

Sweet Syndrome Subsequent to Relapsing Polychondritis and Myelodysplastic Syndrome in a Japanese Patient

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Sir,

Sweet syndrome is characterized by tender, erythematous plaques, most often on the head, neck or extremities. It is associated with haematological malignancies in more than 20% of cases (1, 2). Relapsing polychondritis (RP) is a rare rheumatological disorder in which recurrent episodes of inflammation result in destruction of cartilage of the ears and nose (3). Myelodysplastic syndrome (MDS) is a clonal disorder of haematopoiesis characterized by peripheral cytopaenias and dysplastic bone marrow, which is usually hypercellular. Diebold et al. (4) demonstrated that there was frequent evidence of MDS in their bone marrow study of RP patients. We report here a case of a patient with Japanese Sweet syndrome found subsequent to RP and MDS.

CASE REPORT

An 80-year-old Japanese man presented with a 1-month history of flu-like illness followed by vertigo, joint pain and auricular swelling. Physical examination at our hospital revealed fresh red areas of erythema, with swelling and tenderness on the left ear, except the earlobe (Fig. 1a). Histopathologically, dense inflammatory infiltrations on the subcutaneous cartilage were observed along with degeneration of the marginal chondrocytes in the cartilage (Fig. 1b). Ophthalmological and otolaryngological examination revealed uveitis and moderate sensorineural deafness. In laboratory examinations, biochemical tests detected high levels of C-reactive protein (11.0 mg/dl). The patient demonstrated auricular chondritis, ocular inflammation, hearing loss and seronegative inflammatory arthritis, which fulfilled the diagnostic criteria of RP according to Michet et al. (5). An enzyme-linked immunosorbent assay (ELISA) was performed as described using type II collagens as substrates

(6). Results of the ELISA showed a high titre of antitype II collagen antibodies in the patient's serum: titres in sera from the patient and from normal individuals were 2.3 and 0.06 ± 0.03 ($n=10$) for antitype II collagen antibodies. Thrombocytopaenia and leukocytosis were detected. A bone marrow aspiration revealed MDS. Thirty mg/day of prednisolone was successful in suppressing the external ear inflammation and other organ symptoms, including eye, inner ear and joint symptoms, had rapidly subsided. Three months after his initial presentation to our institution, the patient often experienced coughing, hoarseness, aphonia, dyspnoea, wheezing, or tenderness over the trachea. Chest radiographs and computed tomography scans of the chest showed a left lower lobe infiltrate with pleural effusion. Exhaustive analysis of sputum, blood, urine, pleural fluid, and broncho-alveolar lavage fluid were negative for any infectious organism. Bronchoscopy with trans-bronchial biopsy for persistent left lower lobe infiltrate revealed bronchiolitis obliterans organizing pneumonia (BOOP). Eight months after admission at our institution, the patient presented with high-grade fever and painful cutaneous lesions on his neck, chest, back and extremities. Physical examination revealed multiple, erythematous, pseudovesicular plaques on his neck, extremities and trunk (Fig. 2a). Histopathological evaluation of the plaques demonstrated diffuse neutrophilic infiltration with nuclear dust in the dermis without vasculitis (Fig. 2b). Blood tests revealed an elevated C-reactive protein (17.0 mg/dl), neutrophilic leukocytosis and anaemia (haemoglobin, 6.3 g/dl). The patient was diagnosed with Sweet syndrome. MDS continued to progress to more aggressive acute myelogenous leukaemia. The patient was unresponsive to a variety of treatment regimens and died following infective exacerbation of BOOP.

DISCUSSION

The appearance of certain dermatoses has heralded either the diagnosis of a previously unsuspected malignancy or

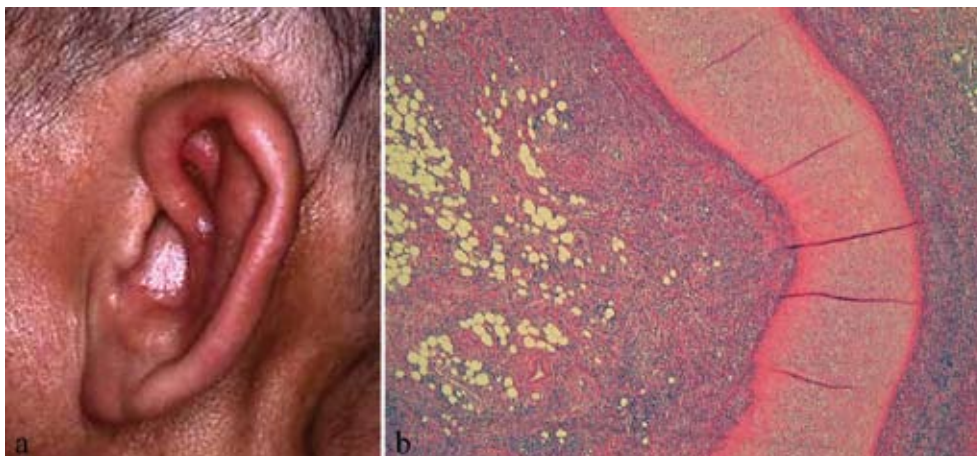


Fig. 1. (a) Erythema of cartilaginous portion of left pinna sparing the earlobe. (b) Biopsy of left pinna revealed degenerated cartilage and dense inflammatory infiltration in dermis close to subcutaneous cartilage (haematoxylin and eosin; H&E, $\times 40$).

