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Case Report

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Protein-Losing Enteropathy, Anasarca and Dermatological Manifestations on People of Advanced Age: Don't Overlook the Diagnostic Hypothesis of a Cronkhite Canada Syndrome

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Abstract

Cronkhite-Canada syndrome is a rare and non-genetic syndrome of unknown etiology, characterized by diffuse gastrointestinal polyposis, the dermatological triad (nail distrophy, hyperpigmentation, alopecia), diarrhea, weight loss and abdominal pain.

Herein, we describe a late-onset case that experienced relief after prednisone treatment.
It is very important keep in mind the clinical hypothesis of this syndrome, because an early diagnosis can help reduce morbidity and mortality associated with this pathology, which is often life threatening.

Keywords: Cronkhite-Canada syndrome; dermatological triad; gastrointestinal polyposis syndrome.

Background

Cronkhite-Canada syndrome (CSS) is a rare and non-genetic syndrome of unknown etiology, characterized by diffuse gastrointestinal polyposis, the dermatological triad (nail distrophy, hyperpigmentation, alopecia), diarrhea, weight loss and abdominal pain.

More than 500 cases have been reported in the literature, but after a sensitive search on Pubmed there are only 4 papers (1-4) in English language describing a late onset on people over the age of 80 years, in the last 10 years.

We describe an 87-year-old man in observation for cachexia, anasarca and diarrhea, who after clinical manifestations (cutaneous and gastrointestinal), experienced relief after prednisone treatment.

Although the pathology is unusual and the manifestation on people of advanced age does not suggest a syndrome, the recognition of the association between cutaneous and gastrointestinal manifestations may lead to early diagnosis and can help reduce morbidity and mortality associated with this pathology, which is often life threatening.

Case report

An 88-year-old patient came to our attention, referred by the general practitioner, for cachexia, persistent diarrhea and edema of the lower limbs.

History showed: dysmetabolic syndrome (hypertension, dyslipidemia, diabetes mellitus II), mild chronic kidney disease.
In the previous year he performed an esophagogastroduodenoscopy, positive for multiple polyposis and duodenal brunneroma and a colonoscopy, positive for multiple colon polyps and ileocecal valve polyp.

A physical examination showed pitting lower limb edema, sarcopenia, globular abdomen with palpable liver , dry skin and mucous membranes, onycholysis. It also showed skin with dyschromia and melanosis, especially on the palm of the hand, alopecia and nail dystrophies.

Laboratory tests showed: *hypoalbuminemia and hypoprotidemia (protein 4 g/dl, albumin 48.6%), hypokalemia (1.9 mEq/l), macrocytic anemia (Hb 12.9 g/dl, MCV 108), mild thrombocytopenia (119,000-87,000/mm3), hypophosphoraemia (1.8 mg/dl), hypomagnesemia (1.3 mg/dl), non-significant proteinuria (649 mg/24 hours), mild monoclonal component non IgGk, low cholesterol levels (total cholesterol 69 mg/dl, HDL 23 mg/dl, LDL 33 mg/dl), Bence Jones negative, calprotectin increased (996 ug/g : grey area 50-100), slight reduction in faecal elastase (113 microg/g), lipase, calcitonin, gastrin within the limits, elevated chromogranin during proton-pump inhibitor therapy (> 700 ug/l), clostridium and 5 OH indoleacetoacetic negatives, slight elevation of IgG4 (144 mg/dl; normal 8-140 mg/dL).*

Abdominal ultrasound showed ascites and Thorax X ray minimal pleural effusion.

We formulated the clinical problem: presence of a dermatological triad (changes in the skin, hair and nails), anasarca and diarrhea in a old man with dysmetabolic syndrome (fig 1,2) No: 3,4

