

Ulcerative subcutaneous zygomycosis: Development of hypothyroidism induced by potassium iodide (Wolff-Chaikoff effect)

Sir,

Chronic subcutaneous zygomycosis (Phycomycosis, Entomophthoro-mycosis) is an uncommon subcutaneous mycosis caused by ubiquitous molds of the order Entomophthorales.^[1,2] Rational management of such uncommon mycoses requires confirmation of diagnosis by demonstrating fungal elements on histopathology as cultures are not always positive.^[3] We came across an unusual presentation of subcutaneous zygomycosis that responded well to a combination of potassium iodide and itraconazole administration followed by skin grafting. Hypothyroidism was encountered as a side effect of potassium iodide therapy and has been reported infrequently in the dermatology literature.^[4]

A 29-year-old, non-diabetic housewife hailing from West Bengal presented with a large fungating mass over left upper arm and shoulder of eight months duration. [Figure 1] There was no history of trauma or surgical intervention of the involved extremity. There was no history suggestive of tuberculosis or significant contact with a tuberculosis patient. Patient gave no history of taking steroid or immunosuppressant drugs. On

examination, there was a large fungating ulcerated mass occupying the whole left upper arm and axillary fossa. The mass showed areas of hemorrhagic crusting, necrosis and purulent discharge. The skin around the mass showed diffuse, erythematous and indurated swelling of approximately 25 cm in diameter extending upto anterior chest wall, scapula and infra-axillary area on the same side. On palpation, the boundary of this diffuse swelling could be felt well and fingers could be insinuated beneath the swelling on upper back. Regional lymph node examination was not possible due to severe soft tissue edema and limb enlargement.

Her general and systemic examinations were unremarkable except for moderate degree of pallor. Complete hemogram revealed anemia with hemoglobin of 8.6 g/dl. Routine blood biochemistry and urinalysis were normal. Her serology for HIV, hepatitis B and hepatitis C was negative. Peripheral smear and buffy coat preparation did not show any abnormal cells. Chest roentgenogram was normal and tuberculin skin test was negative. To rule out deep venous thromboses venous doppler of left arm was attempted, but it was not possible to visualize the vessels due to massive edema. Abdominal ultrasound was normal. X-ray of the arm showed gross soft tissue edema with poor visibility of underlying bones. Histopathological examination of skin biopsy revealed nodular and interstitial tuberculoid eosinophilic granulomatous infiltrate composed of lymphocytes, eosinophils, plasma cells, epitheloid cells, Langhans giant cells and foreign body type giant cells in whole of the dermis and subcutaneous fat. [Figure 2] Non-septate, twisted, collapsed ribbons like hyphae typical of zygomycetes were observed on Gomori methenamine silver (GMS) stain under 40 magnification [Figure 3]. However, fungal culture of the tissue did not show any growth at the end of four weeks.

With a working diagnosis of subcutaneous zygomycosis, we started the patient on saturated solution of potassium iodide (SSKI) along with itraconazole 200 mg twice a day for two months and then stepped down to 100 mg twice a day for one month. Oral potassium iodide was started with five drops t.i.d. and increased by one drop daily upto a maximum of 15 drops t.i.d. Intravenous amoxicillin (1g) plus clavulanic acid (200 mg) b.i.d and metronidazole 500 mg (100cc) b.i.d were instituted on the basis of antibiogram. Cleaning and dressing was done daily with hydrogen peroxide and normal saline.

However, one month later the patient developed iodide-induced hypothyroidism along with signs of

iodism in the form of rhinorrhea for which the patient was started on thyroxine 75 μgm once a day and dose



Figure 1: A large fungating mass on left upper arm with woody induration of surrounding skin on chest wall

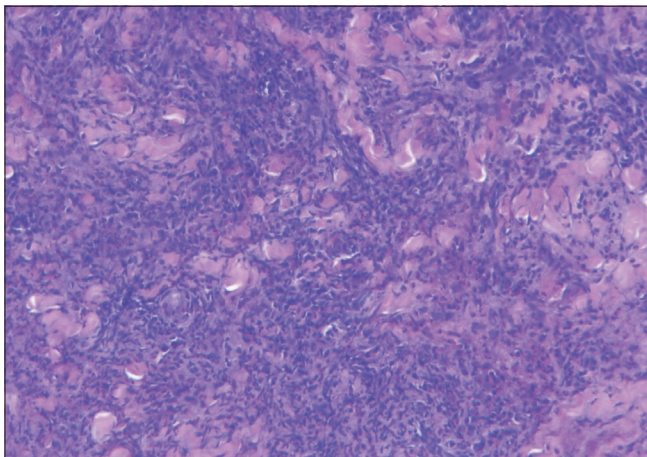


Figure 2: Nodular and interstitial tuberculoid granulomatous infiltrate composed of lymphocytes, eosinophils, plasma cells, epithelioid cells on HandE stain ($\times 10$)



