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CASE REPORT

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Severe adverse reaction to dapsone in the treatment of leprosy

Reação adversa grave à dapsona no tratamento da hanseníase

Reacción adversa severa a la dapsona en el tratamiento de la lepra

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ABSTRACT

Introduction: leprosy is caused by the bacillus *Mycobacterium leprae* and affects the skin and/or peripheral nerves. Adverse reactions to medications used in the treatment of the disease have been reported in the literature. **Objective:** to report the case of a patient who experienced a severe adverse reaction to dapsone in the treatment of leprosy. **Case description:** a 51-year-old female patient sought care at the dermatology outpatient clinic of Lauro Wanderley University Hospital of the Federal University of Paraíba, linked to the Brazilian Hospital Services Company, complaining of spots on her lower limbs for three years. Physical examination revealed erythematous-brown macules with altered sensitivity in the lower limbs. A biopsy of the lesions and a skin smear bacilloscopy were performed, confirming the diagnosis of

leprosy, leading to the initiation of multidrug therapy, a single regimen. After three weeks, the patient developed hemolytic anemia caused by dapsone, necessitating the suspension of multidrug therapy, a single regimen, and the prescription of two hemoconcentrates and intravenous hydrocortisone, with satisfactory progress. **Discussion:** there are reports in the literature of adverse reactions to multidrug therapy, single regimen, with an emphasis on dapsone. Hemolytic anemia is one of the most common adverse effects. However, the patient's low hemoglobin levels differed from findings in previous studies, making it necessary to suspend the medications. **Conclusions:** the case highlights severe anemia, emphasizing the relevance of an interdisciplinary approach and meticulous attention to patients undergoing such therapeutic regimens.

Keywords: *Neglected Tropical Diseases. Lepromatous Leprosy. Dapsone. Drug Side Effects. Hemolytic Anemia.*

RESUMO

Introdução: a hanseníase é causada pelo bacilo *Mycobacterium leprae* e afeta pele e/ou nervos periféricos. Reações adversas às medicações utilizadas no tratamento da doença têm sido relatadas na literatura. **Objetivo:** relatar o caso de paciente que apresentou reação adversa grave à dapsona no tratamento da hanseníase. **Descrição do caso:** paciente do sexo feminino, 51 anos, buscou atendimento no ambulatório de dermatologia do Hospital Universitário Lauro Wanderley da Universidade Federal da Paraíba, vinculado à Empresa Brasileira de Serviços Hospitalares, com queixa de manchas em membros inferiores há três anos, sendo identificadas, em exame físico, máculas eritêmato-acastanhadas com alteração de sensibilidade em membros inferiores. Foi realizada biópsia das lesões e a baciloscopia de esfregaço dérmico, que confirmaram o diagnóstico da hanseníase, procedendo-se ao início da poliquimioterapia, esquema único. Após três semanas, a paciente apresentou anemia hemolítica causada pela dapsona, sendo necessária a suspensão da poliquimioterapia, esquema único e prescrição de dois hemoconcentrados e hidrocortisona endovenosa, com evolução satisfatória. **Discussão:** há relatos na literatura de reações adversas à poliquimioterapia, esquema único, com ênfase à dapsona. A anemia hemolítica corresponde a um dos efeitos adversos mais comuns. Porém, os baixos níveis de hemoglobina da paciente diferiram dos achados de estudos prévios, sendo necessária a suspensão das medicações. **Considerações finais:** o destaque trazido pelo caso enfoca a anemia severa, evidenciando a relevância de uma abordagem interdisciplinar e da atenção minuciosa aos pacientes sob tal esquema terapêutico.

Palavras-chave: *Doenças Negligenciadas. Hanseníase Virchowiana. Dapsona. Efeitos Adversos. Anemia Hemolítica.*

RESUMEN

Introducción: la lepra es causada por el bacilo *Mycobacterium leprae* y afecta la piel y/o los nervios periféricos. Se han reportado reacciones adversas a los medicamentos utilizados en el tratamiento de la enfermedad en la literatura. **Objetivo:** reportar el caso de una paciente que presentó una reacción adversa grave a la dapsona en el tratamiento de la lepra. **Descripción del caso:** paciente de sexo femenino, 51 años, busca atención en el ambulatorio de dermatología del Hospital Universitario Lauro Wanderley de la Universidad Federal de Paraíba, vinculado a la Empresa Brasileña de Servicios Hospitalarios, con queja de manchas en las extremidades inferiores desde hace tres años, identificándose en el examen físico máculas eritémato-castañas con alteración de la sensibilidad en las extremidades inferiores. Se realizó una biopsia de las lesiones y una baciloscopia de raspado dérmico, que confirmaron el diagnóstico de lepra, procediéndose al inicio de la poliquimioterapia, régimen único. Después de tres semanas, la paciente presentó anemia hemolítica causada por la dapsona, siendo necesaria la suspensión de la poliquimioterapia, régimen único, y la prescripción de dos hemoconcentrados y hidrocortisona endovenosa, con evolución satisfactoria. **Discusión:** hay reportes en la literatura de reacciones adversas a la poliquimioterapia, régimen único, con énfasis en la dapsona. La anemia hemolítica corresponde a uno de los efectos adversos más comunes. Sin embargo, los bajos niveles de hemoglobina de la paciente diferían de los hallazgos de estudios previos, siendo necesaria la suspensión de los medicamentos. **Consideraciones finales:** el caso destaca la anemia severa, evidenciando la relevancia de un enfoque interdisciplinario y de la atención minuciosa a los pacientes bajo tal esquema terapéutico.

