Vasculitis in erythema induratum of Bazin: A histopathologic study of 101 biopsy specimens from 86 patients

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Background: Erythema induratum of Bazin is a mostly lobular panniculitis. There is considerable controversy in the literature about whether or not vasculitis is a histopathologic requirement to establish the diagnosis of erythema induratum of Bazin. Even accepting vasculitis as a histopathologic criterion, there is no agreement about the nature and size of the involved vessels.

Objective: The main goal of our study was to investigate whether or not vasculitis was present in a large series of cases of erythema induratum of Bazin and, when vasculitis was found, to determine the nature and localization of the involved vessels.

Methods: We studied 101 skin biopsy specimens from 86 patients with clinicopathologic diagnosis of erythema induratum of Bazin. Histopathologic criteria required in each case to be included in this study were: (1) a mostly lobular panniculitis with necrotic adipocytes at the center of the fat lobule; (2) inflammatory infiltrate within the fat lobule mostly composed of neutrophils in early lesions and granulomatous infiltrate in fully developed lesions; (3) significant fat necrosis; and (4) absence of other histopathologic findings that allow a specific diagnosis of other lobular panniculitis different from erythema induratum of Bazin. We also recorded the nature of the inflammatory cells involving the fat lobule, and the lesions were classified into two main categories: (1) early lesions, when the inflammatory infiltrate was mainly composed of neutrophils, with or without leukocytoclasis; and (2) fully developed lesions, when histiocytes and lipophages were the predominant inflammatory cells within the involved fat lobule.

Results: Some type of vasculitis was evident in 91 cases (90.09%). A total of 47 biopsy specimens (46.5%) showed a mostly lobular panniculitis with necrotizing vasculitis involving the small vessels, probably venules, of the center of the fat lobule. Thirteen biopsy specimens (12.8%) showed a mostly lobular panniculitis with vasculitis involving both large septal veins and small vessels, probably venules, of the center of the fat lobule. Twelve biopsy specimens (11.8%) showed a mostly lobular panniculitis with vasculitis involving large septal veins, with no involvement or other septal or lobular vessels. Ten biopsy specimens (9.9%) showed a mostly lobular panniculitis with vasculitis involving large septal veins, both arteries and veins, and necrotizing vasculitis involving the small vessels, probably venules, of the center of the fat lobule. Nine biopsy specimens (8.9%) showed a mostly lobular panniculitis with vasculitis involving large septal vessels, both arteries and veins, but with no involvement of the small blood vessels of the center of the fat lobule. Finally, 10 biopsy specimens (9.9%) showed a mostly lobular panniculitis without evidence of septal or lobular vasculitis in serial sections. Associated diseases included history of extracutaneous tuberculosis (including tuberculosis of the lung, lymph nodes, kidney, or bowel) in 12 cases (13.9%), previous episodes of superficial thrombophlebitis of the lower legs in 3 cases (3.72%), rheumatoid arthritis in one case (1.16%), Crohn disease in one case (1.16%), chronic lymphocytic leukemia in two cases (2.32%), hypothyroidism in two cases (2.32%), and positive serology for hepatitis B virus in 4 cases (4.65%) and for hepatitis C virus in 5 cases (5.81%).

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**Limitations:** Serial sections were not performed in all cases. At least 10 sections were studied in each case. When vasculitis was evident in some of these first 10 sections, no further sections were cut, but when histopathologic features of vasculitis were not found in the first 10 sections, serial sections throughout the specimen were performed looking for vasculitis. Because some type of vasculitis was evident in the first 10 sections of 91 cases, serial sections were performed only in the remaining 10 cases and they failed to demonstrate clear-cut histopathologic features of vasculitis. On the other hand, this is a retrospective study that was performed from the histopathologic slides of our files, and only the clinical information contained in the report accompanying the biopsy specimen could be recorded.

**Conclusions:** In our experience, vasculitis is present in most lesions of erythema induratum of Bazin, and the nature, location, and size of the involved vessels is, from more to less frequent, as follows: (1) small venules of the fat lobule; (2) both veins of the connective tissue septa and venules of the fat lobule; (3) only veins of the connective tissue septa; (4) veins and arteries of the connective tissue septa and venules of the fat lobule; and (5) veins and arteries of the connective tissue septa. However, in some cases with all clinicopathologic features of erythema induratum of Bazin vasculitis could not be demonstrated with serial sections throughout the specimen and, therefore, the presence of vasculitis should be not considered as a criterion sine qua non for histopathologic diagnosis of erythema induratum of Bazin. (J Am Acad Dermatol 2008;59:839-51.)

