Folliculotropic Mycosis Fungoides

Sir,

Folliculotropic Mycosis fungoides (F-MF) is a rare variant of Mycosis Fungoides (MF) with distinct clinical and histological findings, treatment responses, and survival rates.[1,2] It is characterized histologically by atypical T lymphocytes that preferentially infiltrate the follicular epithelium and the interfollicular epidermis is usually spared.

A 60-year-old male, presented with persistent and recurrent swelling of lips and eyes, with severe itching over the face, neck, and ears for 3 months. For the past one-year patient is developing episodes of intermittent swelling over the face and neck. He was diagnosed to have diabetes mellitus and hypertension for 1 year and was on oral hypoglycemic agents, telmisartan, and amlodipine for the same.

In view of his cutaneous symptoms of itching and swelling over face, he was diagnosed as chronic urticaria and angioedema. He received multiple treatments with oral antihistamines, prednisolone in dosage of 30 mg and azathioprine 50 mg daily with temporary relief in itching and swelling but recurred after tapering steroids. He had history of weight loss of 4 kg in the past 2 months.

Cutaneous examination revealed diffuse erythema and edema over the entire face, scalp, ears, and neck with predominant periorbital and upper lip edema [Figure 1a & 1b]. The facial skin appeared thickened and infiltrated especially over the ears and retro-auricular area [Figure 1c]. Patient also had superciliary madarosis and multiple seborrheic keratosis on both cheeks. Lymph node examination revealed discrete mobile non tender upper cervical lymph nodes less than 1 cm in diameter. There was no evidence of generalized lymphadenopathy, thickened peripheral nerves, or sensory impairment. Differential diagnosis of scleromyxedema, papular mucinosis, granulomatous diseases (Lepromatous leprosy and cutaneous leishmaniasis), and mycosis fungoides were considered.

Skin biopsy from the papules present on the posterior aspect of the right ear revealed dense nodular infiltrate of lymphocytes in a perifollicular location and extending into deep dermis. The inflammatory infiltrate showed presence of atypical lymphocytes with larger convoluted nuclei [Figure 2a, 2b & 2c]. On immunohistochemistry the lymphocytes were CD3 and CD4 Positive. CD20 positivity was seen in perifollicular location while CD8, CD56, and c-kit were negative.

His baseline laboratory investigations (complete hemogram, erythrocyte sedimentation rate, peripheral smear for atypical lymphocytes, liver and renal function tests, urine examination.), thyroid profile, serum cortisol levels were normal. Slit skin smear did not reveal acid-fast bacilli. Ultrasonography of neck revealed multinodular goiter and fine-needle aspiration cytology (FNAC) showed Bethesda II goiter. Peripheral smear showed no evidence of atypical lymphocytes. Bone marrow biopsy was normocellular. CT-Scan (thorax, abdomen, and pelvis) revealed no significant abnormality. Final diagnosis of folliculotropic mycosis fungoides was considered. Patient was referred to the oncologist for further management. There patient received 6 cycles of chemotherapy with gemcitabine followed by alternate day radiotherapy (30.6 Gy). In spite of treatment patient continue to worsen and died after 1 year of diagnosis.

F-MF differs from classic MF with distinctive clinical and histological features, more refractory to standard treatment and worse prognosis than classic MF. F-MF is a rare form of CTCL that represents less than 10% of patients with MF.[3,4] It is more common in men than in women.[5] At the time of diagnosis, 92% of patients have skin-limited disease, whereas 8% patients have nodal or visceral disease at first presentation.[6]

Number of lesions can vary from single lesion to extensive involvement. Clinical presentation includes different

