

Pregnancy as a Trigger of Epidermolysis bullosa acquisita

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A 38-year-old woman developed epidermolysis bullosa acquisita (A-EBD) in connection with her third pregnancy. The activity of visible blistering disappeared at menopause. Direct immunofluorescence examination showed linear deposition of IgG and C'3 in the basement membrane zone. The light and electron microscopical findings of the disease were consistent with A-EBD. We assume that the bullous scarring eruption was triggered by a hormonal mechanism. *Key words:* Pregnancy; *Epidermolysis bullosa acquisita.* (Received September 18, 1982.)

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Epidermolysis bullosa dystrophica acquisita (A-EBD) has been accepted as a special form of the large heterogeneous group of mechanobullous diseases (4) commonly called epidermolysis bullosa.

The criteria for the diagnosis have been presented by Roenigk & Pearson (12); 1) trauma-induced bullae over the hands, feet, elbows and knees with atrophic scars, milia and nail dystrophy; 2) adult onset; 3) negative family history; 4) exclusion of other bullous diseases; 5) the finding of IgG in the basement membrane zone by direct immunofluorescence microscopy; 6) deposition of IgG in the amorphous zone beneath the basal lamina, demonstrable by immunoelectron microscopy; 7) demonstration of blister formation beneath the basal lamina with a zone of amorphous material.

There are many reports on associations of A-EBD with internal systemic diseases, amyloidosis, multiple myeloma, malignancies and Crohn's disease (1, 2, 12, 13). There are fewer observations on associations between A-EBD and hormonal events (7). The recently discussed suspicions about the nature of A-EBD, suggesting that it is an autoimmune skin disease (10, 12), are of interest. In this case report A-EBD began in connection with pregnancy.

CASE REPORT

A 38-year-old woman was admitted for examination at the dermatological department because of bullous eruption which had appeared on the second day after her third delivery. The first bullae, caused by minimal traumas, were situated on the dorsal aspects of hands and fingers and also on the back. Later the bullae on the trunk disappeared, but blistering continued on acral parts of extremities. Erosions were found on the oral membranes.

Blisters left atrophic scars with milia. Most disturbing was the scarring of nailbeds and destruction of the nails. The patient's two earlier pregnancies had been normal. At the age of 40 she had her fourth pregnancy, ending in spontaneous abortion. About 10 years later at menopause, the development of new, visible bullous eruptions suddenly ended and scars were left on the skin. Family history as far as similar skin findings were concerned was negative.

Laboratory examination showed normal complete blood cell count, differential count, GPT and chest X-ray examination. Antinuclear antibodies, cryoglobulins and uroporphyrins of urine were negative. In the urine there was unaccountable microscopic haematuria. Serum electrophoresis was within normal limits; in immunoelectrophoresis, IgG was polyclonally elevated. Direct IF of a skin biopsy specimen, which was taken 20 years after the onset of the disease from the edge of scarring sequelae, revealed IgG and weakly positive C'3. An indirect IF test indicated that in the serum of the patient there were no circulating basement membrane antibodies.

The first biopsy specimen of a bulla was examined by light microscopy 3 years after the onset of blistering. It revealed a large subepidermal separation with a well preserved epidermis. At the margin