Currently, the terms “erythema induratum of Bazin” and “nodular vasculitis” are used as synonyms by a majority of authors to describe the most common variant of mostly lobular panniculitides with vasculitis. This has not always been the case, however. This form of panniculitis was originally described by Bazin1 in 1861, as subcutaneous indurate erythematous plaques appearing mainly on the back of the lower aspect of legs of middle-aged women. He classified the process as one of the erythematous benign scrofulids, using “scrofulids” as a descriptive term to refer to deep erythematous nodules, and it seems that he did not consider this panniculitis as a tuberculid. The link between tuberculosis and erythema induratum was emphasized later, around 1900, mostly by French dermatologists who included erythema induratum within the spectrum of the tuberculids.2 Almost simultaneously, identical clinical cases with no evidence of tuberculosis were reported by English authors,3,4 which led later to the development of the concept of erythema induratum as nontuberculous in origin by Whitfield.5 In 1945, Montgomery et al6 in the United States proposed the term “nodular vasculitis” for Whitfield erythema induratum and described its clinical and histopathologic features as different from those of erythema induratum of Bazin. Since then, most textbooks of dermatology described erythema induratum of Bazin, erythema induratum of Whitfield, and nodular vasculitis as 3 different entities.7 Still, some current authors have proposed keeping the name “erythema induratum of Bazin” for those cases in which a causative relationship with tuberculosis is demonstrated and refer to the remainder of cases as nodular vasculitis. In recent years, however, there seems to be a consensus considering erythema induratum of Bazin and nodular vasculitis as the same entity,8,9 an opinion that we shared.10 Like erythema nodosum, erythema induratum of Bazin is currently considered to be a reactive disorder related to several causative factors, one of which may be tuberculosis, especially in some geographic areas.11 In our country, tuberculosis is by far the most important causative factor for erythema induratum of Bazin, and recent polymerase chain reaction investigations have demonstrated Mycobacterium tuberculosis DNA in 77% of the cutaneous biopsy specimens of patients with this variant of panniculitis.12 Although the frequency varies from some geographic areas to others, in many countries tuberculosis is still the main causative factor for erythema induratum of Bazin.13-20 In contrast, in those countries with low prevalence of tuberculosis, this type of panniculitis may be a reactive process as a result of other causative factors such as obesity, cold climate, chronic venous insufficiency, or history of thrombophlebitis of the lower limbs.

Typical erythema induratum of Bazin is a disease of middle-aged obese women in whom erythematous subcutaneous nodules and plaques appear on the back of the lower aspects of the legs. Erythrocyanosis, heavy columnlike calves, erythema surrounding follicular pores, and cutis marmorata are frequently associated changes and may be predisposing factors. Although nonulcerated lesions may heal without scarring, often subcutaneous nodules become adherent to the skin surface and ulcerate. Healing of these ulcers is usually a slow process resulting in atrophic scars that allow retrospective diagnosis in nonactive cases. Erythema induratum of Bazin is more frequent in obese women with some degree of venous insufficiency of the lower extremities, and subcutaneous nodules with ulceration develop mostly during the winter months. Lesions
are usually tender but may be indolent or painful only on pressure. The course is protracted and recurrent episodes over years, even decades, are common. Individual lesions tend to involute, but new crops appear at irregular intervals. Patients with erythema induratum of Bazin are otherwise in good health.

From a histopathologic point of view, erythema induratum of Bazin is a mostly lobular panniculitis. At an early stage, the fat lobules are punctuated throughout by discrete collections of inflammatory cells, mostly neutrophils. There may be extensive necrosis of the adipocytes of the fat lobule. These necrotic adipocytes call for histiocytes that ingest lipid and become foamy. Epithelioid histiocytes, multinucleated giant cells, and lymphocytes contribute to the granulomatous appearance of the inflammatory infiltrate in fully developed lesions of erythema induratum of Bazin. When intense vascular damage is present, extensive areas of caseous necrosis appear and the lesions show all the histopathologic attributes of a tuberculosis granuloma. Caseous necrosis may extend to the overlying dermis and secondarily involve the epidermis with ulceration and discharge of liquefied necrotic fat.

