Acta Derm Venereol 2015; 95: 1015–1017

SHORT COMMUNICATION

A Case of Neonatal Linear IgA Bullous Dermatosis with Severe Eye Involvement

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Accepted Feb 16, 2015; Epub ahead of print Feb 24, 2015

Linear IgA bullous dermatosis (LABD) of childhood is a chronic autoimmune blistering disease characterised by linear deposition of IgA at the cutaneous basement membrane zone (BMZ) (1–4). Although LABD is rare, it represents the most common autoimmune blistering disorder of childhood (1–3, 5, 6). The childhood variant of LABD has a mean age of onset between 4 and 5 years (1, 3, 4). The clinical presentation is characterised by a sudden eruption of clear vesicles and blisters on normal or erythematous skin, affecting at first the perineum and perioral area. Typically, new blisters develop around resolving lesions resulting in an annular or "rosette-like" configuration. Mucosal involvement is common and manifests with conjunctivitis, oral and nasal erosions (2, 3, 4, 6). Ocular lesions can be severe leading to symblepharon, trichiasis, shrinkage of fornices and, rarely, corneal opacities (6). The disease has a chronic relapsing course and in the majority of cases resolves before puberty (1, 5). A few neonatal cases of LABD have been described (7–13). Mucosal involvement was predominant in these patients. We present a rare case of LABD in a neonate with severe ocular manifestations.

CASE REPORT

A 3,800 g full-term Italian male was born to a 36-year-old healthy woman after *in vitro* fertilisation. Pregnancy started with triplets, but miscarriage of 2 foetuses occurred at week 10. Family history was negative for skin diseases. At day 3, several vesicles and tense blisters were noticed in the diaper area, neck and face. Bilateral mucopurulent conjunctivitis developed at the same time. The following day, the newborn presented nasal secretion and oral erosions. At first, a viral or bacterial infection was suspected, and intravenous ampicillin and acyclovir were started while blood tests were pending. Blood polymerase chain reaction (PCR) for herpes viruses (HSV, HHV6, HHV7, HHV8, VZV) and bacterial cultures were negative, and no bacteria or viruses were isolated from swabs of the vesicles. Results of routine laboratory tests (complete blood count, C-reactive protein, and urine analysis) were normal for age. New clear vesicles appeared in the next few days on the head (ears, scalp and nose) and neck, together with sparse elements on the trunk and limbs; oral erosions and conjunctivitis were persistent. In addition, the patient manifested laryngeal stridor due to upper airway involvement. At day 14, a chest X-ray showed bilateral perihilar and basal atelectasis. Progressive respiratory compromise led to intubation of the newborn, who was transferred to the neonatal intensive care unit of our hospital. On admission, the baby presented widespread serous vesicles, blisters and crusted erosions mainly localised to the head, neck, diaper and periumbilical areas and extremities (Fig. 1A–D). Bullous lesions frequently arose on erythematous skin and presented a "rosette-like" pattern with central clearing. Skin erosions were treated with antiseptics. Ocular examination revealed a bilateral blepharoconjunctivitis with ulcerative keratitis of the right eye, for which dexamethasone, tobramycin and trehalose eye drops were administered 3 times daily. Improvement of respiratory symptoms allowed extubation 3 days after admission. Due to persistent laryngeal stridor and wheezing, aerosol therapy with salbutamol 150 μg/kg/day and beclomethasone dipropionate 400 μg/day, in 4 divided doses was started. In parallel, because of dysphagia and oral feeding difficulty, the patient was in part fed by nasogastric tube until week 6 of age. Gastroesophageal reflux was treated with sodium alginate and lansoprazole. New skin and oral lesions ceased to develop by day 25 and cutaneous lesions healed rapidly without scarring.

Upon admission, a skin biopsy of a vesicular lesion of the trunk was performed for routine histopathological examination, followed by a biopsy from perilesional skin for direct immunofluorescence (DIF). Histopathology showed a subepidermal blister with neutrophils and eosinophils admixed with mononuclear cells. DIF revealed linear IgA deposition along the cutaneous BMZ, in the absence of IgG and C3 deposits (Fig. 1E), consistent with a diagnosis of LABD. No circulating anti-BMZ antibodies could be detected at 2 months of age by indirect immunofluorescence on salt-split skin. Immunoblotting assays using normal keratinocyte extracts and medium also proved negative at the same age. Finally, the mother's serum was negative in both assays.

Respiratory manifestations recovered slowly with aerosol therapy. Indeed, bronchoscopy examination performed 6 weeks post-treatment showed minimal inflammatory changes of the larynx and residual tracheal mucous secretions. The infant was discharged at the age of 2 months with complete resolution of skin and oral lesions, normal weight for age, but persistent right eye involvement and mild wheezing.

At monthly follow-ups, no relapses of skin disease were observed. The patient continued aerosol therapy with gradual respiratory improvement until 8 months of age. Despite treatment with trehalose and antibiotic eye drops for several months, an eye examination under general anaesthesia displayed a right corneal leucoma with deep neoangiogenesis. To date, at 17 months of age the child is performing occlusion therapy for amblyopia and visual acuity has not been measured due to young age.

