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Histiocytoid neutrophilic dermatitis, an unusual histopathology in neonatal lupus erythematosus

The authors reported histiocytoid neutrophilic dermatitis in neonatal lupus erythematosus (NLE). One-month-old male infant presented with annular erythematous plaques at the face and trunk. Serologic studies revealed positive anti-ribonuclear protein antibodies (RNP) and antinuclear antibodies (ANA). Histopathology showed predominant myeloid lineage mononuclear cells admixed with segmented neutrophils. This finding is uncommon in cutaneous NLE. Cutaneous NLE and LE should be included in the differential diagnosis of histiocytoid neutrophilic dermatitis. Additional immunohistochemistry studies with clinical and serologic correlations are important to differentiate histiocytoid neutrophilic dermatitis from the other diagnoses, especially leukemic cutis in young patients.

Keywords: dermatopathology, histopathology, SLE

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Neonatal lupus erythematosus (NLE) caused by transplacental autoantibodies has heterogeneous clinical manifestations. The disease can affect several organ systems, including the skin, blood cells, cardiac conductivity and hepatobiliary system. Various cutaneous presentations have been described, e.g. macules, patches, plaques, discoid lesions, persistent cutis marmorata and petechiae.[1] Typically, NLE with cutaneous involvement has two distinct histological findings. The first one is basal vacuolar change with superficial lymphocytic infiltration, which is similar to subacute LE. The latter is superficial and deep perivascular infiltration without epidermal alteration which resemble urticaria.[2] In the literature, neutrophilic dermatitis associated with NLE has been rarely reported.[3] The authors therefore reported histiocytoid neutrophilic dermatitis in NLE.

Case report

A 1-month-old male infant presented erythematous plaques for 10 days. Physical examination showed multiple annular erythematous papules and plaques with central scales on the chin, right cheek and trunk (Fig. 1). Serologic studies revealed positive anti-ribonuclear protein antibodies (RNP) and antinuclear antibodies (ANA) titer was 1 : 1000 with coarse speckled and nucleolar patterns. Anti-Ro/SSA, anti-La/SSB, anti-histone and anti-dsDNA antibodies were negative. Complete blood count revealed neutropenia (absolute neutrophil count 640

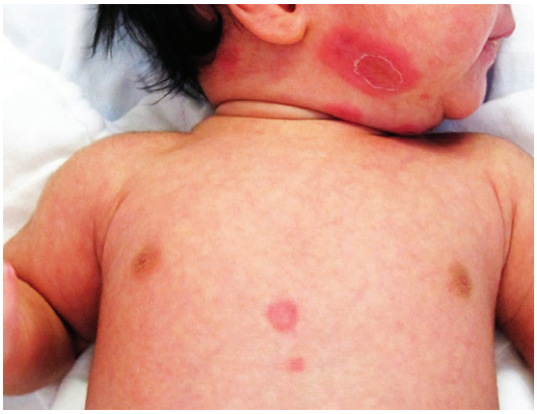

Fig. 1. The patient presents with annular erythematous papules and plaques with central scales on the chin, right cheek and trunk.

cells/mm^3). Liver function test had no abnormality. Chest X-ray and electrocardiography were unremarkable. There was no cardiac conduction defect or structural abnormality. His mother had been healthy and had no history of autoimmune disease. Maternal serologic studies displayed positive anti-RNP antibody and high ANA titer the same as the patient. Up to date, she has not presented enough criteria suitable for diagnosis of any autoimmune disease.

Histopathology of skin biopsy showed diffuse interstitial dermal infiltration by mononuclear cells with some segmented neutrophils (Fig. 2A,B). There was no evidence of vasculitis. No basal vacuolar change was detected at the overlying epidermis (Fig. 2C). These mononuclear cells marked with CD68 (Fig. 2D), CD33 and myeloperoxidase (Fig. 2E), whereas CD34, CD117 and CD1a stains were negative. CD123 showed some clusters of plasmacytoid dendritic cells (PDC) (Fig. 1F) in the periadnexal and perivascular areas. Direct immunofluorescence of the skin biopsy revealed negative result for IgG, IgA and IgM antibodies and colloid bodies.