Controversy persists in the literature about whether or not vasculitis is a histopathologic requirement to establish the diagnosis of erythema induratum of Bazin. Even accepting vasculitis as a histopathologic criterion, there is no agreement about the nature of the involved vessel. Some investigators consider vasculitis as a characteristic histopathologic finding, but they fail to establish the nature and the size of the involved vessels. When the nature of the involved vessel is specifically stated, some authors believe that they are arteries, whereas other authors favor a venous involvement, and still others consider that both arteries and veins are involved. The main goal of our study was to investigate whether or not vasculitis was always present in our cases of erythema induratum of Bazin and, when vasculitis was found, to determine the nature and localization of the involved vessels. This study also describes the histopathologic features of the largest published series of erythema induratum of Bazin.

METHODS

Skin biopsy specimens of 86 patients with clinico-pathologic diagnosis of erythema induratum of Bazin were retrieved from the archives of the departments
of dermatology at Hospital del Mar, Barcelona, Spain (22 biopsy specimens from 16 patients: 12 patients with one biopsy specimen, 2 patients with two biopsy specimens, and 2 patients with three biopsy specimens) and Fundación Jiménez Díaz, Madrid, Spain (79 biopsy specimens from 70 patients: 63 patients with one biopsy specimen, 5 patients with two biopsy specimens, and two patients with 3 biopsy specimens). From a clinical point of view, all patients showed characteristic cutaneous lesions, mostly consisting of erythematous nodules on the back of the legs. Eighty patients showed positive cutaneous delayed hypersensitivity reaction to purified protein derivative (positive Mantoux test result), whereas 3 patients showed negative Mantoux test result and this test was not performed in another 3 patients. Clinical data were obtained from patient’s medical records and, in each case, the demographic data, including age and sex, location of the lesions, and associated diseases, were recorded.

From a histopathologic point of view, the following criteria were required to include each case in this study: (1) a mostly lobular panniculitis with necrotic adipocytes at the center of the fat lobule; (2) inflammatory infiltrate within the fat lobule mostly composed of neutrophils in early lesions and granulomatous infiltrate in fully developed lesions; (3) significant fat necrosis; and (4) absence of other histopathologic findings that allow a specific diagnosis of other lobular panniculitis different from erythema induratum of Bazin. Other types of mostly lobular panniculitis, including pancreatic panniculitis, alpha-1-antitrypsin deficiency-associated panniculitis, sclerosing panniculitis, and lupus panniculitis were ruled out on the basis of the histopathologic findings. Infective panniculitis was ruled out when Gram and periodic acid–Schiff stains failed to demonstrate micro-organisms in cases of a mostly neutrophilic lobular panniculitis. Foreign body material was ruled out throughout polarization in those cases of a
mostly lobular panniculitis with granulomatous infiltrate.

Histopathologic criteria required to establish a diagnosis of vasculitis included swelling of endothelial cells, leukocytoclasis, fibrinoid changes in vessel walls, and neutrophils in and around vessel walls. This vasculitis, the main goal of our study, was not initially considered as criterion sine qua non to include a case in this study when all other characteristic histopathologic features of erythema induratum of Bazin were present. However, because vasculitis was evident in most cases, we recorded in all those cases the nature, size, and localization of the involved blood vessel. We also recorded the nature of the inflammatory cells involving the fat lobule, and the lesions were classified into two main categories: (1) early lesions, when the inflammatory infiltrate was mainly composed of neutrophils, with or without leukocytoclasis; and (2) fully developed lesions, when histiocytes and lipophages were the predominant inflammatory cells within the involved fat lobule. Skin biopsy specimens were fixed in 10% buffered formalin, processed, and paraffin embedded according to conventional techniques. Hematoxylin-eosin stain was performed in sections of each case and, in selected cases, elastic tissue stain with orcein was performed to determine the nature of the vessels involved by vasculitis. At least 10 sections were studied in each case. When vasculitis was evident in some of these first 10 sections, no further sections were cut, but when histopathologic features of vasculitis were not found in the first 10 sections, serial sections throughout the specimen were performed, looking for vasculitis.

RESULTS

Briefly, the clinical features of the 86 patients were the following: 69 patients were female and 17 were male. Age ranged from 23 to 81 years (median 55.8 years). All patients showed erythematous subcutaneous nodules in the back of the legs, and in 10 cases there were also some scattered erythematous nodules on the front of the legs or on the thighs. Two female patients also showed erythematous nodules involving the buttocks and one female patient had lesions involving both the lower and upper limbs and the trunk. Most patients had new bouts of lesions or worsening of pre-existing nodules during the winter. Associated diseases included history of extracutaneous tuberculosis (including tuberculosis
of the lung, lymph nodes, kidney, or bowel) in 12 cases (13.95%), previous episodes of superficial thrombophlebitis of the lower legs in 3 cases (3.72%), rheumatoid arthritis in one case (1.16%), Crohn disease in one case (1.16%), chronic lymphocytic leukemia in two cases (2.32%), hypothyroidism in two cases (2.32%), and positive serology for hepatitis B virus in 4 cases (4.65%) and for hepatitis C virus in 5 cases (5.81%).

