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Case presentation

Acquired acrodermatitis enteropathica after gastric bypass surgery responsive to IV supplementation

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Abstract

Nutritional deficiency is rare in developed countries, but can be acquired from decreased nutrient intake, reduced absorption, and increased gastrointestinal excretion. We report a patient with acquired acrodermatitis enteropathica (AE) who exhibited low plasma zinc levels and concurrent nutritional deficiencies (pyridoxine, selenium and fatty acids). Our patient had undergone Roux-en-Y gastric bypass 13 years prior to presentation. The rash, consistent with AE clinically and histologically, nearly resolved one week after starting IV zinc supplementation, total parenteral nutrition, and micronutrient supplements. This case highlights the importance of long-term post-operative follow-up for gastric bypass patients who are at high risk for micronutrient and macronutrient deficiencies and illustrates the potential for rapid improvement with IV supplementation.

Keywords: acrodermatitis enteropathica, gastric bypass, zinc deficiency

Introduction

Malabsorptive bariatric procedures including Roux-en-Y gastric bypass (RYGB) place patients at risk for micronutrient and macronutrient deficiencies. Exclusion of the duodenum following bypass places patients at risk for zinc deficiency, which is often subclinical [1], but may have dermatologic manifestations.

We present a case of acquired acrodermatitis enteropathica (AE), a dermatitis classically caused by zinc deficiency, in a patient with concurrent pyridoxine, selenium, and fatty acid deficiencies and a remote history of gastric bypass. We present this case to highlight that AE caused by nutritional deficiency can manifest years after gastric bypass and may not respond to oral zinc repletion, requiring aggressive IV supplementation.

Case synopsis

A 39-year-old obese woman with a history of malnutrition with marked hypoalbuminemia secondary to RYGB for obesity 13 years prior presented with acute worsening of a chronic, symmetrical, erythematous desquamating eruption of three years' duration. Prior treatment with clobetasol ointment and prednisone did not result in improvement.

She reported a low-protein diet that mainly consisted of soups and had not been evaluated by a nutritionist, surgeon, or gastroenterologist for several years. At the time of evaluation, her only oral nutritional supplements were a multivitamin and iron. In the months prior to presentation, her desquamating rash progressed and failed to improve on an unknown dose of oral zinc, which was prescribed by a physician after her serum zinc was found to be low. She denied any new medications, oral lesions, or diarrhea. She did not drink alcohol.

Physical exam revealed (1) perioral and periorbital erythema and scaling, (2) large areas of denuded skin in the inguinal folds, gluteal cleft, and right antecubital fossa, and (3) erythematous papules and plaques with overlying scale on her chest, abdomen, and extremities (Figure 1). She also had diffuse scale with fissures on her palms and soles, onycholysis and yellow discoloration of her nails, and diffuse alopecia of her scalp without scarring. A punch biopsy was taken from her lower back that showed pallor and vacuolation of keratinocytes in the upper epidermis with associated parakeratosis and mild inflammation, consistent with a necrolytic erythema (Figure 2).

