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Hereditary Ichthyosis With Gastrointestinal Manifestations

A Case Report

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Abstract: Gut inflammation and defect in the gut mucosal barrier appear to have a correlation with skin diseases and vice versa. The coexistence of hereditary ichthyosis with active colitis has never been reported. We present a 17-year-old female with ichthyosis since birth, abdomen pain for 3 months, with acute colitis. After the initial diagnosis, the patient was started on antituberculous therapy (ATT), steroids, and mesalamine. She followed up with us for 1 year where there was resolution of symptoms. Steroids were stopped after 16 weeks, mesalamine was stopped after 20 weeks in view of low absolute neutrophil counts and ATT was stopped after 1 year. She was asymptomatic post 18 months of stopping ATT.

Key Words: gut-skin axis, ichthyosis, colitis, intestinal tuberculosis, Crohn disease

INTRODUCTION

Many dermatological ailments may have associated gastrointestinal issues. Inflammatory bowel disease has a well-known association with various skin manifestations, whereas gluten sensitivity is known to be associated with dermatitis herpetiformis (1). Alterations in gut functions may be due to primary dermatological diseases (1). To understand the relationship between this gut-skin axis for various cutaneous diseases, in association with gut manifestations, may aid in a new opportunity for developing various novel therapeutic strategies. Ichthyoses represents a group of cutaneous disorders with abnormal epidermal differentiation with the cutaneous scaling resembling to the scales of a fish (2). Scaling can be generalized, or localized, and can be associated with a variety of additional cutaneous and/or systemic manifestations (2). We present a 17-year-old female with ichthyosis since birth and abdomen pain for 3 months with acute colitis.

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CASE REPORT

A 17-year-old female presented in December 2020 with diffuse scaly lesions all over her body since birth (Fig. 1) and periumbilical and epigastric intermittent abdominal pain for 3 months not associated with food intake. There was also presence of mucus on passing stools without blood in stools or diarrhea. She had not achieved menarche. She is first born of 3 siblings of third-degree consanguineous marriage. Younger sister aged 15 years also had similar scaly lesions since birth. Youngest brother (11 years) was asymptomatic. On examination, the girl had a height of 142 cm (<3rd centile as per Indian Academy of Pediatrics growth charts) and weight was 24.5 kg (<3rd centile as per Indian Academy of Pediatrics growth charts), and sexual maturity rate of 11. She had dry scaly lesions suggestive of ichthyosis present all over her body. On abdominal system examination, she had tenderness in epigastric region and bowel sounds were normal. There was no organomegaly. Other systems were normal. On admission, investigations showed hemoglobin was 7.8 g/dL, total leukocyte count of 7500 cells/cumm (polymorphs 76%, lymphocytes 17%), platelets of 668 000 cells/μL, erythrocyte sedimentation rate 32 mm at end of 1 hour. Biochemistry showed serum bilirubin 0.4 mg/dL, aspartate aminotransferase 55 U/L, alanine aminotransferase 29 U/L, total protein 6.4 g/dL, albumin 2.7 g/dL, alkaline phosphatase 212 U/L, sodium 133 mEq/L, potassium 4.7 mEq/L, total calcium 10.55 mg/dL, phosphorus 3 mg/dL, pH 7.41, bicarbonate 22 mmol/L, lactate 3 mmol/L, amylase 57.63 IU/L, and lipase 16 IU/L. Hormonal work-up for primary amenorrhea revealed follicle-stimulating hormone.=0.56 mIU/mL, luteinizing hormone <0.1 mIU/mL, estradiol <5.0 pg/mL, Free T3 = 1.57 pg/mL, Free T4 = 1.12 ng/dL, thyroid stimulating hormone = 3.12 μIU/mL. Stool for calprotectin was 84.9 mcg/g and tuberculin skin test was 20 mm induration at 48 hours. Xpert MTB/Rif assay of gastric lavage was negative. X-ray chest showed right upper lobe infiltrates. Ultrasound abdomen showed hepatomegaly with increased echotexture along with long segment bowel wall thickening involving distal ileum, cecum, and ascending colon and chronic small bowel obstruction suggestive of tuberculosis (TB). Contrast-enhanced computed tomography abdomen and pelvis showed diffuse circumferential wall thickening in the terminal ileum and ileocecal junction, maximum wall thickness of approximately 11 mm with luminal narrowing with dilatation of the proximal ileal loop. Few enlarged mesenteric lymph nodes were seen out of which few were necrotic (Fig. 2). Upper gastrointestinal endoscopy was normal. Flexible colonoscopy could be negotiated only till the transverse colon. Erythematous mucosa with large ulcers with irregular punched-out margins with gray dirty looking base with narrowing seen in the transverse colon (Fig. 3). Biopsy from the colon tissue was negative for MTB on Xpert Rif/MTB. Histopathology of duodenal mucosa showed mild lymphoplasmacytic infiltrates without ulceration, crypt distortion, or granuloma. Transverse colon showed distorted architecture with crypt branching, moderate to dense lymphoplasmacytic infiltrates with many eosinophils, neutrophils, and lymphoid aggregates with cryptitis without granulomas. Esophagus, pylorus, descending colon, sigmoid, and rectum showed normal histopathological findings. Whole

