Case Report

Virchowian leprosy and erythema nodosum leprosum in a 34-week pregnant woman without any previous diagnosis

Hanseníase virchowiana e eritema nodoso hanseníco em gestante de 34 semanas sem diagnóstico prévio

Gustavo Moreira Amorim¹, Thaynara Maestri², Amanda Oppitz³, Matheus Leye⁴, Filipe Luis Merini⁵, Luan Junior Vignatti⁵

ABSTRACT: We report a case of a pregnant female patient in the third trimester undergoing regular prenatal care at a Basic Health Unit, with good gestational evolution, but presenting skin lesions for approximately a year accompanied by changes in sensitivity, in addition to facial infiltration and madarosis. Considering Brazil as an endemic country for leprosy, ranking 2nd in the world concerning the number of new cases, late diagnosis of the patient in question stands out. We use this emblematic case report to discuss important aspects concerning the treatment of leprosy during the gestational period (multidrug therapy according to the Ministry of Health manual, without any changes due to pregnancy), obstetric outcome, guidelines regarding breastfeeding (not contraindicated with the mother in treatment; on the contrary, it should be stimulated) and care for the newborn.

Keywords: Neglected tropical diseases; Leprosy; Virchowian leprosy; Erythema nodosum leprosum; Infectious complications of pregnancy.
INTRODUCTION

Leprosy is a chronic and infectious disease caused by bacteria Mycobacterium leprae and Mycobacterium lepromatosis, acid-alcohol resistant bacilli and obligate intracellular parasites that present tropism for the peripheral nervous system, especially Schwann cells. The disease mainly affects the superficial skin nerves and peripheral nerve trunks (located on the face, neck, middle third of the arm and lower portion of the elbow and knee), and may also affect the eyes, bones, spleen and liver, among other organs.

Prevalence of the disease is higher in developing countries, such as Brazil, which ranks 2nd among the countries that recorded the highest number of new cases in 2018. Early diagnosis and treatment are necessary to prevent transmission, minimize possible complications, and reduce the chances of sequelae.

The operational classification proposed by the World Health Organization (WHO) divides patients into Paucibacillary (PB) and Multibacillary (MB). The first is defined by five or fewer skin lesions without detectable bacilli in skin smears, while the second is characterized by six or more lesions and/or positive bacilloscopy.

Transmission occurs mainly through the respiratory route or nasal secretions emitted by patients who are not receiving treatment. Occasionally, transmission can also occur by damaging the skin’s protective barrier. Some factors such as prolonged intimate contact, advanced age, immunosuppression and genetic predisposition can increase the risk of developing the disease. The incubation period is approximately between 5 and 10 years and, in some cases, it can manifest after decades.

Diagnosis can be established through clinical history and physical examination in areas of greater prevalence. Among the clinical findings is the presence of hypopigmented or reddened patches on the skin; decreased thermal, painful and/or tactile sensitivities; paresthesias; painless skin lesions; nodules or edema in the ears or face and peripheral nerve thickening with altered sensitivity. Late sequelae may also include decreased strength in the hands, associated with claw fingers, facial palsy or lagophthalmia, madarosis, collapsed nose or perforated nasal septum.

Treatment is carried out through the association of antimicrobial drugs and should be started as soon as the clinical diagnosis is established, without histopathological confirmation in areas where the disease has a high prevalence. For the PB form, the recommended treatment consists of Rifampicin (supervised monthly dose) and Dapsone (self-administered daily dose and supervised monthly dose), totaling six multidrug therapy (MDT) sessions, which can be offered in up to 9 months. For the MB form, in addition to Rifampicin and Dapsone, Clofazimine is added (self-administered daily dose and supervised monthly dose), totaling 12 MDT sessions, within a maximum interval of 18 months.

Considering the epidemiological relevance of leprosy in Brazil and its occurrence in both genders and all age groups, it is expected that it occurs or, at least, is diagnosed during the gestational period. In terms of public health and Primary Health Care, pregnancy and prenatal care represent an opportunity for diagnosing neglected diseases, especially in areas of greater endemicity. Despite this, the management and peculiarities of the gestational period can still be a reason for doubt, both concerning the diagnostic workup and the therapeutic recommendation.

In this sense, we report the case of a pregnant patient with a late diagnosis of Virchowian Leprosy (VL), despite regular prenatal care at a Basic Health Unit (BHU), drawing the attention to this endemic condition in our country that still generates so much difficulty in its diagnosis and treatment.

