

Epidermolysis Bullosa Acquisita

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Introduction

Autoimmunity to type-VI collagen is characterized by autoantibodies predominantly of IgG class to the non-collagenous domain of type-VI collagen present in the anchoring fibrils which bind basement membrane lamina densa to the anchoring plaques in the dermis¹. This results in a sublamina densa split with a blister formation. Type VI collagen autoimmunity is heterogeneous in its clinical spectrum presenting as epidermolysis bullosa acquisita (EBA) or a subtype of bullous lupus erythematosus². . EBA, the commoner of the presentations, was first described by Elliot in 1895³. In its classical form it is characterized by increased skin fragility and non-inflammatory blisters that heal with scarring and milia, occurring predominantly over the trauma prone sites. In addition to its classical form it may clinically mimic bullous pemphigoid or cicatricial pemphigoid. Histologically there is a subepidermal blister with a variable infiltrate. Direct immunofluorescence (DIF) and indirect immunofluorescence (IF) of perilesional salt split skin (SSS), or the substrate respectively demonstrate linear deposition of IgG and sometimes IgA and IgM on the dermal side of the blister. Immunoelectron microscopy shows the immunoreactants to be in the sublamina densa zone. We describe a case of EBA whom we believe is the first confirmed case from Pakistan.

Case Report

A 46 years old male presented with 3 months history of an itchy blistering eruption over the neck, scalp, upper trunk, knees and elbows. He also had a blister on the tongue. On examination tense blisters on normal looking skin were seen on the above mentioned sites. Scarring and milia were also noticed on these sites. A tense haemorrhagic blister was also seen on the lateral aspect of the tongue (Figure 1).



Figure 1. A solitary haemorrhagic tense blister on the lateral aspect of the tongue. The mucosa was otherwise normal looking. During his stay in the hospital he also developed small vesicular eruption on the forearms in addition to the larger bullae. Systemic examination did not reveal any abnormality. Routine histopathology of a fresh lesion showed a subepidermal blister with a dense neutrophilic infiltrate. DIF studies of perilesional and lesional skin revealed linear deposition of IgG and C3 at the dermoepidermal junction (Figure 2)



Figure 2. FITC conjugated IgG deposited in a linear fashion at the dermoepidermal junction of the perilesional skin (Magnification-X 200).
extending into the floor of the blister cavity (Figure 3).

