CASE REPORT

Cronkhite-Canada Syndrome- The first case from Pakistan: a case report

Hassan Tanvir Ramzi, Yumna Zainab, Sana Manzoor, Akram Malik

Abstract

Chronkhite-Canada Syndrome is characterised by diffuse gastrointestinal polyposis, dystrophic changes of the fingernails, cutaneous hyperpigmentation, alopecia, diarrhoea, weight loss, and abdominal pain. This disease is also associated with peripheral neuropathies and autoimmune disorders. Its association with other diseases may cause the polyps to turn into malignant tumours and worsen the condition. The first-line treatment is a combination of prednisone and mesalamine. NSAIDs and antibiotic administration is based on the symptoms and needs of patients. Here, we describe a 51-year-old male who presented to us with abdominal pain and significant weight loss. His physical examination showed dystrophic nails, alopecia and hyperpigmentation. Endoscopy and colonoscopy showed multiple polyps.

His manifestations were consistent with Cronkhite-Canada syndrome. We prescribed oral corticosteroids, which improved his condition.

Keywords: Cronkhite-Canada syndrome, CCS, polyps, Pakistan.

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Introduction

Cronkhite–Canada syndrome is a non-heritable condition characterised by gastrointestinal polyps along with alopecia, diarrhoea, hyperpigmentation, and onychodystrophy. The condition has a high morbidity rate and occurs more commonly in the male population compared to females, at a ratio of 3:2. Cronkhite–Canada syndrome was first described by a physician Leonard Wolsey Cronkhite Jr. and radiologist Wilma Jeanne Canada in 1955[1]. Since its discovery, only 500 cases have been recorded globally; with this condition being more prevalent in the Japanese population[2,3].

The pathogenesis of Cronkhite–Canada syndrome might be intricate, since many variables play a role in its occurrence and advancement. According to pre-existing literature, Cronkhite–Canada syndrome is thought to have an autoimmune aetiology due to its link with other autoimmune diseases like membranous nephropathy, neuropathies, and hypothyroidism[4,5].

However, the aetiology is still unclear. Physical and psychological stress can also be the causes of this syndrome. Some cases have reported symptoms occurring after psychological stress, heel bone fracture, or a colectomy[6,7]. Even without any treatment, a patient can show improvement in the symptoms just after relief from a stress factor. One of the important causes that cannot be ignored is the imperative role of Helicobacter Pylori in the pathogenesis of Cronkhite–Canada syndrome[8]. Some case studies have shown a correlation with Helicobacter pylori infection; with 54% of the patients having presented with symptoms of Cronkhite–Canada syndrome, along with H. pylori infection. Improvement in symptoms was observed after H.pylori eradication therapy[8,9]. Additionally, allergic reactions to some medications, for instance, oral Thyroxine and some Chinese traditional medicines, can also initiate symptoms[10].

There are no documented case reports or literature reviews about Cronkhite Canada syndrome in Pakistan. Our report suggests that Cronkhite Canada syndrome is mostly overlooked in practice, and though it is linked with autoimmunity and malignancies (10-15%), its prognosis improves with early treatment.[10,11]

Case Report

A 51-year-old male presented to Ibn-e-Siena Hospital and Research Institute, Multan in August 2021, with complaints of hair loss and hyperpigmentation for 1 year; along with a 2 year-long history of abdominal pain and loose stools. Informed consent for the publication of the present study was taken. He had developed abdominal pain,localized to the epigastrium, 2 years prior. It was gradual in onset, progressive in nature, and non-radiating. In addition, it was associated with watery diarrhoea and, according to the patient, weight loss of about 30-35 Kilograms over the course of 2 years. There was a mild loss of taste as well. However, it was not associated with vomiting, fever or melena.

The patient also complained of male pattern baldness

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and loss of hair from his eyebrows, axilla, extremities and pubic area. Moreover, he started developing hyperpigmentation one year earlier.

His past medical, surgical, drug, and family history were unremarkable.