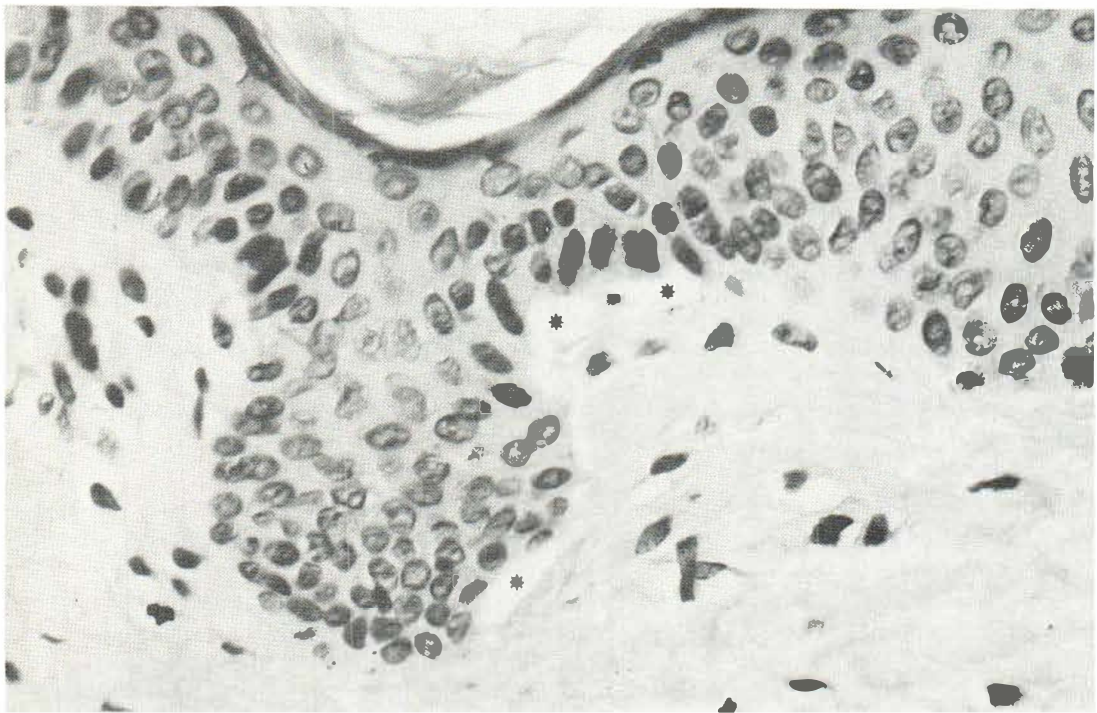


Fig. 1. Subepidermal blistering (*) at the margin of the bulla. Hematoxylin-eosin. $\times 675$.

of the bulla there was vacuolar blistering and the inflammatory cell infiltration was sparse (Fig. 1). In another biopsy 2 years later a blister of the same type was found and this time there was moderate infiltration of eosinophils and round cells beneath the bulla.

The electron microscopy showed that the blister formation occurred beneath the basal lamina even 20 years after the onset of the disease, although clinically visible bullous eruptions had ceased. The hemidesmosomes, basal lamina and lamina lucida were normal, but the anchoring fibrils were sparse in the lesional area (Fig. 2). Focal penetration of the blister was surrounded by amorphous materials of low to high density and by a dermal cell process (Fig. 2).

Treatment attempts with prednisolone, 40 mg daily, dapsone (Avlosulfon, IC1) 100 mg daily and vitamin E were of no avail.

DISCUSSION

The sudden appearance of bullous eruptions in a healthy middle-aged woman immediately after parturition suggests herpes gestationis (HG). In the case presented, the scarring feature and persistent blistering after parturition are not characteristic of HG, which usually disappears within 2 months after childbirth (5). An interesting overlap form between HG and bullous pemphigoid (BP) persisting 8 years after pregnancy was presented by Holmes et al. (9). Furthermore, HG responds well to prednisolone. In the case presented, the morphology of skin eruption and the post-traumatic etiology of blisters suggest epidermolysis bullosa dystrophica Cockayne-Touraine (EBD-CT). The clinical course of the disease rules out HG and BP. Both HG and BP and cicatricial pemphigoid (CP) have an immunofluorescent finding similar to A-EBD containing IgG and C'3 at the basement membrane (8). In this case the immunoelectron microscopic examination which ought to show the levels of immunodeposits was not made. In A-EBD they are below the basal lamina, while in BP, HG and CP they are found on the level of lamina lucida (10, 11).

