Linear IgA dermatosis

What is linear IgA dermatosis?[1]

Synonym: linear IgA bullous dermatosis

Linear IgA bullous dermatosis (LABD) is a rare subepidermal autoimmune blistering disease characterised by linear deposition of IgA along the basement membrane zone. Although most reported cases are idiopathic, there is a subset of patients with drug-induced LABD and various drugs have been associated with the drug-induced form of the disease.

The disease affects both children and adults. In the non-drug-related category the cause is mostly unidentified. However, several cases have been reported following an episode of infection (eg, typhoid, brucella, tuberculosis, varicella, herpes zoster, gynaecological infections, upper respiratory infections). In children, the condition has been known historically as chronic bullous dermatosis of childhood.

Histopathology[2]

LAD is an autoimmune disease histopathologically characterised by the linear deposition of IgA at the BMZ. One function of the BMZ is to maintain the contiguity of the dermal-epidermal junction; antibody deposition causes complement fixation and neutrophil chemotaxis (rapid migration of neutrophils to sites of inflammation), eventually resulting in blister formation. It has recently been found that IgA autoantibodies from patients with LAD induce granulocyte-dependent dermal-epidermal separation in cryosections of human skin.

At the molecular level, various antigens have been identified, some of which are also seen in patients with bullous pemphigoid. Various types of dermal proteins have been identified as antigens. It is increasingly acknowledged that LAD can be divided into various subtypes depending on antigen targets and histopathology.

The immune pathology appears to be identical in adults and children.

How common is linear IgA dermatosis? (Epidemiology)[3]

This is a rare condition with an incidence in Western Europe of 0.5 per million.

The distribution of the age of onset seems to follow a bimodal pattern:

- In children, the age range is from 6 months to 10 years, with a mean of 3.3-4.5 years.
- In adults, the range is from 14-83 years with a mean of 52 years. Drug-induced disease is more prevalent in older people, probably because they are most likely to be on medication.

Symptoms of linear IgA dermatosis (presentation)[4]

History

Before the appearance of the rash, there may be chronic pruritus or acute itching or burning. Patients developing ocular lesions may initially note pain, grittiness or discharge.

As with any patient presenting with a rash, a detailed medication history should be taken. The rate of spread of the blisters is variable. They tend to appear quickly in drug-induced cases. In vancomycin-induced cases the onset ranges from 1-13 days after the first dose.

Examination

Several skin presentations may occur:

- Clear round or oval blisters on normal underlying skin.
- Small blisters (vesicles) or large ones (bullae), often target-shaped, surmounting an erythematous area of skin which is flat or raised.
- New vesicles developing in a ring around an old one (the 'string of beads' sign).
- A crop of vesicles developing close together ('cluster of jewels' sign).

- Crusts, scratch marks, sores and ulcers.
- Lesions which mimic erythema multiforme, bullous pemphigoid and dermatitis herpetiformis.
- 50% of patients have blisters and ulcers around the mouth and lips.
- Ophthalmological findings may include subconjunctival fibrosis and shrinkage of the fornices.

The distribution of the skin lesions varies between children and adults. Children tend to get them on the lower abdomen, anogenital areas, perineum, hands, feet and face. In adults, lesions tend more commonly to develop on the trunk and limbs. In both age groups the distribution may be symmetrical or asymmetrical.

Differential diagnosis

A number of skin conditions have an almost identical appearance. These include:

- Bullous pemphigoid.
- Dermatitis herpetiformis.
- Lupus erythematosus.
- Epidermolysis bullosa acquisita.

Diagnosing linear IgA dermatosis (investigations) [3] [5]

- Histopathology of a skin biopsy shows subepidermal blistering, differentiating the condition from diseases in which blistering occurs within the epidermis (eg, pemphigus).
- Direct immunofluorescence remains the gold standard for diagnosis. Direct immunofluorescence reveals IgA deposition along the basement membrane.
- Serum IgA levels may be raised but this occurs more often in the childhood version.

- Techniques to identify individual antigens within the BMZ are available but these are more research tools than diagnostic investigations.

Associated diseases[6] [7]

- Chronic kidney disease.
- Immune complex glomerulonephritis.
- Lymphocytic colitis.
- Lymphoma.
- Other malignant tumours.
- Psoriasis.
- Rheumatoid arthritis.
- Sarcoidosis.
- Ulcerative colitis.

Associated drugs [8]

Vancomycin is the most common drug involved. Other drugs implicated include:

- Amiodarone.
- Atorvastatin.
- Captopril.
- Cefamandole.
- Ceftriaxone.
- Furosemide.
- Glibenclamide.
- Interleukin-25.
- Lithium carbonate.
- Metronidazole.

- Non-steroidal anti-inflammatory drugs.
- Penicillin.
- Phenytoin.
- Somatostatin.
- Trimethoprim-sulfamethoxazole.

Linear IgA bullous dermatosis may occur after COVID-19 vaccination.[9]

Management of linear IgA dermatosis[6]

Ruptured lesions and erosions may require sterile dressings. Large bullae do not require any particular treatment if intact. Infection lesions should be treated with topical mupirocin and sterile dressings twice-daily.

Dapsone is a commonly used treatment, but many therapeutic agents have emerged in recent years. Rituximab, omalizumab, etanercept, IVIg, sulfonamides, topical corticosteroids, and others have been used successfully with varying disease severity. Sulfonamides have been used in places without access to dapsone.[5]

In drug-related disease, removal of the offending drug usually results in resolution, although this can take up to two weeks. Corticosteroids have been required to hasten resolution in severe cases.

Hospital referral

- Dermatological referral will be required for the initial diagnosis.
- An ophthalmological opinion will be required once diagnosis has been made, irrespective of whether the patient has any eye symptoms, as changes may be detected on examination (eg, subconjunctival fibrosis) before complications arise.

Complications of linear IgA dermatosis[10]

Complications are usually the result of scarring. Lesions on the gums can result in desquamative gingivitis resulting to damage to the teeth. Ocular linear IgA may mimic cicatricial pemphigoid and lead to blindness. There have been reports of involvement of the pharynx, larynx, nose, rectum and oesophagus.

Prognosis[11] [12]

In children, most idiopathic cases resolve within two years. In adults the disease can be more protracted and in some cases can be refractory.

LDA may improve during pregnancy. No fetal damage occurs as a result of the treatment (dapsone) or the disease.[13]

Further reading

- Linear IgA disease; DermNet NZ
- Bernett CN, Fong M, Yadlapati S, et al; Linear IGA Dermatosis. StatPearls, Aug 2022.

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