Physical examination revealed the presence of malnutrition and dermatological features as pigmentation on his hands and feet (Fig.1) along with onychodystrophy (Fig.2).

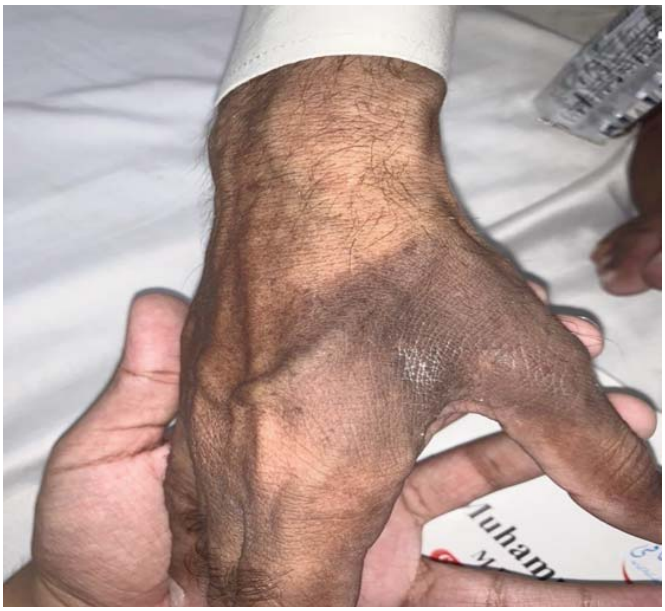

Figure-1: Hand with hyperpigmented lesions

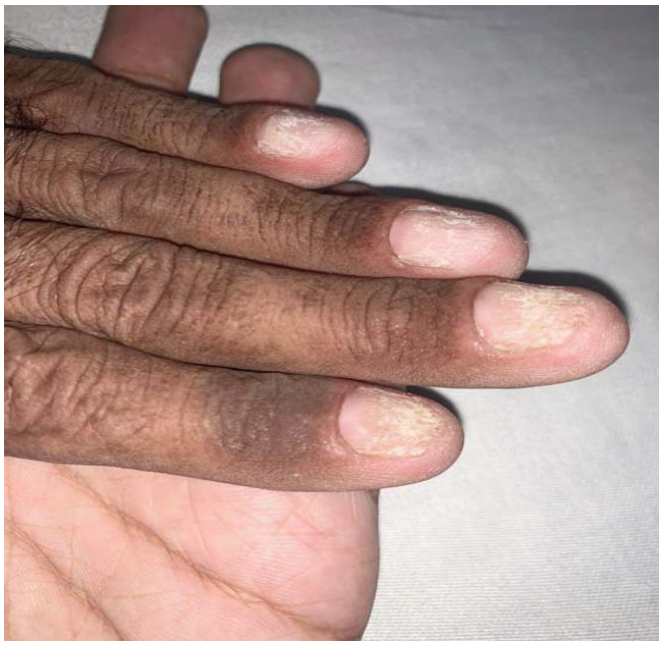

Figure-1: Finger nails showing onychodystrophy

His blood workup presented: haemoglobin 15.1 g/dl (12-16 g/dl), TLC 12,610/mm(4000-11,000 /mm) with neutrophilic predominance 70%; MCV 91 fl (80-102 fl); MCH 30pg(27-34 pg) ; MCHC 33pg (31-35 g/dl) ; Bilirubin 0.9mg/dL (0.1-1.0 g/dl) ; SGPT 69 U/L (upto 40 U/L); SGOT 59 U/L(up to 35 U/L) ; ALP 253 U/L (86-306 U/L). Stool examination was positive for occult blood. Coeliac disease work up was negative, with Serum Anti-Transglutaminase IgA 0.60 U/ml (< 2.6 U/ml); Serum Anti Transglutaminase IgG 0.5 U/ml (<2.6 U/ml) and faecal Calprotectin 8.30 ug/g (43.2 ug/g). Due to financial constraints further testing for an autoimmune profile could not be undertaken. CT abdomen and pelvis showed extensive and innumerable polyps that involved the stomach (relatively sparing the fundus) and large intestine. Esophagogastroduodenoscopy and colonoscopy also showed multiple polyps in stomach, duodenum, terminal ileum, caecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum. Histopathology showed polypoidal gastric mucosa with moderate chronic active gastritis and markedly hyperplastic small and large bowel mucosa with dysplasia. As this patient presented with diffuse gastrointestinal polyposis along with ectodermal changes, including hyperpigmentation and onychodystrophy, the diagnosis of Cronkhite–Canada syndrome was determined.

