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Leprosy Reactions: Clinical and Therapeutic Profile of Patients Registered at a Dermatology Reference Center in Brazil

ORIGINAL

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Abstract

Introduction: During the course of leprosy, 10 to 50% of individuals can be surprised by reaction states, which are immune system reactions of the patient to *Mycobacterium leprae*. Leprosy reactions constitute the main cause of nerve damage and disability caused by leprosy.

Objective: To analyze the clinical and therapeutic profile of patients with leprosy reactions registered in a Dermatology Service in the city of Belém-PA.

Methods: This is a cross-seccional, descriptive study. It was investigated through analysis of medical records, 52 patients who fit the established inclusion criteria. Data were collected in July and August 2016.

Results: It was found a predominance of men, from the metropolitan region. The clinical form most common of Leprosy was Borderline, and the leprosy reaction type 1. The most of reactions occurred right after the introduction of multidrug therapy,and more than a half of patients with type 1 reaction showed edema of limbs. Regarding the type 2, fever and general symptoms were the most common, present in all cases. The frequency of neural damage was evident, showing reduction of motor force level andloss of protective sensation.

Conclusion: Early diagnosis and appropriate therapeutic management of reactive events is critical to the prevention of disabilities.

Keywords
Leprosy; Leprosy Reaction; Dermatology.

Introduction

Leprosy is a chronic disease caused by *Mycobacterium leprae* and has a clinical course dependent on the interaction between the host immune response and that pathogen, which predominantly infects cutaneous and peripheral nerve cells, causing injuries [1].

During the course of the disease, 10 to 50% of leprosy individuals may be surprised by reactional conditions or states [2], which are the main cause of disability caused by leprosy [3]. In addition, they are also important risk factors for retreatment of leprosy, and have a great responsibility on treatment abandoning [2].

Reaction states or leprosy reactions are reactions of the patient's immune system to Mycobacterium leprae [4]. They are alterations of the immune system, externalized as acute and subacute manifestations [5], localized or systemic, occurring commonly before, during or after the specific treatment of the disease. They bear relation to the bacillary quantity and the immune response of the host [6].

There are two types of leprosy reactions: reverse (RR) or type 1, which is an exacerbated response of the cell type immune system, characteristic of patients with tuberculoid and dimorphic forms; and the type 2 or erythema nodosum reaction (ENH), which translates into a hypersensitivity of humoral type immunity, and affects carriers of virchowian and dimorphic-virchowian forms [7].

Type 1 reactions present the following clinical features: infiltration of old lesions associated with the appearance of new lesions in the form of stains, or infiltrated plaques accompanied by edema and pain, erythema, vesicle-bullous lesions, ulcerations, hyperesthesia, paresthesia, malaise, pain or thickening of peripheral nerves with loss of sensory-motor function and, more rarely, deficiency of neural function in absence of symptoms (silent neuropathy), mainly affecting the ulnar and posterior tibial nerves, and hands and feet edema [2].

Type 2 or Erythema Nodosum reactions are characterized by red and painful nodules, which may progress to necrosis in the more severe forms [2]. They may also be accompanied by symptoms related to ocular, hepatic and splenic involvement of lymph nodes, peritoneum, testes, joints, tendons, muscles, bones and kidneys. In addition, they may cause fever and/or alteration of the general state, leukocytosis and, usually present in multiple episodes [4].

Reactional states are the leading cause of nerve damage and disability caused by leprosy. Therefore, it is important to perform an early diagnosis, in order to prevent incapacities [3]. Motor disturbances are visualized through paresis and paralysis, along with atrophies, retractions and joint fixations. Vascular and sweat changes are found when there are autonomic disorders [8].

The diagnosis of the reactional states is clinical and the treatment adopted varies according to the type of reaction [9]. In type 1 reactions, the choice drug is prednisone at 1-1.5 mg/kg/day, with gradual withdrawal after the disappearance of inflammatory signs. In cases of type 2 reactions, the drug of choice is Thalidomide, except in fertile women, at a dose of 100-400 mg/day [10].

Although the implications of leprosy reactions on the generation of disabilities and the consequences for quality of life are recognized, since they produce pain, deformities and abstention to work, national studies about this problem are still scarce [11].

