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Clinical and Histologic Variations Among Thirty Patients with Lucio's Phenomenon and Pure and Primitive Diffuse Lepromatosis (Latapi's Lepromatosis)¹

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ABSTRACT

The clinical and histologic experience with 30 patients who had Lucio's phenomenon, and pure and primitive diffuse lepromatosis (Latapi's lepromatosis) has been reviewed. The unanticipated clinical findings were a male to female ratio of nearly 1:1, a 21 month median time of onset of erythema nodosum leprosum (Type 2 reaction) after starting antibacterial treatment, and an absence of a stocking-glove pattern of anesthesia in 7 patients. The only unanticipated histologic finding was a lepromatous-granulomatous vasculitis, occurring in comparatively large vessels, or in vessels made large by pathologic changes, located near the dermal-subcutaneous interface. This finding was present in 6 of the 22 patients with histologic material available for review. In 2 of these 6 this vasculitis was identified before the onset of Lucio's phenomenon. With one conspicuous exception, the onset of treatment with a microbical agent was associated with a cessation of new lesions of Lucio's phenomenon within one week. Long-term morbidity, other than Type 2 reaction, was found in 22 of the 25 patients followed for more than 1.3 years. Usually this was the consequence of Latapi's lepromatosis, specifically venous insufficiency and/or loss of protective sensation, and only rarely from Lucio's phenomenon, specifically scar formation. Briefly summarized are the seven patients who had had a skin biopsy before the onset of Lucio's phenomenon, as well as the two patients who were considered to be atypical. Criteria for the diagnosis of Latapi's lepromatosis, in the absence of Lucio's phenomenon, are also considered.

RÉSUMÉ

Cet article s'est attaché à faire la revue de l'expérience clinique et histopathologique de 30 patients atteints de phénomène de Lucio et/ou de lèpre lépromateuse pure et primitive-

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ment diffuse, encore appelée lèpre lépromateuse de Latapi. Les données cliniques surprenantes furent un ratio homme-femme de presque 1:1, un temps médian de 21 mois entre la mise en ouvre d'un traitement antibactérien et le déclenchement d'un érythème nouveau lépreux (réaction de type 2), et l'absence d'une anesthésie distribuée en bas-résille chez 7 patients. La lésion histologique non anticipée a été la découverte d'une vasculite lépromateuse et granulomateuse atteignant des vaisseaux de diamètre relativement élevé ou bien des vaisseaux élargis par les changements histopathologiques, situés près de l'interface derme/hypoderme. Cette lésion était présente chez 6 des 22 patients qui présentaient du matériel histologique pour une revue. Chez 2 de ces 6 individus, cette vasculite fut identifiée avant le déclenchement du phénomène de Lucio. Lors de phénomène de Lucio et à l'exception d'un cas plutôt remarquable, l'apparition de nouvelles lésions a été interrompue dans la semaine qui a suivi la mise en place d'un traitement avec un agent bactéricide. Une morbidité à long terme, autre que les réactions de type 2, fut trouvée chez 22 des 25 patients qui ont été suivis pendant plus de 1,3 ans. Le plus souvent, cette morbidité était la conséquence de la lèpre lépromateuse de Latapi, spécifiquement l'insuffisance veineuse et/ou la perte de sensibilité protectrice, et seulement rarement les conséquence du phénomène de Lucio, spécifiquement l'apparition de cicatrices. Brièvement résumés sont les 7 patients qui ont eu une biopsie cutanée avant l'apparition d'un phénomène de Lucio, ainsi que les 2 patients qui furent considérés comme atypiques. Les critères pour le diagnostic de lèpre lépromateuse de Latapi, en l'absence de phénomène de Lucio, sont également présentés.

RESUMEN

Se hizo una revisión de los datos clínicos e histológicos de 30 pacientes que habían tenido el fenómeno de Lucio y lepromatosis difusa pura y primitiva (lepromatosis de Lucio). Los hallazgos clínicos no anticipados fueron: una relación masculino: femenino casi de 1:1, un tiempo promedio de aparición de eritema nodoso leproso (reacción de tipo 2) de 21 meses después del inicio del tratamiento antibacteriano, y ausencia del patrón de anestesia "media-guante" (stocking-glove) en 7 pacientes. El único hallazgo histológico no anticipado fue una vasculitis lepromatosa-granulomatosa, presente en vasos comparativamente grandes o en vasos agrandados por los cambios patológicos, localizados cerca de la interfase dermo-subcutánea. Este hallazgo estuvo presente en 6 de 22 pacientes con material accesible para revisión. En 2 de estos 6 pacientes la vasculitis fue identificada antes de la aparición del fenómeno de Lucio. Con una sola excepción, el tratamiento con un agente microbicida estuvo asociado con la suspensión, en la primera semana, de nuevas lesiones del fenómeno de Lucio. La morbilidad crónica, diferente a la reacción de tipo 2, se encontró en 22 de 25 pacientes seguidos por más de 1.3 años.

Usualmente la insuficiencia venosa y/o la pérdida de sensación protectora fueron consecuencia de la lepromatosis de Lucio y sólo raramente del fenómeno de Lucio en cuyo caso la consecuencia más frecuente fue la formación de cicatriz.

Se describen brevemente los casos de los 7 pacientes que habían tenido una biopsia de piel antes de la aparición del fenómeno de Lucio, y de dos pacientes considerados como atípicos. También se discuten los criterios para el diagnóstico de la lepromatosis de Latapi en ausencia de fenómeno de Lucio.

Since reporting 10 patients with Lucio's phenomenon ⁽²⁵⁾, seen in this institution from 1969 through 1977, a further 20 had been observed by the end of 2004. The primary purpose of this report is to describe the kinds and the extent of the clinical and histologic findings in all these 30 patients with Lucio's phenomenon as well as in the underlying diffuse lepromatosis. In addition, this report presents data on long-term follow-up, and details information concerning patients who had had a skin biopsy prior to the onset of Lucio's phenomenon.

Also, a higher incidence of a lepromatous-granulomatous vasculitis (L-GV) was found in patients with Lucio's phenomenon than was present in those with erythema nodosum leprosum (Type 2 reaction) or non-reactional lepromatous leprosy.

Concerning history and nomenclature, in 1852 Lucio and Alvarado ⁽¹⁶⁾ reported a necrotic skin reaction that occurred in leprosy, as judged by the concomitant changes of peripheral neuropathy, eyebrow loss, and nasal involvement. These authors also described the absence of the nodular, dermal

lesions expected in leprosy, as well as the associated fatal termination. Latapi and Zamora⁽¹⁵⁾ established that the necrosis was a result of vascular involvement, and that the absence of dermal nodules was a part of a diffuse lepromatous infiltrate, which they described in considerable detail. Also, they reported a much better prognosis with dapsone therapy. Latapi and Zamora called the necrotic skin reaction "Lucio's phenomenon" or "erythema necroticans" and the diffuse, non-nodular lepromatous infiltration "pure and primitive diffuse lepromatosis." For the latter expression, the synonym "Latapi's lepromatosis" is proposed, and will be used hereafter herein. This gives an appropriate and brief eponymic recognition of Latapi's important contributions. Also, having "Lucio" in two closely related eponymic terms, i.e., "Lucio leprosy" and "Lucio's phenomenon," often is a needless source of confusion.

The initial report of Lucio and Alvarado was virtually forgotten in 50 years⁽¹⁵⁾. In the over 50 years following the report of Latapi and Zamora⁽¹⁵⁾, both Lucio's phenomenon and the underlying Latapi's lepromatosis have been recognized in diverse ethnic groups, and in a wide geographic distribution, including, but not limited to, Louisiana⁽⁸⁾, Hawaii⁽³⁾, Brazil^(1, 9, 31), Greece⁽¹¹⁾, the Near East⁽³⁰⁾, India⁽²⁹⁾, Singapore⁽²⁾, Indonesia⁽¹³⁾, and Polynesia⁽⁶⁾. Apparently the condition remains rare except in Mexicans, Costa Ricans⁽²⁸⁾, and Cubans⁽¹⁸⁾, where its incidence is aptly described as "not common."

This retrospective study is somewhat incomplete because of the institutional policy of "deep" storage of charts, and the Northridge earthquake of January 1994 trashed the room holding both histologic glass slides and paraffin blocks. The material available was considered sufficient to illustrate a range of clinical and histologic findings, the responses to treatment, and the long-term morbidity encountered.