CASE REPORT

Female subject aged 29 years old, 34-week pregnant, without previous comorbidities, attending regular prenatal care at a BHU in Greater Florianópolis, Santa Catarina. The patient had complained about skin lesions for approximately one year, seeking medical care several times, being diagnosed in these situations with impetigo and secondary syphilis. Cephalexin and two therapeutic regimens with intramuscular benzathine penicillin were prescribed in these consultations.

She denied injuries or similar symptoms in household contacts.

The physical examination revealed nodular lesions with an exulcerated surface, covered by crusts on the upper limbs, lower abdomen and lower limbs, accompanied by changes in the infiltrated face and thermal, painful and tactile sensitivity. The face was infiltrated and hyperpigmented. Bilateral madarosis, infiltration and small nodules were identified in both ears, in addition to persistent and hardened edema of the lips (Photos 1, 2, 3 and 4). Two deep ulcers with hyperkeratotic and painless edges were observed in the plantar region, compatible with plantar perforating malformations, configuring grade 2 disability.

When actively asked, the patient reported nasal obstruction and serosanguineous rhinorrhea.
Figure 1 - Infiltrated face, hyperpigmented, with important bilateral madarosis.

Figure 2 - Left hearing pavilion infiltrated with nodulations clinically compatible with hansenomes.

She was subjected to a biopsy of one of the skin lesions in the right upper limb region, which presented dermis with mononuclear infiltrate, lymphohistiocytic with perineural disposition, and AFB search with positive Fite-Faraco staining, 6+/6.

Figure 3 - Bilateral hansenomas on the back of the hands.

Figure 4 - Ulcered hyperpigmented nodules in lower limbs, clinically compatible with necrotizing erythema nodosum leprosum.

VL diagnosis was then established, with a multibacillary operational classification, grade 2 disability (plantar anesthesia/plantar perforating malpractice) associated with a type 2 reaction, necrotizing erythema nodosum leprosum (ENL). PQT was initiated for the MB form.
The patient’s contacts were instructed to seek a Health Service for a dermatological and neurological examination. Among the family members evaluated, the patient’s 11-year-old daughter had poorly defined hypochromic patches on her face and forearm, associated with hypoesthesia. The complementary workup showed an incomplete histamine test compatible with indeterminate leprosy (PB).

The patient had a spontaneous vaginal delivery at term, with the newborn weighing 2.9 kg, measuring 47 cm, with APGAR 6 in the first minute and 9 in the fifth, and with no visible skin lesions. Breastfeeding was initiated on demand 18 hours after birth, and the child was referred to the Neonatal Intensive Care Unit due to respiratory distress. The infant was diagnosed and treated for early sepsis at the unit, returning to rooming-in after five days.

DISCUSSION

In 2018, approximately 208,000 new cases of leprosy were recorded in the world, of which 28,000 were in Brazil. The MB form corresponded to approximately 70% of the cases.

The diagnosis of leprosy is essentially clinical and epidemiological, performed through anamnesis and dermato-neurological examination, seeking to identify lesions or skin areas with altered sensitivity and/or involvement of peripheral nerves, with sensory and/or motor and/or autonomic alterations. As part of the approach strategy to eliminate leprosy as a public health problem is decentralization of diagnosis and treatment, attributing a prominent role to the primary care health team, which must be present and close to the patient. We emphasize that leprosy, together with tuberculosis, is a priority within the Family Health Strategy. Unfortunately, the reported case of late diagnosis represents an example of the need to maintain continuous and exhaustive health education in the context of leprosy.

Following the diagnosis, treatment is provided by the Unified Health System and is carried out on an outpatient basis at the BHU that serves the area of residence of the diagnosed and notified case. Both PB and MB cases can be adequately treated in a primary care setting, with only the most complex being referred to more specialized services.

A peculiarity of the reported case, which is the reason for this communication, is the identification of the disease during pregnancy. Women in the gestational period present physiological immunological suppression mainly related to cellular immunity due to negative feedback from Th1 helper lymphocytes (Th1) and consequent decrease in interleukin 2 (IL-2) production. Such changes are more marked between the third trimester of pregnancy and the twelfth week postpartum, thus constituting the period of greatest risk for infection, reactivation and progression of leprosy.

Once diagnosed with leprosy, pregnant women should undergo more frequent prenatal consultations to monitor fetal development and the presence of complications secondary to the treatment. The patient in this report was referred to the high-risk pregnancy clinic linked to the institution where she was referred for delivery.

