

Octreotide-LAR-Associated Erythema Multiforme in an Acromegalic Subject: Case Report

apresentação de caso

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ABSTRACT

Long-acting somatostatin analogs are often used for treating acromegaly, either as adjuvant to surgery or radiotherapy or, more recently, as a primary therapeutic option. These drugs seem to be reasonably safe, but new adverse effects not yet described may occur during the use of the relatively new long-acting formulations. In this case report, we describe a severe cutaneous reaction (erythema multiforme) in a patient treated with long-acting release (LAR) octreotide, and also discuss the need of previous "testing" with short subcutaneous preparation of octreotide. (**Arq Bras Endocrinol Metab 2008;52/1:138-140**)

Keywords: Octreotide/adverse effects; Erythema multiforme; Acromegaly; Somatostatin/analogues and derivatives

RESUMO

Eritema Multiforme Associado ao Octreotide- LAR em uma Paciente Acromegálica: Relato de Caso.

Análogos da somatostatina de longa duração são freqüentemente usados no tratamento da acromegalia, como adjuvante à cirurgia ou à radioterapia ou, mais recentemente, como opção terapêutica primária. Essas drogas parecem ser razoavelmente seguras, mas podem ocorrer efeitos colaterais ainda não descritos com o uso das relativamente novas formulações de ação prolongada. Neste relato de caso, descrevemos uma reação cutânea grave (eritema multiforme) em uma paciente tratada com octreotide de liberação prolongada (LAR) e discutimos a necessidade de submeter os pacientes previamente a um "teste" com a formulação subcutânea do octreotide de ação rápida. (**Arq Bras Endocrinol Metab 2008;52/1:138-140**)

Descritores: Octreotide/efeitos adversos; Eritema multiforme; Acromegalia; Somatostatina/análogos e derivados.

INTRODUCTION

SOMATOSTATIN ANALOGS, as octreotide and lanreotide, are currently used worldwide as a therapeutic option for subjects with active acromegaly, before or after transsphenoidal surgery (1-4). Most authors agree that somatostatin derivatives are efficient and reasonably safe medications, based mainly on extensive data on subcutaneous preparations of these drugs. However, long-acting (LAR) formulations of octreotide and lanreotide have been in clinical use only for about a decade

CASE REPORT

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A 40-year-old white woman was first evaluated for nasal obstruction due to septal deformity. On the occasion, she also complained of enlargement of

both her hands and feet and a change in her facial appearance in the last few years. Acromegaly was confirmed by elevated IGF-I and not suppressible GH after an oral 75g-glucose load. Magnetic Resonance Imaging (MRI) showed a pituitary macroadenoma (1.7 x 1.5cm) with invasion of left cavernous sinus. In view of the low probability of complete surgical removal of the adenoma, we preferred to treat the patient preoperatively with long-acting octreotide (Sandostatin LAR®, Novartis) aiming to reduce the tumor mass. On the second day after gluteal intramuscular injection of a 20mg dose of octreotide-LAR, the patient developed round, nonscaling erythematous pruriginous plaques, 1.5 to 3cm diameter, with central areas of normal skin on dorsal and ventral sides of the trunk and proximal parts of limbs. She also presented with arthralgia and periarticular edema in hands, wrists, elbows, knees and ankles, without hyperemia or increased temperature. She denied using other medications or having any infectious symptoms. She had no antecedents of hypersensitivity to any drug. The patient was referred to the Dermatology service in our institution, where the clinical diagnosis of drug-related erythema multiforme was made. She was treated with oral antihistaminic drugs and glucocorticosteroids (prednisone, 40mg qid for a week, followed by 20mg qid for another week). There was a rapid improvement of the articular symptoms, but the skin lesions persisted during 40 days, in spite of the corticosteroid treatment. After the reported instance, neither did the patient receive octreotide again nor did she have further cutaneous abnormalities.

The adverse event was immediately reported to the farmacovigilance bureau of Novartis, which informed us that this type of cutaneous reaction had not been previously reported in association with the use of Sandostatin-LAR®.

The patient was subsequently treated with cabergoline, but failed to achieve biochemical improvement. A new MRI performed 22 months after the first one revealed an increase in tumor size (2.6 x 2cm). She then underwent transsphenoidal surgery, but the post-operative CT still showed a large residual tumoral mass (2.1 x 1.5cm), and the serum GH and IGF-I remained above normal. Pegvisomant and external radiotherapy are currently being considered.

DISCUSSION

Cutaneous reactions are the most common adverse effects of drugs. However, serious events as erythema mul-

tiforme or Stevens-Johnson syndrome are relatively rare. The rapid recognition of these reactions, along with immediate withdrawal of the culprit drug and supportive measures are essential for a good prognosis (5).

Erythema multiforme is an acute eruption characterized by sudden appearance of fixed erythematous bullous target lesions in skin and/or mucosae. The condition is generally restricted to dermatologic manifestations, with minimal general symptoms and a good clinical evolution, but mucosal and cutaneous involvement may be extensive and associated to major systemic disturbances and poorer prognosis in some cases (6).

Somatostatin analogs are generally well tolerated. Their main adverse effects are gastrointestinal symptoms as diarrhea, nausea, abdominal cramps and flatulence, which are usually light or moderate and transient. The most important complication of somatostatin analogs is gallstones development, affecting 20-30% of patients (7). Cutaneous reactions may occur, but the reports in literature are restricted to the site of injection (8,9). Other cutaneous adverse effect related to octreotide is transient hair loss (10,11). We found no reports of octreotide-related erythema multiforme. The manufacturers of the drug (Novartis) also informed us that they were not aware of any previously described reaction like the one presented by our patient, although other adverse events had been associated with the use of octreotide, like, for instance, manic episodes. (12)

We decided to report this unexpected adverse effect because several authors have recently suggested that the treatment of acromegaly with somatostatin analogs can be safely started with initial administration of long-acting release (LAR) formulations of octreotide or lanreotide, since these preparations have a better dose schedule and are more efficacious than the immediate release formulations for subcutaneous injection (13,14). In the reported case of a patient treated with a long-acting release formulation there were symptomatic and potentially severe hypersensitivity skin lesions which persisted during six weeks, the approximate length of the drug effect. Since then, as a measure of precaution, we have administered the long-acting preparation of octreotide only after a short-course (2-3 days) proof treatment with the short-acting subcutaneous preparation, during which we assess the occurrence of hypersensitivity reactions. If they do occur, they are much shorter and easier to handle than those induced by high-dose, long-acting preparations. We must further consider that the reported hypersensitivity reac-

tion may not have been caused by the octreotide itself, but by other components of the long-acting formulation, as, for instance, polylactic acid microspheres.

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