MATERIALS AND METHODS

The subjects were patients in the Hansen's Disease Clinic or the Dermatology Clinic of the Los Angeles County-University of Southern California Medical Center. Included in this study were all patients who had one or more characteristic

lesions of Lucio's phenomenon, i.e., serated hemorrhagic infarcts usually arising in crops, and at least one characteristic sign of Latapi's lepromatosis (*see below*) or of lepromatous leprosy, but no lepromatous nodules. The diagnosis of Latapi's lepromatosis was made after the fact of Lucio's phenomenon. No criteria for exclusion were established.

The data base for the clinical information in this study was compiled from five sources: the available charts, data abstracted from charts for previous publications, clinical photographs obtained before starting treatment, patients currently being followed in clinic, and available histologic specimens. The summary of the histologic changes was compiled from the material available for review.

RESULTS

The results will be presented in two ways. First will be 9 brief case reports. Following the case reports, the available data on all patients will be summarized in narrative form.

CASE REPORTS

The initial 7 case reports concern those patients who had had skin biopsies taken prior to the development of Lucio's phenomenon. Five of these biopsy specimens had been seen by one of us (THR), and 3 of these 5 were available for review. Among these 7 patients, 4 had a diagnosis of leprosy established and treatment initiated before the onset of Lucio's phenomenon (Cases 2, 3, 6, and 7), whereas 3 had had a biopsy but the diagnosis of leprosy was not made until the onset of Lucio's phenomenon (Cases 1, 4, and 5). The remaining 2 case reports (Cases 8 and 9) concern those who were considered to be atypical.

Patients with skin biopsies prior to Lucio's phenomenon

Case 1. An 18 year old woman sought care because of numbness of the hands and feet of several months duration. Neurologists interpreted her findings to be a peripheral neuropathy secondary to a systemic disease. Consultation with many medical specialties could identify no systemic illness. After 18 months, a skin biopsy taken from an area of diminished sensory perception, but otherwise clinically normal skin,

TABLE 1. Frequency of clinical signs of Latapi's lepromatosis.

	Number of patients evaluated	Number (%) positive	Number (%) Negative	Number (%) not recorded or sought	Comment
I. Clinical <i>sine qua non</i> for Latapi's Lepromatosis					
A. Diffuse non-nodular Lepromatous leprosy	30	30 (100)	0	0	peau d'orange change in Case #8
II. Highly suggestive of Latapi's lepromatosis					
A. Telangectasias	28	10 (3)	0	18 (69)	May be more common
1. eruptive		3			
2. mats on face and trunk		7			
B. Not visible subcutaneous plaques	28	8 (29)	0	20 (71)	May be more common
C. Signs of diffuse infiltration	28	22 (79)	0	6 (21)	May be more common
1. non-marginated induration of cheeks		4			
2. widening of nasal root		9			
3. swollen backs of hands		9			
4. dusky swelling of feet		1			
III. Consistent with Latapi's lepromatosis					
A. Alopecia of eyebrows	30	27 (90)	0	3 (10)	Perhaps universal
1. total		20 (67)			
2. partial		7 (23)			
B. Rhinitis	30	25 (85)	0	3 (10)	Perhaps universal
C. Septal perforation	25	9 (36)	8 (32)	8 (32)	
D. S-GPSI with little motor change	30	20 (67)	7 (23)	3 (10)	

was interpreted as "normal skin." Three years after her initial presentation crops of infarcts of Lucio's phenomenon quickly led to the correct diagnosis. A Fite stain then done on the "normal skin" material demonstrated acid-fast bacilli (AFB) and globi within nerves and endothelial cells (slide not available for review).

Comment: this case illustrates the difficulty of making a diagnosis of leprosy in the absence of a sign more readily associated with leprosy.

Case 2. A 22 year old woman presented to the obstetrical service in labor with an incidental complaint of eyebrow alopecia, progressing from medial to lateral, of 2 months duration. Because rhinitis was also present, leprosy was considered. A biopsy of clinically normal skin showed AFB and globi in some endothelial cells and perivascular macrophages (slide not available for review). No AFB were found in placental endothelium. One month after initiating dapsone monotherapy, erythema nodosum leprosum (ENL) developed, which was managed with thalidomide. Eight months later the patient was lost to follow-up, only to return after a 13 months absence with the necrotic lesions of Lucio's phenomenon and ulcers (biopsy not available for review).

Comment: This case confirms the possibility of considering a diagnosis of Latapi's lepromatosis without the infarcts of Lucio's phenomenon, as suggested by others (⁹). Also, this is the only patient seen in this series who had ENL prior to having Lucio's phenomenon. Because of the absence of AFB in placental endothelial cells, but their abundance in cutaneous endothelium, the predilection of AFB for endothelial cells is likely to be organ specific.

Case 3. A 45 year old woman presented with eyebrow alopecia, rhinitis, and palpable but not visible, indurated lesions in the subcutis. Skin biopsy showed, in addition to an extensive lepromatous infiltrate, an AFB-positive, lepromatous-granulomatous vasculitis (L-GV) in the subcutis, characterized by endothelial proliferation, macrophages dissecting between the smooth muscle cells of the media, and macrophages infiltrating the adventitia (Fig. 1a, b). Also present was an aneurysmal lepromatous-granulomatous

vessel (Fig. 1c), as well as signs of new vessel formation. Our working diagnoses were lepromatous leprosy and a reactionary state of unknown type. She was treated with daily dapsone and rifampin, as well as prednisone and thalidomide. The unknown reactionary state was managed with decreasing doses of thalidomide and prednisone, the latter being discontinued after 5 months. Seven months after initiating treatment, and 2 months after stopping prednisone, but still taking thalidomide 100 mg daily, the patient developed Lucio's phenomenon (Fig. 1d). Her new Lucio infarcts ceased within 2 weeks upon resuming prednisone at 40 mg daily; the dose being tapered slowly over the ensuing 5 months.

Comment: This patient made us aware of involvement in larger vessels, or vessels made large by pathologic changes, than previously recognized by us. Also, the previous suggestion that viable bacilli might be a *sine qua non* for Lucio's phenomenon (²⁵) appeared to be incorrect. In retrospect, what was called a reactionary state of unknown type was perhaps the L-GV.

Case 4. A 37 year old woman sought care because of what was described in her chart as nodular lesions on the arms and legs suggestive of erythema nodosum. The report of a skin biopsy at that time noted inflammation and was interpreted as suggesting erythema nodosum. The patient was treated with a saturated solution of potassium iodide. When seen 2 years later for another problem, it was noted that the erythema nodosum had resolved. After an additional 2 years, crops of Lucio's infarcts developed. Of the 2 biopsy specimens obtained at this time, both showed characteristic changes of the Lucio's phenomenon, and the one which was available for review also demonstrated subcutaneous vessels with endothelial proliferation and lumen occlusion (Fig. 2a). Also, the biopsy taken four years before the onset of Lucio's phenomenon was available for review, showing a focal lobular panniculitis consisting of macrophages and, in the dermis, an arcuate, perivascular infiltrate of lymphocytes and foamy macrophages (Virchow cells) (Fig. 2b, c). The latter was interpretable as evidence of a lepromatous change. The tissue blocks were not available.

