

Dermato-neuro syndrome in a case of scleromyxedema

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Abstract

Scleromyxedema is an uncommon connective tissue disease characterized by mucin deposits, fibrosis, and proliferation of fibroblasts in the dermis. Although it shares similar sclerodermoid features, it is a different clinical entity than scleroderma. A monoclonal gammopathy is almost always present; however, progression to multiple myeloma is rare. It may have many systemic manifestations, of which the most notable being the dermato-neuro syndrome because of its rarity and potential fatal outcome. We present a case of a 50-year-old woman with scleromyxedema in whom the dermato-neuro syndrome developed.

Keywords: Scleromyxedema, dermato-neuro syndrome, connective tissue

Introduction

Scleromyxedema is a rare and chronic connective tissue disease of unknown etiology, which is characterized by widespread erythematous papules, dermal fibroblast proliferation, and monoclonal paraproteinemia (1). Scleromyxedema should be distinguished from localized lichen myxedematosus, a form of lichen myxedematosus that presents with waxy firm papules and plaques involving limited areas. Unlike scleromyxedema, sclerotic features, systemic involvement, and monoclonal gammopathy are absent in localized lichen myxedematosus. Scleroderma and scleredema are additional disorders that present with sclerodermoid features but are unrelated to scleromyxedema. Scleromyxedema is also distinct from myxedema of thyroid disease. It is often associated with many systemic manifestations, including neurologic, rheumatologic, cardiovascular, gastrointestinal, pulmonary, and renal manifestations (2). Although rare, the most important form of central nervous system involvement is the dermato-neuro syndrome, which may have a fatal outcome (3). We would like to present a case of a 50-year-old woman with scleromyxedema and the dermato-neuro syndrome attributable to scleromyxedema.

Case Presentation

A 50-year-old woman presented to a dermatology clinic with a 2-year history of widespread papular eruptions over the whole body. She received multiple medications for 2 years, including systemic corticosteroids, but did not benefit from them. She complained of exacerbation of her lesions in the last 2 months and loss of exercise capacity. On physical examination, she had symmetric, flesh-colored, monomorphic, firm, 2-3 mm in diameter, closely-spaced, and linearly arranged papules on the periauricular areas, face, arms, legs, and trunk; "leonine-like" face (Figure 1); and sclerodactyly due to induration, tightness, and infiltration of the skin (Figure 2). She was hospitalized at the dermatology clinic for further investigation. Multiple skin biopsies taken from lesions revealed a diagnosis of scleromyxedema. Routine laboratory investigations, including complete blood count, erythrocyte sedimentation rate, biochemical parameters, thyroid function tests, hepatitis serology, and HIV tests, were normal, except for hypochromic microcytic anemia. Antinuclear antibody (ANA), Antineutrophil cytoplasmic antibody (ANCA), and extractable nuclear antigen antibody (ENA) panel tests were negative. Further examinations revealed proximal sensorimotor polyneuropathy and minimal pericardial effusion. Pulmonary function test results revealed forced expiratory minute volume in 1 s (FEV1): 1.42 l (64%), forced vital capacity (FVC): 1.64 l (62%), FEV1/FVC: 86% and diffusing capacity of carbon monoxide (DLCO): 52%. A high resolution computed tomography of the chest showed no parenchymal pathology. The interpretation of these results indicated a restrictive pulmonary disease due to probable interstitial lung disease accompanying scleromyxedema. Serum and urine electrophoresis due to the known accompanied monoclonal gammopathies showed IgG λ monoclonal gammopathy, and a bone marrow evaluation revealed involvement by abnormal monoclonal λ -producing CD38-positive neoplastic plasma cell infiltration. Multiple myeloma was



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Figure 1. "Leonine-like" face of the patient due to scleromyxedema

diagnosed and chemotherapy was planned. Before the treatment for multiple myeloma could be started, she developed an intractable fever (38.5°C) and generalized convulsions, which were hard to control by anticonvulsant medications. Her cognitive status started to deteriorate and ended up in a comatose state for days. She aspirated her gastric content during a tonic clonic convulsion and was intubated. She was transferred to our intensive care unit for further investigation and treatment. Mechanical ventilation support was started. To rule out meningoencephalitis of an infectious etiology or a vascular pathology, magnetic resonance angiography and magnetic resonance imaging of the neck and head and lumbar puncture for cerebrospinal fluid (CSF) examination were performed; however, no pathological finding was reached. CSF was also examined for leptomenigeal disease due to multiple myeloma or autoimmune encephalitis but revealed no diagnosis. Electroencephalography (EEG) showed bilateral periodic discharges, alpha waves, and diffuse slowing of the baseline rhythm but no epileptic activity, which was consistent with diffuse encephalopathy. After the exclusion of other etiologies for neurological deterioration, the dermatoneuro syndrome was diagnosed and methylprednisolone at a daily dose of 2 mg/kg (intravenous) and plasmapheresis treatment was administered immediately. She developed septic shock and related acute respiratory

distress syndrome. Broad spectrum antibiotic therapy and vasopressor infusion was started. On the second day of plasmapheresis treatment, sudden cardiac arrest occurred, and despite all efforts, she died.