The type of delivery must be defined by obstetric indication, and there is no contraindication to vaginal delivery. Some additional care may be required in the case of fetuses with intrauterine growth restriction, and newborn support by a neonatology team may be necessary.

Treatment of leprosy, as in the case, does not change due to pregnancy, being carried out with MDT according to the operational classification of the disease. Therefore, pregnancy and breastfeeding do not contraindicate usual treatment. MDT is highly effective and considered safe for the maternal-fetal binomial. A small portion of the drugs can be eliminated through breast milk, without additional risks to the newborn, except for momentary discoloration of the child due to clofazimine.

Another interesting aspect to be pointed out was diagnosing a reactional state in the patient in question. ENL is understood as an immunological hypersensitivity reaction to Mycobacterium leprae antigens. This pathology is a common complication of MB forms of the disease and manifests itself through erythematous and painful subcutaneous nodules that can progress to ulceration. In addition to the dermatological condition, ENL is part of the signs and symptoms of type 2 reactions: fever, lymph node enlargement, neuropathy and joint, liver and kidney involvement, among others. Reactional states can occur before, during and after treatment with MDT. However, its discontinuation is not recommended due to the leprosy reaction. In ENL, thalidomide is recommended as a first-line treatment until remission of the reactional condition, which naturally was not an option in the reported case.

In Brazil, since 2003 thalidomide can only be prescribed for women of childbearing age after medical evaluation, excluding pregnancy through a sensitive method and upon proof of using at least two effective contraception methods. The use of this drug is associated with severe fetal limb defects and organ deformities. If it is impossible to use thalidomide, the Brazilian Ministry of Health recommends using prednisone. Among other available options are pentoxifylline (also inadequate for the case in question; category C; therefore, it is contraindicated in pregnancy) and clofazimine, with a triple-daily dose in a decreasing scheme. As there was a significant improvement in the patient’s clinical condition after initiating MDT-MB, it was decided to conduct her treatment without specific medication for the leprosy reaction.

Histopathological analyses have already demonstrated the presence of Mycobacterium leprae on
the fetal surface of the placenta, although the placental barrier is effective in preventing vertical transmission of the bacillus\textsuperscript{14}. Prophylactic administration of drugs that make up the MDT scheme to the newborn is not indicated\textsuperscript{10,14}.

There is no contraindication to breastfeeding or restrictions on the mother’s contact with the infant if she is undergoing adequate treatment. However, care must be taken regarding the newborn’s contact with exulcerated/exudative skin lesions, as these can be infection sources, although transmission is unlikely considering the current treatment\textsuperscript{11}. In agreement with the Neonatology team, taking into account the regular use of MDT-MB since the 34th gestational week, it was decided to allow breastfeeding.

Diagnosis of leprosy is clinical, and its treatment and follow-up require a low level of health complexity. Health professionals who provide prenatal care must diagnose, treat and monitor the maternal-fetal binomial.

CONCLUSION

We present this interesting case of a 34-week pregnant woman diagnosed with lepromatous leprosy and erythema nodosum leprosy, discussing the peculiarities of the gestational period and the mother-child binomial. We highlight the high prevalence of leprosy in Brazil and the need for accurate and early diagnosis for effective treatment in BHUs. Health professionals who provide prenatal care must diagnose, treat, and monitor the maternal-fetal binomial because pregnant women who suffer from such infection and immunological alterations inherent to the gestational period can interfere with the evolution of the disease. We emphasize again that there is no contraindication to the use of MDT during the gestational period.

Authors’ participations: Gustavo Moreira Amorim: study conception and design; effective participation in research guidance; intellectual participation in propaedeutic and/or therapeutic conduction of the case studied; critical literature review; critical participation in propaedeutic and/or therapeutic conduction of the case studied; critical literature review; drafting the manuscript or reviewing it critically for important intellectual content. Amanda Oppitz: data collection, or data analysis and interpretation; intellectual participation in propaedeutic and/or therapeutic conduction of the case studied; critical literature review; drafting the manuscript or reviewing it critically for important intellectual content. Matheus Leye: data collection, or data analysis and interpretation; critical literature review; drafting the manuscript or reviewing it critically for important intellectual content. Filipe Luis Merini: data collection or data analysis and interpretation; critical literature review; drafting the manuscript or reviewing it critically for important intellectual content. Luan Junior Vignatti: writing or critical review; critical literature review; final approval of the version to be published.

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