Comment: Two explanations for the sug-

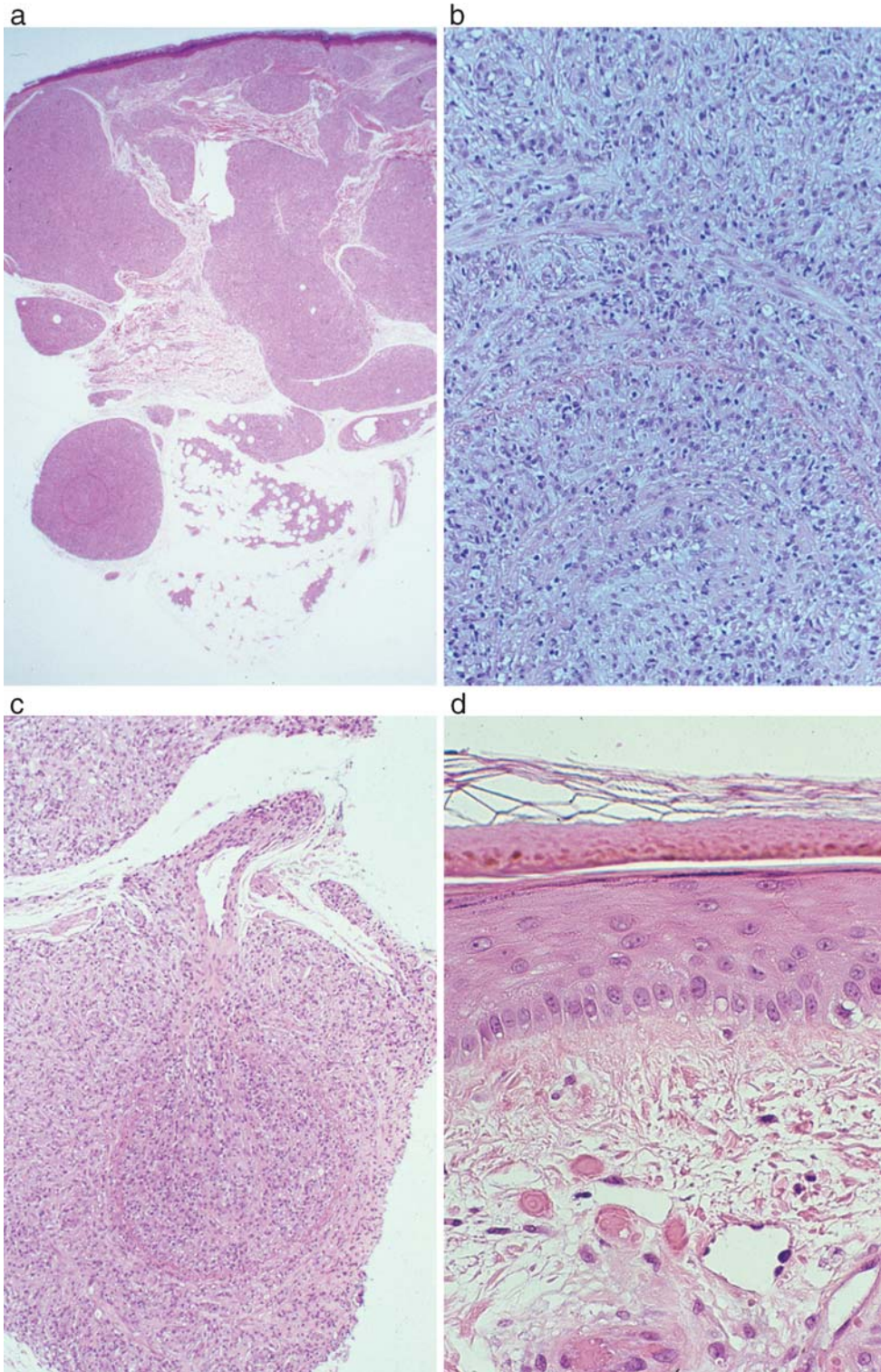


FIG. 1. From Case 3. a) A low power view of a biopsy from a palpable, but not visible, subcutaneous lesion, on the right arm, which shows in the lower right corner an enlarged vessel in the subcutis with a conspicuous internal elastic lamina. The lumen is occluded, and adventitial involvement is apparent. Heavy infiltration of the dermis is evident. 1.25x objective. b) A high power view of the same vessel as shown in "a." The now less conspicuous internal elastic lamina is indicated by wide arrows, but is readily seen in color. The lumen is occluded

gested "erythema nodosum" appear possible. A leprologic hypothesis is the development of mild, neutrophil-free, transient ENL in a patient who had yet to express other clinical manifestations of leprosy. An alternative explanation is that of a leprosy-unrelated inflammatory disorder occurring on a lepromatous background.

Case 5. A 28 year old man sought care because of the development of palpable, but not visible, nodules in the subcutaneous tissue of his legs. The clinical impression was a vasculitis. A skin biopsy was interpreted as "nodular vasculitis," the pattern consisting of endothelial proliferation with occlusion of the lumen, as well as a dense infiltrate of macrophages in the adventitia (Fig. 3a). He was begun on an anti-inflammatory regimen, which included methotrexate and prednisolone. Five months later he developed an acute, febrile illness, diagnosed as a *Salmonella* non-typhoid bacteremia, secondary to the ingestion of snake powders. He responded well to intravenous ciprofloxacin, and was discharged on ciprofloxacin 500 mg twice daily orally, methotrexate 5 mg twice daily, and prednisone 80 mg every other day in the morning. One day after discharge he abruptly developed extensive and widely distributed infarcts of Lucio's phenomenon. These involved about one-third of his body surface area, most extensive on the legs (Fig. 3b), and arms, but present also on his ears, face (Fig. 3c), trunk, scrotum, and the urethral meatus. This patient was promptly readmitted, and 1 day later his right hand was affected by apparently complete arterial occlusion. Circulation was restored by prompt intervention, but deep necrosis eventually resulted in the loss of the 5th right distal metacarpal head and the right 5th finger. His left patella was also lost, as a consequence of extensive tissue necrosis over the left knee. A Fite stain on the tissue initially interpreted as "nodular vasculitis" was pos-

itive for AFB in endothelial cells and adventitial macrophages.

Comment: This one patient recapitulates three prior case reports. 1) Leprosy may mimic nodular vasculitis⁽³⁴⁾. 2) Occlusion of large muscular arteries may occur in association with Lucio's phenomenon⁽⁸⁾. 3) Lucio's phenomenon may occur in a setting of convalescence from serious infection, i.e., in 2 cases of erysipelas managed with penicillin⁽¹⁾. (These 2 patients, and Case 5, received antibiotics ineffective against *M. leprae*.) New infarcts ceased when rifampin was begun. This patient was the only one whose prognosis was poor when first seen.

Case 6. A 37 year old woman presented to another clinic because of eyebrow alopecia and rhinitis. A skin biopsy confirmed the impression of lepromatous leprosy (slide not available for review). She took 100 mg of dapsone daily for 18 years. At age 68, 13 years after stopping dapsone, she presented to this clinic with Lucio's phenomenon, occurring intermittently for one month.

Case 7. A 15 year old boy presented to a dermatology clinic in Mexico City because of eruptive telangiectasias and eyebrow alopecia. A skin biopsy (not available for review) established a diagnosis of leprosy. Dapsone treatment was initiated at that time but he took it infrequently. At age 21 he presented to our clinic because of leg ulcers and skin infarcts of 6 months duration; telangiectasias were prominent at that time. Dapsone was resumed, but he was seen infrequently. At age 35 he made 2 visits to our clinic because of leg ulcers. Two skin biopsies performed at that time were negative for AFB (not available for review).

The atypical patients

Case 8. This 45 year old woman satisfied entry criteria for this study on clinical grounds because she had one 8 mm characteristic infarct, a perforated nasal septum, total alopecia of eye lashes and eye lids,

←

by endothelial proliferation. The lepromatous infiltrate is dissecting between smooth muscle bundles, shown by thin arrows, and is infiltrating the adventitia. 20× objective. c) Elsewhere in the same specimen an aneurysmal change in a vessel is shown by the relatively dark internal elastic lamina. 10× objective. d) A high power view of a re-epithelized Lucio's phenomenon lesion which shows, from outside inward, the old stratum corneum, the now shrunken infarcted epidermis with a hint of cellular ghosts and persistent melanin, a very thin new stratum corneum, and new granular cell, prickle cell and basal cell layers. The dermal repair is not complete. Five occluded or congested small vessels are evident. 40× objective. (Images available in color in the electronic edition, www.leprosy-ila.org)

