Chapter 94
Chronic Diarrhea

Nasrin Behniafard and Majid Aflatoonian

A 5-month-old male infant was referred with a chief complain of chronic diarrhea, failure to thrive and irritation during defecation. He was born from consanguineous parents and he was on regular formula. His weighed 5700 g which was under 3rd percentile, his head circumference was 42 cm, between 25th and 50th percentile and his height was 64 cm which was at 25th percentile. The patient was pale and had oral candidiasis and mild to moderate eczematous lesions on his face. His BCG vaccine scar was not visible.

The boy was the result of cesarean section from consanguineous parents with normal anthropometric measures at birth. He had early meconium passing and received routine vaccination. He also had a history of recurrent oral candidiasis with poor response to medications and one admission due to pneumonia and chronic diarrhea. Hepatosplenomegaly, abdominal distension or other abnormal findings were not detected in physical examination. Anal fissure was visible at 4 o'clock (Fig. 94.1a).

Q1. What is the least likely diagnosis?

A. Food allergy
B. Immunodeficiency
C. Inflammatory bowel disease
D. Celiac disease

Answer: *The correct answer is* ***D.***

N. Behniafard (✉)
Department of Allergy and Clinical Immunology of Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

M. Aflatoonian
Department of Pediatrics Gastroenterology of Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

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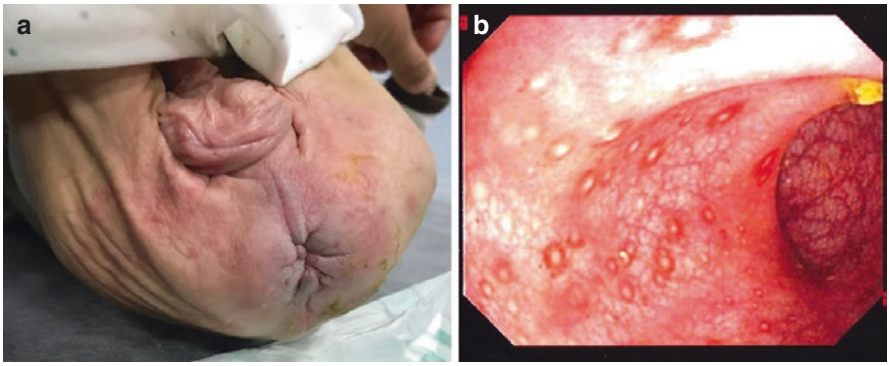

Fig. 94.1 (**a**) Anal fissure was visible at 4 o'clock and (**b**) Colonoscopy showed fragile mucosa and multiple ulcers and aphthous lesions in ascending and transverse colon, in a 5-month-old boy

Non-IgE-mediated food allergy such as food-protein induced enterocolitis syndrome can be one of the diagnoses, presenting with vomiting, bloody diarrhea and failure to thrive. This condition is most commonly provoked by cow's milk or soy protein-based formulas. Stool examination is often positive for occult blood, neutrophils and eosinophils. Diagnosis can be established when elimination of the responsible allergen leads to resolution of symptoms and also by oral food challenge test provoking similar symptoms [1].

Severe combined immunodeficiency usually presents within the first few months of life with chronic diarrhea, pneumonia, otitis media, and sepsis. Anthropometric measures are normal at birth, but failure to thrive usually develop as a result of infections and persistent diarrhea [2]. Proper workup for primary immunodeficiency is mandatory in this patient due to the history of failure to thrive, parental consanguinity, chronic diarrhea and failure to thrive.

Inflammatory bowel disease (IBD) is rare in infants but should be considered in any patient complaining of chronic diarrhea with/without defecation complaints [3]. Early onset IBD can therefore be one of the likely diagnoses.

Celiac disease is an autoimmune disease induced by ingestion of gluten. Gluten is not yet included in the infants diet as he was on regular formula exclusively, ruling out celiac as a differential diagnosis [4].

Neutropenia or lymphopenia were not detected in CBC and further workup, including immunoglobulin levels, antibody responses, lymphocyte subset counts, nitroblue tetrazolium test, and anti-*Saccharomyces cerevisiae* antibodies were in normal ranges. Positive findings were inflammatory pattern of stool and high level of stool calprotectin.

The patient was prescribed amino acid based formula with an impression of food allergy and was visited 1 month later due to refractory diarrhea and prolonged fever with no improvement of his symptoms. He was admitted for further workup. Physical

examination at the time of admission revealed oral candidiasis and persistence of an unusually deep anal ulcer, along with poor weight gain during the last month.

Q2. Which are the following evaluations is least necessary in this patient?

A. Endoscopy
B. Small bowel follow through
C. HIV PCR
D. Rectal manometry

Answer: *The correct answer is* ***D.***

Upper and lower endoscopy are essential due to inflammatory pattern of stool and unresponsiveness to amino acid based formula. Small bowel follow-through is recommended in patient suspected for IBD [4].

Rectal manometry helps in the diagnosis of Hirschprung disease or functional defecation disorders. Our patient did not have a history of delayed meconium passage or abdominal distension, and deep and unusually located anal ulcer is rare in Hirschprung [5]. Chronic diarrhea, oral candidiasis and failure to thrive are common presenting features of HIV infection in infants and should prompt proper workup, which is either qualitative HIV-1 DNA PCR or HIV-1 qualitative RNA assays [6].

Colonoscopy showed fragile mucosa, multiple ulcers and aphthous lesions in ascending and transverse colon (Fig. 94.1b). Pathology of colonic tissue biopsy showed villous blunting and acute on chronic inflammation. Cytomegalovirus and mycobacterium PCR from colonic tissue was negative along with HIV DNA testing.

Q3. All of the following statements are true regarding the most possible diagnosis, except:

A. Ileal involvement is common
B. Therapeutic response to salicylates is poor
C. The etiology of this condition is commonly monogenic
D. Resection surgery is contraindicated

Answer: *The correct answer is* ***A.***

Q4. What is the best treatment option in this patient?

A. Prescription of prednisolone
B. Prescription of azathioprine
C. Prescription of anti-TNF
D. Hematopoietic stem cell transplantation

Answer: *The correct answer is* ***D.***

Ileal involvement is not uncommon in very-early-onset IBD (VEO-IBD) [7]. Targeted gene panel revealed a homozygous null mutation in IL-10 receptor subunit beta (IL10RB) gene and the patient was referred for bone marrow transplantation [3].

Practical Points

- Very-early onset inflammatory bowel disease (VEO-IBD), refers to the onset of IBD under 6 years of age
- Presence of non-specific colitis, higher frequency of pan-colitis, perianal involvement, and fistula resistant to biologic agents distinguish VEO-IBD differs from other types of pediatric-onset IBD
- Early onset IBD (EO-IBD), i.e. onset of IBD before 10 years of age, and VEO-IBD account for most of the genetic causes of IBD
- Early-onset IBD is associated with immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX), X-linked lymphoproliferative (XLP) disease and chronic granulomatous disease (CGD)
- Hematopoietic stem cell transplantation can eliminate signs of intestinal involvement in IBD associated with mutations in either of the *IL10*, *IL10RA*, or *IL10RB* genes

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