Dermpath & Clinic

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Answer: Neonatal lupus erythematosus

Neonatal lupus erythematosus (NLE) refers to a clinical spectrum of cutaneous, cardiac, and systemic abnormalities observed in neonates whose mothers have autoantibodies, which are transmitted across the placenta. Approximately 98% of affected infants have maternal transfer of autoantibodies against Ro/SSA, La/SSB, and, less commonly, U1-RNP. However, only 1-2% of mothers with these autoantibodies have neonates with NLE, regardless of whether the mothers are symptomatic or not [1]. Approximately 40-60% of mothers are asymptomatic when the infants are diagnosed with NLE [1].

The skin lesions of NLE generally present as erythematous patches or plaques with an annular or discoid morphology on sun-exposed areas, and periocular erythema is considered a distinctive feature. The cardiac manifestations include conduction abnormalities and cardiomyopathy. Other abnormalities include haematological and hepatobiliary disturbances [2].

The differential diagnosis of NLE includes seborrheic dermatitis, atopic dermatitis, tinea corporis, psoriasis, granuloma annulare, erythema multiforme and congenital syphilis [3]. Treatment for skin lesions is usually not necessary, but sun protection is essential. Non-cardiac manifestations usually resolve with clearance of the maternal autoantibodies. Rheumatic or autoimmune diseases may subsequently develop in childhood, and follow-up is suggested until adolescence. ■

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Dermpath & Clinic: Pemphigus herpetiformis with vacuolar interface dermatitis and autoantibodies against desmoglein 1 and 3

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Pemphigus is a group of autoimmune blistering diseases characterized by circulating autoantibodies targeting the desmosomal adhesion molecules desmoglein-1 (Dsg1) and desmoglein-3 (Dsg3), leading to loss of keratinocyte adhesion and intra-epidermal blister formation [1]. While pemphigus vulgaris (PV) is most common, other variants include pemphigus foliaceus, pemphigus erythematosus, pemphigus herpetiformis (PH), paraneoplastic pemphigus (PNP), and IgA pemphigus. Here, we present a woman diagnosed with PH, who displayed features of all of these pemphigus variants.

An otherwise healthy 69-year-old Indian woman was admitted with severely itching blisters and painful erosions, present for three weeks, which did not respond to flucloxacillin and valaciclovir given for one week in combination with antihistamines and tramadol. Dermatological examination revealed widespread erythema, both flaccid and firm bullae, some partly filled with pus (hypopyon), and confluent erosions and crustae in a herpetiform pattern on the trunk, extremities and scalp (*figure 1A*). Nikolsky's sign on perilesional skin and Asboe-Hansen's sign on a blister were both negative. Face, palms and soles, and mucous membranes were unaffected. Lesional histopathology revealed neutrophilic spongiosis, and both subcorneal and suprabasal blistering (*figure 1B*). Remarkably, we observed basal vacuolization and dyskeratotic keratinocytes, indicating interface dermatitis. Direct immunofluorescence microscopy (DIF) of perilesional skin demonstrated intra-epidermal immunoglobulin (Ig) G deposits on the epithelial cell surface (ECS), with more granular aspects in the lower layers (*figure 1C*). Indirect immunofluorescence (IIF) on monkey oesophagus demonstrated IgG deposits at the ECS. In the keratinocyte binding assay, IgG bound in the typical PV pattern (*figure 1D*) [2]. ELISA showed antibodies against Dsg1 and Dsg3 (*table 1*). On revision of a previous histopathology specimen taken in the referring dermatology clinic, we observed similar blistering, however, there were no signs of an interface dermatitis. Nevertheless, we felt the need to exclude PNP and systemic lupus erythematosus (SLE). Immunoblotting was negative for PNP, as was IIF of serum on rat bladder substrate. Underlying neoplasm was excluded based on negative PET/CT, m-protein and free light chains. The patient had a weakly positive antinuclear antibody test, but no further signs of SLE. Based on clinical, histopathological, immunofluorescence and serology findings, we diagnosed the patient with PH, accompanied by a lichenoid drug reaction [1, 3].