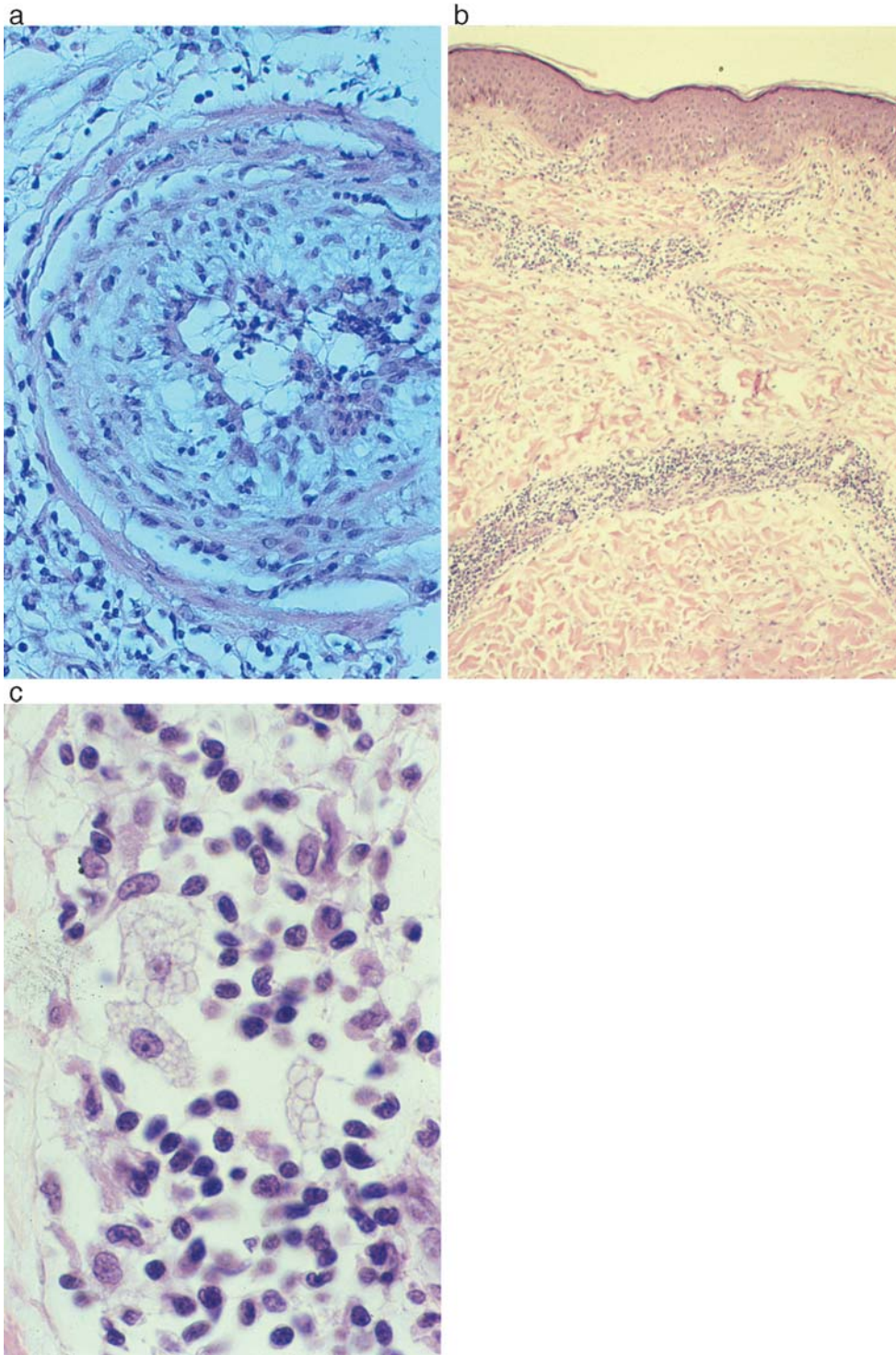


FIG. 2. From Case 4. a) From a Lucio's phenomenon lesion, a vessel in the subcutis with prominent endothelial proliferation, and adventitial infiltration. 40× objective. b) A low power view of an earlier biopsy obtained from a red dermal nodule 4 years before the onset of Lucio's phenomenon, showing epidermal thickening, a superficial infiltrate in the upper dermis, and an arcuate infiltrate in the mid dermis. 10× objective. c) An oil-immersion view from the arcuate infiltrate showing 2 nucleated Virchow cells and the cytoplasm of a 3rd. Lymphocytes are evident, but no neutrophils were found. 90× objective.

several stellate scars, and 3 large leg ulcers, each approximately 10 cm in diameter. Biopsy showed a heavy infiltrate of macrophages, AFB and globi in some endothelial cells, but no endothelial proliferation. She is considered to be atypical because of a "peau d'orange" appearance to the skin of her forehead and cheeks, as well as beading on corneal nerves (¹⁵). Also, she is the only patient in this series with just one infarct, and one of two without endothelial proliferation.

Comment: At present it is unknown if any of these atypical findings, or a combination thereof, would constitute valid criteria for exclusion.

Case 9. A 24 year old man presented to this clinic with typical Lucio's phenomenon, and giving a history of similar clinical findings, as well as intermittent dapsone use for 4 years. A lesional biopsy did not show epidermal necrosis (probably exfoliated during processing), or congestion of superficial vessels, or extravasation of erythrocytes, but did demonstrate AFB in proliferating as well as in non-proliferating endothelial cells, globi in endothelial cells, and passive congestion of deep dermal vessels. Also present were larger vessels with lumens occluded from endothelial proliferation, and macrophage infiltration of the adventitia, but no infiltration of the media (Fig. 4a). New lesions ceased to form 4 weeks after starting dapsone monotherapy. To this point, on balance, the patient was considered to be typical. Eight years later, in the setting of seemingly good compliance with dapsone monotherapy, new Lucio's phenomenon-like infarcts developed on the trunk and extremities. With the working diagnosis of a relapsing Lucio's phenomenon, and an inference of dapsone resistance, dapsone was discontinued, being replaced by daily rifampin and daily minocycline, and the new lesions ceased after 8 weeks. Biopsy now showed epidermal necrosis, passive congestion of superficial vessels, and endothelial proliferation in deep dermal vessels, but stains for AFB were repeatedly negative (slides not available for review).

Comment: No support for dapsone resistance was found. A self-limited process of unknown type, unrelated to leprosy, but mimicking Lucio's phenomenon must be considered.

SUMMARY OF ALL CASES

Demographic data

Sixteen men and 14 women satisfied inclusion criteria. Twenty-five were born in Mexico, 2 in Cuba and 3 in the United States, each of the latter 3 also having resided in known leprosy-endemic areas of Mexico for more than 5 years. Age at the time of diagnosis of Lucio phenomenon, leprosy was known in 29 and ranged in duration from 15 to 71 years, with a median of 34 and an average of 33.7 years.

First sign or symptom of leprosy, and time to diagnosis

The first sign or symptom attributed to leprosy was alopecia in 16 (eyebrows in 15, extremities in 1), leg ulcers in 4, sensory impairment in the hands and/or feet in 3, nasal symptoms in 2 (1 with nose bleeds, 1 with congestion), eruptive telangiectasias in 2, and infarcts of Lucio's phenomenon in 2, but was not recorded in 1. The elapsed time from the initial sign or symptom to the diagnosis of leprosy ranged from a minimum of 2 months to a maximum of 10 years, with a median of 3 years and an average of 4.1 years.

Mode of presentation

Of the 28 patients presenting to our clinic with Lucio's phenomenon, the presenting complaint was leg ulcers in 14 (duration 2 months to 7 years, median 8 months and average 19.7 months). The other 14 complained of the infarcts of Lucio's phenomenon, usually occurring in intermittent crops (duration 5 days to 10 years, median 4 months, and average 4.1 months). Both infarcts and ulcers were characteristically present at presentation, excepting Case 5, who had no ulcers at presentation. The infarcts were hemorrhagic, slightly indurated, not tender, but sometimes painful. Sharply marginated, irregularly serrated borders were characteristic, such that an observer viewing the infarct, whether large or small, from "normal" skin would see a concavity (Fig. 3b, c). Early, pre-hemorrhagic lesions were seen in only one patient, being slightly indurated, light blue in color, and having an erythematous halo. (Previously published photomicrographs of this specimen are figs. 4 and 5 in Rea and Levan (²⁵), and figs. 3 and 4 in Quismorio, *et al.* (²³)) The least

number of infarcts recorded was one, in Case 8. In all other patients the lesions were multiple, arising in crops, most commonly on the legs, but less frequently on the thighs and forearms. In one patient, Case 5, the infarcts were numerous (over 100), widely distributed, and clearly placed his life in peril. In another patient, 24 infarcts were counted. And in yet another patient the infarcts were small, and present only below the ankles. Infarcts on the arms resolved rapidly, behaving more like erosions than ulcers. In 2 patients the infarcts became bullous. Infarctions in organs other than the skin were not evident.

