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Acquired acrodermatitis enteropathica due to zinc deficiency in a patient with pre-existing Darier's disease

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Abstract

Background: Acrodermatitis enteropathica is characterised by inflamed patches of dry red skin which then become crusted and blistered before revealing a pustulent eroded lesion. Typically these patches start near the body's orifices before migrating to other sites, however in this patient the presentation was atypical thus delaying the diagnosis.

Observations: We report a case of an atypical presentation of acrodermatitis enteropathica (AE) due to acquired zinc deficiency in a 65 year old female patient with a previous diagnosis of histologically confirmed Darier's disease. This patient's rash began on the limbs and trunk before progressing to include the perineum, oral mucosa and nose. Diffuse loss of hair on scalp, eyebrows and eyelashes was observed.

Acrodermatitis enteropathica typically presents in infants, either due to an autosomal recessive genetic disorder, or after the cessation of breast feeding. In adults acquired zinc deficiency can be caused by glucagonoma syndrome, poor nutritional state, intestinal malabsorption, nephrotic syndrome and after major trauma (i.e. burns or significant surgery). In our patient low zinc levels confirmed hypozincaemia and the diagnosis of acrodermatitis enteropathica. The patient started oral zinc replacement. Within a few days her symptoms began to improve, and her hair has started to grow.

Conclusion: We believe this to be an unusual presentation of acrodermatitis enteropathica due to a probable dietary zinc deficiency in a lady with pre-existing Darier's disease which may possibly have influenced the uncharacteristic clinical presentation.

Introduction

Acrodermatitis enteropathica (AE) is characterised by inflamed patches of dry red skin which then become crusted and blistered before revealing a pustulent eroded lesion. Typically these patches start near the body's orifices before migrating to other sites,[1] however in this patient the presentation was atypical thus delaying the diagnosis. This is a case of a 65 year old woman with a known diagnosis of Darier's disease (keratosis follicularis), who presented with an atypical rash. Darier's disease is an autosomal dominant condition causing greasy, hyperkeratotic papules in seborrheic regions, with a variety of nail changes including white and red longitudinal bands, longitudinal nail ridges, longitudinal splitting, and subungual hyperkeratosis. V-shaped nail abnormalities are the most pathognomic finding.[2]

Case report

This patient's Darier's had been well controlled, with no skin lesions for the past few years. She complained of a new rash of nine months duration which had started on her limbs and spread to her trunk. The rash was becoming more prolific and what had initially started as scaly red patches was beginning to blister and show pustulent debris in eroded lesions. The patient complained of severe pain and was very distressed by these symptoms, particularly a new alopecia. Other than the presence of a widespread rash over the arms, legs and trunk, severely ridged

and broken nails (probably Darier's related) and the diffuse alopecia there were no abnormalities on clinical examination and she was systemically well. Due to concerns about the possibility of pemphigus vulgaris or possibly paraneoplastic pemphigus (and the speed with which the disease had progressed) the patient was admitted, blood samples and biopsies for histology and direct immunofluorescence taken and a course of high dose steroids (80mg prednisolone) started.

Despite this initial therapy the patient failed to show any response and the rash progressed to include her buttocks, perineum and perioral regions (Fig. 1-2). In the perineum and posterior thighs the rash coalesced into one large eroded site that made any form of movement or contact painful. The returned biopsies failed to show any evidence of histological characteristic abnormality. Direct immunofluorescence was negative. Swabs and blood cultures confirmed the presence of staphylococcus aureus colonisation. Appropriate antibiotic therapy was added to the high doses of steroids but again the patient's condition deteriorated with an increased number of erosive, sloughy ulcerations with other smaller inflammatory papules that Koebnerised when scratched. The patient was requiring morphine for analgesia due to the lesions.