Figure 4: Same patient three months after treatment. The size of the mass has decreased considerably. (Compare with Figure 1)

of potassium iodide was reduced to 13 drops t.i.d. Her baseline TSH was 2.70 $\mu\text{IU/ml}$ (17/2/09), whereas one month later TSH was 16.8 $\mu\text{IU/ml}$ (25/3/09). Two months after starting thyroxine, her TSH level dropped down to 6.78 $\mu\text{IU/ml}$, though it was higher than normal values. (0.3-5.5 $\mu\text{IU/ml}$)

Three months post-treatment, the mass had melted down by almost 90% and then she underwent plastic surgery for skin grafting to promote faster wound healing and better cosmesis. [Figures 4 and 5] Patient was discharged on oral itraconazole 100 mg b.i.d and potassium iodide 13 drops t.i.d. and was advised monthly monitoring of liver enzymes and thyroid profile. The patient followed up with our department in July 2009 with satisfactory response to treatment.

In our patient, the diagnosis of subcutaneous phycomycosis was suspected due to a painless large subcutaneous swelling showing the finger insinuation

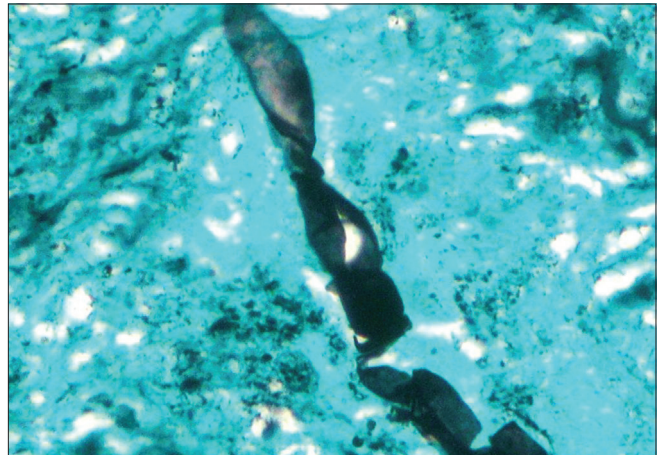


Figure 3: A single black staining ribbon like hypha on Gomori methenamine silver stain ($\times 40$)



Figure 5: Graft *in-situ* on second day of post-operative period

sign. It was proved by demonstration of typical hyphae in biopsy and favorable response to the therapy. However, culture of biopsy tissue and that from the ulcer floor or crust was negative. This is not entirely surprising as zygomycetes have large coenocytic hyphae which often get damaged and become nonviable during biopsy procedure and thereby giving a negative report on fungal culture.^[5]

There are various clinical presentations of zygomycosis: ecthyma gangrenosum like lesion, cellulitis, facial edema, necrotic papulonodules, plaques, large hemorrhagic crust and targetoid morphology.^[6,7] Our case presented with an unusual ulcerated form of chronic subcutaneous zygomycosis with massive edema of the involved extremity due to venous obstruction.

It is proposed that potassium iodide has direct antifungal activity and also possess anti-fibrotic and proteolytic action and thereby concentrating the drug at tissue level.^[8] One month after treatment, our patient was screened for iodide-induced hypothyroidism and was found to have raised TSH level and was started on oral thyroxine 75 μ gm. Hence there was transient iodide-induced hypothyroidism known as Wolff- Chaikoff effect (WCE)^[8] reflecting inhibition of organification by exogenous iodide. In patients with documented iodide-induced hypothyroidism, serum T₃, T₄ and TSH concentration returns to normal within one month of iodide discontinuation.^[9] There exists an autoregulatory mechanism within the thyroid gland itself which serves to maintain a pool of organic iodine within the thyroid gland. The inhibition of organification of iodine in tyrosine residues results in cessation of thyroid hormone synthesis.^[10] Less commonly, iodides may also induce hyperthyroidism (Jod-Basedow effect).^[10] Therefore, for patients needing SSKI therapy, one should specifically ask about any history of thyroid diseases or taking amiodarone or thyroxine and preferably screen them for thyroid function at baseline and after a month of starting therapy.^[8]

The dosing of potassium iodide (KI) ranges from 360 to 900 mg/day,^[9] though higher dosages may be used in tolerant patients. Although KI is usually well tolerated, many adverse cutaneous side effects have been noted i.e. erythematous, urticarial, acneiform, nodular, pustular, purpuric, carbuncular and vegetative skin lesions.^[10] Other reported adverse effects include fever, weakness, unusual tiredness, swelling in the neck or throat, mouth sores, skin rash, nausea, vomiting, stomach pains, irregular heartbeat, numbness or

tingling of the hands or feet, a metallic taste in the mouth, acneiform eruption, sneezing, coryza, parotid gland swelling, increased lacrimation and salivation, brassy taste, eructation, non-inflammatory lid edema; all these constellation of signs and symptoms are commonly referred to as iodism.^[9,11,12] Most of the side effects can be controlled by stopping the drug for few days and then again reinstating therapy at lower dose.^[11] To conclude, successful treatment strategy includes rapid diagnosis, prompt institution of systemic antifungal therapy and surgical resection of involved areas if appropriate.

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