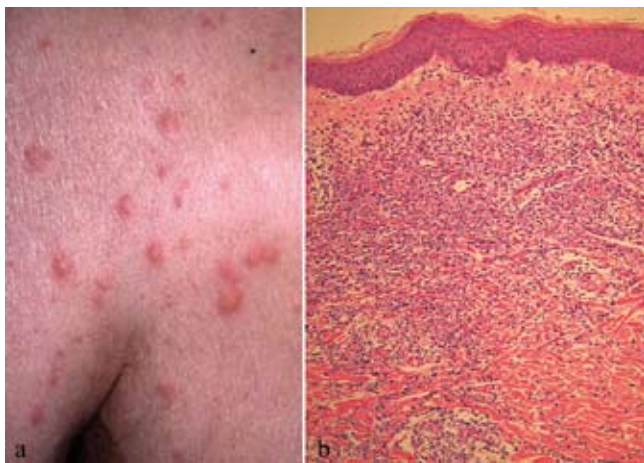


Fig. 2. (a) Clinical appearance of erythematous plaques on the patient's shoulder. (b) Histologically, diffuse neutrophilic infiltrate of the dermis is seen in association with mild dermal oedema (H&E, $\times 100$).

the detection of cancer recurrence in an oncology patient. These associated mucosal and cutaneous conditions are referred to as mucocutaneous paraneoplastic syndromes. Zappasodi et al. (7) reviewed some mucocutaneous paraneoplastic syndromes that occur in patients with haematological malignancies. Sweet syndrome and RP are included in the group of haematological malignancy-associated mucocutaneous paraneoplastic syndromes. Our patient who was diagnosed with both RP and Sweet syndrome developed MDS, which progressed to acute myelogenous leukaemia. Although uncommon, more than one mucocutaneous paraneoplastic syndrome has been described in patients with malignancies; therefore, it is not surprising that both of these conditions frequently developed in patients with haematological dyscrasias (8). We speculate that the appearance of Sweet syndrome lesions in some patients with RP may be the initial sign of MDS progression. Vignon-Pennamen et al. (9) suggested lymphocytic infiltrates with a clinical aspect of Sweet syndrome should lead to the research of atypical myeloid cells in skin infiltrate, blood, and bone marrow for the early detection of an associated MDS. Awareness that these conditions based on MDS may be the initial manifestations of MDS progression may prompt the clinician to consider this possibility. Mucocutaneous paraneoplastic syndromes are of practical clinical importance and may help in the early diagnosis of malignancy and management of patients.

The cause of RP is unknown. An autoimmune origin has been proposed and antibodies to collagen types II, IX and XI have been demonstrated (10, 11). The antibody to type II collagen (the collagen restricted to cartilage) was found in our patient. The antibody may be correlated with the disease pathogenesis and cartilage destruction. RP and Sweet syndrome even in patients who do not suffer from malignancies could be aetiologically related to each other (8, 12). We have suggested that neutrophil apoptosis dysfunction appears to be involved in the

pathogenesis of Sweet syndrome (13). Histopathological evaluation of RP in our case demonstrated moderate to diffuse neutrophilic infiltration with nuclear dust in the dermis to subcutaneous cartilage. The present apparent relationship between Sweet syndrome and RP may imply a common cause or pathogenesis, possibly related to neutrophil infiltration based on autoimmunity to components of the cartilage.

Pulmonary involvement in Sweet syndrome is the common extracutaneous manifestation. Non-infectious lung infiltrates in Sweet syndrome consist of neutrophilic interstitial infiltrates and BOOP (14). Our patient had Sweet syndrome subsequent to RP and MDS with BOOP. The BOOP seemed to have accelerated a paraneoplastic phenomenon in myelodysplasia in addition to airway obstruction or collapse and pulmonary infections. We speculate that this case could be just a case of BOOP in association with Sweet syndrome/RP with myelodysplasia, and the progression to myeloid leukaemia may be relevant to BOOP. Additional reports documenting the occurrence of these conditions in patients with MDS will be helpful to determine whether there is indeed a genuine association between them.

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