

## Amiodarone-induced angioedema: Report of two cases

Sir,

Amiodarone, a class II long-acting anti-arrhythmic, capable of blocking both  $\alpha$  and  $\beta$  -adrenoceptors is an iodine-containing highly lipophilic benzofuran derivative.<sup>[1,2]</sup> Adverse reactions are common and are duration-dependent. Frequent reactions include nausea and other GI symptoms. Ten percent of patients may develop photosensitization (possibly due to phototoxicity) and bluish skin pigmentation, but allergic skin reactions are rare.<sup>[3-6]</sup> The most serious side-effect related to amiodarone is pulmonary alveolitis and fibrosis.<sup>[4]</sup> Only a single case of amiodarone-induced angioedema has been reported in the literature.<sup>[2]</sup> We came across two unrelated cases of angioedema triggered by the use of amiodarone in the last couple of years.

A 65-year-old lady was admitted with pericardial effusion and after a positive pericardial tap antitubercular drugs (ATD) were started (isoniazid 300 mg, rifampin 600 mg, ethambutol 800 mg and pyrazinamide 1500 mg). She developed atrial fibrillation and an alteration in the ventricular rate. She was put on amiodarone 800 mg twice daily for 15 days and then the dose was tapered to once daily. Facial angioedema appeared within a couple of weeks and she complained of anorexia. Chest roentgenogram was done and was non-contributory. Laboratory evaluation was normal (blood analysis and serum chemistry, stool examination for parasites, IgE, thyroid tests (T3, T4 and TSH), and urinalysis). Liver function tests yielded a mild rise in liver enzymes like ALT, AST and serum alkaline phosphatase; which were 93, 97 and 371 respectively. She was anicteric. Fundoscopy was normal. Symptoms of angioedema were unrelated to any physical activity, stress or ingestion of any particular food. She was not an atopic and had no clinical history of nasal polyps, chronic rhinitis, sinusitis, asthma or chronic and chronically relapsing dermatitis. After another four weeks ATD were stopped. Then they were again started

one by one. No improvement was noticed. Angioedema persisted. All medicines were stopped and she was put on prednisolone in a reducing dosage. Within another four weeks that was also completely tapered off. She improved dramatically and was completely symptom-free within 10 days. ATD were started again. No angioedema was noticed then but it appeared within a day when she was given a single dose (400 mg) of oral amiodarone. Again this symptom improved when amiodarone was taken off. Now she is without any symptoms since the last two years.

The second patient was a 73-year-old woman with a history of recurrent episodic facial swelling since one year. This was treated with oral steroids, resulting in clinical improvement. However, facial swelling reappeared after discontinuation of the steroids for which steroids were continued for a year. She presented to our clinic with typical cushingoid habitus. A complete clinical history was taken, and she was carefully questioned about past history and recent symptoms. Symptoms of angioedema were found to be unrelated to any food ingestion, activity, or stress. She had no clinical history of nasal polyps, chronic rhinitis, sinusitis, or asthma. It was found that she was taking oral corticosteroids and amiodarone 200 mg/day. This last drug had been started by a general practitioner 3 years back for cardiac rhythm abnormalities and had never been discontinued. Her chest radiograph was normal and all the laboratory tests (including blood analysis and serum chemistry, stool examination for parasites, IgE, thyroid profile and urinalysis) were within range except mild hyperglycemia and low ACTH level. Suprarenal glands were normal. A diagnosis of iatrogenic Cushing's syndrome was made. Complete physical examination, ECG and echocardiography were non-contributory. Skin patch tests with common allergens were done and found to be negative. In view of the patient's previous history, the diagnosis of amiodarone-induced angioedema was considered. Amiodarone was discontinued, and the symptoms disappeared with the reduction of steroids, which were finally discontinued. In order to confirm that amiodarone was the cause of the patient's reaction, a double-blind oral challenge with amiodarone was undertaken. Within 30 min of receiving the dose (200 mg), she began to experience facial flush and facial

angioedema. A cardiologist was consulted and as her ECGs were normal, amiodarone was withdrawn permanently. The patient is fine even after one year follow-up.

Amiodarone is currently a widely prescribed medicine, being used in ventricular and supraventricular arrhythmias and to maintain sinus rhythm in atrial fibrillation.<sup>[3]</sup> The pathogenetic mechanism was thought to be metabolic rather than immunologic, because body tissues may act as a large reservoir of this drug under chronic administration, and several of the adverse effects of amiodarone are attributable to the deposition of amiodarone conjugated phospholipids in the tissues.<sup>[3,7]</sup>

Our observation indicates that a serious complication like angioedema due to this drug may not be as rare as is thought to be. However, it may be under-reported due to the unawareness of such an adverse effect of the drug or simple lack of documentation. It is very important to know and recognize these rare adverse effects of a fairly widely prescribed drug at an early stage to avoid a serious outcome. To the best of our knowledge, this is only the second report in the literature about facial angioedema induced by amiodarone use.

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## Sparfloxacin induced blue/black discoloration of all nails: Report of three cases

Sir,

Discoloration of nails is usually seen as an adverse reaction to drugs.<sup>[1]</sup> Pigmentation can occur either in the nail plate or vascular nail bed. The term *chromonychia* indicates an abnormality in color of the substance and / or the surface of the nail plate and / or subungual tissues. When the cause is endogenous, discoloration often corresponds to the shape of the lunula. Melanonychia is increased melanogenesis in the nail matrix.

Chloroquine produces blue-black nail bed,<sup>[2]</sup> silver induces dark blue nail bed (argyria), amodiaquine causes hyperpigmentation, phenolphthalein - dark blue discoloration, and zidovudine (AZT) produces brown-black longitudinal streaks in the nail plate.<sup>[3]</sup> Hyperpigmentation due to an increase of melanin pigment in nail and nail bed has been noted in children after six weeks' treatment with doxorubicin.<sup>[4]</sup> Carbamazepine was reported to have produced yellow discoloration in the nails which cleared within 6 months after stopping therapy.<sup>[5]</sup> We report blue / black discoloration of nails in 3 patients due to sparfloxacin, which has not been reported so far in the literature to the best of our knowledge.

## Case 1

A 16 year old boy presented with recurrent boils on the scalp. He was prescribed sparfloxacin 400 mg as a loading dose, followed by 200 mg daily for 15 days. He