

# Tea tree oil dermatitis associated with linear IgA disease

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## Summary

Tea tree oil dermatitis is an increasingly common finding, reflecting the strong demand for natural remedies and aromatic substances. Linear immunoglobulin A (IgA) disease is a rare acquired subepidermal blistering disorder, characterized by basement membrane zone IgA deposition. We describe a patient in whom linear IgA disease appears to have been precipitated by a contact reaction to tea tree oil.

## Introduction

We present an 18-year-old female patient who developed an acute bullous eruption following the application of tea tree oil to her recently pierced umbilicus. Patch testing confirmed her allergy to tea tree oil; however, immunofluorescence of both peri-lesional and nonlesional skin revealed the typical features of linear immunoglobulin A (IgA) disease.

The dramatic increase in consumer demand for natural remedies and aromatic substances over the last few years has prompted an increase in the commercial production of tea tree oil, the essential oil distilled from the leaves of the *Melaleuca alternifolia cheel*. It is not surprising to find that the number of case reports describing allergic contact dermatitis to tea tree oil is also increasing.<sup>1,2</sup>

Linear IgA disease was first described by Bowen in 1901; however, it was only recognized as an entity distinct from dermatitis herpetiformis in 1979. Most cases are of unknown aetiology, but recognized precipitating factors include infection, local skin trauma,<sup>3</sup> and a wide range of drugs, including penicillin,<sup>4</sup> vancomycin, phenytoin, lithium, captopril, diclofenac and somatostatin.<sup>5</sup>

Drug-induced linear IgA disease tends to resolve on cessation of the offending drug and is associated with a lower morbidity.<sup>6</sup>

As far as we are aware, this is the first case of linear IgA disease precipitated by a topical agent.

## Case report

An 18-year-old female patient attended the Accident and Emergency Department with a pruritic blistering rash over her umbilical region. She had had her umbilicus pierced 3 weeks earlier with a silver ring, and was advised to apply tea tree oil for 2 weeks followed by Ster-Zac (SSL Internation plc, Oldham, UK) powder.

During the latter part of the 2-week period she developed a pruritic erythematous rash over the umbilical region, which gradually spread, with the development of blisters (Fig. 1).

This prompted a visit to her general practitioner who prescribed erythromycin and advised her to restart applying the tea tree oil to the area. The subsequent increase in the size and number of blisters prompted her to attend her local hospital.

On examination there were multiple bullae, some of which were deroofed, in the umbilical and peri-umbilical region (Fig. 1). A separate vesicular eruption was present on the left flank at the site of contact with tape used for her dressings.

It was initially thought that she had developed a contact reaction to one of the agents to which she had been exposed (i.e. metal, tea tree oil or Ster-Zac powder), but some of the blisters were distant from the sites of contact.

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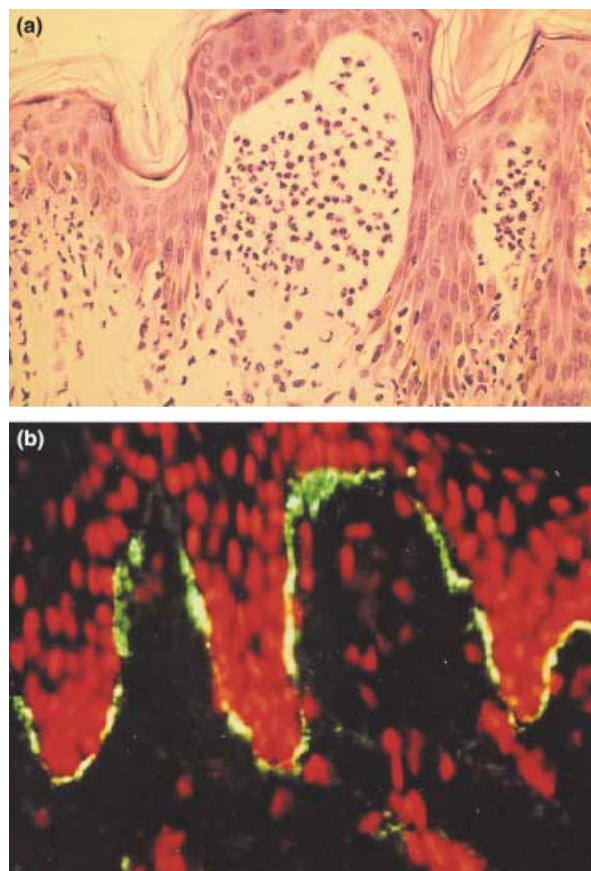
**Figure 1** Acute bullous eruption on the abdomen.