DISCUSSION

To date only 7 cases of neonatal LABD have been described in the literature (7–13) (Table SI[1]). In all patients the disease at first affected the skin, manifes-

[1]https://doi.org/10.2340/00015555-2074

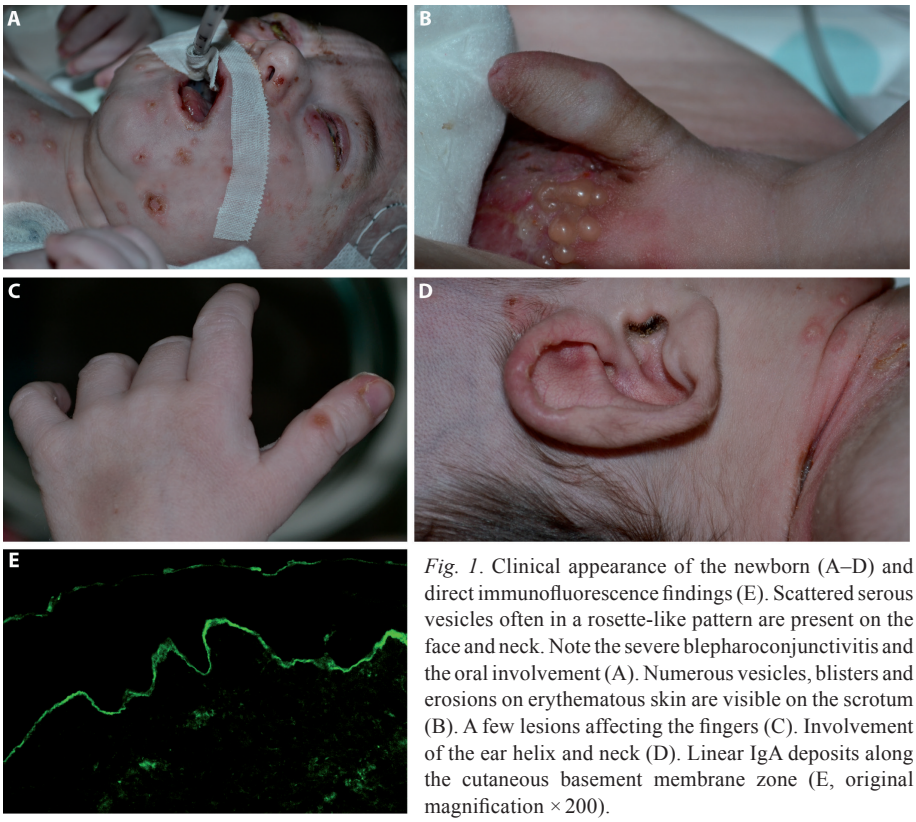

Fig. 1. Clinical appearance of the newborn (A–D) and direct immunofluorescence findings (E). Scattered serous vesicles often in a rosette-like pattern are present on the face and neck. Note the severe blepharoconjunctivitis and the oral involvement (A). Numerous vesicles, blisters and erosions on erythematous skin are visible on the scrotum (B). A few lesions affecting the fingers (C). Involvement of the ear helix and neck (D). Linear IgA deposits along the cutaneous basement membrane zone (E, original magnification × 200).

ting within day 10. The skin manifestations of neonatal LABD seem to resolve rapidly: in 5 patients, including ours, they subsided within the first month of life (7, 8, 12, 13). In our patient and in the case described by Kishida et al. (7) regression occurred in the absence of a specific systemic therapy. On the other hand, all reported cases, except one, were characterised by the severity of mucosal involvement, which followed the skin eruption and persisted longer. Seven patients, including ours, presented upper airway involvement with respiratory compromise leading to intubation and, in one case, tracheostomy (7–10, 12, 13). Death due to respiratory distress was reported in one patient who was also affected by VATERL syndrome (vertebral, anal, tracheoesophageal, renal and limb defects) and hypoplastic nasal sinuses (13). Four patients presented feeding difficulties and oesophageal involvement requiring gastrostomy in 3 of them (7–10). In addition, the severity and persistency of upper aerodigestive tract manifestations resulted in permanent scarring sequelae in 2 patients (7, 8). In our case, aerodigestive complications were less serious and resolved without scarring. In contrast, eye involvement was remarkably severe, leading to right eye corneal leucoma. Ocular manifestations with subsequent scarring and blindness have been reported in a single patient to date.

Systemic treatment with corticosteroids and/or dapsone was required in all neonatal LABD patients with significant mucosal involvement (Table SI[1]). Treatment-related complications included methemoglobinaemia and, likely, pneumonia and sepsis (7, 8, 10, 14). The relatively short disease course, in most cases ranging from a few weeks to approximately one year (Table SI[1]), supports a rapid tapering of systemic therapy needed for aerodigestive manifestations. In our patient, respiratory involvement could be satisfactorily managed with corticosteroid aerosol therapy after short-term intubation. In view of the poor bioavailability of systemic corticosteroids in corneal tissue, ocular lesions were treated with topical corticosteroids.

Almost no data are available on the target antigen in neonatal LABD. Circulating anti-BMZ IgA antibodies could be detected by indirect immunofluorescence in 3 out of 4 cases tested (7–10), and were localized to the epidermal side of salt-split skin in one case (9) and to the dermal side in a second one (7). In addition, immunoblotting studies performed in 2 patients did not allow to identify any target antigen (7, 9). No circulating antibodies could be detected in both our patient and his mother by indirect immunofluorescence and immunoblotting assays. The origin of IgA deposits in the skin in neonatal LABD also remains speculative, as the low levels of IgA detected in newborn cord blood have been reported to be of both foetal and maternal origin (15).

ACKNOWLEDGEMENTS

This study was supported by grants from Italian Ministry of Health (Ricerca Corrente Program) to ODP and MEH.

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