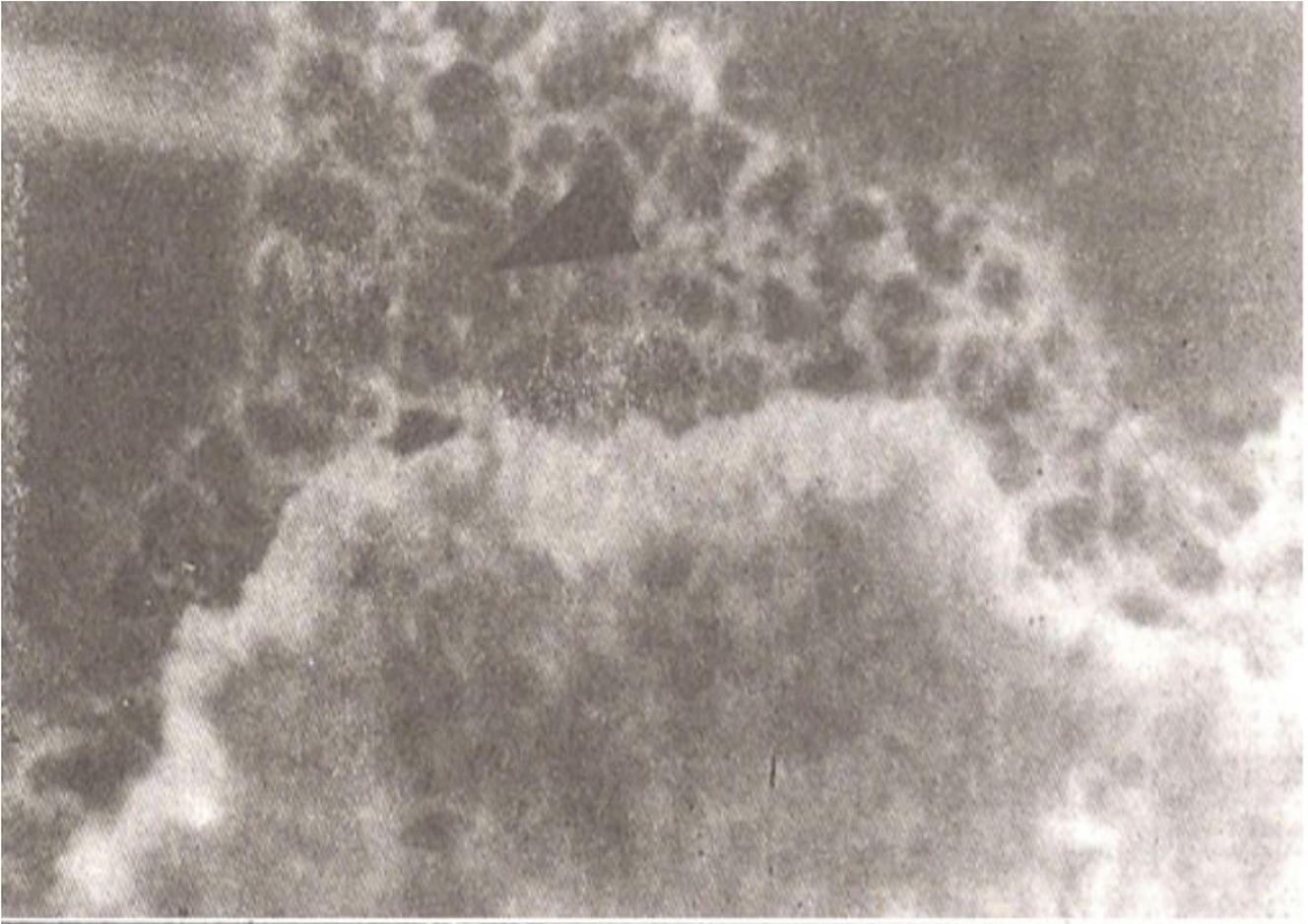


Figure 3. Section of a lesional skin. FITC conjugated IgG staining the floor of the blister cavity in a linear fashion. Blister cavity is marked by the black arrow head (Magnification X 400).

DJF of 1.0 molar NaCl split perilesional skin showed the immunoreactants to be confined to the floor of the split. Similar findings were seen in the vesicular lesions of the forearms. IIF was negative. These findings were consistent with the diagnosis of epidermolysis Bullosa Acquisita (EBA). Other investigations including blood counts, urinalysis, chest radiograph, autoimmune profile, liver functions tests and ultrasound abdomen were within normal limits. The patient was given tablet prednisolone 80 mg/day. The vesicular lesions were first to heal followed by the other lesions. After 3 weeks the steroids were tapered to 10mg every alternate day. With this treatment the patient is in remission with an occasional blister every now and then. The patient is being followed-up since 10 months.

Discussion

The diagnostic criteria for EBA are (a) A late onset mechanobullous disorder; (b) No family history of a mechanobullous disorder; (c) A subepidermal blister on routine histopathology; (d) A positive DIF with IgG at the dermoepidermal junction of perilesional skin; (e) deposits localized to lower lamina densa/sublamina densa zone on immunoelectron microscopy; (f) Alternative to (e) are indirect or direct immunofluorescence on SSS and/or western blotting⁴.

EBA is the prototype and the most common disease associated with autoimmunity to type-VII

collagen⁵. The age of onset varies widely from early childhood to late adult life, but most cases begin between the fourth and fifth decades. Classical presentation of EBA includes skin fragility, trauma induced blisters and erosions mainly on extensor aspects. The lesions are characteristically non-inflammatory and heal with scarring and milia. Scarring may be absent in the early stages of the disease. Mucosal surfaces may be affected including oral, pharyngeal, laryngeal, nasal, conjunctival, esophageal, genital and urinary bladder mucosa⁶. Lesions may resemble dominant dystrophic EB, porphyrias and bullous amyloidosis, but other clinical features and immunofluorescence can differentiate between the various conditions. Other variants of EBA include a bullous pemphigoid like picture⁷ or a mixture of classical EBA and bullous pemphigoid. EBA may clinically resemble cicatricial pemphigoid in producing scarring of the mucosae⁸. Routine histopathology shows a subepidermal blister, which is a feature shared by so many other disease and therefore, is of no diagnostic value. DIF shows deposition mostly of IgG but also C3, IgM, or IgA^{9,10}, at the dermoepidermal junction. About half the patients have no circulating auto-antibodies¹⁰ and therefore, the HF on SSS is of no help in such patients. This was the case in our patient for whom a modified DIF test was done which can distinguish between EBA and bullous pemphigoid with certainty¹⁰. Perilesional skin was incubated in 1M NaCl for 48 hours at 4°C. This procedure separates the epidermis from the dermis at the lamina lucida. The specimen was then frozen and cryosections were treated with reagents for DIF. Because the immunoreactants in EBA are in the sub-lamina densa area, they are seen on the dermal side of the saline induced split. In this patient the modified DIF showed deposition of IgG and C3 on the dermal side of the split. C3 deposition is not very common in EBA. IIF was negative in this patient because of lack of detectable circulating auto-antibodies. Our patient responded to standard immunosuppressive therapy, but this may not always be the case. Other therapies that may be effective and can be tried in resistant cases include, cyclosporin¹¹, dapsone, coichicine, phenytoin, vitamin E, gold, plasmapheresis¹² and intravenous immunoglobulin¹³. This is the first confirmed report of EBA from this county. In the absence of facilities for immunoelectron microscopy and immunoblot analysis, immunofluorescence studies on SSS are the minimum essential for the diagnosis of this disease.

References

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