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Case Report

A Case Report of Hereditary Palmoplantar Keratoderma with Esophageal Melanosis

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Abstract

A 70-year-old man, a known case of diabetes mellitus since 10 years ago, presented with lower limb swelling and dyspnea on exertion for one month and dysphagia to solids associated with early satiety for 2 weeks. The patient had palmoplantar keratosis (PPK), which was present since birth with a similar family history. The patient was admitted to rule out esophageal malignancy. Upper gastrointestinal gastroscopy revealed esophagitis and esophageal melanosis with gastric mucosal erythema. Biopsies samples were taken. Histopathological examination revealed reflux esophagitis and chronic active *Helicobacter pylori* gastritis with no evidence of malignancy. His symptoms improved following *H. pylori* eradication and treatment for coronary artery disease and heart failure. The patient was advised of regular follow-up as he had risk factors for the development of esophageal melanoma or squamous cell carcinoma.

Keywords: Palmoplantar keratosis, Esophageal melanosis, Carcinoma

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Introduction

Palmoplantar keratoderma (PPK) is a rare condition involving the skin of palms and soles characterized by excessive epidermal thickening.[1] The association between PPK and oesophageal squamous cell carcinoma is well-known.[2] Howel-Evans syndrome is an inherited condition characterized by the presence of palmoplantar keratoderma and associated esophageal malignancy.[3] In our case, we present an old man who had isolated (limited to palms and soles), diffuse keratosis (affecting the entire surface of palms and soles) since birth.

Gastroscopy was done-to rule out esophageal malignancy, which revealed oesophageal melanosis. Esophageal melanosis is a rare lesion observed in 0.5%-2.1% of gastroscopies characterized by melanocyte proliferation in the squamous epithelium of the esophagus and melanin accumulation in the esophageal mucosa.[4] Esophageal melanosis may be considered a pre-malignant lesion as it was seen in 27% of esophageal carcinoma specimens in Japan and 25%-30% of primary malignant melanoma of esophagus surgical specimens.[4]

Case Report

A 70-year-old man, a known case of diabetes mellitus (DM) since 10 years ago, and with left below-knee amputation presented with complaints of swelling of the right leg, dyspnea on exertion (NYHA class III), easy fatigability for a one-month duration and dysphagia to solids for 2 weeks. The patient also experienced an unquantifiable loss of weight. He denied smoking or alcohol intake. On examination, the patient had hyperkeratosis of palms and soles (Figures 1 and 2). He also gave a strong family history of similar palmoplantar lesions among the members of the family. There was no history of malignancy-related deaths in the family.

On examination, the patient was poorly nourished with temporal wasting and body mass index (BMI) of 17.6 kg/m^2, pallor, pitting pedal edema up to knees, and raised jugular vein pressure (JVP) (12 cm of water). Vital signs include pulse rate-110/min and blood pressure-90/60 mm Hg. Virchow's node was not palpable. On cardiovascular examination, the patient had an S3 gallop with no thrills or murmurs. The respiratory examination did not reveal any basal crepitations and on abdominal examination, there were no ascites or hepatosplenomegaly. CNS examination was unremarkable.

Provisional Diagnosis

A 70-year-man presented with dyspnea and pedal edema with raised JVP, dysphagia, and palmoplantar keratoderma. The diagnosis was considered as heart failure secondary to coronary artery disease and to rule out esophageal or gastric malignancy.

Investigation

Hemogram showed anemia with hemoglobin 8.1 g/dL with mean corpuscular volume (MCV) of 82 fl, a total count of 4790 cells/mm^3 and a platelet count of 2.08 lakh/mm^3.

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Peripheral smear showed normocytic anemia with normal WBC morphology and count and adequate platelets. Iron studies showed reduced serum iron of 15.64 µg/dL, elevated serum Ferritin levels of 526 µg/L, and reduced total iron binding capacity (TIBC) of 132 µg/dL. Renal function tests were normal. ECG had biphasic T waves in the chest leads V3-4 and T wave inversion in V5-6. Cardiac markers showed a moderately elevated HS troponin T of 51.6 ng/L and brain natriuretic peptide (BNP) was > 35000 pg/mL (normal < 100). A transthoracic echocardiogram revealed regional wall motion abnormality and moderate LV systolic dysfunction (ejection fraction of 35%) with grade II diastolic dysfunction.

