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Histiocytic disorders of the gastrointestinal tract

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Summary The morphologic diagnosis of histiocytic lesions of the gastrointestinal tract can be challenging, and several disorders have to be considered in their differential diagnosis. We present one of the most widespread examples of xanthomatosis of the gastrointestinal tract published so far and give a short review on histiocytic disorders of the gastrointestinal tract in general. The primary histiocytic disorders of uncertain origin, Rosai-Dorfman disease, Langerhans cell histiocytosis, and Erdheim-Chester disease, are addressed. Reactive and infectious conditions such as xanthomatosis, xanthogranulomatous inflammation, juvenile xanthogranuloma, Whipple's disease and malacoplakia are discussed as well. We also briefly go into primary histiocytic disorders of neoplastic origin, systemic diseases with secondary gastrointestinal tract involvement like the lysosomal storage disorders, and pigmented lesions. Using a panel of histochemical stains and immunohistochemical markers, together with conventional microscopy, clinical information, and imaging studies, the diagnosis of histiocytic disorders of the gastrointestinal tract can be established in most instances.

1. Introduction

Intestinal histiocytic disorders comprise a quite diffuse group of disease entities, and their diagnosis can be challenging. *Histiocytes* comprise roughly the cells of the mononuclear phagocyte system. They differ in phenotype and function in health and disease. Macrophages and dendritic cells represent two of the most important of these cell types [1]. Macrophages process antigens by phagocytosis and produce cytokines, which play an important role in inflammation, fibrogenesis, and other processes [1,2]. Dendritic cells present antigens to T cells and play a major role in the activation of the immune response to external stimuli, contributing to the maintenance and initiation of immunity and tolerance [3,4].

Xanthomatosis and xanthogranulomatous inflammation are among the most frequent intestinal histiocytic proliferations. However, only a limited number of cases with xanthomatosis involving larger segments of the gastrointestinal tract (GIT) have been published [5]. Our index case is a case of xanthomatosis involving the colon, appendix, and ileum, thereby representing one of the most widespread examples published so far. Afterward, we briefly review the literature on intestinal histiocytic disorders in general. First,

Abbreviations: CD, cluster of differentiation; ECD, Erdheim-Chester disease; GIT, gastrointestinal tract; LCH, Langerhans cell histiocytosis; PAS, periodic acid–Schiff; RDD, Rosai-Dorfman disease.

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we address the primary histiocytic disorders of uncertain origin, Rosai-Dorfman disease (RDD), Langerhans cell histiocytosis (LCH), and Erdheim-Chester disease (ECD). Reactive and infectious conditions such as Whipple disease and malacoplakia are discussed as well. We also shortly go into primary histiocytic disorders of neoplastic origin and systemic diseases with secondary GIT involvement, like Tangier disease and some of the lysosomal storage disorders. Our review ends with discussion of pigmented histiocytic aggregates.

2. Report of a case

2.1. Patient history

Our index case is a 24-year-old man with "partial" albinism, presenting with pale skin and yellow hair. He had early reduced growth and underwent growth hormone treatment. His adult height is 158 cm. His face shows some dysmorphic features with a short philtrum and a flat nose. He has mild psychomotor retardation. His serum cholesterol and lipids are in the reference range. At 8, 16, and 24 years old, he was treated by myotomy for achalasia. At the age of 13 years, he had xanthomatous osteomyelitis of the right humerus and underwent surgery and systemic antibiotic treatment. Roughly from the age of 16 years, he had recurrent diarrhea and abdominal pain. Colonoscopy performed at ages 16 and 20 years showed accumulation of foamy histiocytes, chronic inflammation, and ulcerations. Systemic antibiotic treatment, 5-aminosalicylic acid, and steroids were not effective. At the age of 22 years, his complaints changed for the worse. He had watery diarrhea, right-sided megacolon, and fever and underwent subtotal colectomy. The postoperative period was uneventful.

2.2. Pathologic and genetic findings

The subtotal colectomy specimen was 46 cm long after fixation and consisted of 3 cm of the distal ileum, the cecum including the appendix, the ascending and transverse colon, and the proximal part of the descending colon. The mucosal surface was pale yellow and slightly edematous. The colon was dilated and measured up to 12 cm in circumference.