He was started on azathioprine, mesalamine and prednisolone. After 2 months his gastrointestinal symptoms reduced, and hyperpigmentation reverted. Surveillance colonoscopies are planned annually.

Discussion

Cronkhite–Canada syndrome may tend to be malignant as the complications may get worse in the presence of other diseases. The prevalence of worst-case scenarios involving progression to GIT cancers is 10%-20%; Among those, the most common is gastric cancer, which is mostly limited to the T1 level.[12,13] The presence of multiple polyps in the gastrointestinal tract including the oesophagus, the stomach, small intestine and colon may lead to other symptoms of Cronkhite-Canada syndrome, such as, abdominal cramps and diarrhoea. Diarrhoea may further lead to electrolyte imbalance. The initial phase of the disease presents with dysgeusia, anosmia, and peripheral oedema. The patient may also present with severe loss of appetite, which, if prolonged, may cause malnutrition and profound weight loss. Recent studies state that, people with Cronkhite–Canada syndrome can also present with coexisting autoimmune diseases, as, rheumatoid arthritis, scleroderma, SLE, and hypothyroidism.[14]

Changes in the mucosa of intestine may cause malabsorption and a decrease in vitamin C and calcium levels in the body. This can lower bone mineral density and cause fractures. Some case studies also reported the coexistence of pulmonary embolism, arteriovenous thrombosis, and vestibular dysfunctions with Cronkhite–Canada syndrome.[15,16] Furthermore, some studies have shown alteration in motor and sensory responses, leading to the conclusion that it may also be complicated by neuropathies such as mononeuritis multiplex. The reason behind the peripheral neuropathies is not well established, but some authors have attributed it to a decrease of myelinated nerve fibres in the sural nerve[17].

Other complications of Cronkhite–Canada syndrome are: Haematochezia, hypoproteinaemia, anaemia, gastrointestinal Bleeding, intussusception, major duodenal papillary prolapse, recurrent pancreatitis, hypocalcaemia, malnutrition, Heart Failure, repeated infection, and sepsis.[18]

There is no approved treatment of Cronkhite–Canada syndrome, however, there is some preferred general and symptomatic management provided in previously reported cases. The key drug that should be considered is prednisone. Drug dosage must be managed according to the severity of the condition and tapered down, as the patient shows improvement in symptoms[19].

In Cronkhite–Canada syndrome, anti-TNF-alpha therapy has proven to be quite effective. According to literature, great therapeutic impact was reported after the administration of infliximab[20].

As mentioned above, the eradication of H.Pylori can help in relieving symptoms of Cronkhite–Canada syndrome. In some cases, a combination of mesalazine and prednisone was effective in gradual recovery of hair and nails, as well as management of diarrhoea.

Conclusion

Cronkhite-Canada syndrome should be considered as soon as gastrointestinal symptoms and skin changes start to show up. It is important to pay attention while examining a patient with this syndrome. Early diagnosis and management can improve the prognosis. Constant monitoring of this condition and follow-ups may also help in a better prognosis. Any negligence can lead to severe complications being overlooked, such as malignancy. To conclude, our patient, who had being diagnosed with Cronkhite-Canada syndrome, symptomatically improved after commencing medical treatment and had no aforementioned complications throughout the follow-ups.

Disclaimer: Informed consent from patient had been taken for publishing his case history.

Conflict of Interest: None to declare.

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