

Teledermatology Nuevo Leon. Clinic case: erythema nodosum leprosum

Manuel Rolando García Garza
Luis José García Morales
José Antonio Bello Castellanos
Genaro Nájera Montero

Member of Telemedicine Nucleus – Nuevo Leon – Mexico
Member of Telemedicine Nucleus – Nuevo Leon – Mexico
Medical Coordinator of Telemedicine – Nuevo Leon – Mexico
Chief of Dermatology Metropolitan Hospital Department of Health – Nuevo Leon – Mexico

Abstract

The erythema nodosum leprosum (ENL) is a kind of leprosy reaction and it is told that it affects between 30 and 50% of patients with lepromatous and limitrophe lepra. It could be developed in whatever stage of treatment, but it is usually present during the first year, and it is recurrent. The clinic symptoms start with fever and feeling bad in general followed with the appearance erythematous nodules, typically over the extensor surfaces of extremities. The ENL has as main characteristic the deposition of immune-complexes getting to produce vasculitis, iridocyclitis, orchitis, lymphadenitis, glomerulonephritis. The state of Nuevo Leon is pioneer in the area of Telemedicine in Mexico and nowadays there have been reported three hundred and fifty cases of lepra. At next it is presented one of them, which was followed by the department of Telemedicine, specifically by Teledermatology, and which distinguishes for having the particularity of having developed this kind of leprosy reaction.

Key words: Telemedicine; Remote Consultation; Dermatology; Erythema Nodosum; Leprosy; Health Services; México.

Resumen

Teledermatología en Nuevo León. Caso clínico: erythema nodosum leprosum

El erythema nodosum leprosum (ENL) es un tipo de reacción leprosa y se indica que afecta a entre el 30 y el 50% de los pacientes con lepra lepromatosa y limitrofe. Puede desarrollarse en cualquier etapa del tratamiento, pero usualmente se presenta durante el primer año, y es recurrente. Los síntomas clínicos comienzan con fiebre y malestar generalizado, seguidos de la aparición de nódulos eritematosos, típicamente en la superficie de las extremidades. El ENL tiene como característica principal la deposición de inmunocomplejos que producen vasculitis, iridociclitis, orquitis, linfadenitis y glomerulonefritis. El Estado de Nuevo León es pionero en el área de Telemedicina en México, y actualmente se han informado trecientos y cincuenta casos de lepra. A continuación, presentamos uno de esos casos que fue seguido por el departamento de Telemedicina, específicamente por el sector de Teledermatología, y que se distingue por la particularidad de haber desarrollado este tipo de reacción leprosa.

Palabras Clave: Telemedicina; Consulta Remota; Dermatología; Eritema Nudoso; Lepra; Servicios de Salud; México.

Resumo

Teledermatologia em Nuevo Leon. Caso clínico: eritema nodoso hansênico

O eritema nodoso hansênico (ENH) é um tipo de reação hansênica e afeta entre 30 e 50% dos pacientes com hanseníase e lepra limitrofe. Pode desenvolver-se em qualquer fase do tratamento, mas é geralmente presente durante o primeiro ano e é recorrente. Os sintomas clínicos começam com febre e mal-estar em geral seguidos do aparecimento de nódulos eritematosos, típicamente nas superfícies de extremidades. O ENH tem como principal característica a deposição de imuno-complexos que produzem vasculite, iridocilite, orquite, linfadenite e glomerulonefrite. O Estado de Nuevo Leon é pioneiro na área da telemedicina no México e até recentemente foram notificados trezentos e cinquenta casos de hanseníase. Na sequência será apresentado um deles, que foi acompanhado pelo serviço de Telemedicina, especificamente por Teledermatologia, e que se distingue pela particularidade de ter desenvolvido este tipo de reação hansênica.

Palavras-chave: Telemedicina; Consulta Remota; Dermatologia; Eritema Nodoso; Hanseníase; Serviços de Saúde; México.

CLINIC CASE

It is about a twenty six years old masculine patient who goes to consultation the day 24th January 2006 to the Metropolitan Hospital of the Health Services of Nuevo Leon presenting lesions that he describes as "little balls" in the arm, thorax and ears of one year of evolution. The patient, from the Municipality of Montemorelos, Nuevo Leon (which is located in the south of the State), single, works in the field and without important familiar pathologic antecedents. The physical examination demonstrates disseminated dermatosis to face, neck, thorax, abdomen and the four extremities, characterized by nodular lesions and plaques of irregular borders without sintomatology. He presented hypoesthesia without differencing between pricking and touching the lesions with a pin. It was suspected to be lepromatous lepra and there were required general labs, bacilloscopy and biopsy. One week later, the bacilloscopy result demonstrates Alcohol and Acid Resistant Bacilli (AARB) of one + only in nasal mucosa. The biopsy took from a lesion in the arm confirmed the diagnosis of lepromatous lepra through Ziehl-Nielsen tint. The treatment was initiated conform the established by the World Health Organization (WHO) and which consists of dapsona, rifampicin, and clofazimine. The patient does not refer any complication in the beginning, and three months after initiated the treatment, the nodular lesions remitted, leaving only areas of postinflammatory hyperpigmentation. Due to the good evolution and the fact of not having complications, it was decided to follow the treatment monthly via Telemedicine. After fourteen months of treatment it is observed new nodular erythematous lesions referring that are painful and hyperthermics. The patient was asked to assist to a personalized examination; he abandoned the following and treatment for four months. Finally he went to the examination, finding lesions with the same characteristics of the beginning of his disease, and it was decided to reinstate the treatment. Two weeks later, he assists to Telemedicine and refers the suspension of treatment for presenting dyspnea, and acrocyanosis, so it is suspected methemoglobin secondary to sulfone (dapsona). Presents new inflammatory lesions, erythematous and painful accompanied with feeling bad in general, hyperthermia, hyporexia, arthralgia, and weight loss. To the physical examination hyperpigmented nodules were observed, the same as nudosities in ears, thorax, abdomen and the four extremities. The patient was transferred to the Metropolitan Hospital for a new biopsy, because it is suspected Erythema Nodosum Leprosum (ENL) due to leprosy reaction. There are prescribed Thalido-

mide and Ofloxacin, waiting to the biopsy result. In January of the present year, assists again to control consultation by Telemedicine where the patient has got a favorable evolution of lesions and the biopsy result of one of the nudosities confirmed the diagnosis of ENL.

EPIDEMIOLOGY

"In May 1991 the WHO adopted the resolution to establish the goal to eliminate lepra as a problem of public health by the year 2000".¹ The annual number of cases detection is six hundred and fifty thousand new cases per year, being circa 75% cases of the Hansen disease, located in descendent order in India, Brazil, Bangladesh, Indonesia and Myanmar with a ratio of two to one in men against women, being more common in infancy.

"The prevalence of the illness has decreased 90%: from 21,1 for ten thousand inhabitants to less than one per ten thousand inhabitants in 2000".² For Latin America, meant for the Pan American Health Organization (PAHO), the situation in the year 2006 had as relevant characteristics a total of 64,715 cases in treatment with poliquimioterapia; detection of 47,612 new cases, being the 8% of these in children minors of fifteen years and 53% of them were multibacillar (MB). Then, in 2006, the detection of lepra rate for the PAHO was 0.02 in Mexico, while other countries as Argentina presented 0.11, Paraguay 0.04 and Brasil 2.35 to cite some examples. This organization announces that the states in the Mexican Republic with a major charge of lepra are: Sinaloa, Michoacan, Nayarit, Nuevo Leon, Jalisco, Tamaulipas, Guerrero, Sonora, Guanajuato and Colima.³

According with the statistics recollected by the Secretariat of Health in the state of Nuevo Leon, in 2007 exist hundred and eighty six registered cases in treatment, thirty registered cases without treatment, and one hundred and thirty four registered cases in post treatment surveillance.

ETIOLOGY

Lepra is a chronic infectious disease produced by the intracellular acid resistant bacilli *Mycobacterium leprae*. "Lepra is probably transmitted from person to person through aerosol particles of lesions from the superior respiratory tract. The inhaled *M. leprae* [...] is captured by the alveolar macrophages and disseminated through the blood growing relatively only in the skin and extremities tissues".⁴

Kumar explains that it does not release toxins and its virulence is based only in the characteristics conferred by its cellular wall. In the same way, the response of T-lymphocytes to mycobacterium will determine if the individual develop tuberculoid or lepromatous leprosy. Furthermore “exists an inverse correlation between the number of lymphocytes and the number of acid bacteria present in the skin lesions”.⁴

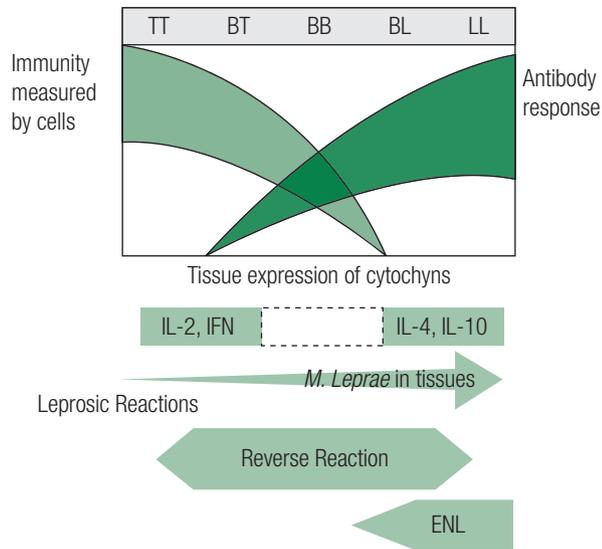


Figure 01 - El espectro clínico inmunológico de la lepra.
 * Cohen & Powderly, Infectious Diseases. 2nd edition. 2004. Mosby, Elsevier.

More to the point, Goldman⁶ indicates that tuberculoid lesions have abundant lymphocytes with well formed granuloma and few mycobacteriums in contrast with lepromatous lesions that present inverse characteristics; leaving two extremes of the disease, the group denominated *borderline* that presents mediated particularities. “[...] tuberculoid leprosy exhibits few lesions (less than five) while the lepromatous leprosy characterizes for multiple lesions (from five to hundreds)”.⁶ Also the disease could be acquired and hold because “its incubation period fluctuates between three months and forty years with an average of seven years”.¹

The lepra cases are given particularly in families due they share the same environment and exposition although it could be added the genetic susceptibility as a determinant. Rakel says that the susceptibility to lepra is connected to the NRAMP1 gen, which through the numerous tests in rodents, indicates the degree of innate control to the mycobacterial infections. In the other hand, the variants in

alleles add as factors of such susceptibility the TNF and two genes linked and correlated PARK2 and PACRG as Goldman illustrates.⁶

CLINIC SYMPTOMS

The beginning of lepra is gradual. The lesions affect the coldest corporal tissues: skin, superficial nerves, nose, pharynges, larynges, eyes and testicles. Pale anesthetized macular lesions from 1 to 10 cm of diameter could occur; infiltrated erythematous nodules well defined from 1 to 5 cm of diameter, or diffuse cutaneous infiltration. The infiltration and enlargement of nerves cause neurologic alterations, with resulting anesthesia and motor anomalies. The bilateral cubital neuropathy is highly suggestive. In patients without treatment disfiguration by cutaneous infiltration and nerves affection could be extreme and it takes to the appearance of trophic ulcers, bone resorption and loss of fingers. “In lepromatous leprosy could be present loss of eyelashes and eyebrows (madarosis), as well as anesthetic affected areas along with anhidrosis”.¹

DIAGNOSIS

The confirmation of lepra is still based in a detailed clinical record with the physical examination; however, it is required to demonstrate BAAR in the cutaneous biopsy. The skin biopsy or of an enlarged affected nerve shows a precise histopathologic image. *M. Leprae* does not grow in artificial cultures.

The disease for the WHO is subdivided in paucibacillar defined as patients with less than five skin lesions and without bacillus in the lab test and multibacillar with six or more lesions in skin and probably positive result in the lab test of the cutaneous biopsy. Clinically and by lab tests it is separated in: indeterminate, tuberculoid (paucibacillar, intense inflammation, few but well defined cutaneous lesions), tuberculoid borderline, lepromatous borderline and lepromatous (multibacillar, inadequate response, few and diffuse cutaneous lesions).⁷

The lepromatous type occurs in persons with defective cellular immunity. The evolution is progressive and malign, with nodular cutaneous lesions; affects slowly and symmetrically the nerves; abundant acid resistant bacillus from the cutaneous lesions and a test of negative cutaneous lepromine. In the tuberculoid type, the cellular immunity

Table 1 - OMS

WHO Classification	Ridley and Jopling	Characteristics of the skin lesion	Modifications in the Ziehl-Nielson dye	Nerve involvement
Undetermined (1)	Hypo pigmented Macular lesions	Negative	None	
	Tuberculoid (TT)	Anular hypo-pigmented lesions	Negative	Localized one or more wide nerves around the skin lesions
Paucibacilar (PB)	Borderline tuberculoid (BT)	Anular lesions with less distinguished borders	Negative	Similar to tuberculoid disease
	Borderline (BB)	Spectrum between borderline	Negative or positive	Spectrum between tuberculoid disease and lepromatose
	Borderline (BB)	Borderline lepromatose		
Multibacilar (MB)	Borderline lepromatose (BL)	Infiltrated parches	Positive	Tends to be diffuse and asymmetrical
	Lepromatose	Diffuse, symmetrical skin infiltration	Positive	Difuse and symmetrical, slow, progressive poly-neuropathy

* Rakel, et al. Conn's Current Therapy 2007. 59th edition. 2007. Saunders, Elsevier.

is intact and the evolution is benign and less progressive, with macular cutaneous lesions, sudden asymmetry and intense affection of the nerves, with few bacilli in lesions and positive result of the lepromine cutaneous test. Intermediate cases ("bordering") are frequent. Ocular affection keratitis and iridocyclitis.

In the possibilities to consider a differential diagnosis exists a lot of comparative possibilities with the Hansen diseases, such as sarcoidosis, rheumatoid arthritis, systemic lupus erythematosus, carpal tunnel syndrome, fungus infections, etc.

TREATMENT

"Until 1980 the treatment for patients with lepra was monotherapy with dapsone. The multiple therapy treatment recommended by WHO surged in 1982 because the growing resistance to dapsone of 40% in some countries".⁵ Nowadays it recomends three drugs with dapsone, 50 to 100 mg/day, clofazimine 50 mg/day and rifampicin, 10 mg/kg/day, all of them via oral. This is for two to three years, and ideally until all biopsies are negatives to BAAR. For indeterminate and tuberculoid lepra it is recommended the combination of dapsone and rifampicin during six to twelve months, followed by a cycle of dapsone during two or more years.

The rifampicin is one of the most effective bactericides against *M. leprae* and although the standard dose in this treatment increases to 600 mg monthly, there is no rela-

tive toxicity though in secondary effects unusual times have been reported renal fails, thrombocytopenia, hemolytic anemia and hepatitis. The dapsone is a slow action and mid-short life bacteriostatic that has reported collateral effects as moderate hemodialysis, methemoglobinemia, agranulocytosis and cutaneous reactions of allergic type. At least, the clofazimine has similar characteristics to dapsone but add an anti-inflammatory feature in its activities; it causes cutaneous pigmentation and concentrates where there is a high number of bacteria, it is not common but it could present intestinal obstructions when taken in high doses.⁵

LEPROSY REACTIONS

The leprosy reactions in lepra are acute or sub-acute episodes mediated immunologically in a superimposition to the previous inflammation, during or after the quimiotherapy and it can occur in one third of patients as Rakel says in the book Conn's Current Therapy 2007.¹ In this reactions, explains the author, exist two types that are reverse reactions (type 1) and the erythema nodosum leprosum (type 2 or ENL in the successive). The reactions type 1 there is generally worsening of signs and symptoms of the existent disease, as the appearance of new skin injuries and at nervous levels that can be related with augmentation of immunity mediated by cells. As well, the ENL reactions are exclusive almost in their totality to the range of lepromatous patients with clinical presentation of ery-

mathosus painful papuls outburst associated with fatigue, acute neuropathy, fever, uveitis, lymphadenopathy, etc. In difference to reactions type 1, the ENL reactions are related with formation of immune complex that are responsible of the clinical symptoms.

The Lucio phenomenon is a reaction in the multibacillar leprosy that though not common is severe and causes death. Its clinical manifestations present hemorrhagic violaceous plaques followed of necrotic ulcers. Due to the presence of acid resistant bacillus, there is necrotic epidermis, vasculopathy or vasculitis with endothelial proliferation and thrombus formation.⁸

ERYTHEMA NODOSUM LEPROSUM (CASE)

It is a type of leprosy reaction and it affects from 30 to 50% of patients with lepromatous lepra, however the frequency and severity of the ENL has been reduced since the use of clofazimine begins. It can develop in any stage of treatment, but usually appears during the first year, and tends to be recurrent. The clinical symptoms start with fever and feeling bad in general followed of the appearance of erythematous painful nodules, typically over the extensor surface of extremities. In several cases, these nodules can form pustules and then ulcers. The most common complication is the neuritis. The ENL has as main characteristic the deposition of immune complex, getting to produce vasculitis, iridocyclitis, polyarthritis, orchitis, lymphadenitis and glomerulonephritis.

The ENL in its slight form responds very well to aspirin or AINE, increase of the clofazimine dose and rest. In its moderate and severe forms and those with neuritis prednisone is required, initiating with a dose of 40-60 mg/day. The response is fast, but due to the fact the ENL tends to be dependent to steroids, the prednisone must be suspended in a lapse of two to three months. The clofazimine in a diary dose of 300 mg suppress the ENL after four to six weeks and it could be used as prophylaxis for later episodes.⁸

If the ENL does not get under control or if it is recurrent, it usually responds well to thalidomide, 400 mg/day for two to three weeks and then 100 to 200 mg/day as maintenance dose. The thalidomide suppresses the secretion of TNF from the macrophages. However, its use is severely limited due to its teratogenicity and must be restricted with exception of men and postmenopausal women under strict supervision. The thalidomide may cause peripheral neuropathy, but it has not been reported in leprosy patients.

CONCLUSIONS

Although some countries are not along with the recommended treatment of the OMS, the majority of therapies consist in the base of drugs though the change of some of them is to avoid secondary effects as the commented in the case clinic here explained. Due this fact, it is important to be alongside the patient because the appearance of any leprosy reaction (type 1, type 2 or Lucio phenomenon) may cause such a disillusion to the patient that brings the treatment abandonment, requiring then a change on it to avoid the evolution of reaction.

Related to Telemedicine in Mexico, the state of Nuevo Leon is pioneer at national level to make possible a telehealth network with the today magnitude and importance. This project began in the year 2002, and nowadays it is a tangible reality that benefit all the population from Nuevo Leon, because it hast access to the main hospitals, primary health centers and social readaptation centers (SO.RE.CE) of the state. Public hospitals from the Health Services of Nuevo Leon as the Metropolitan Hospital (site of the Telecommand center), Children's Hospital, Maternal and Children Hospital, Psychiatric Hospital and the University Hospital are linked to this network. In the private sector it has access to the San Jose-Tec de Monterrey Hospital, where it receives the support of the most recognized specialists in the state. Also there are connected some municipalities of the metropolitan area and the rural zone of the state as: Allende, Anahuac, Cerralvo, Dr. Arroyo, Galeana, Linares, Montemorelos, Sabinas Hidalgo and Santiago. We have linked too three SO.RE.CE, in which we provide medical care to people in prison.

In this way, the versatility that offers telemedicine is to have different subspecialties as ideal tool for the adequate following of patients. In the precise case of teledermatology, that covers the majority of the consultations in our state, allowed us to follow the symptomatology as well to detect quickly the leprosy reactions. Besides, it is an instrument that reflects the conditions of the patient at a distance, avoiding the transfer that in case of the communities to which applies this program, generates a set of factors (work absence, economic expenses, etc.) that in many occasions make patients to desist the medical treatment.

There are three elements that impede, nowadays, the program to get into a status of ideal utopia. The first one is the need of having enough trained personnel in both sides of the program, that allows, with absolute confidence, the specialist to carry the interrogatory and the physical ex-

amination without the possibility of the minimum mistake, whenever or not the other person belongs to the medical specialty of the consultation. The second element is the rejection of the majority of specialist physicians to have a consultation through this program, particularly the ones with more experience, because they argument a patient can not been seen if he is not in front of them; the truth is that teledermatology and telehealth offer a 100% real interaction and the only thing the physician is limited to do is *to touch* the patient. The third and least element would consist in having an organized telehealth network, standardized and connected at national level that allows increasing de consultation quality, to provide specialties in the states where there is a lack of them, making possible a constant communication between the health authorities that helps us to solve our national and regional problems, such as epidemiologic outbreak, natural disasters, and others.

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