Gastroscopy revealed grade-A esophagitis with oesophageal melanosis and gastric erythema with edema (Figure 3).

Histopathological examination of the biopsy revealed chronic active *H. pylori* gastritis, and reflux esophagitis with no evidence of esophageal squamous cell carcinoma or malignant melanoma (Figure 4).

Treatment

The patient was initially admitted to High Dependency Unit in view of acute coronary syndrome- non-ST-elevation myocardial infarction (NSTEMI) with heart failure and started on a high-dose statin, dual antiplatelet, and furosemide infusion with close blood pressure (BP) monitoring. Because of the history of dysphagia to solids, weight loss, and the presence of anemia, esophageal malignancy was strongly suspected. Once the patient's condition improved after adequate diuresis, a gastroscopy was done, which revealed grade A esophagitis, esophageal melanosis, and gastric erythema with edema. There was no esophageal ulcer or mass. Esophageal biopsy revealed reflux esophagitis and gastric biopsy showed *H. pylori*-associated chronic active gastritis with focal intestinal metaplasia for which the patient was started on amoxicillin 1000 mg, tinidazole 500 mg, and omeprazole 20 mg twice daily, orally. He received one unit of packed cell transfusion and was started on oral iron supplements. On discharge, the patient had improvement in cardiac failure symptoms, and dysphagia, and his hemoglobin level improved from 8.1 g/dL to 9.6 g/dL.

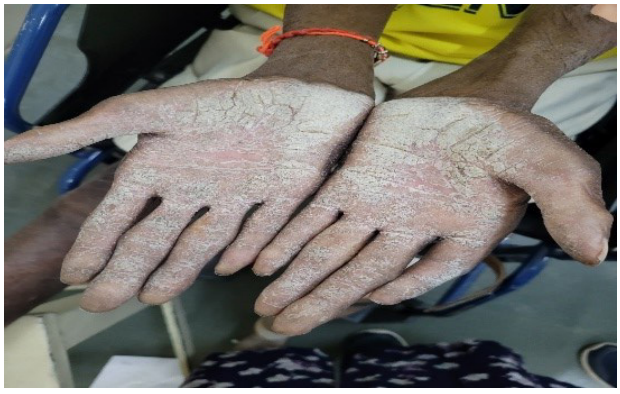

Figure 1. Palmar keratosis

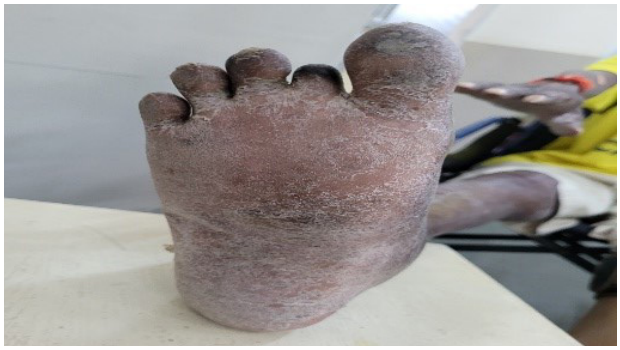

Figure 2. Plantar keratosis

Outcome and Follow-up

After two weeks of *H.pylori* eradication therapy, the patient's symptoms of dysphagia had resolved. He was able to ambulate at home and was able to carry out his activities of daily living. The patient was prescribed oral pantoprazole 40 mg once daily, to continue for 4 more weeks, and was advised regular follow-up.