Ulcers were common on the legs, but occasionally on the thighs. Ulcers of recent onset appeared to be the direct sequelae of the infarcts, being ovoid and irregular in shape, not exceeding 5 cm in greatest diameter. If of long standing, ulcers were round in shape and up to 10 cm in diameter, perhaps being complicated by neglect and unsuitable topical therapy.

In two patients the onset of Lucio's phenomenon was associated with pregnancy, each ending with a normal delivery. In Case 5, the onset occurred while the patient was convalescing from a Salmonella bacteremia. No other potentially precipitating events could be identified.

Signs of Latapi's lepromatosis at the time of presentation

Absent nodules. The absence of lepromatous dermal nodules was noted in all 30 patients, with the possible exception of Case 8, who had a "peau d'orange" prominence to the follicular orifices on the face, presumably the result of infiltration or edema, but no dermal nodules in the conventional sense.

Diffuse infiltration. Signs of diffuse cutaneous infiltration were not mentioned as either present or absent in 8 patients. One or more signs of diffuse infiltration were recorded as present in 22 patients. Widening of the nasal root was described in 9 (or retrievable from clinical photographs). Diffuse infiltration in the hands was noted in 9 patients, being variously described as "swelling," or "non-pitting edema," of the backs of the hands, in association with "fusiform fingers." Changes in the cheeks of the face were variously described in 4 as "red plaques, poorly marginated," "in-

durated erythema," or "a cyanotic edema." "Full" or "swollen" ear lobes were stated to be present in 7 patients. A "dusky swelling" of the feet was described in 1. (Swollen ear lobes and fusiform fingers are signs of diffuse infiltration not uncommonly found in patients with ordinary lepromatous leprosy.)

Subcutaneous plaques. Not visible, nontender, subcutaneous plaques were found on the arms or legs in 8 patients, but were not mentioned as absent in any of the 20 other charts available for review.

Telangiectasias. Telangiectasias were described as eruptive in 3 patients; these persisted in 2, but treatment-associated remission occurred in 1. Persistent telangiectatic mats, occurring on the face or upper chest, were noted as present in 7, (masquerading as spider angiomas, but having no central arteriole, and upon expression, filling from the periphery).

Ordinary changes of lepromatous leprosy at time of presentation

Alopecia. Alopecia of the eyebrows was stated to be complete in 20, partial in 7, and was not noted as present or absent in 3. *Rhinitis.* Rhinitis was stated to be present in 25, and was not mentioned as present or absent in 5. Of the 25 with recognized rhinitis, the nasal septum was recorded as perforated in 9, as intact in 8, but was not mentioned as perforated or intact in 8. *Stocking-glove pattern sensory impairment (S-GPSI).* S-GPSI is a withering away of the sensations mediated by the type C sensory fibers, beginning distally and proceeding proximally. S-GPSI was recorded as present to some degree in 20, as absent in 7, not mentioned as present or absent in 3. *Motor impairment.* Motor impairment was present in only three: two patients with ulnar nerve involvement and one with common peroneal nerve involvement. The motor changes were disproportionately few compared with the magnitude of the sensory loss.

Routine laboratory findings at presentation

A mild anemia, normochromic and normocytic, was common. The average leukocyte count (normal range 3.7–11.6 × 1000/mm³) was 6.5 and the median was 6.3, among the 23 initial counts available for review. The highest count, 11.9, was

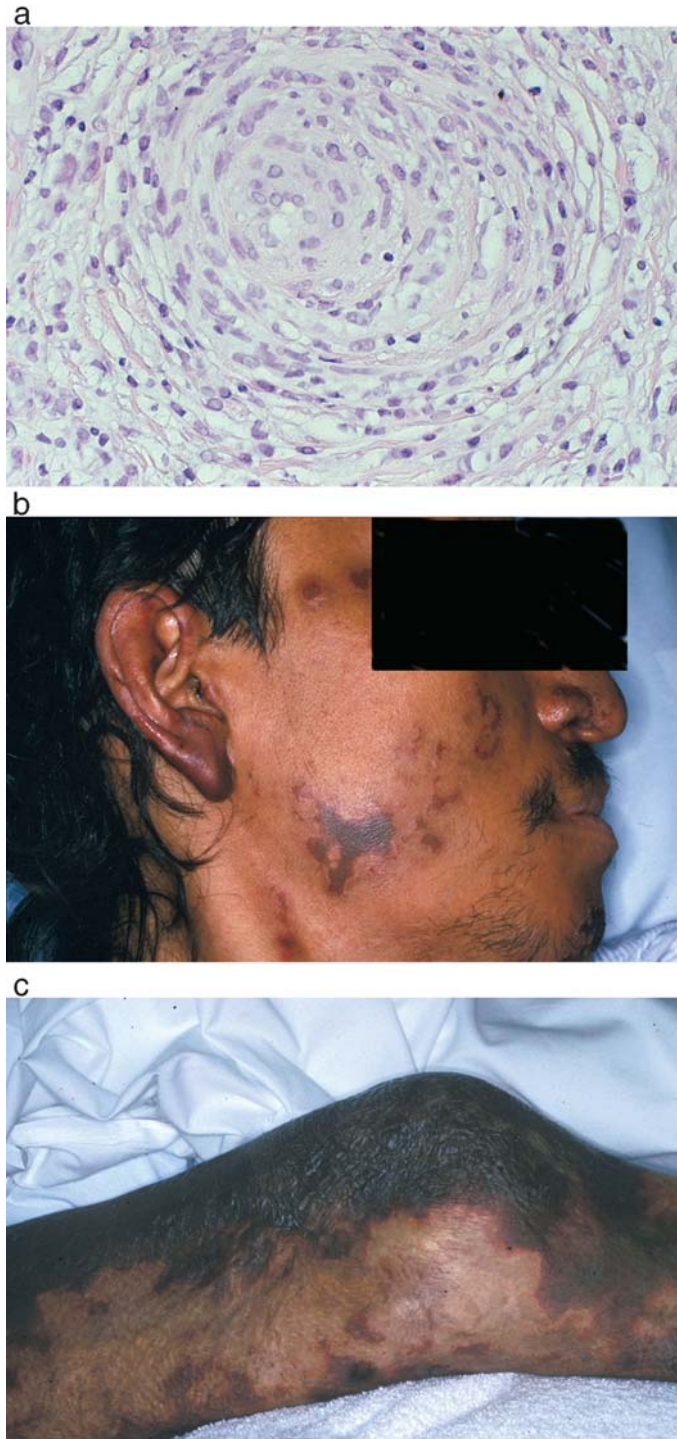


FIG. 3. From Case 5. a) In the center of the field is the largest of several vessels showing endothelial proliferation in the specimen from a palpable, but not visible, subcutaneous lesion obtained from the left thigh, 5 months before the onset of Lucio's phenomenon. 20 \times objective. b) Several lesions of various sizes on the face. Most show the characteristic serrated margins. c) The left knee with adjoining thigh and leg. The skin of the anterior portion is largely necrotic, but the serrations still evident, although farther apart than in "4b." Smaller lesions are evident posteriorly.

seen was in Case 5; the lowest was 3.1. Two counts were above and 2 were below the normal limits. Among 19 patients the cardiophilin-based serologic test for syphilis was reactive or weakly reactive in 15 in 3; of the 15 who were reactive, a *Treponema*-specific test was positive in 3. Hyperglobulinemia was common; in 18 patients the mean value was 4.8 gm/dl (normal 3.0–4.0), the median 5, the high 6.0 and the low 3.2. Serum albumin values were normal in 7, ranging from 3.8 to 4.6 gm/dl, clearly low in 3, ranging from 2.9 to 3.1, and extreme in 1, being 1.8 in the one patient with extensive infarcts, Case 5.

Response to treatment

Cessation of new infarcts. Of the 28 patients who presented to the clinic with Lucio's phenomenon, 19 were begun on dapsone alone. Ten of these 19 had no new infarcts after one week of follow-up. The remaining 9 continued to develop new infarcts for up to 5 months after starting treatment, 2 of which appeared to worsen before they improved. In one of the latter, new lesions ceased at 6 weeks, in association with the addition of daily rifampin.

Of the 7 previously untreated patients with Lucio's phenomenon who were started on a daily microbicidal agent (5 with rifampin, 1 with clarithromycin and 1 with minocycline) no new infarcts were seen after 7 days. (In these 7, a second daily agent was added within 2 weeks, so that all were receiving daily rifampin and daily clarithromycin or minocycline or dapsone.)