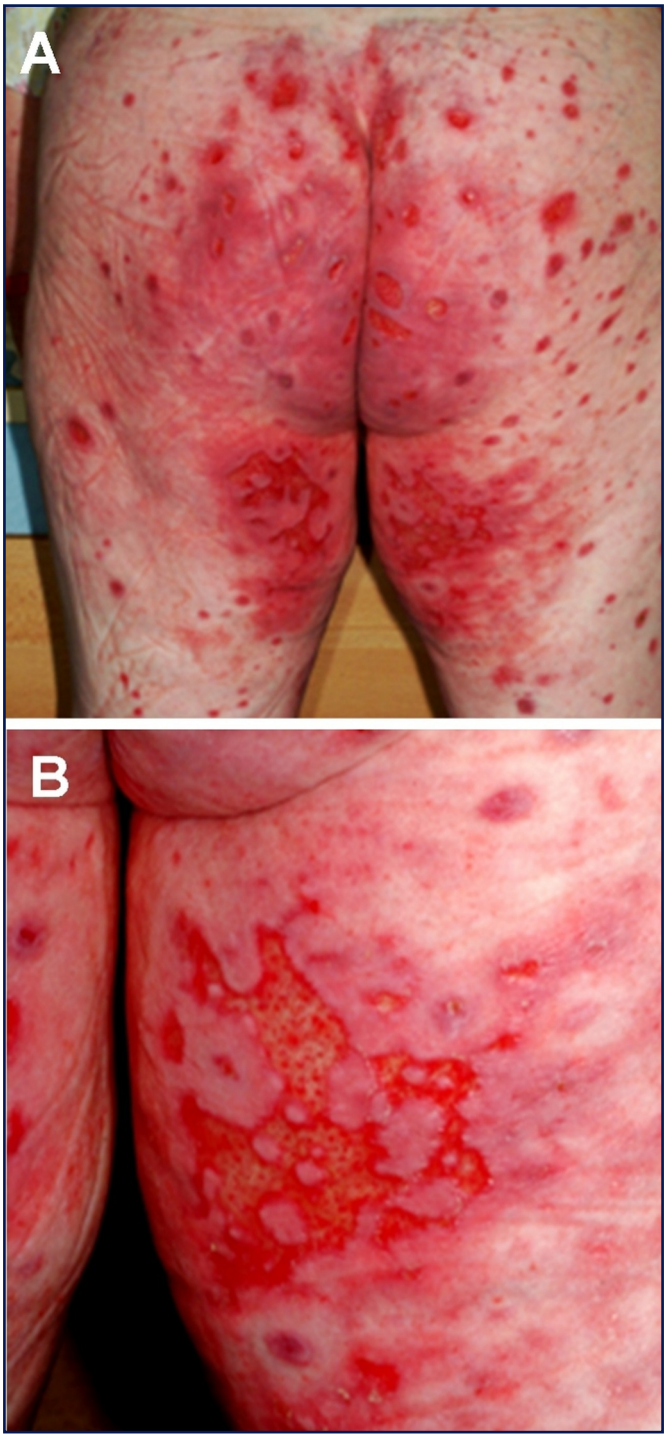

Figure 1

Buttocks and upper thighs (A). Close up of coalesced rash on buttocks containing sloughy pustulent material (B).

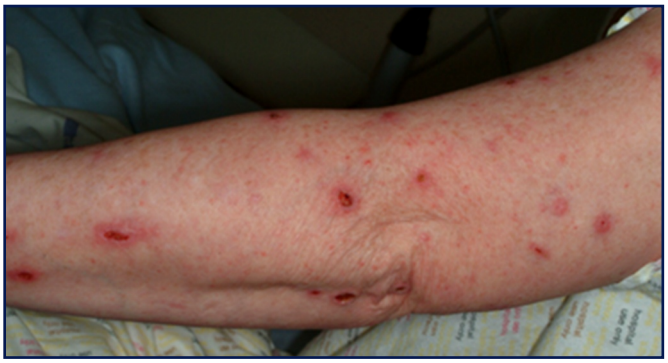

Figure 2

Appearance of rash on limbs.

A familiar looking rash was eventually found following much research, with two possible causes identified; necrolytic migratory erythema due to glucagonoma syndrome or acrodermatitis enteropathica. An abdominal ultrasound followed by an abdominal computer tomography scan revealed no pancreatic masses so after taking blood for assessment of her serum zinc level a trial of oral zinc therapy was initiated whilst the results were awaited, and the antibiotics and steroids were both stopped. Within five days the patient reported improvement of the rash, but mindful of her desperate need for a diagnosis we reacted cautiously. As she continued on the zinc therapy her rash continued to resolve until she was finally discharged two weeks later with just pale purple scars to remind her of what she had suffered. One week post discharge the patient's zinc levels were reported as being 10.2 which is low (Normal Range 11.0-24.0) thus confirming that her problems had been due to zinc deficiency. The patient has now remained well off steroid and antibiotic treatment and she continues to be well whilst remaining on zinc supplementation. Her hair is growing back and her skin continues to be lesion free confirming that this was an atypical presentation of a zinc deficiency state.

