Thalidomide induced xerosis: an unwanted reaction

Nagesh Kamath1, Anurag Shetty1, Harneet Singh1, Shiran Shetty1*, Srinivasa Rao Sirasanagandla2

INTRODUCTION

Gastric antral vascular ectasia (GAVE) typically known as watermelon stomach, is marked by a collection of dilated veins showing as linear red stripes merging in the antrum in a longitudinal manner, giving stomach the look of a watermelon.1,2 Etiology is unknown, nevertheless it has been purported that gastric peristalsis induces prolapse of the loose antral mucosa with consequent extension and ectasia of the mucosal vessels.3 GAVE is an unusual cause of gastrointestinal bleeding seen more so in females than males, and presents mostly as iron deficiency anemia due to the gradual loss of blood.4 GAVE is of two types viz. classic and diffuse type. Classic type earns the name watermelon stomach. Diagnosis is done on the clinical history, endoscopic appearances and histological changes. The preferred endoscopic therapy is argon plasma coagulation (APC). Good response rate depends on the methods used; classic type responds better to APC than diffuse type.

Xerosis makes skin to lose moisture and hence that it cracks and peels. It appears as small fine flakes and dry patches. As skin dryness becomes more severe, cracks and fissures may evolve. As people age, the outer layer of skin loses water, causing the surface to become dry and rough.5 It can be caused by a deficiency of vitamin A, vitamin D, sunburn or some drugs. Xerosis is thought to be related to altered lipid composition of the stratum corneum, in addition to other changes in epidermal differentiation.6 Xerosis does not occur as a result of decreased water in the skin but is the result of abnormal keratinization and desquamation.7 Emollients and moisturizers need to be used. Moisturizers

ABSTRACT

A 59-year-old male exhibited anemia for evaluation. Endoscopy was diagnostic of gastric antral vascular ectasia. He was given a trial of thalidomide after informing about the adverse effects. After starting thalidomide at 100 mg/day, his hemoglobin (Hb) improved. Post 1 month of therapy his Hb normalized, but he developed xerosis. He was given symptomatic treatment, but did not improve. Thalidomide was suspected to cause xerosis, it was discontinued for a month and post-discontinuation of drug he is symptom free for past 8 months. This paper reports a rare case of thalidomide induced xerosis with dermatological and neurological involvement.

Keywords: Anemia, Gastric antral vascular ectasia, Thalidomide, Xerosis

1Department of Gastroenterology and Hepatology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India, 2Department of Anatomy, Melaka Manipal Medical College (Manipal Campus), Manipal University, Manipal, Karnataka, India

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*Correspondence to: Dr. Shiran Shetty,
Email: drshiran@gmail.com

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have water-retaining and lubricating properties suitable treatments for xerotic skin.7

We present a rare case of thalidomide induced xerosis unresponsive to symptomatic treatment with subsequent discontinuation of offending drug resulted in recovery.

CASE REPORT

A 59-year-old male patient presented at our institution with the complaints of fatigue, dizziness, constipation, melena and reported several weeks of anemia, had an episode of loss of consciousness (5 years back). The initial clinical part comprised of a routine medical and drug exposure history, along with a physical examination and routine blood tests. On examination, he had pallor and pedal edema. He was oriented to persons and responded to verbal commands. He was a known diabetic (10 years) on human insulin, non-alcoholic, non-smoker, recently diagnosed to have gynecomastia. He had a history of repeated blood transfusions. Physical examination of the abdomen, lungs and heart was normal. No impairment of intelligence was seen.

Investigations

Admission blood tests showed hemoglobin (Hb) of 5.9 g/dl, erythrocyte sedimentation rate 96, hematocrit (HCT) 16.5%, white blood cell (WBC) 4200/µl, platelets (PLT) 82,000/µl, international normalized ratio was 1.48. Prothrombin time 22.1 (H). Iron 24, total iron binding capacity 456, ferritin was 14.2, serum electrolytes, and creatinine were normal. Albumin 2.7g/dl and total proteins 5.5 g/dl were low, rest of the liver function test was normal. Post-prandial blood sugar was 261 and alpha-fetoprotein of two. Peripheral blood smear showed red blood cell (RBC) sparsely distributed, normocytic normochromic, anisocytosis and polychromasia. WBC were adequate, but PLT were reduced in number.

