

Scleromyxedema complicated by dermatoneuro syndrome during pregnancy

Sirs,

Scleromyxedema (SM) is a rare fibromucinous disorder of unknown etiology and prevalence, associated with monoclonal gammopathy, usually affecting middle-aged adults without gender preponderance (1). SM is characterised by infiltrative skin lesions with mucinous material deposition in the papillary dermis and diffuse thickening of the skin underlying the lichenoid papule, leading to cutaneous papules, plaques, nodules and sclerosis. Skin lesions tend to be chronic and progressive, with rare tendency toward spontaneous remission. SM diagnosis usually requires the presence of a monoclonal gammopathy, the absence of thyroid disorder, and skin biopsy with the triad of mucin deposition, fibroblast proliferation and fibrosis (1-3). Skin manifestations occur, in most cases, prior to the systemic manifestations and rarely after neurologic manifestations. Systemic involvement can occur with pulmonary, gastrointestinal, cardiovascular, musculoskeletal and neurologic findings. Nervous system is involved in 10–15% of cases, mainly with headache, confusion, dizziness, dysarthria, carpal tunnel syndrome, peripheral neuropathy, cognitive decline, memory loss and acute psychosis (4-7). Dermato-neuro syndrome (DNS) is a rare and sometimes fatal neurologic manifestation of SM, characterised by fever, convulsions and coma.

Here, we report on a patient with a 4-year history of SM who had two pregnancies, the second complicated by DNS. To the best of our knowledge, no pregnant patients affected with SM have previously been reported. A 32-year-old woman developed diffuse flesh-coloured firm papules on hands, face, scalp, neck, shoulders, periumbilical region and feet. Cutaneous erythema and sclerodermoid induration of face with “leonine” appearance occurred (Fig. 1). The clinical suspicion of SM was confirmed by skin biopsy and treatment with methotrexate started. IgG λ monoclonal gammopathy was also present.

Due to the worsening of the skin disease, with severe limitation in the joint range of motion and mouth opening, methotrexate was stopped and prednisone (50 mg/day), weekly plasmapheresis and isotretinoin (0.5 mg/kg/daily) started with benefit. Six months later, once improvement was achieved, prednisone was tapered, isotretinoin and plasmapheresis discontinued and monthly high dose (2g/kg) intravenous immunoglobuline (IVIG) started and continued for 4 years.

At age 36, while on prednisone (10 mg/daily) and IVIG, the patient became pregnant. During the first trimester, steroids were

Fig. 1. Cutaneous papules and plaques caused by mucin deposition and a variable degree of sclerosis involving the face.



discontinued and IVIG dosage reduced to decrease the risk of thrombosis. The pregnancy was uneventful and a healthy baby was delivered at term. Three months later the patient complaint of malaise, dysphagia, dysphonia, confusion, visual and auditory hallucinations. She was diagnosed with post-partum psychosis and effectively treated with olanzapine.

At the age of 40, despite the persistence of severe skin involvement, she decided of her own free will to stop treatment and she became pregnant again. Early in the second trimester, she developed confusion, visual and auditory hallucinations. She was admitted disoriented, dysarthric, afebrile, with a slight worsening of diffuse cutaneous papules. Chest x-ray and brain computerised tomography were normal. Fever and tonic-clonic seizure occurred. The patients' neurological status worsened (Glasgow coma score 9) and was admitted to the Intensive Care Unit. Erythrocyte sedimentation rate and C-reactive protein were increased. Cerebrospinal fluid analysis was unremarkable. Brain magnetic resonance was negative. Electroencephalography revealed signs of non-convulsive status epilepticus. After ruling out infectious and metabolic causes, DNS was diagnosed and methylprednisolone (40 mg/day) and monthly IVIG started. At the 18th week of pregnancy, an obstetric echography found a lifeless foetus. The patient underwent hysterectomy and progressively improved. She was discharged on prednisone 10 mg/day and IVIG, alert, collaborative and oriented without cognitive or psychiatric deficits.

At the 5-year follow-up the patient showed no further neurological manifestations, but skin involvement severely worsened compromising mouth opening, eating capability and joint range of motion.

We firstly report on a pregnant woman affected with SM who developed DNS. During the first pregnancy, under treatment with IVIG and steroid, clinical course was negligible, with just a slight worsening of skin features but without systemic involvement. The psychosis, developed during the postpartum period, was not interpreted as related to SM.

During the second pregnancy, a severe neurological involvement and negative foetal outcome occurred. We may speculate that the lack of therapy during this second pregnancy contributed to the severe neurological feature onset. The diagnosis of eclampsia was considered as a potential cause of seizure, but was ruled out due to the early onset during gestation, the absence of the other features of eclampsia, particularly hypertension, and the co-occurrence of other neuropsychiatric manifestations.

The pathogenesis of skin, systemic and neurological involvement of SM remains unclear. The hypothesised role of mucin deposits is not supported by their absence in commonly affected sites (4). It has alternatively been suggested that paraproteins could act as activators of connective tissue diseases, as antibodies against unknown serum antigens or by increasing blood viscosity with central nervous system microcirculation sludging (4, 8).

The occurrence, in our patient, of DNS during pregnancy suggests a possible role of hormonal factors. During pregnancy, an increase in free steroid hormones induces functional changes in B, T cells and monocytes (9). Female gonadal hormones also influence chronic autoimmune diseases as lupus erythematosus, systemic sclerosis and vasculitis (10-12). Indeed, high pregnancy levels of oestrogens can modulate the kinetic of several cytokines including

IL-6 (10). In DNS, Johkura suggested a pathogenic role for IgG crossing a damaged blood-brain barrier mediated by IL-6 and contributing to the sludge of cerebral microcirculation (13). Increased IL-6 levels in CSF were observed in SLE patients with neurological manifestations (14) and IL-6 seems to activate endothelial cells in the blood-brain-barrier and B cells enhancing intrathecal IgG production (15).

However, due to the low incidence of SM and the late onset of the disease, which often occurs after childbearing age, few data on hormone profile and pregnancy outcomes are available, making its pathophysiology difficult to be determined.

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