In this context, the following questions emerged: What are the most observed lesions so that the diagnosis of leprosy reactions can be established early? What is the frequency of patients with neural damage due to leprosy reactions? What is the profile of the patients registered in this Dermatology Center?

To answer the questions, this work aims to analyze the clinical and therapeutic profile of patients registered at a referral center in dermatology of Brazil.

Methods

This is a descriptive study, performed in a Dermatology Service in the city of Belém, Pará, in Brazil. Thus, the following criteria were used in the sample selection: patients belonging to any age group and gender who were part of the spontaneous demand attended at the Dermatology Service of the Universidade do Estado do Pará, from January 2010 to December 2015, and who had leprosy reactions.

The study population was 52 patients with Hansen's disease affected by leprosy reactions, among a total of 144 leprosy patients.

This study was approved by the Ethics Committee in Research of Universidade do Estado do Pará, CAAE Nº 57167316.2.0000.5174 by the provisions of resolution nº 466/2012 of the National Health Council and the rules governing research involving human beings.

The research started from the authorization of the director and the professionals responsible for the Dermatology Service. Data collection was conducted in July and August 2016 in the dependences of the Dermatology Service. A structured protocol with objective questions about the clinical and therapeutic profile of patients with leprosy reactions was used to collect the data. The protocol was divided into two phases: the first phase with questions to identify the socio-demographic profile and the second phase with specific questions about the topic.

The last phase was to organize the findings into a database through Microsoft Excel 2010 software, building graphs, charts, and tables. Descriptive statistics was used for data analysis.

Results

A total of 144 patients with leprosy diagnosis were found, and among these, 52 cases presented leprosy reactions, corresponding to a prevalence of 36.11%.

Regarding the socio-demographic aspects, 38.46% of the total sample was female, and 61.54% was male. In terms of age, a similar distribution was observed, with 15-29, 30-44 and > 60, corresponding to 25% each. All these data are presented in **Table 1** below:

Table 1. Socio-demographic aspects of patients with leprosy reaction. Belém, PA, 2010-2015.

Variables	N	%
Gender		
Male	32	61.54
Female	20	38.46
Age		
0 to 14 years old	6	11.54
15 to 29years old	13	25.00
30 to 44years old	13	25.00
45 to 59years old	7	13.46
>60years old	13	25.00
Origin		
Metropolitan area	36	69.23
Countryside	16	30.77
Profession		
Student	12	23.08
Retired	9	17.31
Housewife/housekeeper	9	17.31
Farmer	3	5.77
Clerk / secretary	3	5.77
Mason	3	5.77
General Services	3	5.77
Others	8	15.38
Not informed	2	3.84

There was a predominance of reactional states in patients with type 1 reactions. The majority of leprosy reactions of this type were present in the dimorphic clinical form, followed by tuberculoid and virchowian. Only five patients with the type 2 reaction were identified, and 60% of the patients presented the virchowian clinical form, while the rest (40%) had a dimorphic form, as shown in **Table 2.**

Table 2. Distribution of clinical forms of leprosy in relation to leprosy, Belém, PA, 2010-2015.

Clinical forms	Type of reaction					
	Type 1		Type 2		Types 1 & 2	
	n	%	n	%	n	%
Undetermined	-	-	-	-	-	-
Tuberculoid	7	16.28	-	-	-	-
Dimorph	31	72.09	2	40	1	25
Virchowian	5	11.63	3	60	3	75
Total	43	100	5	100	4	100

Table 3. Distribution of leprosy reactions among the types of reactions in relation to specific treatment leprosy, Belém, PA, 2010-2015.

Period	Reaction					
	Type 1		Type 2		Types 1 & 2	
	n	%	n	%	n	%
Before	16	37.20	2	40	3	37.50
During	17	39.55	-	-	4	50
After	10	23.25	3	60	1	12.50
Total	43	100	5	100	8	100

As for the onset of leprosy reactions in relation to the beginning of leprosy treatment, it was observed that most of them appeared after the introduction of multidrug therapy, as showed in **Table 3**.

Regarding the clinical manifestations, it was identified that 51.16% of patients with leprosy type 1 had edema and/or pain. Old and recent infiltrated plaques were other clinical findings very common in this reaction. There was also the presence of paresthesia in 39.53% of the patients. The present research showed that fever and general malaise were present in 100% of patients with type 2 and mixed leprosy reactions. There were also the presence of recent infiltrated plaques (40%) and old infiltrated plaques (20%), as shown in **Figure 1**.