Two pint of packed RBC was transfused. Post-transfusion his Hb was 6.8 g/dL; and HCT of 20%. Upper gastrointestinal endoscopy was performed. Endoscopy showed extended vascular ectasias and erythema in the distal part of the antrum that was diagnostic of GAVE (Figure 1), small esophageal varices and edematous duodenum, but no gastric/fundal varix seen. No further complications such as peptic ulcer and necrosis were observed and required one APC (Figure 2) session for GAVE and blood transfusion to control bleeding. GAVE was perceived as a more credible cause for severe anemia resulting from gastrointestinal blood loss. Post-APC Hb was 7.4, HCT 23.5. His HCT and Hb normalized at discharge. Post 1 month he came up with numerous brownish black pigmentation with mosaic like pattern on skin (Figure 3). Pigmentation was seen on the hands, neck, thighs, and legs. In the neck region, forearms (Figure 4) hands pigmentation was abundant and darker in color. Patient was offered referral to Dermatology Department.

Figure 1: Endoscopic image showing gastric antral vascular ectasia.

Figure 2: Endoscopic image showing argon plasma coagulation.

Figure 3: Photograph showing brownish black pigmentation with mosaic like pattern (xerosis).

Treatment

Patient remained as an inpatient for 5 days under observation at a gastroenterology unit. The patient
received conservative treatment that involved parenteral nutrition, broad spectrum antibiotics, and oral hygiene. He was then treated with thalidomide and propranolol. Considering the older age, a low dosage (100 mg daily) was selected to achieve hemostasis, while minimizing toxicity and consequent residual effects. Treatment success, determined by no further need for blood transfusions. Post 1 month of therapy, his Hb was 10.2, but he developed neuropathy and xerosis. Patient was instructed to limit bathing and avoid soap, photoprotection with sun avoidance and appropriate clothing. Multivitamin supplements of vitamin A and D were given. Liquid paraffin emollient was given for local application (3 times daily). But xerosis did not resolve. Hence, we investigated whether thalidomide resulted in xerosis. Thalidomide was discontinued. Xerosis resolved (Figures 5 and 6) on discontinuation of thalidomide. Patient is on continuous follow-up and has not had any further complications. His Hb level has been within the normal limits and is symptom free for last 8 months.

**DISCUSSION**

To the best of our knowledge this is the first case report on thalidomide-induced xerosis. Teratogenic effects of thalidomide are well-reported. However, none of the studies have reported effect of thalidomide on xerosis. Such patients are often a challenge to treat. The antiangiogenic properties may imbue thalidomide with a potential value in the treatment of GAVE.

Thalidomide is an immunomodulating, anti-angiogenic, anti-tumor, and anti-inflammatory drug known for its teratogenic effects. A wide variety of medications have been used to control GAVE-related bleeding viz. Octreotide, hormonal therapy estrogens-progesterone, tranexamic acid, methylprednisolone and cyclophosphamide; however, no study has clearly shown satisfactory results in order to consider medical therapy as a valid alternative to an invasive approach. Thalidomide was hence initiated.

Although thalidomide is generally well tolerated, it can result in different adverse effects, including constipation, sedation, rash, peripheral neuropathy and others. Adverse effects like constipation can be managed by using a laxative and rectifying any folate and vitamin B12 deficiencies to bring down neuropathic symptoms. If patient feels lethargic during daytime, then thalidomide could be taken in evening time. Concomitant drugs, which can aggravate the sedative action of thalidomide viz. alcohol, antidepressants, tranquilizers and other sedatives should be avoided. Peripheral neuropathy is a usual adverse effect of thalidomide. Peripheral neuropathy and xerosis are usually reversible upon discontinuation of thalidomide. The best treatment for GAVE remains unclear hence management decisions are difficult. Iron supplements are the first line therapy of defense. If iron supplementation does not manage anemia, then endoscopic therapy with APC and transfusions may be needed. Treatment failures are infrequent, limited data is available for the first-line use of medical therapies in GAVE. After thalidomide use was prohibited due to its teratogenic effects, it was taken up again for treating erythema nodosa leprosum and showed a satisfactory result. Nevertheless, its use is still very controversial, especially regarding the beneficial and/or adverse effects of the drug, its mechanisms of action and its real therapeutic indications. Regular neurological review and hearing tests are needed.

Figure 4: Photograph showing brownish black pigmentation with mosaic like pattern (xerosis).

Figure 5: Photograph showing the normal skin pattern post discontinuation of drug.

Figure 6: Photograph showing the normal skin pattern post discontinuation of drug.
CONCLUSION

APC is an effective and safe treatment in GAVE patients. Therefore, it be used as first-line treatment in GAVE. Use of thalidomide is controversial; can be used as an alternative in patients not willing for endoscopy or who do not respond to repeated APC; need to be considered on a case to case basis. This case attempts to highlights the necessity for routine monitoring and follow-up of patient who are on thalidomide to prevent neuropathy and xerosis. Reporting every case will help us determine incidence of xerosis with thalidomide use, which is yet unknown. We would like to call attention to the fact that, after halting the drug, xerosis doesn’t recur. Questions remain unanswered whether thalidomide should be used in GAVE patients?

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