Palabras clave: *Enfermedades Negligidas. Lepra Virchowiana. Dapsona. Evento Adverso. Anemia Hemolítica.*

INTRODUCTION

Leprosy is an infectious disease caused by the bacillus *Mycobacterium leprae*. It primarily affects the skin and peripheral nerves. Its incidence is high in Brazil, with over 150,000 new cases diagnosed between 2016 and 2020[1-2].

The definition of a leprosy case begins with a clinical examination. A case is defined when skin lesions with altered color and sensitivity, nerve thickening, and/or a positive bacilloscopy are observed. Classification takes into account the number of lesions and the result of the bacilloscopy: in patients with up to five lesions and a negative bacilloscopy, the case is defined as paucibacillary (PB); if there are more than five lesions or a positive bacilloscopy, the mul-

tibacillary (MB) form is diagnosed[3]. Leprosy is a curable disease treated with uniform multidrug therapy (MDT-U), which consists of three drugs: rifampicin, dapsone, and clofazimine.

Adverse reactions to dapsone in the treatment of leprosy are well documented in the literature and occur more frequently than with other MDT-U drugs. Adverse effects of this drug include hypersensitivity syndromes, gastrointestinal symptoms, and hemolytic anemia, among others[4-5].

We report a case of a severe adverse reaction to dapsone used in the treatment of leprosy in a patient seen at the dermatology outpatient clinic of Lauro Wanderley University Hospital, part of the Federal University of Paraíba and affiliated with the Brazilian Hospital Services Company (HULW-UFPB/Ebserh), as well as at a private hospital in João Pessoa, Paraíba.

METHODOLOGY

This is a case report – an observational study – of a patient who was followed at a university hospital in Paraíba between 2022 and 2023. The Research Ethics Committee of the Center for Medical Sciences (CEP/CCM) at the Federal University of Paraíba approved the report under CAAE number 69458623.5.0000.8069 (approval number 6.104.801).

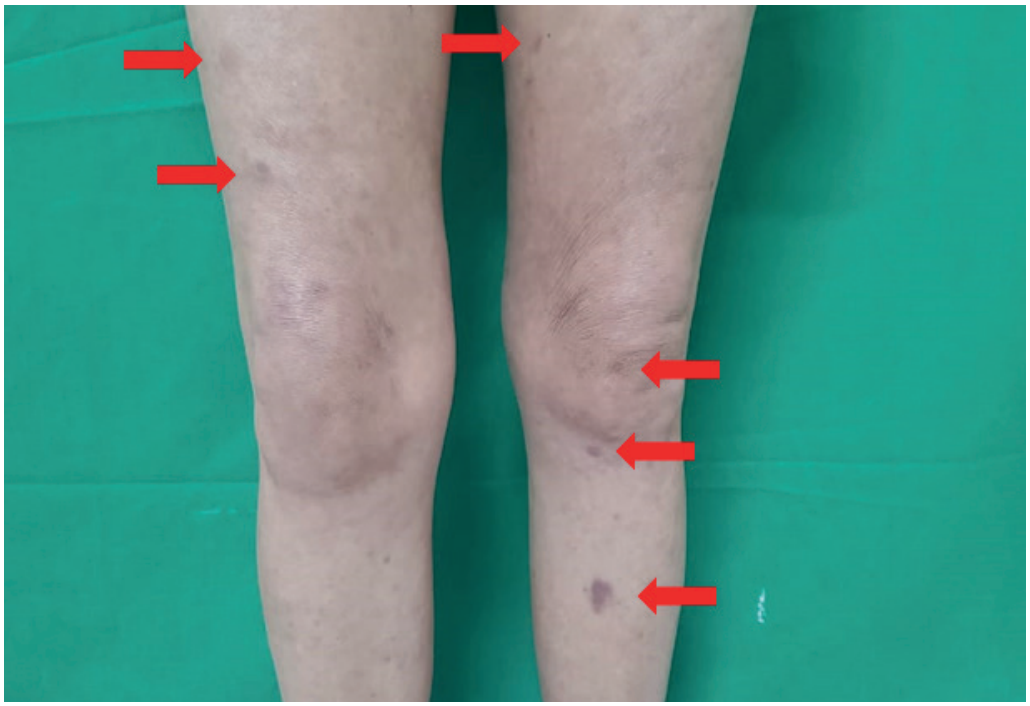
The patient described in this case report provided written informed consent and authorized the publication of her image. The photograph included in this report was taken in a private setting to ensure her privacy and anonymity. All information regarding the case was obtained from her medical records.