The most commonly used drug to treat leprosy reactions was prednisone. For type 1 reaction, prednisone was used in all cases. For the type 2 reaction, thalidomide alone was used in 40% of the cases and in the remaining 60%, prednisone was associated with thalidomide. For type 1 and 2 reactions, the association between prednisone and thalidomide was used in 100% of cases, as presented in **Table 4**.

Figure 1: Main clinical manifestations resulting from leprosy reactions in patients with leprosy, Belém, PA, 2010-2015.

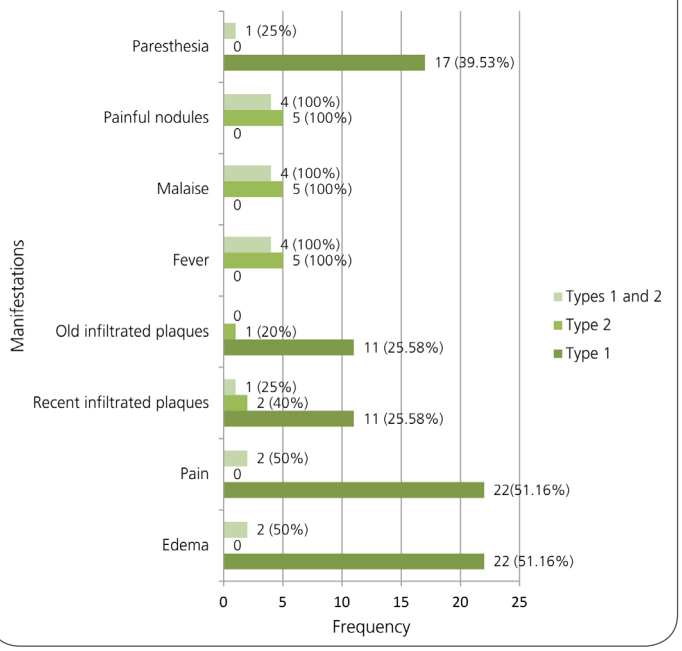

Table 4. Distribution Therapy used for leprosy reactions in patients with leprosy, Belém, PA, 2010-2015.

Medications	Reaction					
	Type 1		Type 2		Types 1 & 2	
	n	%	n	%	n	%
Prednisone 1mg/kg	43	100	-	-	-	-
Thalidomide 100-400mg	-	-	2	40	-	-
Prednisone + Thalidomide	-	-	3	60	4	100
Total	43	100	5	100	4	100

Discussion

The difference between men and women has been shown to be similar to other studies, which also

point to this higher prevalence in men [11, 12, 13]. The predominance of reactional states among men may be associated with a greater delay in the search for health services, which hampers the development of preventive and early diagnosis actions [14].

The largest number of patients (69.23%) came from the metropolitan area of Belém, in the north of Brazil, where the Dermatology Service of the University is located. This situation is similar to the one in the study of Soares [15] and Pires [16], which evidenced a higher demand also coming from the metropolitan region, where the research was carried out, possibly due to greater ease of access.

The clinical forms in which the reactional states occurred most frequently were dimorphic (65.38%) and virchowian (21.16%). There was a divergence from the study by Queiroz [14], who presented a higher frequency in the virchowian and dimorphic forms. The predominance was the virchowian form, with 55.74% of the cases, followed by the dimorphous, with 32.79%.

The predominance of reactional states in the patients studied was type 1, corresponding to 82.69% of the cases. This fact was similar to the study done by Silva and Griep [11], which demonstrated that the majority (58.3%) also presented this type of reaction. However, there was a divergence in the studies of Gonçalves [17], who presented a higher prevalence of type 2 reaction, followed by type 1 reaction, in his study, which was also performed in the southeast region of the country, even though the most frequent clinical form in their study was dimorphic (81.8%).

The present study found that the vast majority (72.09%) of leprosy type 1 reactions were present in the dimorphic clinical form. Only five patients with the type 2 reaction were identified and 60% of them presented the virchowian clinical form. These findings agree with Lima and Aguilar [18], who found that most type 1 reactions were present in patients with dimorphic leprosy (65.71%) and type 2 reactions were more evident in patients with virchowian leprosy (87.58%).

