Neutropenic Enterocolitis in a Child with Acute Myeloid Leukemia Successfully Treated with Early Surgical Intervention

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Received: 31 July 2011 / Accepted: 27 June 2012 / Published online: 15 July 2012
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Abstract Neutropenic enterocolitis (NE) is a life threatening complication of acute leukemia. The case presented here is of a 12 year old boy with acute myeloid leukemia, who developed neutropenic enterocolitis after induction with BFM-93 protocol. Patient underwent exploratory laparotomy during grade 4 neutropenia after failure on conservative line of management of NE. Patient withstood the procedure with supportive care and recovered. This case is reported because NE is a rare but potentially fatal complication and there are no clear guidelines for surgical intervention.

Introduction

NE is a severe gastrointestinal complication in patients who undergo aggressive chemotherapy [1]. It is a condition characterized by inflammation, which usually involves cecum, colon and terminal ileum in patients of leukemia [2]. True incidence is unknown but, in acute leukemias treated with chemotherapy neutropenic enterocolitis incidence rate is about 4 %. Mortality rate varies from 50 to 100 %, with most deaths due to bowel perforation and sepsis. Recently, early recognition and progress in management probably have reduced mortality [3].

Case

A 12 year old boy was brought with complaints of fever of 4–5 days duration. Physical examination was not contributory except for pallor. On laboratory evaluation, his hemoglobin was 9 g%, total leucocyte count 36,700/cumm and platelet count of 50,000/cumm and blasts of 27 %. Serum uric acid, serum creatinine, liver function tests and chest X-ray were normal, S.LDH—1,470 u/l. Bone marrow aspirate showed myeloblasts (55 %) with auer rods, and were sudan black positive and overall diagnosis (morphologically) of AML-M4 was made. However, cytogenetics was inconclusive.

After securing Hickman catheter, patient was started on induction therapy with BFM-93 protocol [4]. Induction was uneventful except on last day (day 8), he developed generalized maculopapular rash, which according to dermatologist opinion was etoposide induced. It was treated symptomatically and the rash subsided. On post chemotherapy day (PCT) 3, patient developed fever and was started on cefepime, amikacin and fluconazole as his absolute neutrophil count (ANC) was zero. Blood and urine cultures were sterile and he developed breakthrough fever on PCT 5, and he was started on amphotericin-B.

On PCT day 10, patient developed abdominal distension and pain in abdomen. Clinical examination revealed distended abdomen, diffuse tenderness and sluggish bowel sounds. At that point of time patient had ANC <100 and hypokalemia, his antibiotics were stepped up to meropenem, levofloxacin and amphotericin-B was continued and potassium was replaced accordingly. Ultrasonography of abdomen/pelvis showed evidence of dilated small bowel loops with no peristalsis, mild inter bowel thickening noted involving cecum (5 mm) with internal vascularity, and overall possibility of typhilitis was suggested. X-ray erect

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abdomen showed multiple air fluid level, suggestive of intestinal obstruction Fig. 1.

Patient was initially managed conservatively. He was kept nil by mouth with continuous Ryle's tube aspiration, higher antibiotics and blood component support was continued. Patients symptoms kept worsening, however he was stable hemodynamically and on PCT 13 pediatric surgeon opinion was sought and an emergency exploratory laparotomy was done with support of G-CSF as patient had ANC <200/cumm with no peripheral blasts. On the day of surgery hemoglobin was 9.9 g% and a platelet count of 48,000 with SDP support, however electrolytes were normal. On exploratory laparotomy, the distal jejunum and ileum was dilated with pre-gangrenous changes secondary to distended and thickened cecal wall, ileo-cecal junction was collapsed and inflamed, and hence bowel contents were milked relieving the obstruction. Thus, the mechanical obstruction which was not managed conservatively was corrected manually during exploration. On PCT day 16, patient's symptoms had subsided and his total leucocyte counts had recovered with ANC of 3,136/cumm. On PCT day 18 patient was started on oral sips of water, which he tolerated well. He was discharged on oral antibiotics. On PCT day 21 his bone marrow was under remission and subsequently patient was put on consolidation therapy.

Discussion

Neutropenic enterocolitis also referred to as typhilitis (from the Greek word "typhlon" that means cecum), is

Fig. 1 Erect abdominal X-ray showing multiple air-fluid levels

characterized by necrotizing inflammation of the cecum especially in leukemic children on chemotherapy [5]. Initially reported in children with acute leukemia, following immunosuppressive therapy for solid malignancies and transplants, but now it is also reported in adults [6]. NE is usually seen 7–10 days after the completion of chemotherapy, during the neutropenic phase. No association is found between the severity of neutropenia and the onset of NE or NE-related mortality. The most frequent symptoms include fever, abdominal pain, diarrhea, and lower gastrointestinal bleeding [7]. Pathogenetic mechanism of this syndrome is poorly understood. The disease appears to be the result of a combination of various host and microorganism's factors that include mucosal injury by cytotoxic drugs, neutropenia, and impaired host defense to intestinal organisms. Diagnostic criteria recommended include three basic elements: fever, abdominal pain, and bowel wall thickness of >4 mm by ultrasound or CT scan. On the other hand the value of bowel wall thickness in the diagnosis of typhilitis remains controversial because there is not a single study validating the sensitivity and specificity of radiologically detected wall thickness in literature yet [8]. The early management is by nasogastric decompression, bowel rest, antibiotics and supplemental parenteral nutrition. Surgery is indicated in cases with persistent gastrointestinal bleeding, bowel perforation, and uncontrolled sepsis [9]. In one study 117 cases of hematologic malignancies were enrolled, who were on various chemotherapeutic regimens, out of which 75.2 % had acute leukemias. The prevalence of NE in patients with acute leukemias admitted for severe neutropenia was 6.8 % and the mortality rate associated with this complication was 37.5 % [10].

Conclusion

Neutropenic enterocolitis is a severe gastrointestinal complication in patients who undergo aggressive chemotherapy. So a high index of suspicion, modern supportive care and timely intervention would save lives in this fatal condition.

Conflict of interest The authors declare no competing interests.

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