

The patient was managed with hemodialysis and discharged after 20 days, with normal renal functions. She remains healthy and well with normal growth and blood pressure on follow up.

Discussion

Severe pneumococcal infections have been associated with HUS, usually with a poor clinical outcome when compared with *Escherichia coli* gastroenteritis associated HUS(1). Association with *S. pneumoniae* is defined by culture of pneumococcus from a normally sterile site within a week before or after the onset of HUS. Clues to a pneumococcal cause, in addition to cultures, may include severe clinical disease, especially pneumonia, empyema, pleural effusion and meningitis; hemolytic anemia without a reticulocyte response; positive direct Coomb's test; and difficulties in ABO cross-matching or a positive minor cross-match(2). Plasmapheresis or administration of fresh frozen plasma may exacerbate HUS caused by *S. pneumoniae* and should be avoided(3).

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Two Children with Invasive Gastrointestinal Aspergillosis

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We report two immunocompromised infants aged six and four months with invasive gastrointestinal aspergillosis. Both patients presented with weight loss and diarrhea. The underlying disorders were combined immunodeficiency and transient hypogammaglobulinemia of infancy. The diagnosis of gastrointestinal aspergillosis was established by gastrointestinal endoscopy and histopathological examination of the tissue specimens. Both children responded well to Amphotericin B.

Key words: *Aspergillosis, immunodeficiency syndromes, gastrointestinal tract.*

Invasive aspergillosis is a life-threatening fungal infection that commonly affects immunocompromised patients. Respiratory tract is usually the main portal of entry and site of infection. But, involvement of gastrointestinal tract is rare(1). We report two infants with histopathologically proven invasive gastro-intestinal aspergillosis infection.

Case 1

A six-month-old male infant presented with weight loss and diarrhea for three months. Parents were third-degree relatives (cousins) and their two

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male children had died in their first year of life due to sepsis. His anthropometric measurements were as follow: weight 4300 gr (under 3rd percentile), height 62 cm (on the 10th percentile) and head circumference 40.5 cm (under 3rd percentile). He looked extremely exhausted and pale with moderate dehydration. Other physical examination findings were within normal limits except pretibial edema and tachypnea. The first laboratory findings were as follow: white blood cells: 20300/mm³, neutrophils: 9000/mm³ and lymphocytes: 9500/mm³, hemoglobin: 8.2 g/dL, hematocrit: 25.6%, platelets: 230000/mm³, blood urea nitrogen: 86 mg/dL, uric acid: 89.22 μmol/L, creatinine: 23.87 μmol/L total cholesterol: 1.06 μmol/L, aspartate aminotransferase (AST): 114 IU/L, alanine amino-transferase (ALT): 151 IU/L, total protein: 37.3g/L, albumin: 13.4 g/L, calcium: 1.675 mmol/L, sodium: 130 mmol/L, potassium: 3 mmoVL, IgG: 310 mg/dL (172-1069), IgM: 3.1 mg/dL (33-126), IgA: 69 (1.1-106) mg/dL, α-1-antitrypsin: 121 mg/dL (30-200). Blood, urine, fundus scanning for metabolic diseases, and abdominal ultrasonographic examination were normal. Microscopic examination of the stool revealed 1-2 leukocytes in every field, no red blood cells, no giardia and no ameba. The stool was not investigated for fungal hyphae or cryptosporidium since the fungal hyphae were seen on endoscopy.

Gastrointestinal system endoscopic examination revealed normal esophageal and antral mucosa but all surfaces of the duodenum were covered with pseudomembranes, Histo-pathological examination of the tissue specimens taken from the duodenum demonstrated mucosa necrosis and aspergillus hyphae, Immuno-phenotyping and other immunologic tests were as follows; anti-HIV negative, beta-2 microglobulin: 1,47 mg/L (1.2-2.5). Nitro blue tetrazolium (NBT) test was 80% with endotoxin and was 60% without endotoxin, CD3:37% (55-82), CD4:12% (27-57), CD8:26% (14-34), CD19:32% (9-29). CD25:2% (2-8). CD16+56:22% (10-22), CD95:7% (40-50), CD11a/CD18:52% (>75), CD11b/CD18:0% (2-5). CD11c/CD18:47% (>75), CD4/CD8:0.5. The expression of major histocompatibility complex class I and class II antigens were low. The diagnosis of combined immunodeficiency-bare lymphocyte syndrome plus

invasive aspergillosis was based on these findings and the child was given intravenous immunoglobulin (1 mg/kg/day for two days), liposomal amphotericin B (3 mg/kg/day intravenously for 3 weeks) along with parenteral nutrition. We have started an intravenous immunoglobulin treatment and prophylaxis against *Pneumocystis carinii* infection and referred him to a university hospital for bone-marrow transplantation.