As for the onset of leprosy reactions in relation to the beginning of leprosy treatment, it was observed that 37.5% of the reactions were present before the moment of diagnosis, while 62.5% appeared after the introduction of the multidrug therapy, 37.5% during treatment, and 25% after discharge. This fact agrees with the study by Queiroz [14], which also showed a lower prevalence of cases before the onset of MDT (26.23%), and a greater predominance after, 73.77% of the cases, being 65.57% during treatment, followed by those who presented after treatment (8.20%).

Isolated prednisone was used only for patients with type 1 reaction, corresponding to 100% of these; isolated thalidomide was used only for type 2 reaction (40%). On the other hand, the association of prednisone and thalidomide was present both in patients with type 2 reaction (60%) and in mixed reaction (100%). This predominance was also evident in the work of Teixeira [2], which demonstrated that in type 1 reactions prednisone was the most used drug, corresponding to 92.7% of patients. For type 2 reaction, the association of prednisone and thalidomide corresponded to 58.1% of the cases followed by thalidomide alone in 19.4% of the cases.

Regarding the clinical manifestations, it was identified that a little more than half (51.16%) of patients with leprosy type 1 had edema and/ or pain. Old infiltrated plaques and recent plaques infiltrated were other clinical findings more common in this reaction, present in 25.58% of patients, each. These clinical manifestations of the type 1 reaction were also the most prevalent in the work of Teixeira [2]; however, old infiltrated plaques and recent infiltrated plaques had a higher frequency in the patients surveyed in relation to edema or pain.

The present study showed that fever and general malaise were present in 100% of the patients with

leprosy type 2 reaction. In contrast, none of the patients with type 1 reaction had such symptoms. There was an agreement with the studies by Foss [19] and Putinatti [20], which showed a compromised general condition with fever and malaise in the type 2 reaction, and absence of general compromise in type 1 reaction; this fact can be explained because the type 1 reaction is better localized, with a sudden increase in cell-mediated immunity; whereas the type 2 reaction presents with involvement of humoral and pro-inflammatory mediators, such as TNF-alpha and IL-6, presenting importance in the immunopathological mechanism and in the symptomatology of ENH [19].

It was evident in the present study that neural involvement is frequent in patients with leprosy reactions: of the 52 patients studied, 22 (42.31%) presented some level of motor force reduction, and 16 (30.76%) already presented loss of protective sensitivity.

Conclusion

The study showed a predominance of males, from the metropolitan area of the city of Belém/PA; there was no predominant age group, but the lowest number of cases was in the 0 to 14 age range.

According to Madrid classification, the clinical form of leprosy most related to the presence of leprosy reactions was borderline, and the main type of leprosy reaction was type 1.

Regarding the clinical manifestations, the most frequent type 1 reaction was the presence of edema and/ or pain, while in the type 2 reaction state, it was the alteration of the general state and fever, besides the presence of erythematous nodules, being an important attention to the quality of life of these patients.

It was observed a higher occurrence of leprosy reactions right after the institution of the therapy, which was recommended by the WHO and the Ministry of Health. For type 1 reactions, the use of Prednisone was recommended, and for type 2 reactions, Thalidomide or its association with prednisone.

As study limitation there is incompleteness of information available in medical records.

Thus, this study contributes to alert about the need of early diagnosis and appropriate therapeutic management of reactional events for sequelae prevention.

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Conflict of interest disclosures

The authors declare that there are no conflicts of interest in this article.

Contribution

Danielle Oliveira de Sousa, Karolyne Moura Rique de Oliveira, Deborah Marques Centeno, Carolina Ribeiro Mainardi, Jean Carlos Alves de Lima Souza, Tiago Galan de França, Lucas Mendonça de Araújo Bellesi: literature review, data interpretation, writing, translation and concept of the manuscript.

Carla Andrea Avelar Pires: Concept and orientation regarding the manuscript, data acquisition and methodological review of the manuscript.

References

1. Júnior LGC, Machado GB, Faria TA. Reação hansênica tipo dois em paciente multibacilar, forma Virchowiana, em vigência de tratamento: relato de caso. Revista de Medicina. 2015; 94(3):197-200.