Discussion

Scleromyxedema is a primary cutaneous mucinosis characterized by a generalized papular and sclerodermoid cutaneous eruption. It is a rare disease of unknown etiology that generally affects middle-aged adults between the ages of 30 and 80 years, with no race or gender predominance. Pathognomonic skin lesions are widespread waxy firm papules and plaques involving the hands, forearms, head, neck, upper trunk, and thighs that demonstrate mucin deposition, increased fibroblast proliferation, and fibrosis on histological examination (1, 2). This histological pattern is characterized by a diffuse, interstitial proliferation of blue-gray histiocytes, giant cells, and lymphocytes within the papillary and mid-reticular dermis forming loose granulomas among collagen fibers and mucin deposits. The pathological examination of skin biopsies in our patient revealed granulomatous scleromyxedema. Scleromyxedema follows a chronic, progressive, and sometimes unpredictable course (1, 2). Depending on the rapidity of onset and the degree of involvement, patients may be either initially asymptomatic or may notice that skin becomes thick and hard and that the face shows a diffuse induration and coarsening in the forehead lines and in lateral portions of the chin, giving the patient a "leonine-like" appearance as in our case. Patients with scleromyxedema can have a number of extracutaneous manifestations, including neurologic, rheumatologic, cardiovascular, gastrointestinal, pulmonary, and renal manifestations of the disease (2). In our case, we diagnosed restrictive pulmonary disease and pericardial effusion. Scleromyxedema is associated with paraproteinemia. The monoclonal gammopathy is generally IgG with a predominance of λ light chains; however, a predominance of IgG kappa also may be observed. A mild plasmacytosis may be found in the bone marrow; however, the disease is estimated to progress to multiple myeloma in less than 10% of cases (4). Our case was diagnosed to have multiple myeloma responsible for IgG λ monoclonal gammopathy. The pathogen-

esis of the extracutaneous manifestations of scleromyxedema is unclear. It has been suggested that mucin deposition in various organs is the cause, although mucin is not consistently found on autopsy in fatal cases. The dermatoneuro syndrome is a rare and occasionally lethal acute neurologic complication characterized by fever, confusion, dysarthria, lethargy, convulsions, and coma. In the dermatoneuro syndrome, brain autopsy has not been contributory, and the pathogenic basis of the encephalopathy remains obscure. It has been proposed that an increased blood viscosity with impaired microcirculation due to paraproteinemia may result in encephalopathy. A pathogenic role for IgG crossing a damaged blood-brain barrier, mediated by increased IL-6 production, also has been suggested (5, 6). Despite many clinical investigations, the pathogenesis of the dermatoneuro syndrome remains to be an enigma because brain imaging results are normal. The diagnosis of the dermatoneuro syndrome typically depends on the exclusion of different etiologies, leading to a comatose state in patients with known scleromyxedema diagnosis. A paroxysmal triad of high fever, seizures, and coma rarely occurs (6). The approach to patients with the dermatoneuro syndrome is not standardized, and various treatments have seemed to yield benefit in case reports, such as intravenous immunoglobulin (IVIg) (7), systemic glucocorticoids plus plasmapheresis or IVIg (8), systemic glucocorticoids plus cyclophosphamide and plasmapheresis (9), melphalan plus IVIg, and bortezomib plus dexamethasone (10). Spontaneous improvement also has been reported (6). Our efforts to clarify the etiology of the patient's neurological deterioration revealed no vascular or infectious pathology, and electroencephalography findings directed us to the diagnosis of the dermatoneuro syndrome. To our knowledge, this is the 22nd case in the literature. We started a treatment protocol by combination of systemic corticosteroids and plasmapheresis but could not succeed. The case we presented further delineates scleromyxedema with the dermatoneuro syndrome and underscores the severity of this condition.

Ethics Committee Approval: N/A.

Informed Consent: Informed consent could not be achieved because the patient was unconscious due to septic shock and relatives could not be reached after the patient died.



Figure 2. Sclerodactyly due to induration, tightness, and infiltration of the skin

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