Fat necrosis: a neglected side effect of intramuscular injections.

Abstract:

# Fat necrosis (FN) is an uncommon etiology of panniculitis. It is mainly caused by trauma and may be associated to other conditions such as pancreatic disease. We report an interesting case of subcutaneous FN caused by intramuscular injections of cefazolin and meglumine antimoniate in a 38-year-old female patient.

# Key words: Fat necrosis, leishmaniasis, meglumin antimoniate, cefazolin

# Introduction :

Fat necrosis (FN) is a localized panniculitis. Most cases are caused by trauma, although some have been described following injection therapy. FN is a benign non suppurative inflammatory disease of adipose tissue. It is a rare condition, affecting all ages. 1 Terminology of FN remains confusing as it is also called ‘nodular-cystic fat necrosis’, ‘mobile encapsulated lipoma’, ‘nodular fat necrosis’ and ‘post-traumatic fat degeneration. 1,2 FN is the consequence of the stimulation of an inflammatory reaction within the adipose tissue, which is due to a local trauma or tissue injury.

Herein, we present a distinctive case of FN occuring after intramuscular injection of meglumine antimoine and cefazolin.

**Case report:**

A 38-year-old female was admitted to our department with asymptomatic multiple ulcerative nodules of 1 month duration. Her medical history was unremarkable. Dermatological examination revealed multiple nodules on the right leg and the left forearm, six were firm, non tender and ulcerated and four ones were non ulcerated extending along the line of lymphatic vessels. The patient had also a paronychia of the big toe (figure. 1a) and an indurated plaque of 70/40 mm on the right buttock (attributed to intramuscular injections of cefazoline 2 times per day during one week). The remaining physical examination was normal except for obesity (Body Mass Index of 30). The diagnosis of cutaneous leishmaniasis (CL) was confirmed by a positive polymerase chain reaction (PCR). Given the clinical form of CL (sprorotrichoid, paronychia and multiple lesions), intramuscular injection of meglumine antimoniate (IMMA) was initiated (at the dose of 30 mg/kg/day for 5 days and 60 mg/kg/day for 8 days). Despite, the deep intramuscular injection afar from the indurated plaque of the buttock (figure. 1b), the patient remained annoyed, which compelled us to stop IMMA. An ultrasound of the right buttock plaque showed a large hypoechogenic mass on the deep tissue away from the muscle without any detectable collection. Local massage by a potent topical corticosteroid (3 months) than oral colchicine (1mg/day) for 9 months led to a slight improvement. Thereby, a limited excision was made 27 months after the onset of the lesion of the buttock. The histology showed extensive lesions of steatonecrosis with a cystic degeneration of adipocytes and numerous multinucleated foreign body type giant cells (figure 2). The diagnosis of fat necrosis (FN) induced by intramuscular injection of an antibiotic and worsened by large quantities of IMMA was made.

**Discussion:**

First described on the breast in 1920, FN is a benign non suppurative inflammatory disease of adipose tissue. It is an uncommon, self-limited panniculitis of traumatic origin, in newborns, while it mainly affects women after a breast surgery. 1

Terminology of FN is still confusing as it is also called ‘nodular-cystic fat necrosis’, ‘mobile encapsulated lipoma, ‘nodular fat necrosis’ and ‘post-traumatic fat degeneration. 2

FN is the consequence of the stimulation of an inflammatory reaction within the adipose tissue, which is due to a local trauma or less frequently a tissue injury. 3 Limb, which are commonly exposed to repeated microtrauma, are the most commonly affected sites. Chemical agents such as vasopressin, human growth hormone, triamcinolone, and insulin are also alleged. 4,6 Numerous diseases have been reported in association with FN: pancreatitis, collagen vascular diseases, myeloproliferative disorders, asphyxia, hypothermia, subcutaneous injections and trauma. 3

Obesity, the only morbidity found in our patient is more likely to be a risk factor. We generated this hypothesis with the belief that the subcutaneous adipose tissue of obese patients has a lower blood flow.

Clinically, FN presents as indurated painful deep nodules of the subcutaneous tissue covered by a normal skin or an ‘orange peel’ appearance, local depression or discoloration of the skin. 1 The acute presentation as a large indurated plaque, as in our patient, is quite unusual. 7

FN has a similar imaging appearance as mature adipose tissue. Ultrasonographic image displays a hypoechoic appearance in most cases (like ours). However, FN of the trunk and in extremities are not fully characterized.4

In our patient, FN was induced by IM injections of cefazolin and compounded by IMMA. Several cutaneous side effects of this MA were reported: either general reactions (including rash, urticaria…) or local ones (infection, rash…). According to the large series of Beheshti et al 5 the most common side effects of MA are skin hypersensitivity and urticaria. Most authors explain this high frequency by the presence of impure heavy metals in the product 5 Cefazolin is an antibiotic known for its allergic reactions and cross-reactivities with betalactams. 7 Local cutaneous side effects aren’t documented in the literature.

The diagnosis of traumatic panniculitis was first proposed in our patient, hence the prescription of colchicine. Given the resistance, a cutaneous calcinosis or foreign body granuloma were suspected. An excision confirmed the diagnosis of FN. And to the best of our knowledge, there were no previous case reports of FN post cutaneous leishmaniasis treatment.

In fact, histopathology findings in FN depend on the stage of the disease. At early stages, FN with cystic spaces and numerous neutrophils in the adjacent fat are seen. Later on, predominant cells become lymphocytes, histiocytes and multinucleated giant cells with lipid vacuoles in some cells. Finally, fibrosis prevails on histology 8

Since FN is a self-limiting condition, a conservative approach can be followed. Surgical intervention is required only in patients with intractable pain and complications 8  or for cosmetic reasons. In our patient, we performed a surgical excision given the impact of the lesion and the unusually persistent character.

**Conclusion:**

We report an original case of FN. It is the first one described after IM cefazoline injections and compounded by IMMA. We believe that the repeated injections on the superficial fat tissue in an obese patient compromised local vascularization and caused a FN with a cystic degeneration and a foreign body reaction. Although, cutaneous leishmaniasis is a benign parasitic infection, lesions can lead to disability and disfiguring scars. Systemic treatment remains the main treatment in these cases. Follow up and early detection of adverse drug reaction of IMG is of a good help for a better management.

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**Legend of figures**

Figure 1A: paronychia of the big toe

Figure 1B: Indurated plaque with red-orange surface of the buttock

Figure 2: Extensive lesions of steatonecrosis. Note the Cystic degeneration of adipocytes and the presence of numerous multinucleated foreign body type giant cells (HE x 50).

**Medical clinical key:**

FN remains rare. We report an interesting case of subcutaneous FN caused by intramuscular injections of cefazolin and meglumine antimoniate in a 38-year-old female patient refered to our department for the management of cutaneous leishmaniasis.