In two patients, followed for less than 4 weeks, no judgement was made as to treatment response.

Of the two patients who developed Lucio's phenomenon after initiating anti-microbial treatment in our clinic, the one, Case 2, who developed the reaction after discontinuing dapsone, responded without new lesions after resumption of dapsone. The other, Case 3, who developed Lucio's phenomenon reaction after 7 months of daily dapsone and rifampin is a glaring exception to the usually favorable outcome of microbicidal treatment. Her response to increased daily doses of prednisone was good, with new lesions ceasing within 2 weeks, and no recurrences in association with a slow tapering of the prednisone over 5 months.

Healing of ulcers. The ulcers usually healed within 4 months, in 3 patients taking as long as 8 months, *the length of time being roughly proportional to ulcer size.*

Follow up data

As of December 31, 2004, 14 patients were still being followed. Of the remainder, 15 had been lost, and 1 was deceased after 20 years of follow up. The length of follow up has been as brief as less than 1 month and as long as 35 years, mean 12.9 and median 10. Five were followed for 1.3 years or less.

Erythema nodosum leprosum

Thirteen of the 30 patients, 7 women and 6 men, were known to have developed ENL. In Case 2 ENL definitely preceded the onset of Lucio's phenomenon. Also Case 4, who might have had mild ENL 4 years prior to developing Lucio's phenomenon, did develop typical ENL 37 months after initiation of treatment with daily rifampin and dapsone. Excepting Case 2, the time of onset of the ENL ranged from 1 to 41 months after treatment was started in our clinic, median 21 months, average 22.1. Apart from this long median time of onset after initiation of treatment, the ENL in these patients did not differ from the ENL seen in ordinary lepromatous leprosy. No patient had lesions of ENL at the time of having new lesions of Lucio's phenomenon.

Long term morbidity

Excluding from analysis the 5 patients followed for 1.3 years or less, some degree of long-term morbidity has been experienced by 22 of the remaining 25 patients. Apart from ENL, the long-term morbidity observed in these patients arose from three mechanisms. Two of these mechanisms, S-GPSI and venous insufficiency, appear to be a part of Latapi's lepromatosis. The third mechanism producing long-term morbidity, scar formation, was the direct consequence of Lucio's phenomenon. Secondary to S-GPSI, 11 have experienced ongoing problems with pathologic plantar callosities and/or ulcers. Also secondary to S-GPSI, 5 have physical impairment in the hands, including fissures, ulcerations, and bone resorption. Morbidity from muscle weakness

or contracture was rare, occurring only in Case 5, and consisted of soft tissue contracture of the fascia and tendinous muscle in the left knee complex. *Recurrent* leg ulcers from venous insufficiency have been an ongoing problem for 10; 4 of these also having trophic problems in their feet. Scar formation led to hand and leg disabilities in one patient, Case 5.

Of the 14 who continue to be followed, 7 have a disability grade 1 or 2 according to the WHO grading system; 3 with a grade 1 disability and 4 with a grade 2 disability. Those with grade 2 disability include one with bilateral finger resorption, one with unilateral finger resorption, one with a resolving plantar ulceration, and one (Case 5) with right hand partial amputation due to ischemic changes.

Histologic changes

Histologic material obtained from lesions of Lucio's phenomenon was available for review in 22 patients. In 15 both H&E and adequately preserved Fite stained material was available, in 5 H&E only, and in 2 adequately preserved Fite stained tissue only. The common source of variation among specimens was the age of the lesion sampled. Most of the features have been described in detail and illustrated elsewhere^(25,26).

In all 22 patients the histologic material demonstrated foamy macrophages in the dermis in association with a few lymphocytes. The volume of the dermis occupied by the macrophages was small in 16 specimens, ranging from 2–10%, with a median value of 5%. In the remaining 6, the volume occupied was larger, ranging from 15–40%, with a median of 23%. In contrast, in biopsy specimens obtained from the indurated, but not visible subcutaneous plaques present before the Lucio phenomenon in Cases 3 and 5, the volume of the infiltrate occupied approximately 70 and 80% of the dermis, respectively. In their Lucio's phenomenon lesions the volume of the dermis occupied by macrophages was approximately 5–10% in both patients.

Epidermal necrosis was present in 18 and absent in 2 but could not be evaluated in 2 because of absent or insufficient epidermis. In the recent lesions, the necrotic epidermis was of normal thickness but manifested the absence of staining of nuclei, nuclear

ghosts, and early regeneration at the periphery, which was an epithelial tongue dissecting between the necrotic epidermis and the dermis. In older lesions, a new keratinizing epidermis was well developed, the necrotic epidermis now located above the new stratum corneum, and identifiable by compacted nuclear ghosts in the former prickle cell layer and melanin in the former basal cell layer (Fig. 1d). Similarly, necrosis of eccrine ducts and/or coils was present to some degree in 16 and absent in 6. In the oldest lesions, the necrotic epidermis was evidently exfoliated in the processing, and necrotic eccrine structures had been absorbed.

Intense passive congestion of vessels was present in 16 and absent in 4, but could not be evaluated in 2. This was usually confined to the superficial dermis, but was present in the deep dermis or subcutis in 3. Extravasation of erythrocytes was present in 12 and absent in 8, but could not be evaluated in 2.

In the medium sized vessels of the dermis and subcutis, endothelial proliferation was identified in 20, but could not present in 2. The proliferation ranged from mild to severe, frequently producing luminal occlusion, and was associated with thrombosis in 7. Inflammatory cells within these vessels were few in number, suggesting that the term "vasculosis" would be better than "vasculitis." The generally sparse inflammatory infiltrate was primarily lymphocytic. Neutrophils or neutrophilic dust were identified in 6 of 22 specimens, but were not associated with vascular changes, but instead were infiltrating necrotic areas in 5, and in the subcutis in 1. Fibrinoid change was present in 1 specimen.

Subcutaneous tissue was present in specimens from 18 patients. The area occupied by the subcutis was estimated to be 20% or less than that of the dermis in 5, 20–50% of that of the dermis in 6, and 50% or more of that of the dermis in 7, respectively. All 18 specimens had some degree of a lobular panniculitis. This was considered to be focal in 9, involving an estimated 15% or less of the panniculus, moderate in 5, involving 20–40%, and extensive in 4, involving 50–80%. The nature of the infiltrate varied considerably, 8 with leptotic macrophages and only a few lymphocytes, 9 with an ob-

vious mixture of leprotic macrophages and lymphocytes, and 1 with leprotic macrophages and neutrophils, the latter infiltrating between the lipocytes, apparently ignoring the vessels.

Concerning specimens with adequately preserved Fite stains, AFB and globi were found in macrophages in the dermis in all 17 specimens, as well as in the macrophages in the subcutis of the 15 specimens so endowed. In all 15 specimens with both endothelial proliferation and a Fite stain, bacilli in some of the proliferating endothelial cells were readily identified in all but 1, often with globi. Similarly, in all 17 specimens with a Fite stain, bacilli could be found in some non-proliferating endothelial cells. Bacilli were most difficult to find in endothelial cells in Case 3, probably the consequence of 7 months of continuous antimicrobial treatment

Histologic changes in large vessels, or vessels made large by pathologic changes, which we have chosen to call L-GV, were present in a total of 6 of the 22 (27%) patients with Lucio's phenomenon. In 2, Cases 3 and 5, the large vessel changes were observed only in non-necrotic specimens, obtained before the onset of Lucio's phenomenon. The fully developed L-GV consisted of endothelial proliferation, macrophages infiltrating the media, and macrophages infiltrating the adventitia. This fully developed change was found in Case 3, (Fig. 1a-c), and in lesions from 2 other Lucio's phenomenon patients. In one of these latter 2, the changes were active, (Fig. 4b, and in the other the changes were considered to be regressing (Fig. 4c). Incomplete expression of the L-GV consisted of endothelial proliferation with a variable degree of adventitial infiltration, as exemplified by Fig. 4a, also found in Figs. 2a and 3a. A similar L-GV was found in 6 of 70 (9%) of histologic specimens obtained from lesions of ENL (Fig. 4d), and as an incipient change in 3 of 51 (6%) non-reactional lepromatous patients (data not shown). These incipient changes were found in comparatively large subcutaneous vessels located near the dermis, and consisted of foci of endothelial proliferation in which AFB were identified, whereas none were found in non-proliferating endothelium. In Lucio-Latapi disease, ENL, and

non-reactional lepromatous leprosy, the vessels involved with L-GV were located in the subcutis, or what was subcutis prior to lepromatous infiltration or connective tissue proliferation. The L-GV involved vessels were largest in the Lucio-Latapi patients, smallest in the non-reactional lepromatous material, and of intermediate size in specimens of ENL.