This case was atypical for several reasons. First, histopathology displayed neutrophilic spongiosis with absence of eosinophils, which is present in about 9% of PH patients [3]. Second, an interface dermatitis is uncommon in PH [1, 3]. We believe that this reflects a lichenoid drug eruption to one of the previously given drugs. An alternative, less likely, explanation could be that Dsg3-specific CD4+ T-cells induce pemphigus vulgaris and interface dermatitis, according to data from a study in mice [4]. Third, the observed autoantibodies against both Dsg1 and Dsg3 have been described in only 4% of DH cases, and may explain the blistering at various intra-epidermal levels [3]. Despite anti-Dsg3 antibodies, which normally cause mucosal lesions, only the skin was involved. This observation does not match the Dsg compensation hypothesis, and it has been

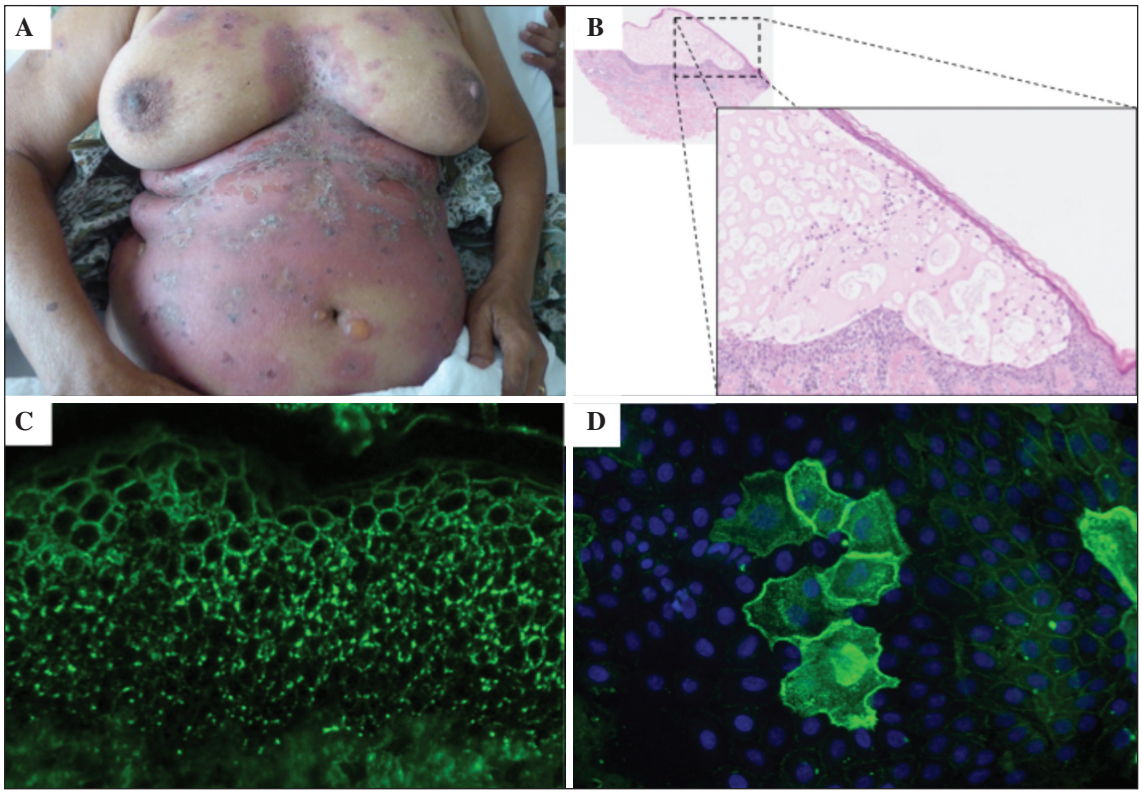

Figure 1. Clinical presentation. **A**) Firm and flaccid blisters, erosions and crustae on an erythematous base. **B**) Histopathology shows a subcorneal blister containing numerous neutrophils. **C**) Direct immunofluorescence shows IgG deposits in a chicken wire pattern, which is granular in the lower layers. **D**) Keratinocyte-binding assay showing a typical PV pattern.