Discussion

Although histopathology of the skin biopsy in this patient revealed histiocytoid neutrophillic dermatitis, a unique finding in acute febrile neutrophillic dermatitis or Sweet syndrome (SS), the clinical and laboratory findings supported the diagnosis of NLE. The patient had erythematous plaques on the face, chin and trunk, which can be found in SS and NLE; however, the patient had no clinical or laboratory criteria for diagnosis of SS. In addition, anti-RNP and ANA titer are positive in the patient and his mother. These findings indicated a diagnosis of NLE rather than SS. SS-like histopathology has been reported in systemic lupus erythematosus (SLE) and NLE.[3–6] Gleason et al. proposed the term of 'non-bullous neutrophillic dermatosis', an unusual pattern associated with LE.[4] Subsequently, two NLE with non-bullous neutrophillic dermatosis were reported by Satter et al.[3] Camarillo et al. reported histiocytoid non-bullous dermatosis in two SLE pediatric patients.[5] Brinster et al. and Pavlidakey et al. additionally described four and seven patients of non-bullous neutrophillic dermatosis and SLE, respectively.[6,7] Coexistences of SS and SLE, and SS and NLE has been described.[8,9] Our patient had no fever and leukocytosis, so SS could be excluded, and histiocytoid Sweet syndrome (HSS)-like histopathology is the most likely diagnosis.

NLE has various cutaneous manifestations, which can mimic benign or malignant skin conditions, thus skin biopsy is a considerable tool to confirm the diagnosis in case of controversial clinical manifestations. Commonly, histopathology of cutaneous NLE is as same as that of subacute LE. The skin biopsy of our patient revealed HSS-like histopathology, which is rarely found in NLE. HSS was firstly described by Requena et al.[10] The term of 'histiocytoid neutrophillic dermatitis' is defined by dermal infiltration by segmented neutrophils and mononuclear cells with myeloid lineage differentiation. A section of the skin biopsy revealed mononuclear cell infiltration and scattered neutrophils. Immunohistochemistry demonstrated that the mononuclear cells marked with myeloperoxidase, CD68 and CD33, whereas they did not mark with CD34 and CD117. The differential diagnosis of HSS-like histopathology includes myeloid leukemia cutis, interstitial granulomatous dermatitis (GD) and granuloma annulare (GA). GD and GA could be excluded clinically and immunophenotypically. The results of immunohistochemistry indicated that the mononuclear cells derived from myeloid lineage, hence myeloid leukemia cutis is a crucial differential diagnosis. However, because there was no blast in the peripheral blood and the patient had no hepatosplenomegaly, myeloid leukemia cutis is unlikely.

We studied CD123, a marker of PDC in the tissue section, and found their aggregations in the periadnexal and perivascular areas. The PDC have a major role in innate and adaptive immune response associated with type I interferon. These cells can be found in several