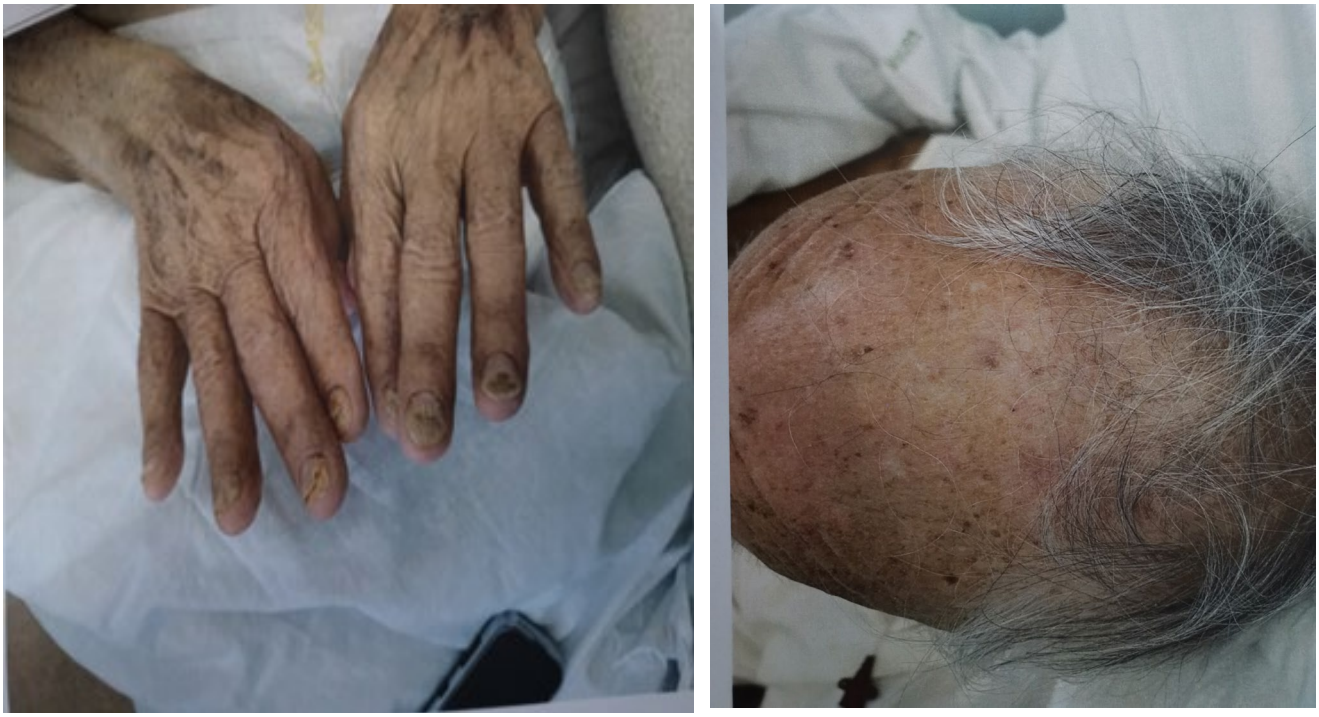

Figure 1 and 2: Dermatological triad of the patient

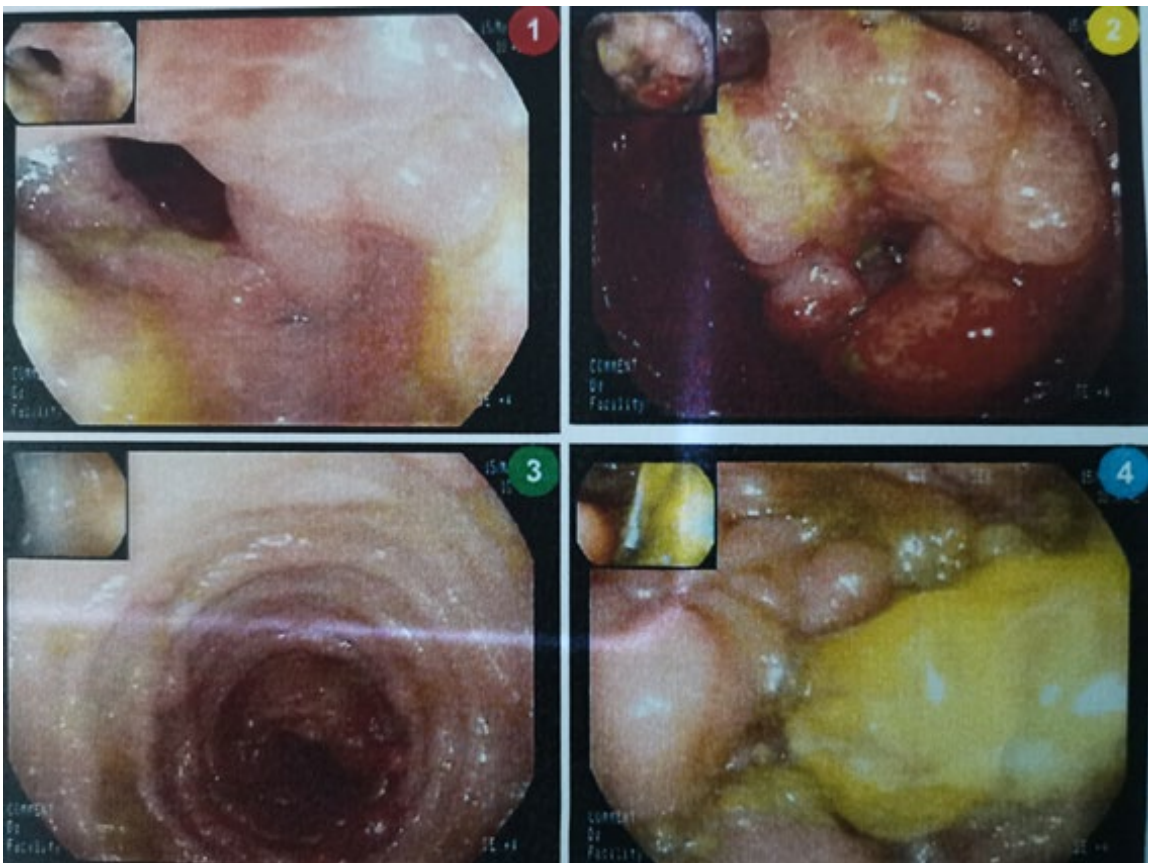

Figure 3: Colonoscopy of the patient

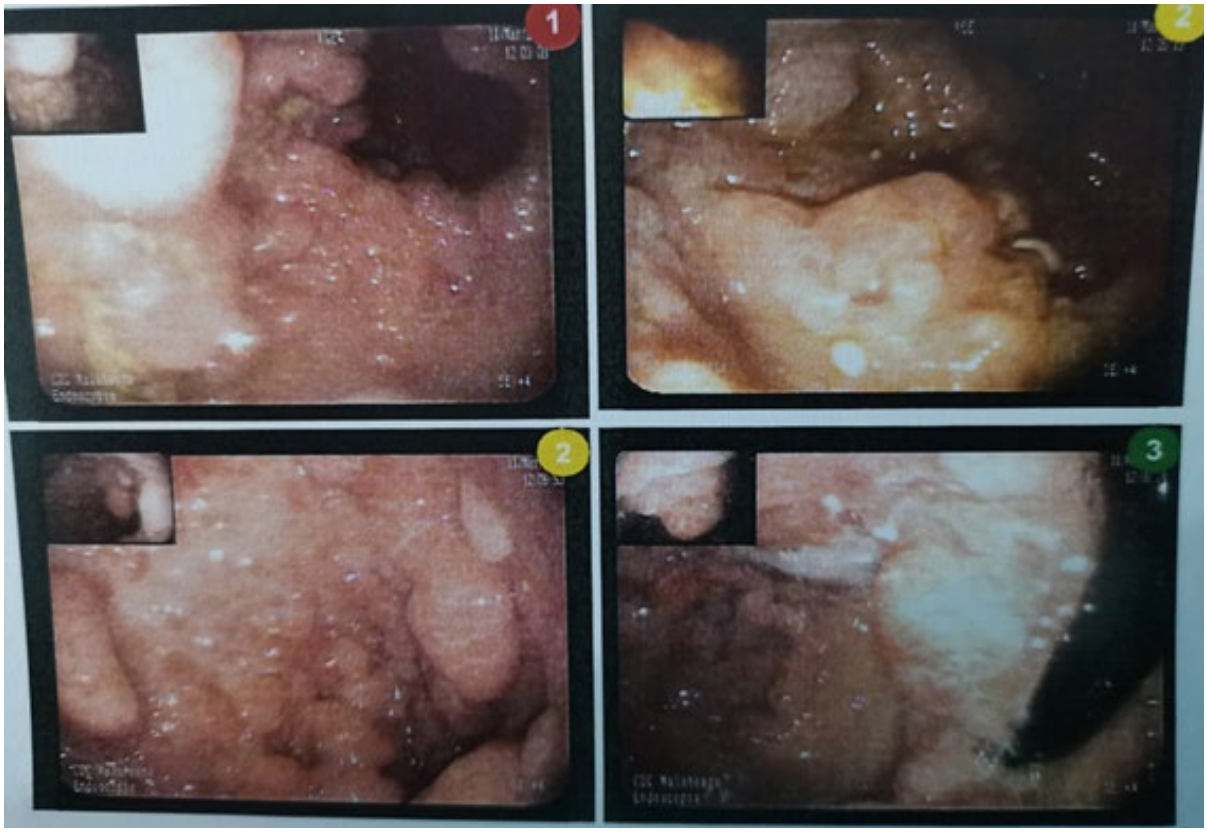

Figure 4: Esophagogastroduodenoscopy of the patient

The diagnostic hypothesis were: a protein-losing enteropathy associated with intestinal infection or a protein-losing enteropathy after neoplastic/inflammatory etiology. However, we noted that the skin manifestations arose with diarrhea and therefore explored the possibles associations.

