of the cases. [1] Evaluation of the patient with suspected chronic meningitis should include a detailed history, physical examination, repeated CSF analysis and brain imaging studies. Early identification of the etiology and rapid treatment are crucial for long- term morbidity and mortality [1,2]. We report a case of six-year-old boy suffering from B cell acute lymphoblastic leukemia who developed chronic pyogenic meningitis during chemotherapy. He was treated with prolonged antibiotic course of 10 weeks before achieving clinical improvement and remission in CSF morphology.

Case Description

Six year old boy was diagnosed to have B Cell Acute lymphoblastic leukemia without CNS or testicular involvement in February 2021 when he was evaluated for complaints of fever and easy fatigability. He was initiated on BFM 95 protocol from first week of February ,2021. He achieved morphological disease remission after induction chemotherapy and remained asymptomatic during his chemotherapy.

On evaluation for his 14th maintenance chemotherapy, he had high grade fever, headache and back pain for 7 days origin. His chemotherapy was stopped. His investigations including routine Hemogram, biochemistry, blood cultures, urine routine, chest X-ray and USG abdomen were normal. As workup for persistent fever in background of headache and backpain, his CSF analysis was done which showed wbc-110/cumm; 50% neutrophils; protein 80mg/dl ;glucose 25mg/dl with corresponding Random blood sugar of 72mg/dl without any evidence of malignant cells. With possibility of pyogenic meningitis, he was treated with inj Ceftriaxone (100mg/kg/dose once daily) and inj Linezolid (10mg/kg/dose every 8 hours) IV for 10 days. Intravenous immunoglobulin (IvIg) was infused in view of low IgG level. His fever responded within two days to the above antibiotics and he remained afebrile for 2 weeks after starting antibiotics.

He developed recurrent spikes of fever 1 week after completion of antibiotic course. His repeat CSF evaluation revealed recurrence of meningitis. Values of CSF analysis revealed wbc-520; 60% neutrophils, protein 65mg/dl; glucose 36mg/dl with corresponding random blood sugar of 60mg/dl. CSF culture did not reveal any growth. In light of partially treated pyogenic meningitis, he was initiated on inj Meropenem (40mg/kg/dose) and inj Vancomycin (20mg/kg/dose) IV 8 hourly for 20 days. After 3 weeks of antibiotics, his CSF wbc counts dropped to 16 cells/cumm with normal sugar and protein. Pediatric Neurology and Infectious disease opinion were sought. His MRI brain with contrast and CT chest were normal. After detailed discussion with multidisciplinary team consisting of Haematologist, Pediatric Infectious disease specialist and pediatric neurologist, it was decided to restart maintenance chemotherapy as he was afebrile and asymptomatic for more than 72 hours. It was also decided to hold Intrathecal chemotherapy till clearance of WBC in CSF during subsequent visits.

Immediately after starting maintenance chemotherapy consisting of Inj Vincristine, oral daily 6- mercaptopurine and oral weekly methotrexate, he developed intermittent fever and back pain from 2nd week onwards which responded to oral antibiotics and antipyretics on Outpatient basis. His CSF evaluation was repeated after 2 months which revealed chronic pyogenic meningitis with wbc– 333cells/cumm; 87% neutrophils; protein-87mg/dl; sugar-33mg/dl along with corresponding random blood sugar-106mg/dl. CSF cultures including aerobic culture, anaerobic culture, tuberculosis culture and multiplex PCR were negative for infective foci. His repeat MRI brain and spine were normal. His chemotherapy was stopped immediately after that.

He was reinitiated on Inj Meropenem (40mg/kg/dose) and Inj Vancomycin (20mg/kg/dose) IV every 8 hourly which was continued for 6 weeks in view of chronic bacterial meningitis. He was also started on Cap Rifampicin along with IV antibiotics for possible intracellular bactericidal effect of drug. He remained afebrile and asymptomatic after that. Repeat CSF analysis was suggestive of wbc - 8 cells/cumm; 100% lymphocytes; Protein -49mg/dl ; sugar 44 mg/ dl along with corresponding random blood sugar 108mg/dl. He was reinitiated on maintenance chemotherapy drugs after that. His subsequent CSF analysis revealed normal CSF picture.

Discussion

Chronic meningitis is defined as symptoms and signs of meningeal inflammation and persisting cerebrospinal fluid (CSF) abnormalities such as elevated protein level and pleocytosis for at least one month. Chronic Meningitis in patients of acute lymphoblastic leukemia receiving chemotherapy regimen has always been challenging aspect for treating Heamtologist [2]. It affects less than 10% of meningitis sufferers and is linked to a large variety of both infective and non-infective causes [3]**.** However, while there are numerous published individual case reports on chronic meningitis, there is a definite paucity of large case series in the literature specially for pediatric patients who develop this kind of disease, while on chemotherapy. Increasing use of immunosuppressant medications for haematological malignancy, post transplantation period and predisposing conditions such as congenital and acquired immunodeficiency syndrome have led to a larger population at risk of chronic meningitis. [1,9] The most common cause of chronic meningitis is Mycobacterium tuberculosis, which accounts for up to 60% of cases. Other infrequent causes include malignancy (8-10%) and cryptococcal infection (6–10%) In up to 33% of cases no underlying cause is identified [4]**.**

The classic triad of clinical features of meningitis which is seen up to 80% of patients presenting with acute bacterial meningitis is uncommon in chronic meningitis. [5] However Focal neurological signs,cranial nerve palsies and abnormal CT brain findings are far more commonly seen in chronic meningitis [6].

There are several additional factors, which make children with acute leukemia more prone to bacterial meningitis. Acute and chronic diseases (e.g. renal or hepatic failure), repeated lumbar puncture for administration of chemotherapy drug, immunosuppressive chemotherapy and reduced cellular and humoral immunity are common predisposing factors. Patients lacking antibody-dependent or complement-mediated lysis (bactericidal activity) are most susceptible to meningococcal disease. [7] Our patient's CSF showed predominantly neutrophils, raised protein, and low glucose for more than 4 weeks, which are seen in only 10% of bacterial meningitis cases [8].

This case highlights the diagnostic challenge associated with bacterial meningitis presenting in immune compromised child. The presentation was uncommon with subtle febrile episodes and absence of any focal neurological deficit. The diagnosis required repeated investigation during follow up visits. Early lumbar puncture has to be encouraged to confirm the diagnosis. Despite a delayed diagnosis appropriate antibiotic therapy can still lead to a good outcome [**9,10**]

Consent

Written informed consent was obtained from patient for publication of this case report.

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