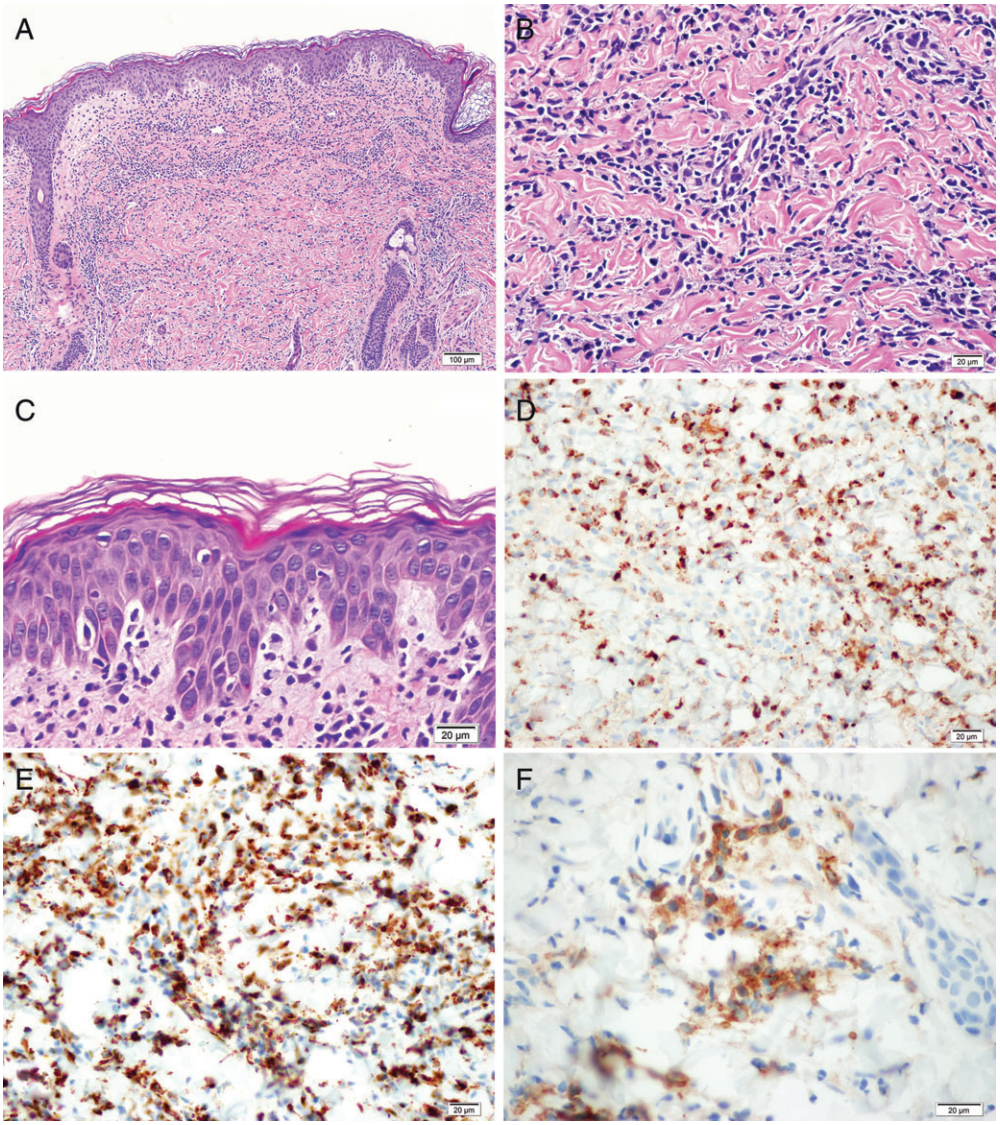

Fig. 2. A) Histology shows diffuse dermal infiltration by inflammatory cells (hematoxylin and eosin, original magnification ×100). B) The inflammatory cells are composed of mononuclear cells with some segmented neutrophils (hematoxylin and eosin, original magnification ×400). C) The epidermis reveals no basal vacuolar change (hematoxylin and eosin, original magnification ×400). D) The mononuclear cells mark with CD68 (CD68, original magnification ×400). E) The mononuclear cells and neutrophils mark with myeloperoxidase (myeloperoxidase, original magnification ×400). F) CD123 reveals plasmacytoid dendritic cells in clusters (CD123, original magnification ×400).

inflammatory skin diseases such as lichen planus, dermatomyositis, psoriasis and LE with different distribution patterns.[11–13] PDC distribution in cutaneous lesion of NLE has not been reported. We found clusters of PDC in NLE, which was similar to cutaneous LE. There was no relationship between clusters of PDC and maternal LE in this patient, because there have been only serologic suggestions of possible maternal connective tissue disorder. NLE is caused by maternal autoantibodies across the placenta to the fetus and damage fetal and neonatal antigen. Aggregations of PDC are triggered by autoantibody nucleic acid and produce interferon-α. Significance of PDC in cutaneous NLE is unknown, in addition to immune response to the maternal autoantibodies.

In conclusion, we reported histiocytoid neutrophillic dermatitis, which is an uncommon histopathology in NLE. Cutaneous lesion of LE and NLE should be included in the differential diagnosis of neutrophilic dermatitis and histiocytoid neutrophillic dermatitis. Clinical correlations and additional laboratory investigations together with immunohistochemistry are needed to render the diagnosis.

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