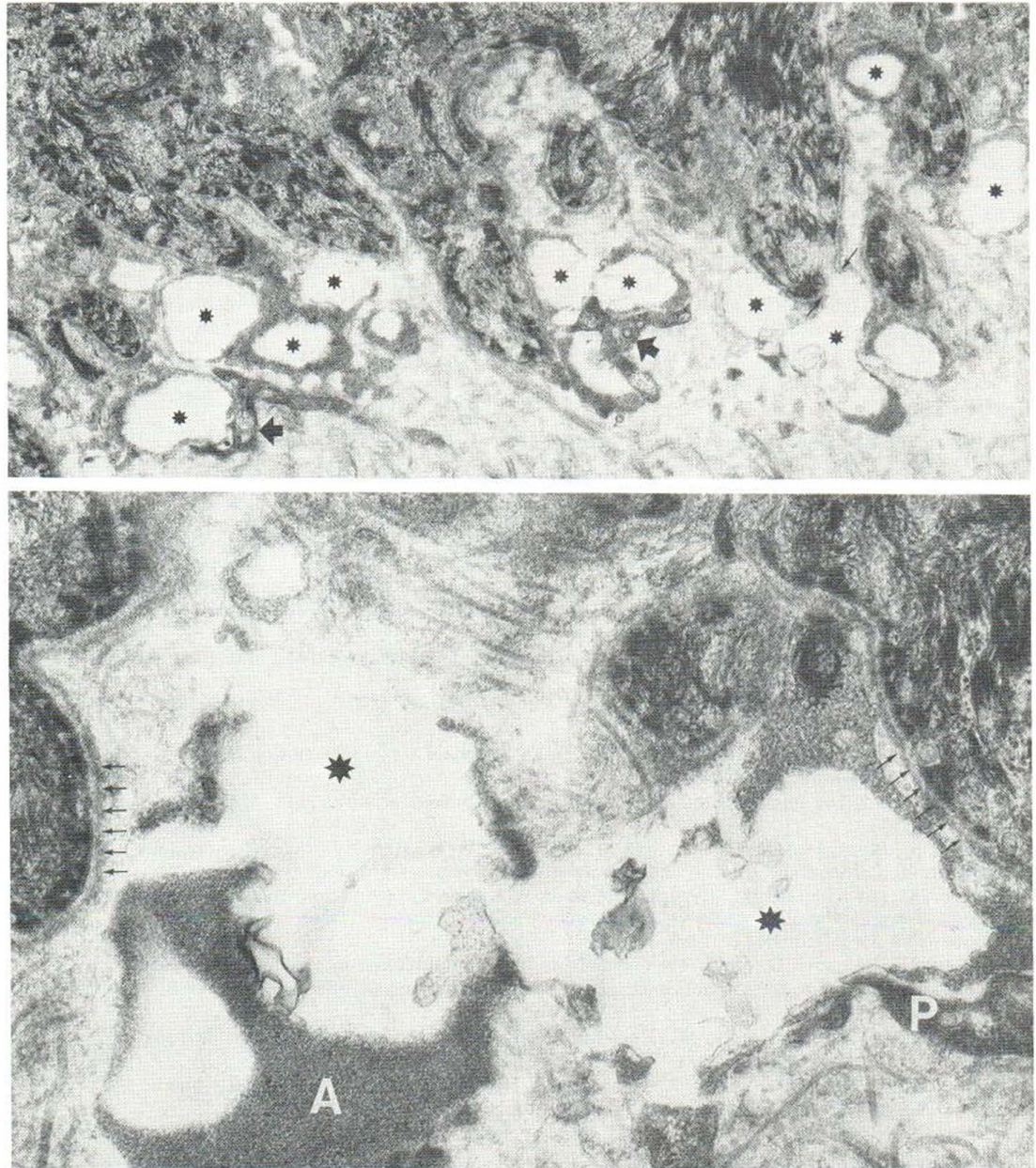


Fig. 2. Top: Several small bullae are surrounded by amorphous substance and a dermal cell process (thick arrow). A focal cleft in the basal lamina is seen between thin arrows. ($\times 10\,500$). *Bottom:* Higher magnification of the clefts (*) surrounded by very dense amorphous material (A) and a cell process (P). Arrow, basal lamina. $\times 27\,200$.

Establishing the immunological or clinical differential diagnosis between A-EBD and CP is even more problematic (3). The immunological character of A-EBD indicates that it belongs rather to the pemphigoid group of diseases than to the non-immunological epidermolysis bullosa group. Although the electron microscope specimen was taken only in a clinically inactive phase of the disease, the skin was fragile, with blisters and amorphous

material, similar to the earlier descriptions of A-EBD (10). Many associations have been suggested to exist between A-EBD and systemic diseases (10). There are few observations of an association between hormonal alterations and A-EBD. In the case presented the appearing of bullous eruptions at parturition and disappearance of visible bullous eruptions at menopause suggest the hormonal basis as a possible trigger of A-EBD in this case. Possibly this persistent blistering A-EBD and the abortion of the patient's fourth pregnancy had a causal connection.

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