Dermato-neuro syndrome associated with scleromyxedema

Sir,

A 50-year-old previously healthy male, presented with skin thickening and waxy papules on his forearms, face and upper aspect of trunk for 2 years [Figures 1 and 2]. A skin biopsy revealed diffuse mucin deposition in the dermis with significant fibroblastic proliferation suggestive of scleromyxedema. Serum protein electrophoresis and immunofixation revealed IgG lambda light chain gammopathy. Bone marrow biopsy specimen was normocellular with evidence of lambda chain gammopathy on immunohistochemical examination. The patient first developed symptoms of encephalopathy one year later in the form of a flu-like prodrome followed by fever, nausea, vomiting, disorientation and dysarthria. Cerebrospinal fluid study and cranial magnetic resonance imaging were unremarkable. He recovered completely within 24 hours on broad spectrum antibiotics and acyclovir. The encephalopathy recurred one year later and again spontaneously recovered in 20 hours. Cranial magnetic resonance imaging and cerebrospinal fluid studies were again normal. He was then started on intravenous immunoglobulin (IVIG) 1 g/kg

Figure 1: Skin thickening over forearms

monthly. After the fifth cycle, he experienced the third attack of encephalopathy lasting for 3 days for which he required admission in the intensive care unit. On admission, he was lethargic, confused and agitated with no motor deficits. The body temperature was 37.8°C. Laboratory investigations including biochemistry, thyroid functions and antibodies, rheumatoid factor, antineutrophil cytoplasmic antibody and antinuclear antibodies was within normal limits, except leukocytosis. The cerebrospinal fluid examination revealed pleocytosis (200 cells, lymphocytes) with high protein (53.3 mg/dl) and normal glucose levels. Microbiologic, virologic, and serologic studies including polymerase chain reaction for herpes simplex virus type 1 and 2, and serology for syphilis were negative. Cerebrospinal fluid IgG index was within normal limits. Electroencephalography and brain magnetic resonance imaging were normal. As the encephalopathy episode had recurred during IVIG treatment, intravenous methylprednisolone (500 mg/day) and plasmapheresis was started. There was no clinical improvement and plasmapheresis was stopped after the fourth session, and IVIG at a total dose of 2 g/kg was given with which the patient quickly improved. At the end of the second week of admission, he was oriented, and could speak and comprehend normally. Intravenous steroid was continued for another 10 days after which it was switched to oral prednisone, 60 mg/day.

Scleromyxedema is characterized by thick papular lesions resulting from dermal fibroblast proliferation and mucin deposition.[1] The exact pathophysiology of scleromyxedema is still unknown. The disorder usually affects middle aged adults with no gender predilection,[2] and monoclonal paraproteinemia (most

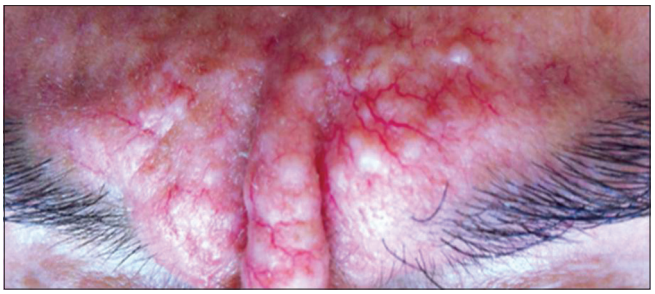

Figure 2: Skin thickening and waxy papules over face

commonly IgG-lambda) is typical.[3] Patients may have extracutaneous involvement, with neurologic, rheumatologic, cardiac, renal, gastrointestinal, and ophthalmologic manifestations.[4,5] Neurological disorders such as encephalopathy, acute psychosis, cognitive disorders, peripheral neuropathy, and carpal tunnel syndrome are seen in 10–15% of the patients.[4,5] Fever, coma, and convulsions following a flu-like prodrome is termed dermato-neuro syndrome and can be fatal.[6,7]

In a recent study, Fleming *et al*.[8] presented 18 patients with findings proposed for the diagnosis of dermato-neuro syndrome, viz. fever, coma and convulsions following a flu-like prodrome and 7 patients with acute neurological deficits but not showing all the features for dermato-neuro syndrome. We believe all scleromyxedema patients with altered consciousness or other neurological deficits that cannot be explained by another disease may be named as dermato-neuro syndrome. All these findings indicate involvement of the central nervous system and no clear-cut proof for the given criteria for dermato-neuro syndrome is present in the literature. Hence, our patient with flu-like prodrome, fever and altered consciousness was diagnosed and treated as dermato-neuro syndrome.

Histopathologic findings in the brain have varied from near normal in one patient with lethal neurologic syndrome[4] to mild demyelination and gliosis in another patient with dermato-neuro syndrome.[6] Hence, the exact pathogenesis of systemic complications is not clear. One of the theories is that the increase in blood viscosity by paraproteins or leukocyte aggregation impairs the central nervous system microcirculation resulting in dermato-neuro syndrome.[7]

Various modalities have been tried for the treatment of scleromyxedema such as melphalan,

bortezomib, intravenous immunoglobulin (IVIG), plasmapheresis, high dose dexamethasone, autologous stem cell transplantation,[9,10] and a combination of these. Clinical response to melphalan and bortezomib suggests that scleromyxedema could be treated with agents which are known to be beneficial in multiple myeloma.[11,12] IVIG[10] and plasmapheresis have been found to be effective for dermato-neuro syndrome with relatively less side effects.[8,9] The mechanism of IVIG remains unclear. It may block an as-yet-unknown factor causing mucin and collagen deposition by stimulating fibroblasts.

If all acute onset neurological symptoms associated with scleromyxedema are taken into account, we found are 25 prior reports of dermato-neuro syndrome in the English literature. Although scleromyxedema is fairly rare, dermato-neuro syndrome should be considered in the differential diagnosis when a patient presents with unexplained neurologic symptoms with skin lesions suggestive of scleromyxedema.

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