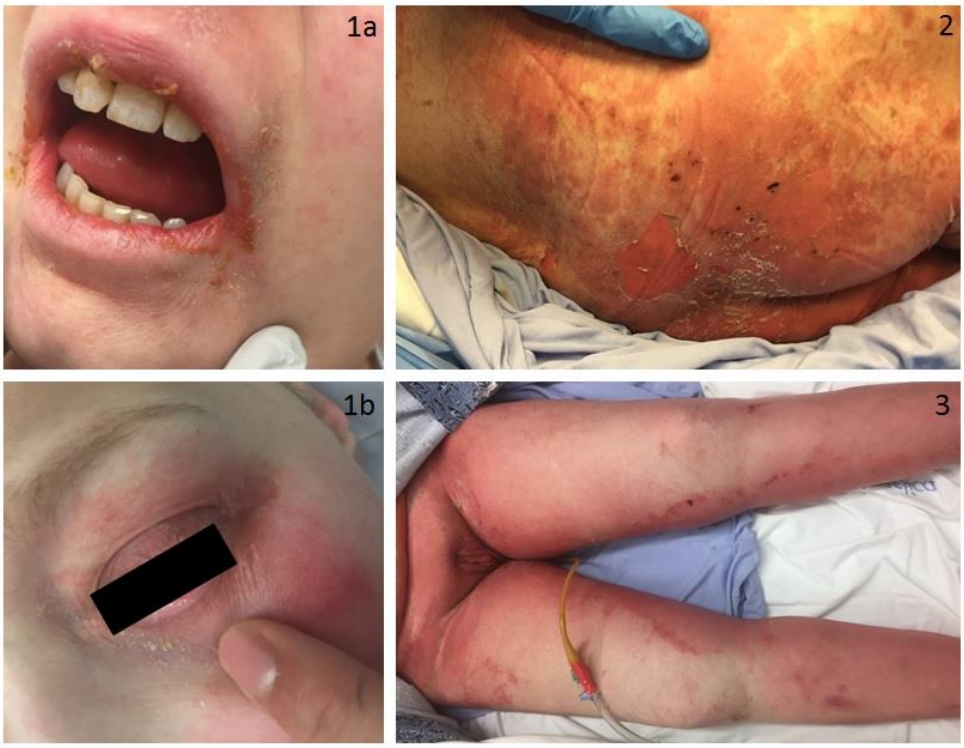

Figure 1. Physical exam revealed (1a) perioral and (1b) periorbital erythema and scaling as well as (2) denuded skin around the gluteal cleft and (3) erythematous plaques with overlying scale on her extremities.

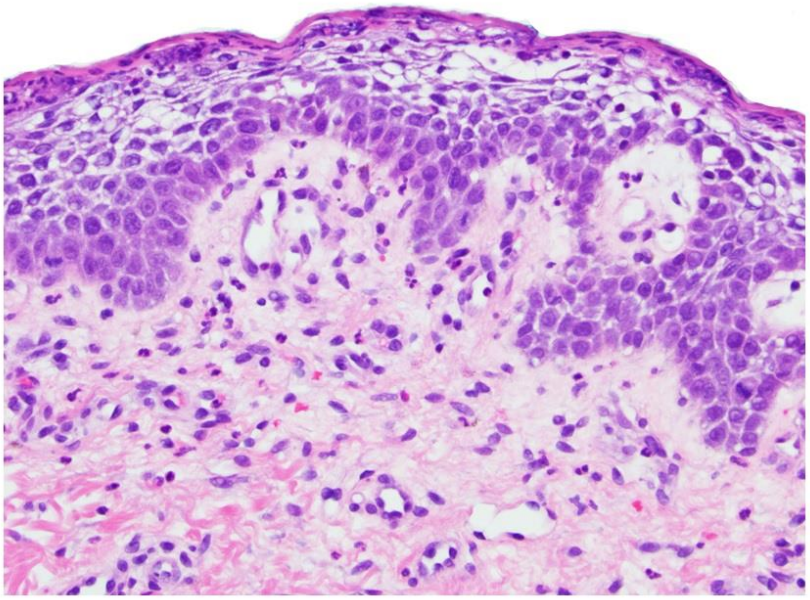

Figure 2. H&E staining of punch biopsy reveals characteristic pallor and vacuolation of the upper epidermis and parakeratosis consistent with a necrolytic erythema.

Laboratory findings demonstrated a serum zinc level of 19 mcg/dL (normal range 60-130 mcg/dL), a prealbumin of <4 mg/dL (normal 17-34 mg/dL), albumin of 1.8 g/dL (normal 3.5-5.2 g/dL), total protein of 2.8 g/dL (normal 6.4-8.3 g/dL), pyridoxine (B6) of <2 mcg/l (normal 5-50 mcg/L), selenium of 40 ng/mL (normal 70-150 ng/mL), and multiple decreased fatty acid levels. Riboflavin (B2) and niacin (B3) were within normal limits. The patient tested negative for hepatitis C (HCV) and completed a negative work-up for glucagonoma at an outside hospital.

The patient's dermatitis rapidly improved within one week after starting 10 mg IV zinc daily, total parenteral nutrition (TPN), and micronutrient supplements (Figure 3). She was continued as an outpatient on altered oral zinc supplementation (440 mg TID) with close follow-up and a low threshold for repeat parenteral supplementation if needed.