Table 1. Serology results.

	Positive results	Negative results
IIF		
– rat bladder	-	IgG anti-ECS, IgA anti-ECS, IgA anti-BMZ
– monkey oesophagus	IgG anti-ECS	IgA anti-ECS
– salt split skin	-	IgA epidermal and dermal side, IgG epidermal and dermal side
– keratinocyte binding assay	IgG binds in a PV pattern	IgA binding
Immunoblot	-	IgG anti-plakin, IgG anti-BP180, IgG anti-BP230
ELISA	Dsg1 >150 U/mL, Dsg3 52 U/mL *	-

**Interpretation: Dsg1 <14 U/mL: negative, 14-19 U/mL: uncertain, >19 U/mL: positive; Dsg3 <7 U/mL: negative, 7-19 U/mL: uncertain, >19 U/mL: positive.Dsg1: desmoglein-1; Dsg3: desmoglein-3; ECS: epithelial cell surface; ELISA: enzyme linked immunosorbent essay; IgA: immunoglobulin A; IgG: immunoglobulin G; IIF: indirect immunofluorescence.*

previously suggested that other pathogenic factors affect acantholysis [5].

PH comprises 6-7% of pemphigus cases and its diagnosis usually takes time, since it resembles other pemphigus variants [3]. Recognition of PH is important because of its milder disease course and better response to corticosteroids or dapsone [3]. Herpetiform arrangement of blisters and erosions combined with histopathology showing eosinophilic and/or neutrophilic spongiosis, sometimes with vesicles or pustules, suggests PH. DIF on perilesional epithelium and serologic testing are required to demonstrate autoantibodies and exclude other forms of pemphigus. ■

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sQuiz your knowledge! A case of dermatitis, psychosis, and diarrhoea

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A 47-year-old man presented with a one-year history of well-defined, symmetrical pruritic scaly erythema on his face (*figure 1A*), neck and limbs (*figure 1B*). He had a long history of alcohol abuse and a history of chronic diarrhoea for one year. Four months prior, he developed depression, anxiety, irritability and delusional parasitosis. Laboratory examinations revealed that erythrocyte count (3.06×10^{12}/L), haemoglobin (80 g/L), and serum albumin (31.2 g/L) were decreased. Liver and renal function tests, thyroid assay, and human immunodeficiency virus status were normal or negative. Histopathological examination showed hyperkeratosis, parakeratosis, telangiectasia and a perivascular chronic inflammatory cell infiltrate in the upper dermis.

What is your diagnosis?

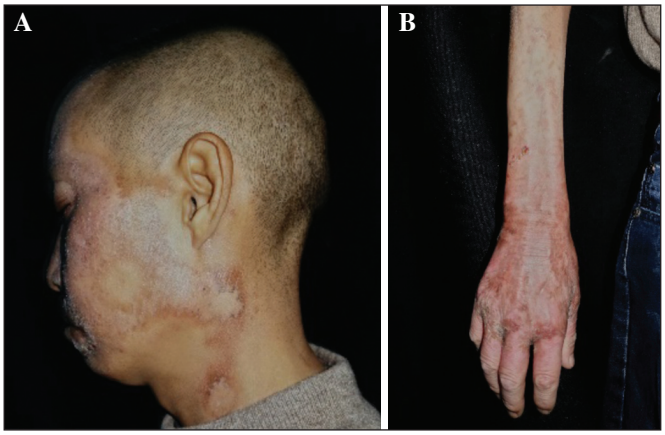

Figure 1. A) Multiple reddish-brown maculae and scaling with well-defined borders on the face and neck. **B**) Lesions on the dorsa of the hands and arms.

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