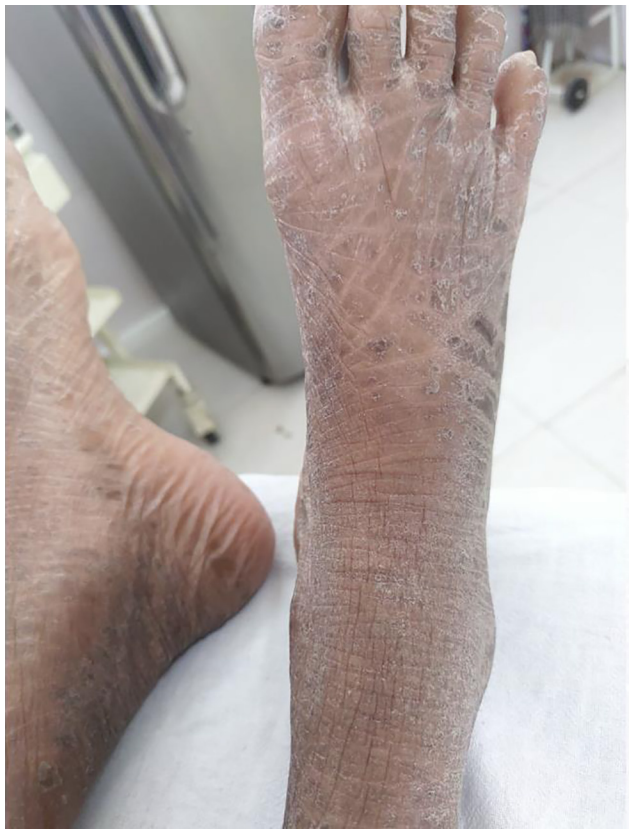

FIGURE 1. Diffuse scaly lesions presented on patient's feet.

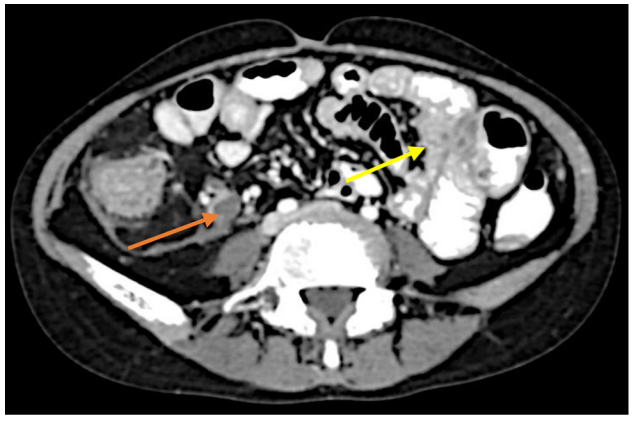

FIGURE 2. Diffuse circumferential wall thickening in the terminal ileum and ileocecal junction with luminal narrowing (yellow arrow) and necrotic lymph nodes (orange arrow) noted in axial section of contrast-enhanced computed tomography (CECT) abdomen.

exome sequencing could not be done in view of nonaffordability. With the consideration of positive tuberculin skin test and radiological features, she was started on antituberculous therapy (ATT) consisting of isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) for 4 months and Isoniazid, Rifampicin, Ethambutol for 8 months. In view of histopathological findings consistent with cryptitis and active colitis, a pulse dose of intravenous (IV) Methyl Prednisolone (2 mg/kg/d) for 3 days followed by oral