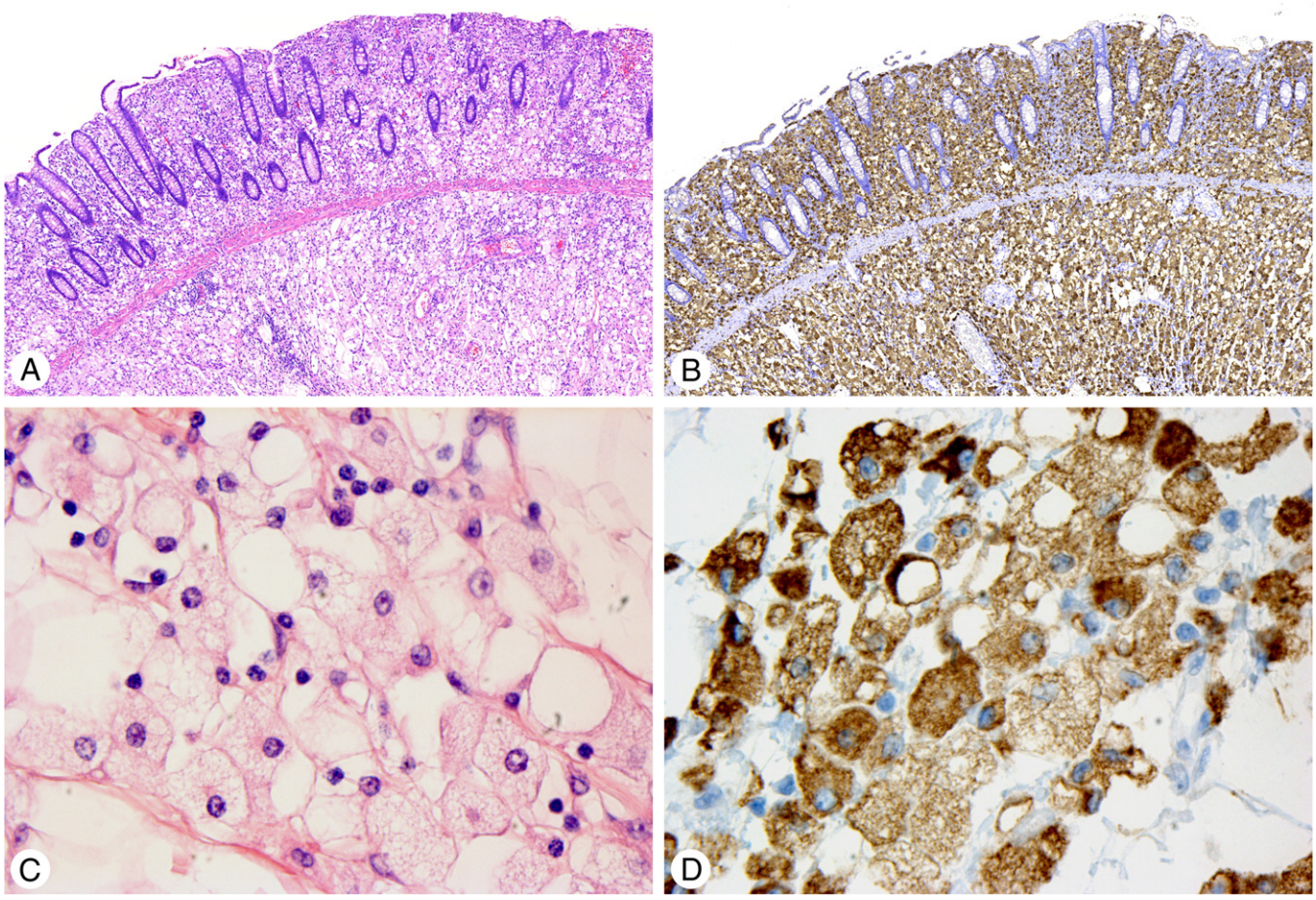

Fig. 1 Xanthomatosis of the colon. A, The lamina propria and submucosa are packed with foamy histiocytes (hematoxylin and eosin [H&E], ×50). B, The histiocytes strongly express CD68PG (×50). C, At higher magnification, the foamy, vacuolated appearance of the histiocytes is appreciated (H&E, ×630). D, The histiocytes express CD163 (×630).