Ashy dermatosis-like pigmentation due to ethambutol

Sir,

A 30 year-old Indian woman presented to us with asymptomatic, multiple, hyperpigmented macules. She had been receiving treatment for abdominal tuberculosis in the form of levofloxacin (750 mg daily) and ethambutol (800 mg daily) for two months, followed by levofloxacin, rifampicin (450 mg daily) and isoniazid (300 mg daily) for eight months. Macular lesions appeared on her forearm about two weeks after starting the initial treatment course. No new lesions had appeared and existing lesions did not enlarge since ethambutol was stopped; however, the pigmentation had persisted.

Multiple, non-scaly, slightly atrophic, muddy-brown to brownish-black macules of round, oval and bizarre shapes and different sizes (0.5-10 cm in size) were present over the face, neck, upper extremities and the trunk [Figure 1]. Some of the lesions, especially those on the abdomen, had perilesional erythematous halos. Palms, soles, scalp and mucosal surfaces were unaffected. Routine investigations were normal. Histopathological examination showed mild epidermal atrophy with a slight flattening of rete ridges and a sparse superficial perivascular infiltrate of lymphocytes. Papillary and deep dermis showed numerous melanophages [Figure 2]. These findings were consistent with ashy dermatosis.

Ashy dermatosis (erythema dyschromicum perstans) is an asymptomatic eruption of oval, polycyclic or irregularly shaped, grey-blue, hyperpigmented macules on the trunk, arms, face, and the neck.\(^{[1]}\) It begins as ash-coloured macules, sometimes with an erythematous or elevated border. The oral cavity and genitals are spared. It has been associated with ingestion of ammonium nitrite, orally administered radiographic contrast media and whipworm infestation.\(^{[1]}\)

Ethambutol has only rarely been reported to cause lichenoid eruptions;\(^{[2,3]}\) however, it has never been reported to cause ashy dermatosis-like eruptions. In one report of ethambutol-induced lichenoid eruption, the eruption consisted of lichenoid papules,\(^{[2]}\) while another report described the eruption consisting of lichenoid papules and hyperpigmented macules.\(^{[3]}\) Some authors believe that ashy dermatosis may be a manifestation of lichen planus.\(^{[1]}\)

The present case appears to be the first in which ethambutol most probably led to ashy dermatosis-like pigmentation. We believe that the pigmentation in the present case may be better called ashy dermatosis-like rather than lichenoid, because of the presence of a perilesional, inflammatory, erythematous halo and inconsistent basal cell degeneration.

A challenge test with ethambutol was considered unethical. Re-exposing a patient with a drug eruption to the suspected drug may be dangerous, and hence, is not usually recommended.\(^{[4]}\) The time course of eruption strongly suggested that ethambutol was responsible for the eruption.

Sometimes, the issue as to whether a particular drug is really responsible for an eruption, is debatable. Although no perfect solution exists, the Naranjo adverse drug reaction probability scale is frequently used to clarify this issue.\(^{[5]}\) In the present case, the likelihood of ethambutol causing the
eruption was considered to be probable, which is one step below the highest certainty provided by this scale.

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REFERENCES


Tumoral calcinosis

Sir,

Calcinosis cutis, a group of disorders in which calcium is deposited in the skin is of four types: metastatic, dystrophic, idiopathic and intraepidermal calcified nodules.[1] Tumoral calcinosis is a special form of idiopathic calcinosis which affects adolescents and young adults[2] and is characterized by massive subcutaneous deposits of calcium phosphate near the joints such as hips, shoulders, elbows, wrists, feet and hands. The deposits consist of pleomorphic calcium phosphate (hydroxyapatite) crystals.

A 26 year-old married male presented with gradually increasing, painless, bony, hard masses over both the elbows and around the right hip joint prevalent since the last two years. There was no history of excessive milk or antacid intake, endocrinal abnormalities, or any history suggestive of any connective tissue disease. There was also no history of any similar condition in the family members.

On examination, there were firm-to-hard, nontender, irregular, tumorous masses over the lateral aspect of the right gluteal region measuring 15 × 15 cm, and over both elbows measuring about 10 × 8 cm with overlying skin showing atrophic scars. There was minimal restriction of movements at the joints [Figure 1]. Systemic examination results were normal.

Hemogram, liver and renal function tests, and the erythrocyte sedimentation rate were normal. Serum phosphorus level was 6 mg% (normal range: 2-4.5 mg%). Serum calcium, uric acid, alkaline phosphatase, parathyroid hormone, calcitonin levels were normal. Antinuclear antibodies and the rheumatoid factor were absent. Radiographs showed large, lobulated, radio-opaque, soft tissue masses of calcific density with radiolucent septae in the juxta-articular position of both elbows and the right hip. Magnetic resolution imaging (MRI) of the right hip showed foci of calcification with infiltration into the gluteus medius and quadratus femoris [Figure 2]. Histopathology from the elbow showed deeply basophilic amorphous granular material surrounded by dense fibrous tissue and infiltration [Figure 3]. Debulking of the elbow regions was done and the patient is now on regular follow-up to detect any recurrence.

Tumoral calcinosis was first described in 1899.[3] The pathogenesis is obscure but the basic defect is thought to be in the proximal renal tubular cell with an elevated renal phosphate reabsorption threshold and increased production of 1, 25-dihydroxyvitamin D.[4] It is classified into three types depending upon the pathogenesis: primary normophosphatemic tumoral calcinosis (NPTC), primary hyperphosphatemic tumoral calcinosis (PHTC) and secondary tumoral calcinosis.[5] Our case is of subtype 2 having hyperphosphatemia with normal levels of serum calcium, parathyroid hormone and alkaline phosphatase. Tumoral calcinosis is often associated with diseases like chronic renal failure, primary hyperparathyroidism, hypervitaminosis D, milk-alkali syndrome, sarcoidosis and massive osteolysis.[5] Typical clinical findings, radiology, fine needle aspiration cytology, and histopathology[3] showing calcification help in the diagnosis. Various treatment modalities like aluminium hydroxide or acetazolamide have been tried but none has been found to be effective. Complete surgical excision has been recommended but recurrences are common.[6]

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