Lesional skin taken from the umbilical region was sent for histopathology, and peri-lesional skin from the umbilical region was sent for direct immunofluorescence. Several weeks later, once the acute episode had settled, serum and nonlesional skin, taken from the left buttock, were also sent for immunofluorescence.

Histological examination of lesional skin showed subepidermal blistering with oedematous dermal papillae containing numerous neutrophils (Fig. 2a). The appearances resembled the papillary tip microabscesses of dermatitis herpetiformis but were more extensive and compatible with linear IgA disease. Direct immunofluorescence showed a bright linear band of IgA at the basement membrane zone in peri-lesional skin (Fig. 2b), and a similar but less prominent band in nonlesional skin, which localized to the floor of the blister on salt split skin. Indirect immunofluorescence was negative. The histological and immunopathological features were characteristic of linear IgA disease.

Patch testing was performed to the standard European battery, as well as to Ster-Zac powder and tea tree oil; readings were taken at 2 and 4 days after application of the test substances. Our patient showed positive reactions to tea tree oil and to colophony.

The patient responded to dermivate topically and was discharged 5 days after admission. Review 1 month later revealed no evidence of blistering and no mucosal involvement. Our patient reported that she had developed several new blisters since discharge from hospital which responded to topical steroids. She was followed up for a further period of 8 months, during which time she experienced no further episodes of blistering.



**Figure 2** (a) Histological appearance of bullae in Fig. 1. The biopsy was taken from lesional skin on the abdomen (haematoxylin and eosin, magnification  $\times 20$ ). (b) Direct immunofluorescence of perilesional skin taken from the abdomen, showing deposition of linear IgA at the dermo-epidermal junction.

## Discussion

It appears that our patient developed a contact dermatitis from exposure to tea tree oil which precipitated linear IgA disease. It is recognized that deposition of immunoreactants may occur as a nonspecific finding in severe contact dermatitis, and also that secondary spread may occur in patients with florid allergic contact dermatitis.

However, the presence of a linear IgA band at the basement membrane zone on direct immunofluorescence of both peri-lesional and nonlesional skin, in conjunction with characteristic histopathological features, supports our hypothesis that the linear IgA disease was precipitated by a contact reaction to tea tree oil.

Linear IgA disease has features in common with other subepidermal bullous diseases; however, certain immunopathologic distinctions, i.e. the deposition of

IgA at the basement membrane zone, have prompted its recognition as a distinct clinical entity. Circulating IgA antibodies may also be present and salt splitting of normal skin reveals epitopes on the epidermal side in the majority of cases.

Kuechle *et al.*<sup>5</sup> described six cases of drug-induced linear IgA disease with a variety of oral medications; they also compared the clinical, pathological and immunofluorescence findings with those in idiopathic linear IgA disease. They proposed that drug-induced linear IgA disease differs from idiopathic IgA in several respects; the absence of conjunctival lesions, spontaneous remission on cessation of the offending drug and disappearance of immune deposits from the skin once the lesions had resolved. In contrast, 10 to 50% of patients with idiopathic linear IgA disease resolve spontaneously, and immune deposits persist in the skin after resolution of the lesions in some to most cases.<sup>3</sup> It is therefore interesting to note that, in our patient, linear IgA was still present in the skin on immunofluorescence once the lesions had resolved; this may suggest that our patient was genetically primed to develop linear IgA disease in the presence of certain precipitants. This aspect clearly needs further investigation.

Bullous pemphigoid is clinically similar to linear IgA disease; however, it demonstrates subepidermal eosinophilic predominance on histology, and IgG deposition along the basement membrane. Drug-induced bullous pemphigoid is a well-described phenomenon; penicillamine, enalapril, phenacetin, frusemide<sup>7</sup> and spironolactone<sup>8</sup> have all been implicated.