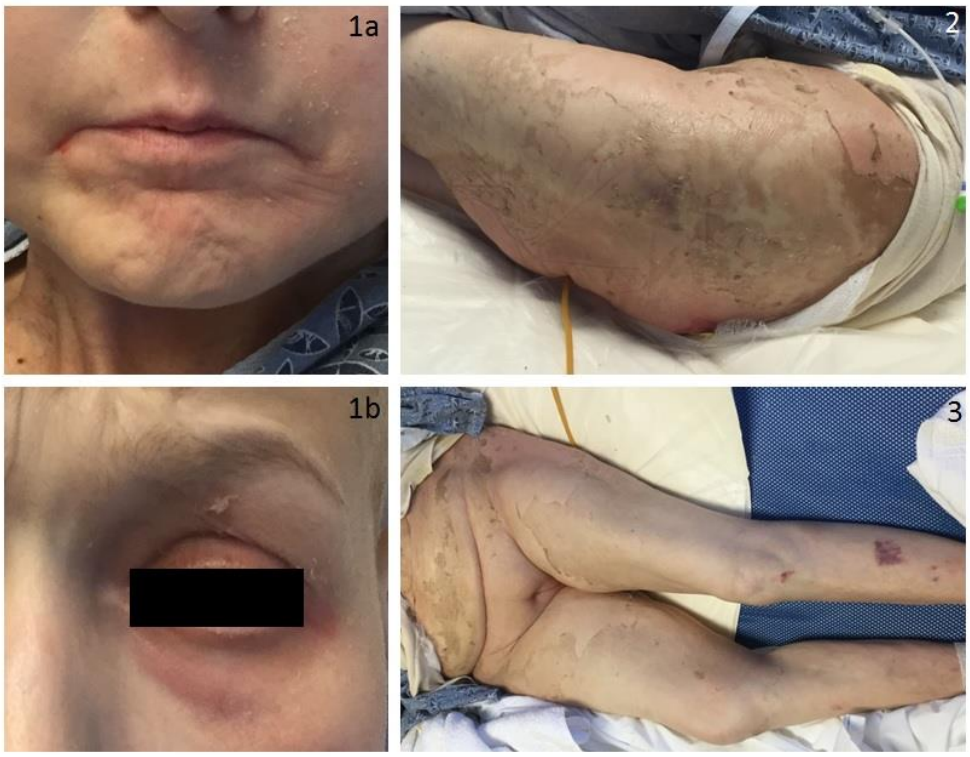

Figure 3. Approximately one week after starting IV zinc and total parenteral nutrition, physical exam revealed improvement in (1a) perioral and (1b) periorbital erythema and scaling as well as (2) healed areas of denuded skin in the gluteal region and (3) near disappearance of erythematous plaques on her extremities.

Discussion

Zinc deficiency can be inherited as an autosomal recessive disorder (owing to loss of an intestinal zinc transport protein, *ZIP4*) or acquired in adulthood from decreased intake, reduced absorption, or intestinal loss [1, 2]. As zinc is a cofactor for metalloenzymes critical for cellular metabolism and replication, zinc deficiency manifests in organs with high metabolic activity and turnover rate (e.g. skin and GI tract), and can result in acrodermatitis enteropathica (AE). The clinical features of both inherited and acquired AE include dermatitis, diarrhea, and alopecia, though all three classic findings are seen in only 20% of cases [2]. From a histological standpoint, AE is classified as a "necrolytic erythema", which is a family of dermatoses (also referred to as "deficiency dermatoses" for their attribution to underlying nutritional deficiencies) that share certain microscopic features, including pallor of the superficial epidermis with or without necrosis, parakeratosis, and epidermal hyperplasia [3].

We identified RYGB as the main risk factor for our patient whose clinical and histological findings were most consistent with zinc deficiency [2, 4]. RYGB is the most common bariatric procedure in the United States and places patients at increased risk for acquired zinc deficiency as it (1) reduces dietary intake owing to a reduced gastric capacity and (2) bypasses the duodenum and proximal jejunum, two key sites for zinc absorption. Bariatric surgery can be restrictive (e.g. gastric banding) or malabsorptive (e.g. RYGB, biliopancreatic diversion). Congruent with the fact that restrictive procedures function to decrease the gastric capacity and malabsorptive procedures bypass portions of the small intestine (e.g. duodenum and jejunum), post-operative macronutrient and micronutrient complications are more common in patients undergoing malabsorptive rather than restrictive bariatric surgery [5].

Our patient also had concomitant pyridoxine, selenium, and fatty acid deficiencies that were also most likely related to malabsorption secondary to RYGB, and which likely contributed to the clinical picture. We could not identify any prior literature associating these or any other nutritional deficiencies with impaired zinc absorption. However, the presentation of concurrent nutritional deficiencies may have a common origin secondary to poor diet and/or physiology of malabsorption.

