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CASE REPORT

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Massive lower gastrointestinal hemorrhage caused by CMV disease as a presentation of HIV in an infant

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Abstract The gastrointestinal (GI) manifestations of acquired immunodeficiency syndrome in children are related to opportunistic infections like cytomegalovirus (CMV). CMV disease of the GI tract is a major cause of morbidity and mortality in immunocompromised patients: it typically produces mucosal ulcerations that can result in pain, bleeding, diarrhea, and GI perforation, often around the cecum. Preoperative diagnosis may be difficult, plain films and barium enema are often nonspecific, and endoscopic evaluation is impossible when there is massive bleeding. The patient usually needs surgery to establish the correct diagnosis and initiate appropriate treatment. The use of gancyclovir for CMV disease in the postoperative period has improved the prognosis.

Keywords Acquired immunodeficiency syndrome · Human immunodeficiency virus · Cytomegalovirus · AIDS · Gastrointestinal hemorrhage

Introduction

Cytomegalovirus (CMV) disease of the gastrointestinal (GI) tract (GIT) causes major morbidity and mortality in immunocompromised children, and its diagnosis should raise the suspicion of acquired immunodeficiency syndrome (AIDS). The incidence of CMV infection associated with symptomatic disease in children with human immunodeficiency virus (HIV) infection is between 30% and 60%. Immunocompromised children with CMV disease of the GIT present with nausea, vomiting, pain, diarrhea, and GI bleeding, which are relatively nonspecific symptoms.

Complications result from ulceration of the GI mucosa, usually in the colon. Lesions may be diffuse or focal, and the cecum may be the only area affected. In more severe cases, CMV may produce ischemic necrosis of the bowel wall, strictures, submucosal hemorrhage, toxic megacolon, and perforation. Surgery is often needed to establish the correct diagnosis. This report describes the case of an infant who presented with severe lower GI bleeding and progressive weight loss, in whom HIV infection was not recognized initially.

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Case report

A 17-month-old girl was admitted to a local hospital with pneumonia, malnutrition and anemia. She was treated with cefaclor, but after discharge developed severe, bloody diarrhea, necessitating readmission with dehydration and mild metabolic alkalosis. She was severely anemic (Table 1). A barium enema was normal. After failing to improve with multiple antibiotics and transfusions, she was transferred to our institution for investigation of the GI bleeding. Rectal examination revealed grossly bloody stool. She had an abnormal clotting profile (Table 1). Initial treatment included packed red blood cells, fresh frozen plasma, vitamin K1, netilmicin, and vancomycin. She continued to pass copious, bloody stools.

An exploratory laparotomy showed a dilated terminal ileum, the colon containing blood, and mesenteric lymphadenopathy. No bowel was resected. Postoperatively, significant GI bleeding continued and the child became increasingly unstable. A second laparotomy identified two cecal ulcers for which a right hemicolectomy, ileostomy, and colostomy were performed (Fig. 1). Histology suggested that the ulcers were due to ischemia. On postoperative day 4 she developed a productive cough and wheezing and perineal lesions suggestive of candidiasis. A chest radiograph showed perihilar and retrocardiac areas of pulmonary consolidation. Amphotericin B was commenced. On postoperative day 10 she began vomiting and had tonic-clonic seizures. A lumbar puncture was normal. Bleeding from the ileostomy increased. CMV infection was confirmed; histopathologically, CMV intranuclear inclusions were seen at the edge of a mucosal ulceration (Fig. 2). A HIV antibody test proved positive, and her parents were also found

Table 1 Laboratory findings (*HB* hemoglobin, *HCT* hematocrit, *WBC* leukocyte count, *PT* prothrombin time, *PTT* partial thromboplastin time)

	Hb (g%)	HCT (%)	WBC (/mm^3)	Platelet (/mm^3)	PT (%)	PTT (s)
Readmission to local hospital + prior to transfer	5.5	18	6900	60,000	95	40.5
At admission to tertiary center	3.4	11	6100	110,000	42	92
Day 1 post-hemicolectomy	16.8	51	6100	36,000	76	85

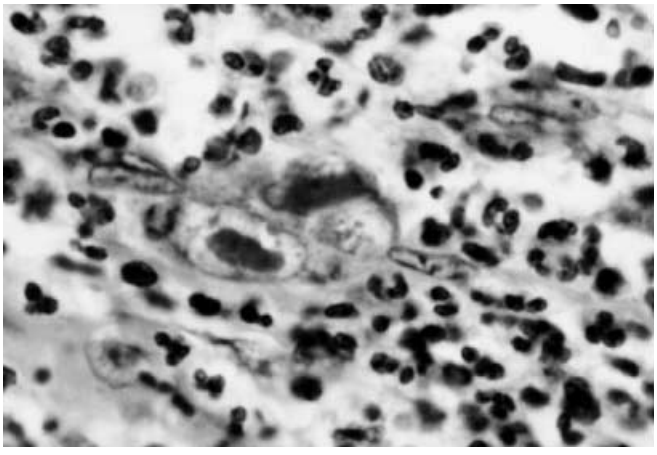

Fig. 1 Macroscopic findings of the resected ileocecal area showing the mucosal ulcerations