Histopathologically, some type of vasculitis was evident in the first 10 sections of 91 cases (90.09%). In the remaining 10 biopsy specimens (9.9%), serial sections failed to demonstrate clear-cut histopathologic features of vasculitis. In all, 47 biopsy specimens (46.5%) showed a mostly lobular panniculitis with necrotizing vasculitis involving the small vessels, probably venules, of the center of the fat lobule. There was no involvement of the septal vessels (small or large septal vessels). This vasculitic pattern was seen both in early lesions (with neutrophilic infiltrate in the fat lobule, 23 cases [22.7%]) (Fig 1) and in fully developed lesions (with granulomatous infiltrate within the fat lobule, 24 cases [23.7%]) (Fig 2). Thirteen biopsy specimens (12.8%) showed a mostly lobular panniculitis with vasculitis involving both large septal veins and small vessels, probably venules, of the center of the fat lobule. This vasculitic pattern was seen both in early lesions (5 cases [4.9%]) (Fig 3) and in fully developed lesions (8 cases [7.9%]) (Fig 4). Twelve biopsy specimens (11.8%) showed a mostly lobular panniculitis with vasculitis involving large septal veins, with no involvement or other septal or lobular vessels. This vasculitic pattern was only seen in biopsy specimens of early stages of erythema induratum of Bazin (Fig 7). Nine biopsy specimens (8.9%) showed a mostly lobular panniculitis with vasculitis involving large septal vessels, both arteries and veins, and necrotizing vasculitis involving the small vessels, probably venules, of the center of the fat lobule. This vasculitic pattern was seen both in biopsy specimens of early lesions (8 cases [7.9%]...
(Fig 8) and in fully developed lesions (one biopsy specimen [0.9%]). In all cases with some type of vasculitis (91 cases, 90.09%), vascular damage was seen in all of the 10 performed sections, it was located at the center of the panniculitic process (Figs 1 to 8), and there was not any case in which vasculitis was identified without inflammation of the surrounding subcutaneous tissue. We did not find any relationship between the presence of histologic ulceration and the nature of the inflamed vessels, because histologic ulceration was evident only in 8 cases (7.9%), and two of them (1.9%) showed vasculitis involving large arteries and veins of the septa of the subcutaneous septa, whereas the remaining 6 ulcerated cases (5.94%) showed vasculitis involving the small blood vessels of the fat lobule without any damage of the large arteries or veins of the connective tissue septa. Extravasated red cells were seen in the vicinity of the inflamed vessels in most cases. Finally, 10 biopsy specimens (9.9%), showed a mostly lobular panniculitis without evidence of septal or lobular vasculitis in serial sections and this pattern with no vasculitis was seen both in early lesions (two cases [1.9%]) (Fig 9) and in fully developed lesions (8 cases [7.9%]) (Fig 10). From these 10 biopsy specimens without evidence of vasculitis in serial sections, two biopsy specimens were from the same patient. Another 3 patients with two biopsy specimens showed septal large venous vasculitis in one biopsy specimen, but no evidence of vasculitis was seen in the other one. The remaining 5 biopsy specimens without vasculitis belonged to patients with only one biopsy specimen. Table I summarized the histopathologic features of our series.

**DISCUSSION**

In our experience, veins of the connective tissue septa and small venules of the fat lobule are the most common blood vessels affected by vasculitis in erythema induratum of Bazin, because 90.9% of our cases showed some type of venous vasculitis, whereas arteries and arterioles were only involved in 18.8% of the cases, and in all these cases with arterial vasculitis, some type of venous vasculitis was concomitantly identified. In other words, no case with exclusive arterial or arteriolar vasculitis was found in our series. It was also remarkable that arterial and
arteriolar vasculitis was mostly seen in biopsy specimens with a predominant neutrophilic infiltrate involving the fat lobule (there was only one case with involvement of both large arteries and veins of the septa and granulomatous infiltrate at the fat lobule), which probably indicates that involvement of arterial vessels of the subcutaneous fat is only present in early stages of the evolution of the lesions. Curiously enough, in 10 biopsy specimens of this series, which showed all stereotypical clinicopathologic features of erythema induratum of Bazin, serial sections throughout the specimens failed to identify clear-cut histopathologic features of vasculitis. Furthermore, in one patient of our series, who showed all classic clinicopathologic features of erythema induratum of Bazin, two biopsies were performed from two separate episodes of the panniculitic process and no evidence of vasculitis was found in either of the biopsy specimens, whereas another 3 patients with two biopsy specimens showed vasculitis of the large septal veins in one biopsy specimen, but no histopathologic features of vasculitis could be identified in the other one. Therefore, although rare, some cases of erythema induratum of Bazin may show all classic clinicopathologic features of the disorder, except vasculitis, and thus the term “erythema induratum of Bazin” is more accurate than “nodular vasculitis” to name this process.