CASE REPORT

A 51-year-old female patient presented to the dermatology outpatient clinic of HULW-UFPB/Ebserh with a complaint of skin lesions on her lower limbs for approximately three years (Figure 1). Her medical history included anxiety disorder, for which she was being treated with escitalopram 15 mg/day. On physical examination, erythematous-brownish macules with altered sensitivity were observed on the lower limbs, abdomen, and flank. She also exhibited leonine facies, with infiltration of the eyebrows, nasal bridge, auricular pavilion, and mild madarosis.

The biopsy of the lesions was performed, showing findings compatible with multibacillary leprosy (Lepromatous leprosy) and a Ridley Bacillary Index (BI) of 4. A slit skin smear bacilloscopy was also conducted, showing a BI of 3, and a simplified neurological evaluation with classification of physical disability grade (Grade I), in which drying of the eyes, skin, and nostrils was noted, along with slight muscle weakness in the right fifth toe, thickening of the left ulnar nerve,

Figure 1 – Lower limbs of the patient. Arrows indicate erythematous-brownish macules.



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and mild loss of sensation in the lower extremities. The patient was started on supervised MDT (multidrug therapy) and instructed on hydration measures and tactile stimulation of the feet.

Twenty-one days after initiating treatment, the patient was admitted to the admissions unit of a private hospital, presenting with fever, anorexia, malaise, and dyspnea. Laboratory investigations revealed an elevated lactate dehydrogenase level of 1932 U/L and a hemoglobin concentration of 5.8 g/dL. A total abdominal CT scan was also performed, demonstrating grade I splenomegaly and mildly enlarged lymph nodes in the left inguinal region.

Given the hemolytic anemia caused by dapsone, MDT-U was discontinued. The patient received two units of hemoconcentrate and 400 mg of intravenous hydrocortisone; the dose was gradually reduced and later replaced with 10 mg of oral prednisone, with satisfactory progress. The patient was discharged after 13 days with a prescription for vitamins B1, B6, B12, and oral folic acid and was advised to return to the referral center for follow-up.

At the subsequent outpatient visit, the patient had a hemoglobin level of 11.6 g/dL and persistent dermatological lesions. A hematology consultation was requested to evaluate the resumption of leprosy treatment, this time using ofloxacin instead of dapsone. Following a lymph node biopsy that tested negative for malignant lesions and an increase in hemoglobin to 13.1 g/dL, the introduction of an alternative regimen was authorized, with no new adverse reactions observed.

DISCUSSION

Leprosy treatment previously recommended by the Ministry of Health varied depending on whether the patient was classified as PB or MB. However, following the publication of new studies, the pharmacological management of both forms of leprosy has been unified in Brazil since 2021[6-7]. The MDT-U regimen now consists of a monthly supervised dose of 600 mg rifampicin, 300 mg clofazimine, and 100 mg dapsone, along with a daily self-administered dose of 50 mg clofazimine and 100 mg dapsone. The treatment duration is 6 months for PB forms and 12 months for MB forms[8].

The literature reports adverse reactions to MDT-U, with particular emphasis on dapsone, especially during the first four months of treatment. Hemolytic anemia is one of the most common adverse effects of dapsone, particularly in women over the age of 45, as observed in the present case[4,9-12].

However, the patient's hemoglobin levels differed from those reported in previous studies. According to Deps et al.[12], most patients with anemia during leprosy treatment had a minimum hemoglobin level of 8.14 g/dL, whereas the patient described here had a level of 5.8 g/dL. Following treatment of the adverse reaction, the hemoglobin level rose to 11.6 g/dL, aligning with findings reported in the literature.

The patient's systemic manifestations required blood transfusions and discontinuation of dapsone. In a previous study, approximately half of the patients who developed hemolytic anemia had to discontinue the medication[11]. Subsequently, the patient benefited from an alternative regimen and continued without any new adverse reactions.

CONCLUSIONS

A case of a severe adverse reaction to dapsone in a patient with MB lepromatous leprosy is reported. The case highlights the occurrence of severe anemia and underscores the importance of an interdisciplinary approach and close monitoring of patients undergoing this therapeutic regimen.

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ETHICAL APPROVAL AND INFORMED CONSENT: *this study was approved by the Research Ethics Committee of the Center for Medical Sciences (CEP/CCM) of the Federal University of Paraíba, under CAAE number 69458623.5.0000.8069 (opinion number 6.104.801).*

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