Case 2

A 4-month-old male infant admitted to the hospital for watery diarrhea (3-4 times a day) and severe vomiting in the last month. The patient had been referred to the pediatric gastroenterology outpatients department for persistent vomiting with a pre-diagnosis of gastro esophageal reflux disease. He was the first child of second degree related parents.

Anthropometric measurements of this case were as follow: weight 5630 gr (between 3rd -10th percentiles). height 64 cm (on the 50th percentile) and head circumference 41.5 cm (on the 50th percentile).

On examination the abdomen was distended, but not tender. Other findings related to systems were normal. Complete blood count revealed white cell count: 11800/mm³, neutrophils: 6500/mm³, hemoglobin: 11.9 g/dL, platelets: 259000/mm³ and renal function tests were normal. This patient's the immunologic studies were as follow: Anti HIV negative, IgG: 315 mg/dL, IgM: 58 mg/dL, IgA: 36 mg/dL, CD3:65% (55-82), CD4:40% (27-57), CD8:23% (14-34), CD19:26% (9-29), CD16+56:7% (10-22) and NBT test 62%.

Abdominal ultrasonographic examination was normal. Gastroendoscopic investigation revealed an antral ulcer with fungal hyphae. Tissue specimen was taken and fungal hyphae were seen on microscopy. The stool was not investigated for the fungal hyphae in this patient either. This patient was also treated with Amphotericin B. The control endoscopic examinations showed normal duodenal mucosa. The child was followed-up for six months with the diagnosis of transient hypogammaglobulinemia of infancy. The second immunoglobulin levels were within normal limits.

Discussion

Extra-pulmonary aspergillosis produces different symptoms according to involved organs. The features of gastrointestinal tract involvement are: fever not responding to antibiotics, diarrhea, abdominal pain and vomiting. There may be signs of gastrointestinal hemorrhage or peritonitis(2). Localized gastrointestinal invasive aspergillosis is rare but involvement of the gastrointestinal tract is not uncommon in disseminated infection(3).

The diagnosis of invasive fungal infections remains challenging. A positive CT scan, culture or microscopic evidence of disease, detection of aspergillus antigens in serum are the ways to show aspergillosis infection. But the histo-pathological evidence of mycelial growth in tissue proves the invasive infection(1).

Symptoms of chronic diarrhea and vomiting in both of our patients were histopathologically explained as a result of localized duodenal aspergillosis infection. Chest radiographs throughout their hospitalization were normal and bowel may have been the initial portal of entry. Both patients did not have a clinical history of documented immunodeficiency. But the immunologic system searches revealed combined immunodeficiency in one case and symptomatic hypogammaglobulinemia in infancy and childhood in the second case. Primary immunodeficiency syndromes should be investigated when approaching an infant with chronic diarrhea(4).

The bare lymphocyte syndrome is a combined immunodeficiency resulting from the lack of expression of class I. HLA antigens at the cell surfaces of the human body(5). Bejaoui M, *et al.*(6) reported nine patients with bare lymphocyte syndrome similar to our first case whose clinical symptoms started at the mean age of 4.5 months with chronic diarrhea.

Opportunistic infections are not commonly reported with symptomatic hypogamma-globulinemia in infancy and childhood. There is a report of *Pneumocystis carinii* pneumonia in a patient with transient hypogammaglobulinemia of infancy, but we couldn't find any report describing aspergillus infection and hypogammaglobulinemia(7). It has been reported that chronic diarrhea has a

high incidence in infants with hypogammaglobulinemia(8).

Conclusion

Since chronic diarrhea may be the initial symptom of primary immunodeficiencies with invasive aspergillosis, endoscopic investigations and biopsies should be performed when suspected of intestinal mycosis. This diagnosis should be considered when immunocompromised patients have abdominal pain with or without distention, chronic diarrhea and fever.

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