We repeated the endoscopic tests in the hypothesis of Cronchite-Canada syndrome:
- Colonoscopy: *ileitis with pancolitis. Rectal ampulla, rectum and sigmoid congested mucosa, multiple hyperemic nodules without ulcers/erosions. In colon congested/hyperemic mucosa, multiple nodular formations and petechiae, hypertrophic, congested, hyperemic ileocecal valve, with petechiae (Fig 3)*
- Terminal ileum histology, ileocecal valve, ascending/descending colon: *edema of lamina propria with focal haemorrhagic areas, mild chronic inflammation and hyperplastic aspects of the epithelium, fragments of low-grade tubular adenoma in the rectum.*
- Esophagogastroduodenoscopy: *multiple stomach (from a few mm to 10 mm) and duodenal polyps with hyperemic, sometimes eroded mucosa (histology: pseudopolyps of the gastric and duodenal mucosa) (Fig 4)*
– EnteroTC: *sections of colon and small intestine with concentric thickening and parietal impregnation, and reduction of the lumen, distal ileum with prestenotic dilatation. Minimal liquid film in the abdomen. Hypervascular polyps of the cecum and ascending.*

During hospital stay

- The patient was kept on fasting and parenteral nutrition, with albumin supplementation.
- Therapy with empiric antibiotic, steroid and intramuscular octreotide was practiced.
- A low-fibre, high-protein and high-glycidic diet was subsequently started, as well as supplementation with medium-chain triglycerides and proteins.

Therefore, there was a progressive improvement in diarrhea, inflammatory indices and protidemia, with reduction of anasarca, up to home discharge.

Discussion

Our case is charaterized by late onset, so it was more difficult to keep in mind the diagnostic hypothesis of a syndrome. More than 500 cases worldwide of CCS are described in the literature: European and Asian peoples are more affected, males slightly more than females. The estimate of average age at onset is 59 years (range 31-85 years).

In our case the symptoms were disabling and similar to those described in the literature: watery diarrhea (up to 4-6 litres, sometimes steatorrhea and melena), dysgeusia, lack of appetite, weight loss (often greater than 10 kg), abdominal pain constant or episodic, asthenia. Diarrhea is usually followed, in variable sequence, by onychodystrophy, alopecia (initially areata, rapidly progressing to complete hair loss), and hyperpigmentation (diffuse light or dark brown patches and plaques and patchy vitiligo), located on the palms of the hands and soles of feet, upper limbs, face and chest. More than 10% of patients develops gastrointestinal cancer (predominantly of the sigmoid colon

and rectum). Neurological signs (numbness and tingling in the extremities, dysphagia, and seizures), autoimmune disorders, hypothyroidism and membranous glomerulopathy are present in some patients. Gastrointestinal lesions are usually generalized, the esophagus is rarely affected. The most common complications are gastrointestinal bleeding, malabsorption, malnutrition, and infections. Dysgeusia and cutaneous signs have been attributed to malnutrition.

Our case is also characterized by a slight increase in IgG4. This data is interesting, because the pathogenesis of CCS is not known, but an immune-mediated process has been hypothesized (as confirmation, in addition to the increase of IG4, the presence of antinuclear antibodies and the frequency of autoimmune diseases).

Finally our case is characterized by a favorable outcome. It is very important to think about this unusual syndrome, since the clinical course of CCS is progressive with rare spontaneous remissions, frequent relapses and evolution towards malignant tumors. The 5-year mortality rate can reach 50% (mainly due to gastrointestinal malignancies, portal vein thrombosis, infections and membranous glomerulonephritis).

Available treatments, either alone or in combination, include steroids, nutritional therapy (fluid, electrolyte, protein, and vitamin supplementation and, if necessary, elemental diet or parenteral nutrition), 5-aminosalicylic acid, antagonists of histamine H2 receptors, anti-tumor necrosis factor alpha agents, immunomodulators and Helicobacter pylori eradication [1-10].

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