DISCUSSION

The findings in the additional 20 patients with Lucio's phenomenon are in good accord with the initial report of 10 such patients⁽²⁵⁾ from this clinic. Hence the 30 patients have been taken together in this report. The additional 20 patients and the follow-up information add detail to the variations in the clinical picture without altering its broad outlines. The one exception to this accord is the finding of large vessel involvement in the subcutis, where it was not found in a previous report⁽²⁶⁾. This failure was not due to a lack of looking, but was probably the result of inadequate sampling of the subcutis with the 4mm in diameter punch biopsy instruments, then in routine use. This contrasts to the more generous amounts, and greater depths, obtained with the 6mm punches, in common use in our clinic for the past 2 decades, as exemplified by Fig. 1a.

What is being called L-GV is not a new pattern. For example, this pattern has been previously observed in non-reactional lepromatous specimens⁽⁷⁾, as well as in specimens of ENL^(17,27). Also it has been observed and illustrated in Lucio's phenomenon⁽¹⁰⁾, and was alluded to by Latapi and Zamora⁽¹⁵⁾. The pattern is similar to, if not the same as, that of the "leprous phlebitis" reported by Mukherjee and his associates^(19,20).

L-GV occurs in larger vessels, or in vessels made large by pathologic changes, primarily in the subcutis. L-GV, and what is interpreted as its variants, was present in 4 of the specimens from 22 Lucio's phenomenon patients with material available for review, and in 2 of the 3 pre-Lucio's phenomenon specimens available for review. However, the importance of L-GV to the pathogenesis of Lucio infarcts, if any, is not known.

An argument can be made to support the hypothesis that the L-GV is not important

TABLE 2. Major histologic findings in 15 Lucio's phenomenon lesions, with both H&E and adequately preserved Fite stained material, with special emphasis on subcutaneous changes.

	Area of subcutaneous tissue expressed as % of dermis	% of subcutaneous tissue infiltrated	Lepromatous-granulomatous vasculitis	Epidermal necrosis	Intense passive congestion	Endothelial proliferation	Endothelial proliferation with lumen occlusion	PMNS infiltrating lesion	Case # in text
A	>50	75	Y	Y	Y	Y	Y	Y	
B	>50	15	N	Y	Y	Y	Y	Y	
C	>50	40	Y	N	Y	Y	Y	N	9
D	0	NA	NA	Y	N	Y	N	N	
E	<20	60	N	Y	N	Y	N	N	
F	20-50	5	N	Y	Y	Y	Y	N	
G	>50	30	Y	Y	Y	Y	Y	Y	4
H	20-50	5	N	Y	Y	Y	Y	Y	3
I	0	NA	NA	N	N	N	N	N	8
J	20-50	30	Y	Y	Y	Y	N	Y	
K	<20	10	N	Y	Y	N	N	N	
L	0	NA	NA	Y	Y	Y	N	N	
M	0	NA	NA	Y	Y	Y	Y	Y	
N	20-50	5	N	Y	Y	Y	N	N	5
O	<20	5	N	Y	N	Y	Y	N	

Major histologic findings in 15 Lucio's phenomenon lesions, with both H & E and adequately preserved fite strained material, with special emphasis on subcutaneous changes.

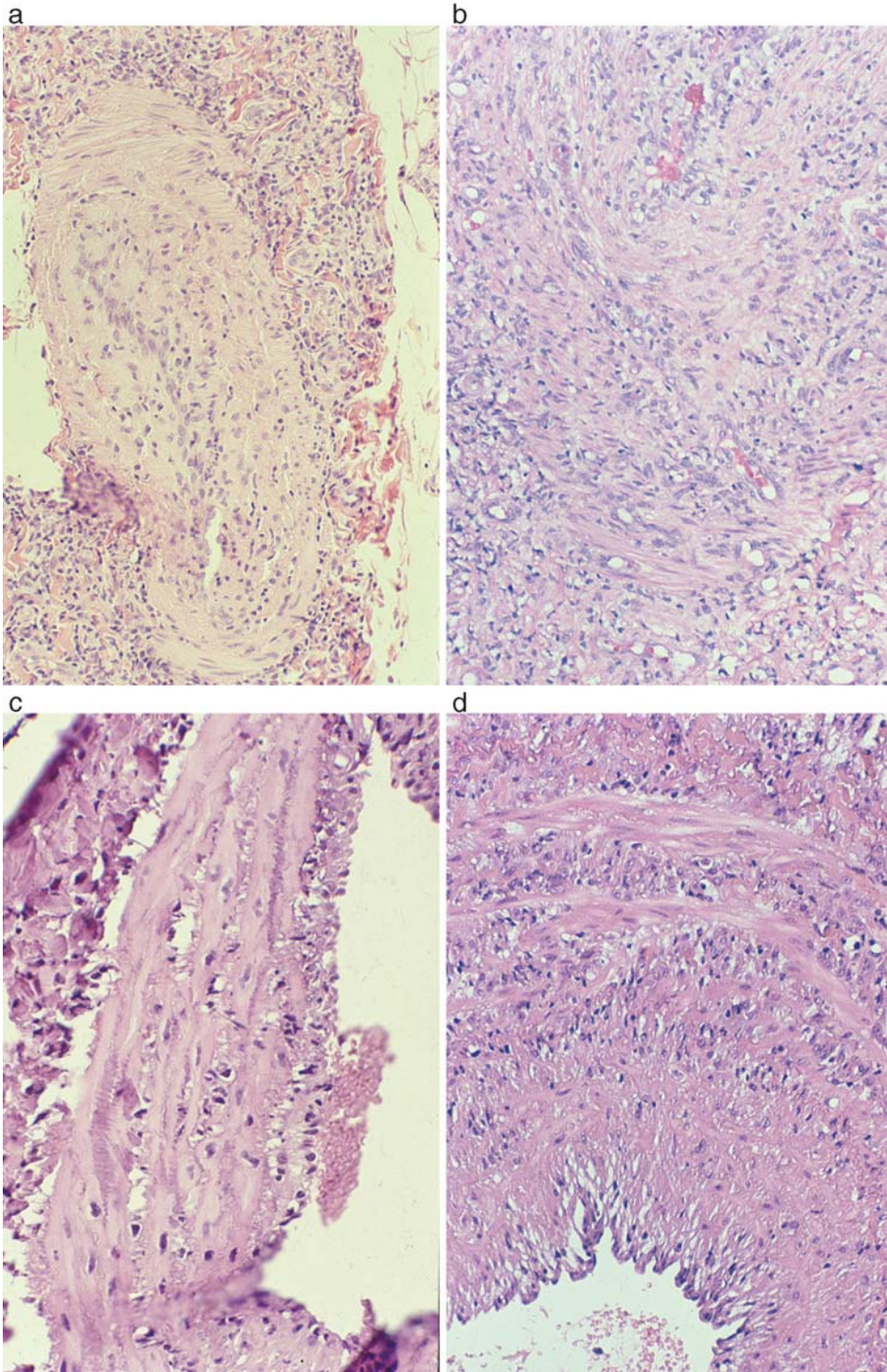


FIG. 4 (a). From Case 9, a Lucio's phenomenon lesion. An obliquely sectioned, subcutaneous vessel showing extensive endothelial proliferation, and heavy adventitial infiltration, but little disturbance in the smooth muscle bundles. 20× objective. b) A panvasculitic vessel from the subcutis of a Lucio's phenomenon lesion showing intimal proliferation, a chaotic infiltration of macrophages among the smooth muscle bundles, and infiltration in the adventitia. c) A high power view of a large subcutaneous vessel which shows modest endothelial change,

to the pathogenesis of Lucio's phenomenon. Because the pattern of L-GV also has been seen in lesions of ENL^(17,27) (Fig. 4d), as well as in non-reactional lepromatous leprosy⁽⁷⁾, and because it has similarities to the leprosy phlebitis reported by others^(19,20) it is not specific for either Latapi's lepromatosis or the Lucio reaction. Also, because its presence in Cases 3 and 5 were not directly associated with necrotic lesions, it is not a change necessarily leading to necrosis. In this context L-GV is most easily interpreted as part of the vascular changes known to be associated with leprosy, from large muscular arteries, to arterioles, to capillaries, to venules, and on to large veins. Such changes have been reported by, among others, Fite⁽¹²⁾, Coruh and McDougall⁽⁷⁾, Kaur, *et al.*⁽¹⁴⁾, Bansai, *et al.*⁽⁵⁾, and Mukherjee and his associates^(19,20).

