Case Report

Acute renal failure due to intermittent use of rifampicin in the treatment of leprosy

Insuficiência renal aguda decorrente do uso intermitente de rifampicina no tratamento da hanseníase

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ABSTRACT

Leprosy is a chronic infectious contagious disease caused by Mycobacterium leprae. Individuals with this comorbidity can be cured thanks to treatment with dapsone, clofazimine and rifampicin. The combination of drugs is known as multidrug therapy and the choice of combination depends on the classification of patients as paucibacillary or multibacillary. Rifampicin is part of standard treatment and renal anomalies secondary to its use are rare. However, the most common of these is acute renal failure. Because it is an unusual and potentially fatal side effect, it is necessary for health teams and patients to be alerted to the possibility of their occurrence, thus ensuring early detection of abnormalities and rapid management of side effects. We present a case of a patient with a diagnosis of dimorphic leprosy in treatment with multidrug therapy who developed acute renal failure after the tenth dose of rifampicin, requiring the suspension of the same.

Keywords: Leprosy, Rifampin, Renal Insufficiency.

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RESUMO

A hanseníase é uma doença infectocontagiosa crônica, causada pelo Mycobacterium leprae. Indivíduos com esta comorbidade podem ser curados graças ao tratamento com dapsona, clofazimina e rifampicina. A associação de fármacos é conhecida como poliquimioterapia e a escolha da combinação depende da classificação dos pacientes como paucibacilares ou multibacilares. A rifampicina faz parte do tratamento padrão e as anomalias renais secundárias ao seu uso são raras. No entanto, dentre elas, a mais comum é a insuficiência renal aguda. Por se tratar de um efeito colateral incomum e potencialmente fatal, é necessário que as equipes de saúde e os pacientes sejam alertados quanto à possibilidade de sua ocorrência, garantindo desta forma, detecção precoce de anormalidades e rápido manejo dos efeitos colaterais. Apresentamos caso de paciente com diagnóstico de hanseníase dimorfa em tratamento com poliquimioterapia que desenvolveu insuficiência renal aguda após a décima dose da rifampicina, sendo necessária a suspensão da mesma.

Palavras-chave: Hanseníase, Rifampina, Insuficiência Renal.

Introduction

Leprosy is a chronic contagious and infectious dermatosis, caused by Mycobacterium leprae, characterized by neurological symptoms and cutaneous lesions, that can induce deformities. Though curable, it is still a relevant public health problem, since it persists as endemic in many countries, among them, Brazil.[1,2]

It was proposed, by the World Health Organization, an operational classification for the endemic disease control purposes, using therapeutic schemes that have as principle the combination of drugs, known as multidrug therapy. Its use quickly reduces the number of bacilli and stops the transmission of the disease. The definition of the combination of drugs to be used depends on the patient's classification in paucibacillary or multibacillary. The first feature up to five skin lesions, absence of bacilli in the bacilloscopy, and will be treated for 06 months with rifampicin 600 mg, in monthly supervised dose, and Dapsone 100 mg, home daily. In the other side, multibacillary have more than five skin lesions, presence of bacilli in bacilloscopy, and require treatment for period of 12 or 24 months, with Rifampicin 600 mg and Clofazimine 300mg,on supervised monthly dose, in addition to Dapsone 100mg and Clofazimine 50 mg, home daily.[2,3,4]

Several adverse effects are attributed to these medications, and renal damage with development of Acute Renal Failure (ARF) is considered rare and serious event, resulting from the use of rifampicin. It is believed that this event is related to the intermittent use of the drug, although it has been described during continuous use. It is assumed that this occurs by immune mechanism: since rifampicin acts as a hapten, connected to plasma protein, it activates the immune system and leads to the formation of antibodies. During the period in which the individual is not receiving the drug, the synthesis of these antibodies reaches critical levels and, when administered again, may lead to hypersensitivity reaction. Immunological tests show antibodies against Rifampicin, but there are patients who do not present them, and others that, although they have, don't develop injuries.[5]

Another drug that can trigger renal injury is Dapsone, due to induction of haemolysis and intravascular coagulation, leading to Acute Tubular Necrosis. The possibility of Dapsone potentiate the toxicity or magnify the immune reaction of Rifampicin cannot, therefore, be deleted.[5,6]The kidney damage in patients with leprosy can also be motivated by the disease itself, and the multibacillary presents greater risk factor, but in this case, specific treatment has an impact on improvement of renal function.[6]

Description

Female patient, 51 years old, leucodermic, born and living in Barbacena, Minas Gerais. She was seen in the dermatology clinic with complaints of stain associated with sensory loss, with onset one year and six months ago. She reported history of Pulmonary Tuberculosis for five years, treated with rifampicin, isoniazid, pyrazinamide and ethambutol for six months, evolving with cure and absence of complication.

Physical examination showed erythematous and infiltrated lesions with depressed center, disseminated, and of varying sizes (Figure 1), associated with thickening of the retro-auricular nerve and ulnar nerve bilaterally. It was established the diagnosis of Borderline Leprosy, confirmed by bacilloscopy (bacillary index of 0.75) and Histopathological examination, which showed perivascular, interstitial and superficial dermatitis, with inflammatory infiltrate, full of neutrophils.