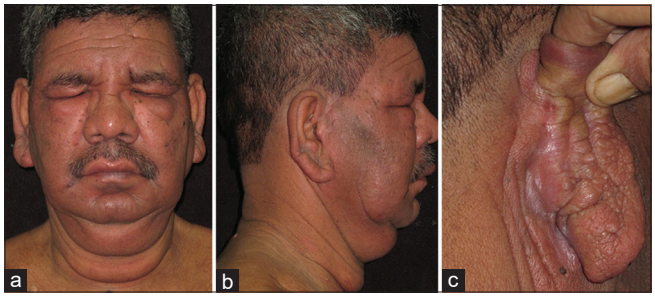

Figure 1: (a) Cutaneous examination showing diffuse erythema and edema over the entire face, ears, and neck with predominant periorbital and upper lip edema. (b) Supraciliary madarosis, infiltration of skin over the cheeks and ears. (c) Thickened and infiltrated skin over the ears and retro-auricular area

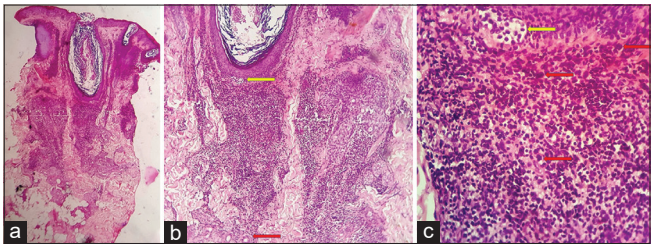

Figure 2: (a) Skin biopsy showing follicular plugging and predominantly perifollicular inflammatory infiltrate in upper and deep dermis. (40X, H&E stain). (b) (100X, H&E stain): Perifollicular mononuclear cell infiltrate (Yellow arrow: Pautrier's Micro-abscess, Red arrow: syringotropism). (c) (400X, H&E stain): Presence of atypical lymphocytes with larger convoluted nuclei (Yellow arrow: Pautrier's Micro-abscess, Red arrow: atypical lymphocytes)

morphologies like infiltrative plaques, acneiform lesions, cysts, alopecic patches, prurigo-like lesions. Other rare presentations include lichen spinulosus-like lesions in association with hypopigmentation and alopecia, pseudotumors, lupus tumidus-like plaques, and rosacea-like lesions.[7] A leonine face has been known to be associated with stage-IV CTCL, and is often accompanied by folliculotropism and blood involvement.[8] Our patient also had similar presentation, however, the investigations did not reveal significant systemic or lymphatic involvement at the time of presentation but the disease progressed rapidly.

Alopecia is a typical feature of FMF, occurring in up to 81% of patients. Involvement of the eyebrows is highly characteristic and may present an early disease manifestation as well as a useful clue in the differential diagnosis. Due to its different clinical presentation from classical MF, diagnosis can be delayed.[9]

The most noticeable difference between F-MF and conventional MF is the distribution of lesion. Conventional MF usually presents in a bathing suit distribution, while F-MF has a predilection for the head-and-neck region.[2,5,10]

Histopathological findings of FMF include perivascular and peri-adnexal localization of dermal infiltrates with variable infiltration of the follicular epithelium by small, medium-sized, or large hyperchromatic cells with cerebriform nuclei; and sparing of the epidermis is common.[2,10]

Histopathological differential diagnosis is follicular mucinosis which shows presence of basophilic granular material (mucin) within hair follicles accompanied by atypical perifollicular and intrafollicular lymphocytes.[11] Peri-eccrine infiltrates (syringotropism) may also be seen in 4% to 33% of cases.[12]

Management is symptomatic and includes the use of PUVA (photochemotherapy) combined with interferon alpha-2a and retinoids, total body electron beam irradiation, and local radiotherapy in cases of persistent tumors. Topical imiquimod has been used successfully in some patients with localized lesions.

Age at diagnosis, large cell transformation, and secondary bacterial infection are independent risk factors for disease progression and/or poor survival. On clinicopathologic correlation, 3 subgroups with significantly different survival have has been identified. Patients presenting with patches and/or follicular papules or plaques with histologically sparse perifollicular infiltrates demonstrated highest overall 10-year survival, followed by patients presenting with plaques with histologically dense perifollicular infiltrates, tumors, or erythroderma. Patients with extracutaneous FMF demonstrated the worst overall 10-year survival.[6]

We report this rare presentation of folliculotropic MF presenting with persistent itching and facial swelling mimicking angioedema.

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Conflicts of interest

There are no conflicts of interest.

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