An argument can be made to support the contrary hypothesis of importance for L-GV in pathogenesis. Anoxia is a final cause of tissue necrosis, however diverse the responsible mechanisms. In patients with Lucio-Latapi disease, anatomical changes with the potential of leading to anoxia have been demonstrated at three levels of the vascular tree. Best described is the endothelial proliferation with lumen occlusion, with or without thrombosis formation, occurring in the mid-sized vessels in the dermis of the necrotic lesions^(25,26,31), as confirmed in the present study. Also, swelling and parasitization, with lumen occlusion, of capillary endothelium has been found by electron microscopy in 3 of 3 specimens of clinically normal skin⁽³³⁾, i.e., Latapi's lepromatosis, from patients with Lucio's phenomenon, and could well be widespread. The subcuticular L-GV found in the present study in both Lucio's phenomenon and Latapi's lepromatosis is a third anatomical change that could contribute to anoxia; this change, if focal, could also be more prevalent than has been observed. All of these changes acting synchronously might result in an ischemia

sufficient to produce necrosis, whereas any one by itself would be less likely do so. In addition, the circulating immune complexes associated with Lucio's phenomenon⁽²³⁾ might interact with the anatomical changes in ways that lead to necrosis.

Perhaps the changes of the L-GV are better developed Latapi's lepromatosis, because this difficult to diagnose lepromatous condition may give more time for bacterial proliferation and for a granulomatous vasculitis to develop.

Three retrospective findings were not anticipated, but emerged only when the comparatively large numbers of patients reported here were gathered together. 1) The near parity of the genders is in contrast to the expected male preponderance, 2 to 1, in lepromatous disease⁽²¹⁾. 2) The absence of S-GPSI in 7 patients was not anticipated to be this common in Latapi's lepromatosis. 3) The median time of onset of ENL, 21 months after initiating treatment, appears to differ considerably, and perhaps significantly, from the 12 months median time observed in this clinic (unpublished data). Good explanations for these three unexpected findings are not available.

Clinically, the ischemic infarcts of Lucio's phenomenon were of a uniform character, varying in size and extent, but always of the same kind, or, in other words, a monomorphic response. Accompanying ulcers, erosions and bullae, were clearly secondary to the infarct.

The report by Diogenes, *et al.*⁽⁹⁾ and our experience with Case 2, raises the possibility of the diagnosis of Latapi's lepromatosis in the absence of Lucio's phenomenon. Usually a diagnosis of Latapi's lepromatosis is made after the fact of Lucio's phenomenon. Which findings or combination of findings might be considered as criteria for a diagnosis of Latapi's lepromatosis in the absence of Lucio's phenomenon?

Either of two findings could be regarded as a *sine qua none* for this diagnosis. Dif-

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spotty infiltration in the wall, and involvement of the adventitia. The process appears to be old and regressing. This impression is supported by the absence of a defined muscular layer, and by the several lines of "hash marks" at different levels in the wall, suggesting repeated reduplication of the internal elastic lamina, (block not available for definitive staining). 40x objective. d) A high power view of a subcutaneous vessel in an ENL lesion, giving an exemplary demonstration of the features of lepromatous-granulomatous vasculitis (L-GV), that is, endothelial proliferation, infiltration of macrophages between smooth muscle bundles, and adventitial infiltration. 20x objective.

fuse non-nodular infiltration is one; the other is heavy endothelial parasitization by *M. leprae*. Neither finding is specific for Latapi's lepromatosis, but the presence of dermal nodules or the absence of endothelial parasitization virtually excludes the possibility of Latapi's lepromatosis.

Three other distinct findings could be regarded as highly suggestive of Latapi's lepromatosis. These are 1) telangiectasias, either eruptive or as mats on the face and chest, 2) palpable but not visible subcutaneous plaques, and 3) as manifestations of diffuse infiltration, widening of the nasal root, poorly defined induration of the facial cheeks, with or without erythema, and swelling of the backs of the hands.

In the presence of the two "*sine qua non's*" other common changes could be regarded as supportive of a diagnosis of Latapi's lepromatosis. These include complete eyebrow and or eyelash alopecia, nasal septum perforation, and significant S-GPSI with little motor change.

In lepromatous patients who present without nodular change and who have heavy parasitization of endothelial cells, (in our experience those who present with spontaneous ENL⁽²⁴⁾), findings which point away from a diagnosis of Latapi's lepromatosis include normal eyebrows and eyelashes, mild or absent rhinitis, and ocular involvement.

Five biopsy specimens obtained before the onset of Lucio's phenomenon were examined by one of us, three being available for review. In all four with a Fite stain, endothelial parasitization by *M. leprae* was evident. As demonstrated by hematoxylin and eosin, three histologic patterns were identified, and each pattern could be related to the clinical findings at the biopsy site. In Cases 1 and 2, where the specimen chosen was from clinically normal skin, the infiltrate was scant, and with little if any other inflammatory change, aptly described as "apparently normal." In Case 4, with the clinical findings of erythematous nodules, a distinct lymphocytic infiltrate was associated with foamy macrophages. In cases 3 and 5, the specimens being obtained from not visible, non-tender, indurated subcutaneous plaques, well developed vascular changes were associated with a heavy infiltrate of macrophages.

Two of the 3 pre-Lucio specimens available for review, from cases 3 and 5, demonstrated endothelial proliferation with lumen occlusion, and were obtained 7 and 5 months, respectively, before the onset on Lucio's phenomenon. In the third specimen, obtained 4 years before the onset of the Lucio's phenomenon, no such vascular change was evident.

The most conspicuous disagreement in the literature concerning Lucio's phenomenon is in regard to its histologic pattern, leukocytoclastic vasculitis (LCV): LCV yes^(2, 18, 31) or LCV no^(10, 22, 25)? The review of our biopsy material is in accord with our previous conclusion that the histologic pattern is not that of LCV⁽²⁵⁾. The most likely explanation for the disagreement is differing criteria for what constitutes LCV. Another possibility is the intellectual difficulty in dissociating or uncoupling the idea of a putatively immune complex disorder of skin⁽²³⁾ from the histologic pattern of LCV. The histologic pattern called LCV is that found in "palpable purpura" and is the same whatever disease may be producing the lesions of "palpable purpura." The lesions of "palpable purpura" were not found in any of these 30 patients.

Clinically, a variety of septic infarcts and thrombotic syndromes⁽⁴⁾ may mimic the infarct of Lucio's phenomenon, being hemorrhagic and having serrated borders. In addition, one recent case report gives strong evidence that other vasculitic conditions may closely mimic Lucio's phenomenon. Tang and Yosipovitch⁽³²⁾, in their report of an acute Churg-Strauss syndrome, have in their clinical photograph (their fig. 1) illustrated changes perfectly consistent with the serrated, hemorrhagic infarcts of the Lucio reaction. In the same report is a photomicrograph (their fig. 2) which shows extravasation of erythrocytes, and in our interpretation, congestion of superficial vessels, and a necrotic epidermis, identified in the legend as "scale crust," a pattern looking much like our Fig. 1d. Viewed in this perspective, the second episode of infarctions in Case 9, would be best regarded as being a Lucio's phenomenon-like tissue response of unknown cause, not a true Lucio's phenomenon.

Comfort may be taken from this series, where by the time of development of

Lucio's phenomenon, overt clinical signs of lepromatous leprosy, without exception, were present. Conversely, anxiety may arise from this series, where, in some cases, the diagnosis of leprosy was not made until the Lucio phenomenon occurred, even though preceding characteristic signs and symptoms, although seen and heard by physicians, were not interpreted as suggesting the possibility of leprosy.

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