Discussion

Palmoplantar keratoderma comprises a diverse group

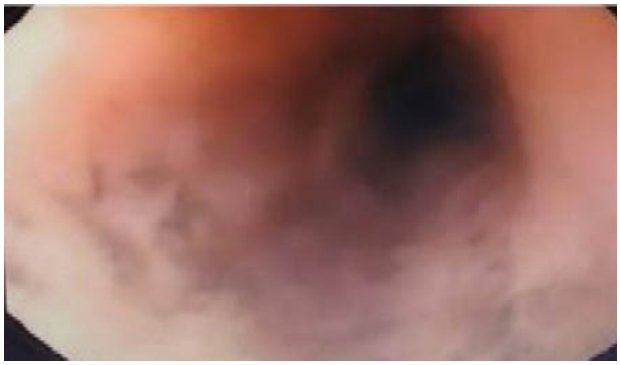

Figure 3. Oesophageal melanosis

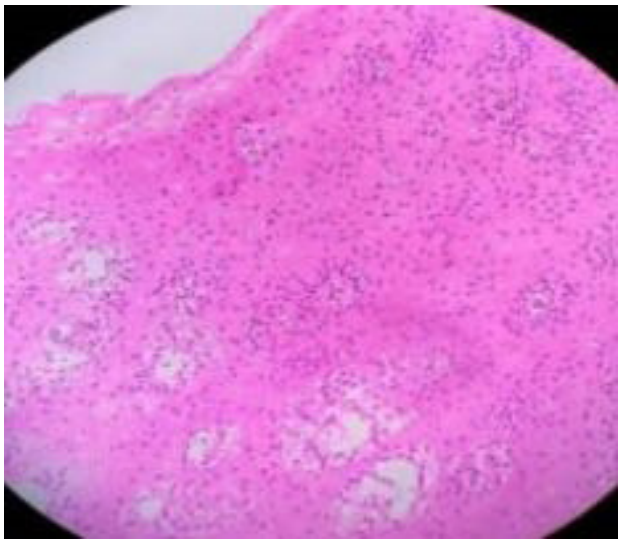

Figure 4. reflux esophagitis

of disorders that can occur in isolation or as part of a syndrome. It is a rare disorder with a prevalence of 5.2 per 10 000 people as published by a study from South India.[5]

The classification of PPK is based on the extent of the disease manifestation, which can be either isolated or syndromic, the morphology of palmoplantar skin involvement, inheritance pattern, and molecular pathogenesis. There are multiple clinic-morphological variants such as diffuse, focal, punctate, trangredient, progrediens, or cicatrizing.

The inheritance of PPK can be autosomal dominant, autosomal recessive, X linked, or mitochondrial. Hereditary PPK is due to mutations either in the intracellular cytoskeletons, adhesion proteins, cell-to-cell communication, or cell signaling proteins. The commonest mutation in the hereditary forms of PPK includes KRT1/KRT9, which encodes for suprabasal keratin (K1 &9).[6]

Our patient had hereditary isolated palmoplantar keratoderma which was diffuse, non-cicatrizing, with no lesions extending beyond palms and soles with no extracutaneous manifestations and probable autosomal dominant inheritance.

Esophageal melanosis is a rare endoscopic finding with a prevalence of 2.1% in India. One case report reported that a patient with esophageal melanosis went on to develop dysplasia, melanoma, and carcinoma over a period of 8 years.[7] Several other studies have also reported esophageal melanosis as a precursor to malignancy.[8-10]

Abnormalities in keratinocyte differentiation and hyperproliferation with an increased number of basal epithelial keratinocytes may predispose to malignant epidermal tumors. There have been more than seven case reports of malignant melanoma arising in the hyperkeratotic lesions of patients with inherited PPK. This suggests a predisposition for malignant melanoma in these patients. It is possible that an inherited PPK along with other risk factors, which lead to a disturbed maturation and proliferation of melanocytes such as oesophageal melanosis, can predispose to esophageal melanoma.[11-14] This will require at least yearly screening upper gastrointestinal endoscopy in our patient.

In our patient, esophageal melanosis along with other risk factors for esophageal malignancy such as reflux esophagitis prompts us to keep our patient on close follow-up with yearly gastroscopy in case he develops a squamous cell carcinoma or a malignant melanoma of the esophagus.

Learning Points

1. Palmoplantar keratoderma can be hereditary or acquired and can be isolated or associated with various syndromes.
2. Esophageal melanosis is a rare condition and its association with esophageal malignancy or its premalignant nature is still unclear.
3. Not all patients with inherited palmoplantar keratoderma are at increased risk of developing oesophageal malignancy.
4. There have been several reports of esophageal melanosis leading to the development of esophageal melanoma or squamous cell carcinoma.
5. In our patient, with multiple risk factors for esophageal malignancy, frequent clinical and endoscopic follow-ups must be carried out.

Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

Informed consent was obtained from the patient for publication of this report.

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