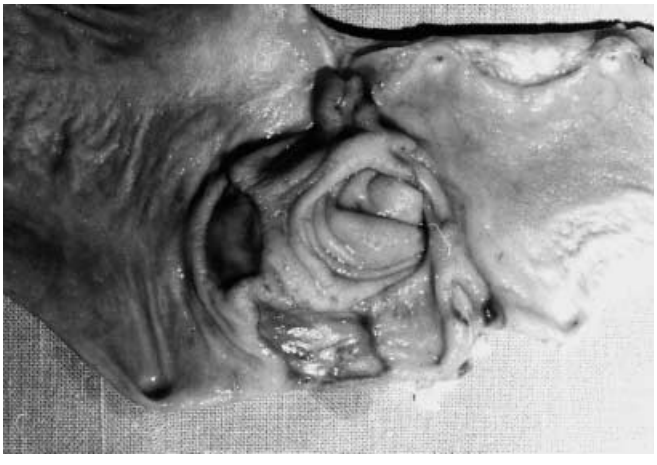

Fig. 2 A huge intranuclear inclusion surrounded by neutrophilic exudate (HE ×100)

to be HIV-positive. Her pulmonary status deteriorated, probably due to *Pneumocystis carinii* infection. Despite trimethoprim-sulfamethoxazole and gancyclovir therapy, she became progressively more hypoxic and developed multiple organ failure, resulting in death 2 days later.

Discussion

By December 1997, over 72,000 cases of AIDS in Brazil had been reported to the Ministry of Health. Approximately 3,700 of these were in children under 12 years, most of whom acquired the infection from their mothers. Perinatal transmission accounted for 88.8% of all cases in children reported up to 1997. This pediatric group comprises 3% of all cases reported to the National Coordination of Sexually Transmitted Diseases and AIDS [1]. Children born to HIV-positive mothers become infected during pregnancy, labor, and breast-feeding. In the United States, during the mid- and late 1980s, 80% of pediatric AIDS cases were vertically transmitted, whereas by the mid-1990s 90% were acquired perinatally. The mean age at diagnosis of perinatally-acquired disease is 18 months; 80% of all pediatric AIDS patients are under the age of 5 years when diagnosed [2]. In Brazil, 81% of new pediatric AIDS cases reported between 1980 and 1997 were in children under the age of 4 years [1].

Many of the GI complications of AIDS are due to the numerous opportunistic infections that occur in these patients. The mucosa of the GIT serves as a reservoir for HIV-infected mononuclear cells. Bacteria and viruses like CMV or their products are potential activators of these cells. Infection results in the release of various inflammatory mediators, which promote and perpetuate the inflammation of the GI mucosa [3]. CMV infections associated with symptomatic disease in children with HIV infection have not been well-documented. Kitchen et al. [4] found a prevalence of CMV in children with HIV infection of approximately 30%, and the incidence of CMV disease was 9%.

The impact of CMV disease on mortality is less clear. Among pediatric patients with positive CMV cultures and evidence of CMV disease, survival is poor: 33% after 1 year and 13% after 2 years [4]. CMV infection of the GIT is associated with ulceration, hemorrhage, and perforation [2]. CMV most commonly infects the endothelial cells of the capillaries and venules of the enteric mucosa and mesenchyme. This causes vasculitis, thrombosis, ischemic necrosis, and ulceration [3, 5]. CMV can infect the small bowel and produce duodenitis and enteritis. Colitis is more frequent in children with AIDS, and is typically heralded by hematochezia, mucous stools, abdominal pain, and fever [3] and may lead to typhlitis, pneumatosis, strictures, and frank perforation [3, 5]. Involvement of the colon by CMV may be diffuse or focal, particularly around the cecum and adjacent terminal ileum [3, 6].

HIV patients with intestinal perforation often have few clinical signs to suggest an acute abdomen; there is minimal abdominal pain, no fever, and a normal leukocyte count [6]. Plain films of the abdomen are non-

specific or show colonic distension with multiple air-fluid levels without evidence of obstruction. On barium enema, mild involvement of the colon may reveal diffuse mucosal granularity, aphthous ulcers, spasm, and thickened folds similar to inflammatory bowel disease. Computed tomography of the abdomen may determine the extent of CMV colitis and its complications [3].

The definitive diagnosis of CMV infection of the GIT can be obtained by cultural isolation of CMV in GI tissue, detection of CMV antigen or the CMV genome in tissue, or detection of typical CMV cytopathology [7]. The massive bleeding makes pre-operative endoscopic evaluation difficult, and many of these patients are referred to surgery with a presumptive diagnosis of colonic angiodysplasia. Surgery will establish the correct diagnosis and enable initiation of appropriate treatment [8]. The appearance of the perforated bowel in CMV infection is typical: there are multiple areas of mucosal ulceration with one or more leakage points within deep ulcers. Construction of a stoma is advisable when resection of the necrotic bowel is required or when there is concern about healing of an anastomosis [6]. The most frequent postoperative complications are sepsis and *P. carinii* pulmonary infection. Intestinal perforation caused by CMV has 70% mortality and 100% morbidity [9]. Intravenous gancyclovir and foscarnet in the postoperative period should be commenced early. Gancyclovir is preferred as it is easier to administer [10]; its main side effect is bone-marrow failure, in which case it may be replaced by foscarnet [11, 12]. Oral gancyclovir is effective in secondary prophylaxis and provides an alternative to intravenous maintenance treatment [10].

Conclusion

In conclusion, pediatric HIV patients often have GI manifestations of their disease including nonspecific diarrhea and malnutrition. Impaired immunity associated with CMV infection can culminate in devastating and fatal complications. It should be remembered that massive lower GI bleeding can be caused by CMV infection in immunocompromised children, especially those who are HIV-seropositive. A high index of suspicion may lead to earlier diagnosis and the prompt commencement of effective therapy to increase survival.

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