Our understanding of linear IgA disease has recently been enhanced by the identification of the target antigens and epitopes that the basement membrane zone antibodies react with. The most common target antigen appears to be BP180.<sup>9</sup> Other target antigens include BP230 and collagen VII.<sup>10,11</sup> It also appears that individuals with linear IgA disease may possess autoantibodies which react with more than one antigen and antigenic site.<sup>12–14</sup>

Other developments include the identification of genetic variations in the HLA system which influence susceptibility to linear IgA disease and clinical features such as disease severity. For example, the autoimmune haplotype HLA B8, CW7, DR3 is thought to be related to early disease onset in childhood.<sup>15</sup> Collier *et al.*<sup>15</sup> also found that the presence of the tumour necrosis factor 2 (TNF2) allele is associated with a longer disease duration.

It is reasonable to suggest that our patient may have been genetically primed to develop linear IgA disease,

with the result that any disruption to her skin, whether it be a contact dermatitis secondary to tea tree oil or colophony in the tape used on her flank, was sufficient to produce blistering.

As far as we are aware, this is the first reported case of linear IgA disease precipitated by contact dermatitis to a topical agent, in this case tea tree oil. This finding is of significance in the context of the increasing use of tea tree oil by consumers which will be accompanied by an increase in the incidence of adverse effects.

## References

- 1 Khanna M, Quasem K, Sasseville D. Allergic contact dermatitis to tea tree oil with erythema multiforme-like ID reaction. *Am J Contact Dermat* 2000; **11**: 238–42.
- 2 Knight T, Hausen B. Melaleuca oil (tea tree oil) dermatitis. *J Am Acad Dermatol* 1994; **30**: 423–7.
- 3 Wojnarowska F, Marsden R, Bhogal B, Black M. Chronic bullous disease of childhood, childhood cicatricial pemphigoid and linear IgA disease of adults, a comparative study demonstrating clinical and immunopathological overlap. *J Am Acad Dermatol* 1988; **19**: 792–805.
- 4 Combemale P, Gavaud C, Cozzani E *et al.* Linear IgA dermatosis induced by penicillin G. *Ann Dermatol Venereol* 1993; **120**: 847–8.
- 5 Kuechle M, Stegemeir E, Maynard B *et al.* Drug-induced linear IgA bullous dermatosis: report of six cases and review of the literature. *J Am Acad Dermatol* 1994; **30**: 187–92.
- 6 Nousari H, Kimyai-Asadi A, Caeiro J *et al.* Clinical, demographic, and immunohistologic features of vancomycin-induced linear IgA bullous disease of the skin. Report of 2 cases and review of the literature. *Medicine* 1999; **78**: 1–8.
- 7 Baz K, Ikizoglu G, Kaya T, Koca X. Furosemide induced bullous pemphigoid. *J Eur Acad Dermatol Venereol* 2002; **16**: 81–2.
- 8 Modeste A, Cordel N, Courville P *et al.* Bullous pemphigoid induced by spironolactone. *Ann Dermatol Venereol* 2002; **129**: 56–8.
- 9 Zone J, Taylor T, Meyer L *et al.* The 97 kDa linear IgA bullous disease antigen is identical to a portion of the extracellular domain of the 180 kDa bullous pemphigoid antigen, BPAg2. *J Invest Dermatol* 1998; **110**: 207–10.
- 10 Hashimoto T, Ishiko A, Shimizu H *et al.* A case of linear IgA bullous dermatosis with IgA anti-type VII collagen autoantibodies. *Br J Dermatol* 1996; **134**: 336–9.
- 11 Ghohestani R, Nicolas J, Kanitakis J *et al.* Linear IgA bullous dermatosis with IgA antibodies exclusively directed against the 180- or 230-kDa epidermal antigens. *J Invest Dermatol* 1997; **108**: 854–8.
- 12 Zhou S, Ferguson D, Allen J, Wojnarowska F. The localisation of target antigens and antibodies in linear IgA disease is variable; correlation of immunogold electron

- microscopy and immunoblotting. *Br J Dermatol* 1998; **139**: 591–7.
- 13 Schumann H, Baetge J, Tasanen K *et al.* The shed ectodomain of collagen XVII/BP180 is targeted by autoantibodies in different blistering skin diseases. *Am J Pathol* 2000; **156**: 685–95.
- 14 Wojnarowska F. What's new in linear IgA disease? *J Eur Acad Dermatol Venereol* 2000; **14**: 441–3.
- 15 Collier P, Wojnarowska F, Welsh K *et al.* Adult linear IgA disease and chronic bullous disease of childhood: the association with human leucocyte antigens Cw7, B8, HLA DR3, and tumour necrosis factor influences disease expression. *Br J Dermatol* 1999; **141**: 867–75.