2. Teixeira MAG, França ER, Silveira VM. Características epidemiológicas e clínicas das reações hansênicas em indivíduos paucibacilares e multibacilares, atendidos em dois centros de referência para hanseníase, na Cidade de Recife, Estado de Pernambuco. Rev Soc Bras Med Trop. 2010:287-92.
3. Castro MD, Braga KP, Barbosa JC, Alencar CHM, Monteiro LD, Heukelbach J. Incapacidades físicas em pessoas acometidas pela hanseníase no período pós-alta da poliquimioterapia em um município no Norte do Brasil. 2013.
4. Souza LWF. Reações hansênicas em pacientes em alta por cura pela poliquimioterapia. Revista da Sociedade Brasileira de Medicina Tropical. 2012; 43(6).
5. Filgueira AA, Paresque MAC, Carneiro SMF, Teixeira AKM. Saúde bucal em indivíduos com hanseníase no município de Sobral, Ceará. Epidemiologia e Serviços de Saúde. 2014; 23(1):155-64.
6. Mendonça VA, Costa RD, Melo GEBA, Antunes CM, Teixeira AL. Immunologyofleprosy. Anais Brasileiros de Dermatologia. 2008; 83(4):343-50.
7. Abraçado MFS, Cunha MHCM, Xavier MB. Adesão ao tratamento de hanseníase em pacientes com episódios reacionais hansênicos em uma unidade de referência. Revista Pan-Amazônica de Saúde. 2015; 6(2):23-8.
8. Sampaio SCC AP, Ararigbóia RE. Dermatologia. 3rd ed. São Paulo: Artes Médicas; 2007.
9. Azulay RD, Azulay RD. Dermatologia. 5th ed. Rio de Janeiro: Guanabara Koogan; 2011.
10. Ministryof Health. Portaria N° 3.125, de 7 de Outubro de 2010 [Internet]. Ministério da Saúde. Brazil; 2010 [cited2017Oct11]. Available from: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2010/prt3125_07_10_2010.html
11. Silva SF, Griep RH. Reação hansênica em pacientes portadores de hanseníase em centros de saúde da Área de Planejamento 3.2. do Município do Rio de Janeiro. Hansenologia Internation alis (Online). 2007; 32(2):155-62.
12. Brito MFM, Ximenes RAA, Gallo MEN, Bührer-Sékula S. Associação entre reação hansênica após alta e a carga bacilar avaliada utilizando sorologia anti PGL-I e baciloscopia. Revista da Sociedade Brasileira de Medicina Tropical. 2008; 41:67-72.
13. Cunha MHCM, Xavier MB, Pires CA, Oliveira MS. Episódios reacionais hansênicos: estudo de fatores relacionados com adesão ao tratamento em uma unidade de referência. Hansen int. 2013; 38(1/2):61-7.
14. Queiroz TA, Carvalho FPB, Simpson CA, Fernandes ACL, Figueirêdo DLA, Knackfuss MI. Perfil clínico e epidemiológico de pacientes em reação hansênica. Revista Gaúcha de Enfermagem. 2015; 36(spe):185-91.
15. Soares CGM. Hanseníase no estado do Pará: perfil epidemiológico da população que demanda interação por reações hansênicas 2001.
16. Pires CAA, Neto FOMJ, de Albuquerque NC, Macedo GMM, Batista KNM, Xavier MB. Leprosy reactions in patients coinfected with HIV: clinical aspects and outcomes in two comparative cohorts in the Amazon Region, Brazil. PLoS neglected tropical diseases. 2015; 9(6):e0003818.
17. Gonçalves SD, Sampaio RF, de Figueiredo Antunes CM. Fatores preditivos de incapacidades em pacientes com hanseníase. Revista de Saúde Pública. 2009; 43(2):267-74.
18. Lima MM, Moreira AM. Perfil Epidemiológico da Hanseníase em um município de Minas Gerais: Uma análise retrospectiva. Revista Prevenção de Infecção e Saúde. 2015; 1(3):1-10.
19. Foss NT. Episódios reacionais na hanseníase. Medicina (Ribeirao Preto Online). 2003; 36(2/4):453-9.
20. Putinatti MSMA, Lastória JC, Padovani CR. Prevenção da repetição de episódos de reação tipo 2 da Hanseníase com o uso da talidomida na dose de 100mg/dia. Hansenologia Internationalis. 2011:76.