Acquired idiopathic generalised anhidrosis (AIGA) is an uncommon entity characterised by an inability to sweat in the absence of any neurological features or sweat gland abnormalities (1). Although its pathogenesis is poorly understood, recent reports suggested the involvement of a T-cell-mediated immune response and the contribution of reduced expression of the acetylcholine receptor and acetylcholinesterase in the eccrine gland (1, 2). In this report, we describe a case of AIGA successfully treated with steroid pulse. Interestingly, immunohistochemical staining revealed the infiltration of IL-17 producing cells, granulysin-bearing cells and pSTAT1 expressing cells around the secretary portion of eccrine glands. Moreover, in parallel with a sweat test by the iodine starch method, decreased reactivity to anti-dermcidin antibody was seen in the secretary portion of eccrine glands before therapy, and was recovered after steroid pulse therapy.

CASE REPORT

A 38-year-old man consulted us with a 6-month history of pruritic eruptions on his whole body. He had been treated in a private clinic for chronic urticaria and administered oral antihistamine with inadequate results. On his initial visit, physical examination revealed no eruptions except for dermographism. The medical interview suggested that he had had hypohidrosis for 6 months. We performed a sweat test by the iodine starch method as previously described (3). As expected, the starch-iodine showed no changes except on the axilla (Fig. 1, top left) and palms. There was no reaction (sweating, wheal) to intradermal administration of acetylcholine on the trunk. There was no sign of orthostatic hypotension or abnormality of the deep tendon reflex. A full blood count and complete biochemical profile including autoantibodies (anti dsDNA Ab, anti SS-A Ab, anti SS-B Ab, anti scl-70 Ab, anti RNP Ab, anti Jo-1 Ab) were within normal ranges. From the above findings, we diagnosed this condition as AIGA. We performed skin biopsy from the abdomen and axilla. The former biopsy specimen revealed dense infiltration of mononuclear cells around the secretary portion of eccrine glands (data not shown). The infiltrating mononuclear cells consisted of IL-17 producing cells, granulysin expressing cells, pSTAT1 expressing cells and HLA-DR+ cells (data not shown). Immunohistochemical staining also revealed that the secretory portions of the eccrine glands in the affected areas had significantly decreased reactivity to anti-dermcidin antibody (Fig. 1, bottom left) compared with the axilla region (Fig. S1). We then intravenously administered methylprednisolone sodium succinate 1,000 mg/day for 3 days, as previously reported (16) followed by oral predonisolone at a dose of 60, 55, 50, 45, 40, 35, 30, 25 mg/day for 3 days each and 20 mg, 15 mg, 10 mg/day for 2 weeks each. Then, we have kept to administered oral predonisolone 10 mg/day without recurrence for 3 months. Five days after the steroid pulse therapy, the patient started sweating. At day 14, we performed a sweat test using the iodine starch method, results which suggested a general ability to sweat (Fig. 1, top right). The biopsy specimen from the abdomen at day 14 revealed an increase in the reactivity to anti-dermcidin antibody (Fig. 1, bottom right) and decrease in the infiltration of IL-17 producing cells (Fig. S1), granulysin-bearing cells (Fig. S1), pSTAT1 expressing cells and HLA-DR+ cells (data not shown).

DISCUSSION

Th17 cells have been characterised in mice as a subset of CD4+ T cells that produce IL-17A, IL-17F and IL-22, and serve as immune effectors in autoimmunity (4). In the dermatological field, the contribution of IL-17 producing cells has been reported in various autoimmune diseases,

Fig. 1. Left: before steroid pulse treatment, right: after steroid pulse treatment. Top: Starch-iodine test in which the starch-iodine combination turns dark in the presence of sweat; sweating only in axillae (left) and additionally on the abdomen, neck and face (right). Bottom: Paraffin-embedded tissue sections from biopsies of the trunk were deparaffinised and stained using anti-dermcidin Ab showing negative staining of sweat gland before therapy which turned positive after therapy. Sections were developed with liquid permanent red (in red) (Original magnification ×200).

http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-2034

© 2015 The Authors. doi: 10.2340/00015555-2034
Journal Compilation © 2015 Acta Dermato-Venereologica. ISSN 0001-5555

Acta Derm Venereol 2015; 95: 743–744
SHORT COMMUNICATION
Acquired Idiopathic Generalised Anhidrosis: An Immunohistopathological Investigation of Periglands Infiltrated with Immunoreactive Cells
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Accepted Dec 10, 2014; Epub ahead of print Dec 18, 2014
including psoriasis, alopecia areata (AA), systemic lupus erythematosus (SLE) and autoimmune bullous disease (5–8). Ambrosi et al. (7) reported the significant roles of IL-17 in cooperation with type 1 interferon (IFN) in maintaining and amplifying the autoimmune and inflammatory response in systemic autoimmune diseases such as SLE. In addition, as we previously reported, IL-17 producing cells, together with IFN-γ producing cells, contribute to the clinical course of AA (5). Taken together, these reports suggested the contribution of IL-17 producing cells in promoting the recruitment of effector cells, such as granulysin-bearing cells, in the immunoreactive areas of the skin.

Granulysin is a cationic molecule present in the granules of cytotoxic T lymphocytes (CTL) and natural killer (NK) cells. Granulysin has homology with other cytotoxic molecules of the saponin-like protein family (9). In addition to eliminating pathogens and tumour cells, granulysin acts as a chemoattractant for monocytes, CD4+ and CD8+ memory T cells, NK cells, and mature monocyte-derived dendritic cells (MoDC) (10). Notably, Nakamizo et al. (11) previously reported a case of AIGA that presented with a dense infiltration of CD4+ and CD8+ T cells around the secretory portion of eccrine glands. In addition, we previously reported 8 cases of acute graft-versus-host disease associated with hypohidrosis, which was accompanied by the infiltration of granulysin-bearing cells around the secretory portion of eccrine glands (12). In aggregate, the infiltration of granulysin-bearing cells in our present case might have contributed to the decrease of sweating.

To assess the destruction of sweat glands, we employed immunohistochemical staining for dermcidin. Dermcidin, the dominant sweat antimicrobial peptide with broad-spectrum activity, is specifically and constitutively expressed in the sweat glands (13–15). In normal skin, like in the axilla of our patient (see Fig. S1), the secretory coils of the eccrine sweat glands are positive for dermcidin (15). In our present case, the decrease in the reactivity to anti-dermcidin antibody was prominent in the secretory portion of eccrine glands before corticosteroid therapy and increased in parallel with the results of a sweat test after therapy.

REFERENCES