Cronkhite-Canada Syndrome

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Introduction:

Cronkhite-Canada syndrome (CCS) is a gastrointestinal polyposis syndrome with distinct ectodermal findings. The course may be rapidly progressive with a grave prognosis. Herein we report a case of CCS.

History of Present Illness:

A 77 year old woman was found to have a rectal polyp. She reported a history of benign but large sigmoid colon polyp which required a partial colectomy in 2002. Later, in 2005, she developed a right colon cancer requiring surgical treatment followed by chemotherapy. She has had loose stools since with frequent incontinence and had been rendered a diagnosis of Crohn disease. However, it is unclear how this diagnosis was reached. She has been on prednisone and Asacol since.

Past Medical History:

Significant for hypothyroidism, hypertension, cardiovascular disease, angioplasty, and severe arthritis.

Sigmoidoscopic Examination:

A large lesion with fronds measuring 5 to 6 cm was noted at 11cms from the anal verge on a sigmoidoscopic examination in late 2008. Due to its large size, it could not be removed endoscopically.

Procedure:

A proctocolectomy with an end ileostomy was performed.

Pathology: The submitted resection specimen revealed broad based polyps and the largest of these measured 8cm. The polyps were remarkable for cystically dilated, tortuous crypts containing inspissated mucin in edematous lamina propria. The intervening non-polypoid lamina propria was edematous too. A tubulovillous
adenoma with high grade dysplasia was also noted, which had features typical of a tubulovillous adenoma and lacked the edematous lamina propria seen in other areas.

Discussion:

Cronkhite-Canada syndrome was first described by Drs. Cronkhite and Canada in 1955 as “An unusual syndrome of polyposis, pigmentation, alopecia and onychotrophia”. The patient age ranges from 30 to 80 years but the syndrome usually presents after 50. Men and women are equally affected. Although it is worldwide in distribution, most cases are reported from Japan, Europe, and the US. All of these cases are sporadic and there is no known genetic link. Distinct ectodermal findings include skin pigmentation, nail changes, and hair loss. The hair loss is rapid and may occur in the first few weeks of presentation. The skin lesions are usually manifested in the form of light to dark brown macules on the extremities, face, neck, palms, and soles.

The usual clinical presentation, however, is that of diarrhea with abdominal pain, protein losing enteropathy and associated weight loss, weakness, paresthesias, and xerostomia. Malabsorption is associated with the degree of small bowel mucosal injury. Patients report 5-7 loose bowel movements per day. The diarrhea may be bloody and the blood loss may be significant to require transfusions. The disease tends to wax and wane but the course may be rapidly progressive. The laboratory findings include hypoproteinemia, particularly hypoalbuminemia, anemia, electrolyte imbalance, and deficiencies of vitamins (vitamin B12) and minerals (zinc and magnesium). It is unclear whether the nutritional deficiency associated with Cronkhite-Canada syndrome is an etiologic factor or a consequence of the syndrome. Importantly, the electrolyte imbalance may be severe and may lead to seizures or tetany.

Differential Diagnosis:

These morphologic findings are not specific and the differential diagnosis includes juvenile polyposis syndrome (JPS), which is the most common GI hamartomatous polyposis syndrome and Cowden syndrome.

Juvenile polyposis syndrome (JPS) was first described by McColl et al in 1964. It is an autosomal dominant polyposis syndrome with germline truncating mutations in DPC4/SMAD4 on chromosome 18 (most commonly), also BMPR1A mutations in some patients. Most cases present before 30 years. Congenital birth defects including malrotation of the gut, heart and GU tract are reported in 15% of the cases.

Cowden Syndrome was described by Lloyd and Dennis in 1963. Like JPS, it too is an autosomal dominant syndrome. It is associated with a germline mutation in the PTEN gene on chromosome 10. The gastrointestinal hamartomatous polyps are quite variable in structure and content, but are usually small and lack the edema of C-C polyps. They show no predilection towards dysplasia or malignancy. However, the hamartomas in Cowden syndrome affect all the three germ cell layers but most commonly arise from the ecto and endodermal elements. Therefore, mucocutaneous lesions namely trichilemmomas, acral keratoses, and oral papillomas are commonly seen. Breast lesions, benign and malignant, affect the majority of female patients with the syndrome and include fibroadenomas, fibrocystic disease, and adenocarcinomas. Other abnormalities including thyroid, central nervous system, genitourinary, and endometrial are also associated with this syndrome.
References:


