Diffuse leprosy of Lucio and Latapí: a histologic study

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Summary
Background and purpose Ladislao de la Pascua described the spotted or lazarine leprosy for the first time in 1844. Later on, Lucio and Alvarado studied and published it with the same names in 1852. Latapí re-discovered it in 1938 and reported it as ‘Spotted’ leprosy of Lucio in 1948. Frenken named it diffuse leprosy of Lucio and Latapí in 1963. Latapí and Chávez-Zamora explained that the fundamental condition of this variety of leprosy was a diffuse generalised cutaneous infiltration, naming it pure and primitive diffuse lepromatosis, upon which necrotising lesions develop, calling these lesions Fenómeno de Lucio or erythema necroticans. A great number of histopathological reports have addressed the study of Lucio’s phenomenon, and few about the histologic changes that take place in the course of diffuse lepromatous leprosy. The purpose of this work is to report the histologic findings observed in the study of 170 cutaneous biopsies of diffuse leprosy of Lucio and Latapí and 30 of Lucio’s phenomenon.

Methods This is a retrospective study, which included the examination of 200 biopsy skin specimens from 199 patients with diffuse leprosy at different course of the disease. These cases were diagnosed in Mexico from 1970 to 2004.

Results The histologic examination revealed a vascular pattern affecting all cutaneous vessels, characterised by five outstanding features: a) colonisation of endothelial cells by acid-fast bacilli, b) endothelial proliferation and marked thickening of vessel walls to the point of obliteration, c) angiogenesis, d) vascular ectasia, and e) thrombosis. Necrotising lesions seen in diffuse lepromatous leprosy displayed two histopathological patterns: one of them, non-inflammatory occlusive vasculopathy and, the other one, occlusive vasculopathy, leukocytoclastic vasculitis, large neutrophilic infiltrate and lobular panniculitis. The first appeared as a result of the course of the occlusive vasculopathy produced by the colonisation of endothelial cells by Mycobacterium leprae. The second, as a result of a previous occlusive vasculopathy plus a leprosy reaction which is considered here as variant of ENL.

Conclusions Endothelial cell injury appears to be the main event in the pathogenesis of diffuse leprosy of Lucio and Latapi. Once M. leprae has entered the endothelial cell, the micro-organism damages the blood vessels, leading to the specific changes seen in this variety of lepromatous leprosy.
Introduction

In 1844, Ladislao de la Pascua, when Director of the ‘Hospital de los Lazarinos’ in Mexico City, described three clinical forms of leprosy, tuberculous (nodular), anaesthetic and a third characterised by the production of painful red spots that went on to ulcerate. These patients were known in Mexico as ‘Lazarinos’.1 Later on, Rafael Lucio, in collaboration with Ignacio Alvarado, published in 1852 a paper entitled ‘Opúsculo de la Enfermedad de San Lázaro o ELEFANCIASIS DE LOS GRIEGOS’,2 in which Lucio described his observations, made during 8 years at the same ‘Hospital de los Lazarinos’ in Mexico City, of which he was Director after de la Pascua. He also distinguished three clinical forms of leprosy: tuberculous (nodular), anaesthetic, and spotted (manchada), and paid special attention to the spotty form, characterised by the presence of red and painful spots undergoing necrosis, and which was striking because the skin underwent characteristic changes according to the stage of the condition. This landmark paper by Lucio and Alvarado was gradually forgotten and this variety of leprosy was completely unknown among leprologists outside Mexico until Latapí and Chevez-Zamora3 brought it to attention at the 5th International Congress of Leprosy held in Havana in 1948. That the authors explained that the underlying condition of this clinical form, unnoticed by Lucio and Alvarado, was generalised diffuse cutaneous infiltration, which Latapí and Chevez-Zamora named ‘pure and primitive diffuse lepromatosis’, upon which secondary cutaneous outbreaks developed. These outbreaks were regarded as a form of lepra reaction produced by multiple, acute, necrotising vasculitis for which Latapí proposed the name of ‘Fenómeno de Lucio or erythema necroticans’. Before Latapí and Chevez-Zamora’s report, Martinez Baez had studied spotted lesions of five patients in 1941,1,3,6,20 noting the basic lepromatous structure, acute vasculitis with nuclear dust, and thickening and occlusion of the larger vessels producing necrosis. He described for the first time the histological changes that occurred in what Latapí would later name Lucio’s phenomenon.

About 1943, Latapí distinguished the pure and primitive diffuse leprosy that always begins as diffuse leprosy, and the secondary diffuse leprosy, which arises from an indeterminate form; both display the same clinical aspect and the same histologic changes during their course.5,7 In 1963, Frenken included both under the name of diffuse leprosy of Lucio and Latapí, having as fundamental characteristic, that the generalised infiltration never develops nodules.1,5,7

Diffuse leprosy of Lucio and Latapí is characterised by a diffuse cutaneous infiltration, without nodules, succulent or atrophic according to the stage of progression. Dysesthesia, anhidrosis, alopecia, destructive rhinitis and telangiectasia, and a special variant of lepra reaction named Lucio’s phenomenon or erythema necroticans (erythema necroticans). Histologically it has been reported that the finding of heavy endothelial parasitisation by Mycobacterium leprae is a peculiar feature to diffuse leprosy.4,5,8–12 Lucio’s phenomenon is clinically characterised by crops of wine-red irregular spots (manchas) with burning sensation, sharply delineated, and capricious centre, which turn purpuric and become necrotic leaving atrophic stellar scars. Histopathologically Lucio’s phenomenon has been reported to have two types of patterns. One of them involves leukocytoclastic vasculitis as the underlying pathologic change,5,13,14 and the other, endothelial cell proliferation, thrombosis, a mild mononuclear cell infiltrate and ischemic necrosis.15,16 The first pattern is thought to be due to an immune complex disease caused by leprae or skin antigens.17 In the second pattern, vascular damage is thought to be due to direct invasion of M. leprae.15,16
Diffuse leprosy is considered to be the most anergic of the all-immunological spectrum of leprosy. In a study on lepromin responsiveness, Leiker reported that not all lepromatous patients are completely anergic to lepromin, as a weak response to lepromin had been observed in many such cases and it seemed that the diffuse lepromatous variety was the only truly anergic type of leprosy. Lucio and other authors believed that this variety of the disease was exclusive to Mexico. Yet it is found not only in Mexico, but also in other countries. The purpose of this study is to describe histological changes seen in 170 cutaneous biopsies of diffuse leprosy of Lucio and Latapí and 30 of Lucío’s phenomenon.

Materials and methods

This is a retrospective study, which included the examination of 200 biopsy specimens of diffuse leprosy of Lucio and Latapí obtained from 199 patients. In one patient two biopsy specimens were taken, one was from infiltrated skin and other from a necrotic skin lesion. The cases were diagnosed between 1970 and 2004 at the Laboratory of Dermatopathology of the Institute for Epidemiologic Diagnosis and Reference (InDRE) in Mexico City. Twenty-six cases were from the archive of the InDRE; 174, were included in a previous report by the National Leprosy Control Programme. Biopsies selected for this study were those that were taken from patients who had two or more physical signs of diffuse lepromatous leprosy without nodules (DLL). The clinical data were obtained from the histology request forms. Specimens were dispatched in glass or plastic vials containing 10% formalin solution from different provinces of the country to the InDRE in Mexico City where all histological processing was carried out. Specimens were processed routinely and stained with haematoxylin and eosin; the first 125 specimens with Fite-Faraco stain, and the other 75 specimens with a modified Fite-Faraco stain using carbol-fuchsin solution to stain acid-fast bacilli, Weigert’s iron haematoxylin to stain nuclei, and metanil yellow solution to stain other tissue elements. The leprosy programme uses the Madrid classification, which considers two polar types: lepromatous and tuberculoid; and two groups: indeterminate and dimorphous. This classification does not include the variety diffuse lepromatous leprosy.

Results

The series was composed of 128 males and 71 females, with a male to female ratio 1.8:1; the ages ranged from 12 to 88 years, with a median age of 37 years and an average of 28.8 years. The elapsed time from the appearance of the first sign or symptom referable to leprosy ranged from 1 week to 12 years, with a median of 3 years and an average of 4.2 years. Out of the 200 cases, 181 (90.5%) were from Pacific Coast states of Mexico and 19 (9.5%) from other states of Mexico. The biopsy specimens were obtained at different times in the course of the illness, and included those that showed apparently normal skin and those with necrotising lesions; 170 were from patients with diffuse leprosy without necrotising lesions, and 30 were from patients with diffuse leprosy with Lucio’s phenomenon. All patients had physical signs of DLL, mainly diffuse infiltration of the skin, impairment of sensation (numbness of the dorsal aspects of the extremities, hypaesthesia, or aesthesia), alopecia of eyebrows and eyelashes, anhidrosis, and destructive rhinitis. All the biopsy specimens were obtained from skin with sensory
impairment associated with another or other physical signs of DLL: 32 from apparently normal skin, 82 from skin with diffuse infiltration, 13 from atrophic skin, 9 from hypochromic macules, 7 from erythematous macules, and 30 from skin with Lucio’s phenomenon, data on 27 cases were missing. Biopsy sites were: 141 from the limbs, 33 from the ear lobe, 12 from the trunk, data on 14 cases were missing. As the clinical diagnosis made by physicians of the control programme did not include diffuse leprosy, 86 of the request forms for histological study only had the clinical diagnosis ‘lepromatous’. Nonetheless, 62 had the clinical diagnosis of DLL and 8 the clinical diagnosis of pure and primitive diffuse lepromatosis (PPDL), because, these specific diagnoses were made by physicians with several years working in the programme. There were other clinical diagnoses: 7 of indeterminate leprosy, 4 of dimorphous leprosy 1 of tuberculoid leprosy, 30 of Lucio phenomenon, and 2 were without clinical diagnosis. The physical signs of leprosy reported by medical staff in the request forms for histological exam, apart from the lesions of Lucio’s phenomenon, correspond closely with DLL, thus, none of the 199 patients had nodular lesions. The 199 (100%) presented impairment of sensation (hypaesthesia or anaesthesia or numbness of the extremities), 132 diffuse cutaneous infiltration with absence of nodules, 36 apparently normal skin, 15 atrophic skin, 9 hypochromic macules, 7 erythematous macules, 87 anhidrosis, 126 alopecia of eyebrows, and 63 destructive rhinitis. The histopathological features were divided into five stages: (1) early, (2) bacillary dissemination, (3) well-developed, (4) necrosis by vascular occlusion and (5) necrosis by vascular occlusion plus leprosy reaction. The changes observed during these different histologic stages are described below.

STAGE 1. EARLY

Fifty-three biopsies comprised 33 males and 20 females (M:F ratio 1·7:1), age range 15 to 88 years, (median 43 years and mean 43). The delay from the appearance of the first sign referable to leprosy was 2 months to 17 years (median 1 year, mean 1.4 years). The skin where the specimens were taken was: diffuse infiltration 36, apparently normal with dysesthesia 3, atrophic 2, hypochromic macule 1, erythematous macule 2, no information 9. Biopsy sites were: inferior extremity 18, upper extremity 19, thorax 4, and ear lobe 9, no information 3.

Histology

Blood vessels looked dilated with a thick wall lined with normal or plump proliferative endothelial cells. Slight and apparently insignificant foci of infiltration were present in the dermis, arranged around dilated blood vessels. Very scarce bacilli could be observed in the endothelial cells in few of the large vessels and in some nerve trunks of the deep dermis.

STAGE 2. BACILLARY DISSEMINATION

Sixty-two biopsies comprised 32 males and 30 females (M:F ratio 1:1:1; the age range 15 years to 85 years, (median 39 years). The delay from the appearance of the first sign referable to leprosy ranged from 1 month to 22 years (median 3 years, mean 3.4 years). The skin where the specimens were taken were: diffuse infiltration 34, dysesthesia, anhidrosis and alopecia 5, atrophic 5, hypochromic macule 7, erythematous macule 3, no information 8. The biopsy sites were: inferior extremity 20, upper extremity 22, thorax 2, abdomen 1, ear lobe 13, no information 4.
Dissemination of acid-fast-bacilli (AFB) extended progressively from the deep plexus to all cutaneous blood vessels, first, into the blood vessels of the subcutis and reticular dermis; then to vessels of the superficial plexus; and finally to capillaries of the papillary dermis. The vessels showed acid-fast bacilli inside swollen endothelial cells, thrombosis, passive congestion and ectasia. The lumen of the large vessels was reduced in size by intimal proliferative thickening. Small infiltrates of mononuclear cells were arranged around blood vessels of the dermis and subcutaneous fat tissue.

**Stage 3. Well-Developed**

Fifty-five biopsies comprised 34 males and 21 females, M:F ratio 1:6:1; age range 12 years to 77 years, (median 28 years, mean 34.6). The delay from the appearance of the first sign referable to leprosy ranged from 4 months to 20 years (median 2 years, mean 3.4 years). The skin where the specimens were taken were: diffuse infiltration 29, dysesthesia, anhidrosis and alopecia 7, atrophic skin with dysesthesia, anhidrosis and alopecia 6, hypochromic macule 1, erythematous macule 2, no information 10. Biopsy sites were: inferior extremity 26, upper extremity 9, thorax 5, ear lobe 7, no information 8.

**Histology**

Well-developed lesions were characterised by vascular ectasia, focal passive congestion, thrombi and an increase in capillaries. The blood vessels of the dermis and the subcutis showed a swollen and prominent endothelium, thick wall and narrowed or obliterated lumen (Figure 1A).

The infiltrate, which was composed of lymphocytes and macrophages, was slight, in the dermis cuffing the blood vessels (Figure 1A), and in the subcutis invading the subcutaneous fat. Variable numbers of Virchow cells were diffusely distributed around blood vessels in the dermis and subcutaneous fat. Acid-fast staining showed bacilli in the perivascular inflammatory infiltrate (Figure 1B) and, in the most cases within one or more of the endothelial cells of the cutaneous blood vessels (Figures 1C–1E).

**Stage 4. Ischaemic Necrosis due to Non-Inflammatory Vascular Occlusion**

Eight biopsies comprised 6 males and 2 females, M:F ratio 3:1; age range 29 years to 67 years, (median 38 years mean 3.1 years). The delay from the appearance of the first sign referable to leprosy ranged from 6 days to 14 years (median 2 years, mean 3.1 years). All had necrotic lesions of the skin, from which the specimens were taken. Biopsy sites were: inferior extremity 2, upper extremity 3, and abdomen 1, no information 2.

**Histology**

The main feature in this fourth stage was a severe damage of blood vessels. The presence of *M. leprae* in endothelial cells seemed responsible for this change. Histological appearance was characterised by necrosis of epidermis and superficial dermis, angiogenesis, ectasia,
passive venous congestion and vascular occlusion caused by luminal thrombi and/or by thickening of the vessel wall. Angiogenesis, ectasia, passive venous congestion, and luminal thrombi were most evident in superficial dermis (Figures 2B, 2C, 3F) and in middle dermis (Figure 2A).

Thickening of vessel wall with reduction of the lumen and sometimes with obliteration was seen in vessels of the dermis (Figures 3B-3E) and of the subcutis (Figure 3A). The inflammatory infiltrate and the presence of bacilli were similar to that of the previous third stage.

**STAGE 5. ISCHAEMIC NECROSIS DUE TO INFLAMMATORY VASCULAR OCCLUSION PLUS LEPROSY REACTION**

Twenty-two biopsies comprised 9 males and 13 females, M:F ratio of 1:1.4; age range 12 years to 75 years, (median 39 years, mean 7.8 years). Delay from the appearance of the first sign referable to leprosy ranged from 3 months to 28 years (median 3 years, mean 7.8 years). All had necrotic lesions of the skin, from which the specimens were taken. The part of the body where the biopsies specimens were taken was: inferior extremity 9, upper extremity 11, no information 2.
Histology

This fifth stage showed changes superimposed on the pre-existing occlusive vascular damage. They included necrosis of epidermis (Figure 4B) and superficial dermis, hyalinisation and/or deposits of fibrin in small blood vessel walls of the dermis and the subcutaneous fat tissue. (Figures 4A–4E).

The cellular infiltrate around these vessels consisted of neutrophils, nuclear dust, a few eosinophils, lymphocytes, and in rare cases red blood cells. Large vessels in the deeper reticular dermis and in the subcutis showed pronounced thickening and intimal proliferation causing reduction in vascular lumen and sometimes complete occlusion; their wall was infiltrated by neutrophils and lymphocytes (Figure 4E). In addition, a dense predominantly neutrophil infiltrate was seen involving the deeper dermis and the lobular portion of the

Figure 2. 2A) third stage lesion, showing a blood vessel distended by thrombus. 2B) this is a transition lesion between third and fourth stages. The epidermis appears stretched and thinned with pyknotic malpighian cells. In the dermis, beneath of epidermis, thrombi (T) occlude the lumina of some superficial capillaries; there is no inflammatory infiltrate. 2C) from a lesion in fourth stage. This superficial lesion shows loss of epidermis, thrombosis and congestion of capillaries papillae Note the absence of inflammatory cells. This lesion heals “restitutio ad integrum”. 2D) from a case in fourth stage, exhibits loss of tissue that includes the epidermis and some superficial dermis, and a superficial vessel occluded by an amorphous homogeneous and acidophilic substance. (2A. H&E; ×100, 2B–2D. H&E; ×250).
subcutaneous fat tissue as a lobular panniculitis. In one case there was a granulomatous reaction within and around a large blood vessel of the subcutis.

CHANGES FOUND IN OTHER STRUCTURES OF THE SKIN

AFB were found not only in blood vessels, but also in lymph vessels, nerves, hair follicles, erector pili muscles, sebaceous glands, sweat glands, and in a few cases in the different layers of the epidermis (Table 1).

Usually, bacilli were more abundant in sections of the biopsy specimens taken from the ear lobe. Nerves and epidermal appendages showed different degrees of invasion, degeneration and destruction by the inflammatory infiltrate, these changes being more noticeable in the ischaemic tissue necrosis stages.

Discussion

Histopathologically, five stages of DLL were considered in this study, each of them having different features. When the clinical data are correlated with the histological changes, the three first stages, early, disseminated, and well-developed, correspond to the phase in which patients have diffuse infiltration of entire skin The fourth and fifth stages of ischaemic necrosis correspond to Lucio’s phenomenon or erythema necroticans. Endothelial cells seem to be the main targets of the organism, and following invasion of M. leprae vascular damage
Figure 4. All sections are from a fifth stage case. 4A) shows necrosis of the epidermis, leukocytoclastic vasculitis in small blood vessels of the dermis and subcutis. In the lower left is an almost occluded blood vessel infiltrated by inflammatory cells. 4B) necrosis of the epidermis and leukocytoclastic vasculitis. 4C) leukocytoclastic vasculitis in the upper dermis. 4D) This illustration shows two small vessels, in the lower dermis, stained acidophilically and surrounded by inflammatory infiltrate composed largely by neutrophils mixed with mononuclear cells. 4E) leukocytoclastic vasculitis in the subcutis. 4F) the subcutaneous blood vessel seen in 4A, shows endothelial proliferation and heavy infiltration by neutrophils, lymphocytes and histiocytes. (4A. H&E; × 35, 4B. H&E; × 160, 4C. H&E; × 400, 4D. H&E; × 160, 4F. H&E; × 250).
occurs, suggesting that the colonisation of the endothelial cells by acid-fast bacilli could be responsible for this damage. At the early stage, the changes consist of dilated vessels, angiogenesis, and congestion. Endothelial bacillation varies considerably with the progression of lesions. In the beginning, there are very few bacilli in the endothelial cells of large blood vessels. As time goes by, organisms increase within the endothelial cells. Later, bacilli spread progressively from the deep plexus to mid and small-sized vessels of the dermis and subcutis to give rise to a well-developed histological lesion in which most of the sections show all blood vessels having a bacillated endothelium, a finding already reported by Martinez-Baez, who said: “. . . every time one sees the picture of a blood-vessel, one can observe that the mentioned bacilli are present in one or more to the endothelial cells”.

The presence and constitution of the infiltrate were variable and did not seem to be related to the age of the lesion. Biopsies of some patients at a well-developed histological stage and with a long clinical evolution up to 10 years showed only a slight perivascular mononuclear infiltrate, while other cases with well-developed histological lesions but with a short clinical history showed a dense mononuclear infiltrate. Relatively few Virchow-cells were seen compared with the great number of bacilli.

The fourth stage of ischaemic necrosis due to non-inflammatory vascular occlusion is characterised histologically by the presence of necrotic cutaneous lesions due to vascular occlusion by endothelial proliferation or thrombosis, and clinically it coincides with the appearance of discrete purple-coloured painful spots, which lead to ulceration of the skin without systemic symptoms. It should be stressed that the fourth stage of ischaemic necrosis due to non-inflammatory vascular occlusion seems to be caused by vascular injury induced by invasion of the endothelial cells by Mycobacterium leprae and that tissue necrosis is due to vascular occlusion by proliferative endothelium or thrombosis. At this stage systemic symptoms do not develop and these are the cases that do not respond to thalidomide. This pattern, the damage of which is seen with or without sparse inflammatory cells, seems to correspond to the one that Rea used the term vasculosis.

The fifth stage of ischaemic necrosis appears as an acute reactional state that may supervene in such patients and aggravates the existing vascular damage. It is manifested microscopically by necrosis of the superficial dermis and epidermis, leukocytoclastic

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vasculitis in small blood vessel of the dermis and of the subcutis, and lobular panniculitis. Mid-sized and large blood vessels show intimal proliferative thickening, a narrow vascular lumen, and walls infiltrated by neutrophils and lymphocytes.

The fifth stage of ischaemic necrosis is considered here as a severe variant of ENL. When this happens the clinical disease is exacerbated; the number of spots increases suddenly in several parts of the body, the pre-existing necrotic cutaneous lesions become aggravated and systemic symptoms appear. It is suggested that ENL and Lucio’s phenomenon may result from similar immunological mechanisms, both show immune-vasculitis resulting from deposits of complement-fixing immune complexes in small blood vessel walls, and both are may respond to thalidomide. In patients with either ENL or Lucio’s Phenomenon, deposits of IgG and C3, as well as circulating immune complexes have been found in the wall of small blood vessels. It is known that immune complexes activate the complement system and become chemotactic for neutrophils, which ingest the immune complexes and are subsequently destroyed in the form of nuclear fragmentation. Activation of the clotting system results in the conversion of fibrinogen to fibrin. The histological picture shows neutrophils, nuclear dust, and fibrin in the wall of small blood vessels, features that establish the diagnosis of leukocytoclastic vasculitis (LCV). Clinically different manifestations are described to LCV, including macules, papules, nodules, vesicles, bullae, and ulcers.

Some immunological, histological and clinical aspects distinguish Lucio’s phenomenon from ENL. Immunologically, Lucio’s phenomenon occurs in patients considered the most anergic of the all-immunological spectrum of leprosy. Histologically, Lucio’s phenomenon starts with heavy colonisation of the endothelial cells by acid-fast bacilli. It develops in a tissue that already has severe vascular damage, and it is always associated with skin necrosis. Clinically, Lucio’s phenomenon is an erythema necorcitans, characterised by red and painful spots (manchas) that progress to necrosis and ulceration leaving atrophic stellar scars, occurring in a skin with diffuse generalised infiltration and complete absence of nodules, and appearing in untreated patients. In this study, one case of granulomatous vasculitis in the subcutis was only observed in patients in this stage; a change that could contribute to anoxia.

Another noteworthy fact, in stages four and five, was the finding of vascular occlusion by thrombi, with no signs of perivascular inflammation. The endothelium has on its surface a number of anticoagulant and procoagulation properties which, when perturbed, may lead to intravascular coagulation. Therefore the activation of the endothelial cell by organisms can trigger a cascade of events leading to the conversion of fibrinogen to fibrin intravascular and thrombosis that occlude arterioles and capillaries. Lucio and Alvarado remarked in their work that in these patients the level of fibrin was always elevated, and the patients bleed less during a surgical amputation.

The nasal mucosa is involved early in the course of Lucio’s leprosy and at least 95% of all patients with lepromatous leprosy have nasal involvement too. Leprosy bacilli may spread though the bloodstream from the nose to another area of the body, among them the skin.

The results of this study support the hypothesis that in Lucio’s leprosy there are leprosy bacilli in endothelial cells throughout the vasculature that promote the liberation of substances by the endothelium that induce vascular reactivity as manifested by distended vessels, morphological changes of the endothelial cells, areas of passive venous congestion and foci of intravascular clotting, which proceed to disseminated intravascular coagulation (DIC). DIC is one of the causes of death among these patients.
It is suggested here that in all cases of lepromatous leprosy, be they nodular or diffuse, the first lesion is the same: the colonisation of the endothelium by bacilli and that the course of the disease be determined by the resistance of each patient to the micro-organism. Suitable treatment can reverse the obliterative changes. Skin biopsies from treated patients show vessels cleared of organisms. Some solid bacilli, however, can remain in the media of great blood vessels, and persist in spite of treatment. In vessels of treated patients thickness of the walls diminishes gradually and the lumen becomes wide and clean, the disease does not progress and necrosis does not occur. Treatment with dapsone and rifampicin is associated with the prompt cessation of new acute lesions. Consequently, the restoration of a normal endothelial cell state would be an important objective in the treatment of a patient with diffuse leprosy of Lucio and Latapi. The two important criteria for this diagnosis are: 1) diffuse non-nodular infiltration, and 2) heavy vascular endothelial parasitisation by M. leprae.

Conclusions

Histopathological findings suggest that diffuse leprosy of Lucio and Latapi is a vascular disorder produced by the invasion of vascular endothelial cells by Mycobacterium leprae. It would seem that once the bacilli have entered the endothelial cell, they induce endothelial cell activation that leads to specific morphologic and functional changes, among which are vascular ectasia, proliferation and swelling of the endothelium with thickness of the vessel walls, angiogenesis, and activation of clotting which gives rise to thrombosis. These changes characterise this variety of lepromatous leprosy. The necrotising lesions of Lucio’s phenomenon are due first, to occlusive vasculopathy, without systemic symptoms, and secondly, to a lepra reaction that aggravates vascular damage and causes systemic signs and symptoms.

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