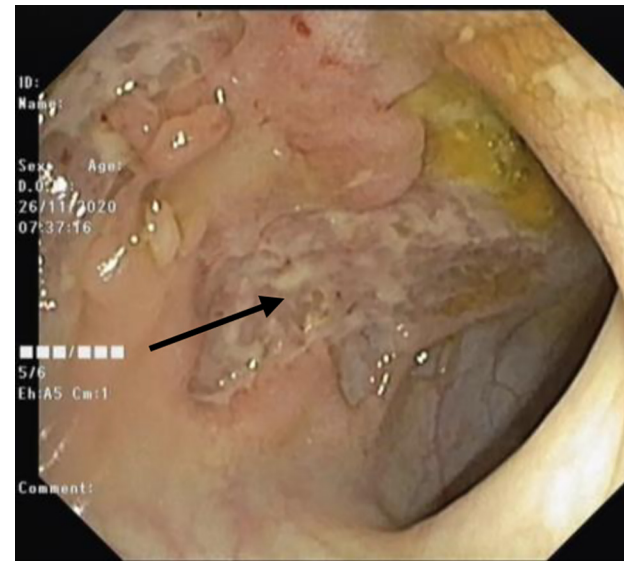

FIGURE 3. Erythematous mucosa with large ulcers with irregular punched-out margins with gray dirty looking base seen on colonoscopy.

prednisolone for a total of 16 weeks (2 mg/kg/d for 4 weeks followed by gradual tapering). Additionally, oral mesalamine (50 mg/kg/d) was given for 20 weeks and stopped in view of low absolute neutrophil count. Ultrasound abdomen on follow-up after 7 months of therapy showed IC valve thickening. A repeat colonoscopy showed narrowing of the ascending colon with pseudopolyps around the narrowing and scope could not be negotiated around the narrowing and hence cecum and ileocecal valve could not be studied. Previously seen transverse colon ulcers were resolved. Histopathology of endoscopic colonic biopsy was suggestive of moderate chronic colitis comprising of lymphocytes, plasma cells and a few eosinophils. There were no crypt architecture distortion, crypt loss, crypt abscess, cryptitis, or granuloma. TB MGIT culture of colonic biopsy did not grow MTB after 6 weeks.

DISCUSSION

Ichthyosis can be congenital (ichthyosis vulgaris or familial ichthyosis) or acquired (secondary, new-onset, or paraneoplastic) (3). Most of the reported cases are quite benign (3). Both familial and acquired ichthyosis (AI) are clinically and histologically similar (3). Various cases of AI coexisting with gastrointestinal tract diseases have been reported like dermatomyositis in a patient with hepatocellular carcinoma (4), ichthyosis with celiac disease (5) and AI with esophageal (6) and gastric carcinoma (7). Menni et al. (5) reported significant improvement in skin lesions after 6 months of gluten-free period. Katsanos et al. (3) reported the first case of AI in a patient with ulcerative colitis in 2004. Their patient was diagnosed case of ulcerative colitis for 3 years and was on sulfasalazine and with use of local preparation with 5% urea and 5% NaCl, they were able to get remarkable results in 2 months (3).

Similarly, Saad et al. (8) reported the first case of AI in association with lymphocytic colitis in 2019. Fry et al. (9) have reported alterations in the jejunal mucosal morphology with ichthyosis and a decrease of succinic dehydrogenase causing altered metabolic activity of the intestine on intestinal biopsies in patients with ichthyosis vulgaris. Netherton syndrome is a severe entity of ichthyosis associated with Gastrointestinal malabsorption because of jejunal villous atrophy (10). Many children had an associated

history of constipation, elevated serum magnesium and calcium levels (10). Intestinal mucosa regulates inflammation by secretion of cytokines (10). Small intestine controls T helper 17 cells (Th17) and their elimination via its mucosa. Interlukin-22 (secreted from Th17) binds to receptors on keratinocytes there by increasing the antimicrobial defense of the skin and thus plays an important role in the clearance of skin infections (10). We were unable to find any case report of association of hereditary ichthyosis with colitis or intestinal TB, whereas all the available case reports showed association with AI.

Our patient was started on ATT in view of positive Interferon Gamma Release Assay with colitis although cultures were negative, and histopathology did not show granulomas. However, inflammatory bowel disease could not be ruled out in the patient, as there was diffuse colitis which is not seen with TB. The mainstay management of hereditary ichthyosis is emollients and treatment of supera-added infection (2). We gave both ATT and mesalamine in our patient due to ambiguity in diagnosis.

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Informed patient consent was obtained from adult if under 18 years in this case report.

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