Discussion

Zinc is essential for the normal function of all cells and is important for the function of vital enzymes such as alkaline phosphatase.[3] Zinc is one of the essential trace

elements[3,4] and can be found in high concentrations in shellfish, green leafy vegetables, legumes, nuts and whole grains.[4,5] Foods which are rich in protein also provide a good source of zinc.[5,6]

Acrodermatitis enteropathica is a rare genetic disorder where there is malabsorption of zinc through the intestinal cells. Weismann *et al*[7] performed absorption studies calculated from retention values recorded in the time interval 8-30 days after oral administration of 65Zn in five patients with AE. Two AE patients (7 and 13 years old) had a low absorption of 3.3% and 1.8% respectively. In three adult AE patients zinc absorption ranged from 28 to 36% (mean 34%). In the healthy controls the range was 27 - 65% (mean 43%).[7] The genetic defect responsible for AE is believed to involve SLC39A4 on 8q24.3 which codes for the transmembrane protein that serves as a zinc uptake protein.[8,9] Although AE presents more commonly in children on weaning; it may be seen in adults as a consequence of glucagonoma syndrome, dietary deficiency, intestinal malabsorption, nephritic syndrome or after traumatic events such as burns or surgery.[1,10]

Clinically AE is characterised by the presence of red and inflamed areas of dry and scaly skin that evolve into blistered lesions containing pus. Other features of the condition include a sharp demarcation between the affected area and normal skin; nail involvement; diffuse loss of hair on scalp, eyebrows and eyelashes; secondary infection; mouth ulcers.[1,10]

Biochemically there are low levels of circulating zinc and this is also reflected in the hair, saliva and urine (although these are rarely tested).[11] As the production of alkaline phosphatase is dependent on zinc these levels may be low too, although our patient always had consistently normal alkaline phosphatase levels. Patients with AE may also test positive for secondary infections such as staphylococcus aureus.[1,10] Histologically cutaneous lesions show intracellular oedema of epidermal keratinocytes but this is not pathognomonic and may be observed in other nutritional deficiencies.[1,10]

Patients who are found to be zinc deficient should be commenced on an oral zinc supplementation for life. Patients should begin to see improvement within the first week of commencing therapy. Problems associated with zinc therapy may include abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, gastric irritation, gastritis, irritability, headache and lethargy.[12]

In conclusion, we believe this to be an unusual presentation of acrodermatitis enteropathica due to a probable dietary zinc deficiency in a woman with pre-existing Darier's disease which may possibly have influenced the uncharacteristic clinical presentation.

References

1. Maverakis E, Fung MA, Lynch PJ, Draznin M, Michael DJ, Ruben B, Fazel N. Acrodermatitis enteropathica and an overview of zinc metabolism. *J Am Acad Dermatol*. 2007; 56: 116-124.
2. Sehgal VN, Srivastava G.. Darier's (Darier-White) disease/keratosis follicularis. *Int J Dermatol*. 2005; 44: 184-92.
3. Stefanidou M, Maravelias C, Dona A, Spiliopoulou C. Zinc: a multipurpose trace element. *Arch Toxicol*. 2006; 80: 1-9.
4. Tuerk MJ, Fazel N. Zinc deficiency. *Curr Opin Gastroenterol*. 2009; 25: 136-143.
5. Wittsiepe J, Schnell K, Hilbig A, Schrey P, Kersting M, Wilhelm M. Dietary intake of nickel and zinc by young children--results from food duplicate portion measurements in comparison to data calculated from dietary records and available data on levels in food groups. *J Trace Elem Med Biol*. 2009; 23: 183-194.
6. Haase H, Overbeck S, Rink L. Zinc supplementation for the treatment or prevention of disease: current status and future perspectives. *Exp Gerontol*. 2008; 43: 394-408.
7. Weismann K, Hoe S, Knuden L et al. 65Zinc absorption in patients suffering from acrodermatitits enteropathica and in normal adults assessed by whole body counting techniques. *Br J Dermatol*. 1979; 101: 573-9.
8. Nakano H, Nakamura Y, Kawamura T, Shibagaki N, Matsue H, Aizu T, Rokunohe D, Akasaka E, Kimura K, Nishizawa A, Umegaki N, Mitsuhashi Y, Shimada S, Sawamura D. Novel and recurrent nonsense mutation of the SLC39A4 gene in Japanese patients with acrodermatitis enteropathica. *Br J Dermatol*. 2009; 161: 184-186.
9. Schmitt S, Küry S, Giraud M, Dréno B, Kharfi M, Bézieau S. An update on mutations of the SLC39A4 gene in acrodermatitis enteropathica. *Hum Mutat*. 2009; 30: 926-933.
10. Sehgal VN, Jain S. Acrodermatitis enteropathica. *Clin Dermatol*. 2000; 18: 745-748.
11. Jacobus P, Van Wouwe JP. Clinical and laboratory assessment of zinc deficiency in Dutch children. A review. *Biol Trace Elem Res*. 1995; 49: 211-225.
12. Maret W, Sandstead HH. Zinc requirements and the risks and benefits of zinc supplementation. *J Trace Elem Med Biol*. 2006; 20: 3-18.