It was started the treatment with multidrug therapy for multibacillary patient, however, in the tenth dose, she started with indisposition, diffuse abdominal pain, throwing

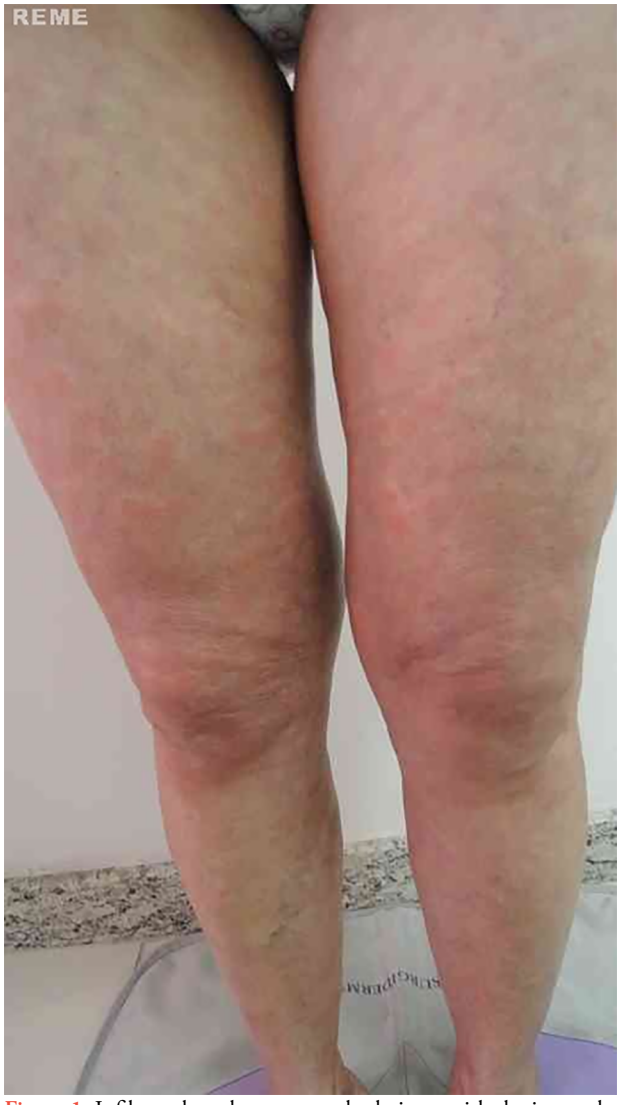

Figure 1. Infiltrated erythematopapular lesions, with the internal and external insertions delimited to the body, disseminated below.

up, developed oliguria, and later, anuria, elevation of urea and creatinine. The patient was hospitalized, in which she was diagnosed with Acute Renal Failure (ARF) by intermittent use of Rifampicin. The medications were suspended, dialysis was started, with total recovery of renal function. She returned, after hospitalization, to the Dermatology's service, with complete regression of the cutaneous lesions. A new bacilloscopy was requested, showing bacillary index of zero. Due to the history of Acute Renal Failure, caused by Rifampicin, we opted for the permanent suspension of multidrug therapy. This decision was also motivated by the detection of bacillary index of zero and proper use of medications.

Discussion

The use of multidrug therapy has an important role in the management of leprosy, allowing even its cure. However, pharmacological aspects, mainly the management of side effects, are poorly studied and addressed, since most of the researches about this disease, in Brazil, prioritizes the clinical and epidemiological features.[3]

Among the drugs used in conventional treatment, the only with bactericidal action is rifampicin. The incidence of adverse reactions to this medication are higher during the intermittent use or re-use. This occurs because a single dose can induce sensitization and may cause immunoallergic reaction after exposure, while the daily administration is able to confer immune tolerance.

The side effects of continuous therapy with Rifampicin are minimal and involve allergic reactions, skin rashes, gastrointestinal discomfort, drug interactions and, mainly, hepatotoxicity. When the use is intermittent, the effects may be more severe and, in this case, the reactions will be immune mediated by IgG and IgM antibodies, and directed against the red cells, platelets and other cells, as the renal tubular epithelial cells. In this case, there may be Flu-like syndrome, hemolytic anemia, dyspnea, shock and renal manifestations; the last is unusual; however, when present, generally represented by ARF.[4,7]

The main histological patterns found in biopsies of patients with renal damage, caused by the use of Rifampicin, is Acute Tubular Necrosis (ATN) and/or Interstitial Nephritis (IN). The ATN is more common and serious, when compared to IN, that has been described as insidious and with similar symptoms to the flu-like syndrome.[6,7,8,9]

The prognosis of the ARF due to the use of multidrug therapy is, in most cases, good. Furthermore, it has low mortality and complete recovery of renal function, in most affected. The main influencing factor will be the duration of anuria. If it is prolonged, there will be need for dialysis, and in this case, the reduction's rate of azotemia will be slow.[7]

This patient made use of Rifampicin intermittently, which is a risk factor for the development of ARF. The intervals between administrations were sufficient for the synthesis of antibodies to reach extreme levels and cause the acute Renal failure. In addition, during the treatment, the patient also made use of Dapsone, which may have broadened or potentiated the reaction to this medication.

The way in which the patient evolved is in accordance with the cases described in the literature, for complete recovery of renal function and the prognosis was good.

Conclusion

Considering that the renal involvement is a serious and potentially fatal complication, physicians should be warned to the suggestive signs and symptoms. For this, it is essential to collect the patient's story, especially the pharmacological. In addition, it is necessary to follow up patients laboratory in use of Rifampicin, especially those with oliguria or anuria. Those who manifest immunoallergic reaction to this drug should have its use permanently suspended, given the potential severity of reactions. Health workers and patients should be aware of side effects, because this allows quick intervention, and, consequently, better prognosis.

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