Pyridoxine (B6) deficiency has been reported secondary to malabsorption and inadequate dietary intake, but cutaneous manifestations (seborrheic-like dermatosis on face, scalp, trunk, and perineal area with nonspecific cheilitis and glossitis) typically occur weeks after initiating a deficient diet [6]. This patient's dermatosis was more consistent with an insidious well-defined necrolytic erythema with acral predilection.

Selenium and fatty acid deficiencies can manifest with AE-like dermatoses clinically and histologically [6, 7]. Rapid improvement with intravenous zinc supports the hypothesis of a dermatosis driven by zinc deficiency, but the patient also received TPN and oral micronutrient supplementation within this window of time, which resulted in simultaneous repletion of her other nutritional deficiencies, confounding our ability to attribute this response exclusively to zinc. Clinically, fatty acid deficiency tends to result in generalized xerosis and scale (this patient had a symmetric predominantly perioral and acral dermatosis) [6], but a selenium deficiency-associated dermatosis can mimic the periorificial distribution of zinc deficiency [7].

In our diagnostic workup, we also considered other causes of necrolytic erythema: necrolytic acral erythema was excluded with negative HCV testing and the most common cause of necrolytic migratory erythema (NME) was excluded with negative glucagon testing. NME and AE are generally indistinguishable histologically, but the acral and periorificial predilection of the patient's desquamating eruption was clinically more consistent with AE [2, 3, 4]. We cannot exclude a possible NME-AE overlap given that she had multifactorial nutritional deficiencies, which have also been cited as precipitating factors for NME [8].

It is unclear why zinc deficiency in our patient manifested with such a delayed onset 13 years after gastric bypass. There are a handful of case reports describing acquired zinc deficiency in patients after gastric bypass, anywhere from 3 to 10 years after surgery [9, 10, 11, 12]. It is plausible the patient's waxing and waning dermatitis flares for 3-4 years prior to diagnosis and 13 years after her RYGB heralded an underlying zinc deficiency, which then became intractable as the zinc deficiency worsened. Notably, clinical symptoms of zinc deficiency may be present even with normal plasma zinc levels that do not adequately reflect cellular zinc stores, and diagnosis is best confirmed with response to zinc supplementation [4].

Data regarding prevalence of zinc deficiency after gastric bypass is limited, but in one prospective study of 56 obese women with a mean body mass index of 45.2 kg/m^2 who underwent RYGB, 12 of the 56 women had low plasma zinc levels at 18 months after surgery (<70 μg/dL) with no reported symptoms [1]. In a random subset of 26 patients in the same study, zinc intestinal absorption was measured and found to decrease from 32.3% of normal capacity at 0 months to 21.0% by 18 months. Decreased absorption (in addition to reduced intestinal surface area for absorption) after gastric bypass may explain, in part, why the patient did not

respond to oral supplementation, ultimately requiring IV zinc. A similar observation was cited in a case report of a 38-year old woman with acquired AE 10 years after gastric bypass who responded to IV zinc supplementation, but not oral zinc supplementation [10]. Supplementation for zinc deficiency can be started at 3 mg/kg/day of elemental zinc (50 mg of elemental zinc per 220 mg of zinc sulfate) and it is common for lesions to rapidly improve within days to weeks [4, 10, 12], as in our patient.

Conclusion

This case highlights the rare presentation of acquired AE in a patient with multiple nutrient deficiencies 13 years after gastric bypass. Although common micronutrient and macronutrient deficiencies (e.g. protein, iron, vitamins A, B12, C, D) in patients after gastric bypass are widely reported in the nutritional and gastroenterological literature [13], there are limited data on the prevalence, timing, and symptoms of zinc deficiency (as well as pyridoxine, selenium, and fatty acid deficiencies) after gastric bypass [1, 14].

A symmetric acral and periorificial dermatitis was the primary manifestation of zinc and concurrent nutritional deficiencies in this patient, suggesting dermatological manifestations may be early markers of nutritional deficiencies in patients undergoing gastric bypass. Standard nutritional supplements decrease incidence of most nutritional deficiencies, but trace elements like zinc may require greater supplementation [1, 13]. Lifelong nutritional follow-up (in absence of other risk factors that predispose individuals to nutritional deficiency) is reasonable for gastric bypass patients.

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