A review of the literature and of the most famous textbooks of dermatology and dermatopathology reveals considerable variation about whether or not vasculitis is present in the cutaneous lesions of erythema induratum of Bazin. Even in those cases in which vasculitis is accepted by the investigators as a characteristic histopathologic feature, controversy exists about the size, the nature, and the location of the involved vessels. Thus, in some textbooks, vasculitis is described as a characteristic histopathologic finding of erythema induratum of Bazin, but the nature, size, and location of the involved vessels are not established. Ackerman believes that “nodular vasculitis is so named because clinically the lesion is a nodule, and microscopically it is an arteritis. This severe vasculitis, in which neutrophils, lymphocytes, and histiocytes participate, involves a muscular artery and eventuates in ischemic changes within the lobule or portions of the lobules supplied by

Fig 6. Fully developed lesion of erythema induratum of Bazin showing mostly lobular panniculitis with vasculitis involving large septal veins, with no involvement of other septal or lobular vessels. A, Scanning power. B, Higher magnification showing lobular panniculitis. C, Granulomatous inflammatory infiltrate involving fat lobule. D, Vasculitis involving large vein at septa. (A to D, Hematoxylin-eosin stain; original magnifications: A, ×10; B, ×40; C and D, ×200.)
the affected artery." In our opinion, however, the involved vessel illustrated by Ackerman\(^2\) as an example of nodular vasculitis (erythema induratum of Bazin) is better interpreted as a vein rather than as an artery. In our view, this is a frequent mistake in the histopathologic study of the panniculitides and vasculitides involving the subcutaneous fat of the lower legs, because in these areas the veins of the connective tissue septa of the subcutis show a thicker and more compact muscular layer than the veins of the subcutis in other areas of the skin and they often are misinterpreted as arteries.\(^2\) Black,\(^2\) in agreement with Ackerman,\(^2\) also considers that arteries are the vessels mainly involved in the lesions of erythema induratum of Bazin. In contrast, Degos,\(^2\) in his textbook of dermatology, considered that erythema induratum of Bazin is a mostly lobular panniculitis with vasculitis mainly involving the veins of the connective tissue septa of the subcutis. A venous vasculitis is also postulated by McKee et al\(^2\) in their last edition of *Pathology of the Skin*, because they wrote: "The histologic features of nodular vasculitis combine septal and lobular changes with the presence of vasculitis being a sine qua non (Fig. 9.79). In a biopsy from an established lesion, the septa are widened and chronically inflamed (Fig. 9.80). Acute vasculitis, affecting veins and venules with a heavy inflammatory cell infiltrate consisting of neutrophils, lymphocytes and histiocytes is typically present, sometimes accompanied by vessel wall necrosis and thrombosis." McKee et al\(^2\) failed to establish the location of the involved vessels, but because they considered that both veins and venules were involved, we deduce that they interpreted that the venous vessels of both the connective tissue septa and the fat lobule were involved. Patterson\(^7\) considered that "vasculitis is frequently present and can involve small or medium-size vessels (Fig. 100.8). It may be predominantly neutrophilic, lymphocytic or granulomatous," but he did not establish whether the involved vessels were arterial or venous, or whether the vasculitic process involved the septa, the fat lobule, or both. Other authors believe that both venous and arterial blood vessels are involved in lesions of erythema induratum of Bazin, but discrepancy still persists about the size of the vessels, because whereas some of them considered that large veins and arteries are affected,\(^2\) others stated that

only small and medium arteries and veins are involved, and finally others described involvement of all sizes of arteries and veins. Curiously, even within the same textbook, there are discrepancies between different chapters, because in a textbook edited by Farmer and Hood, *Pathology of the Skin*, Olsen considered in the chapter of vasculitis that nodular vasculitis was "a panarteritis involving a small to medium-sized artery, typically in the subcutis," whereas Dahl and Su, in their chapter of panniculitis, dealing with erythema induratum of Bazin-nodular vasculitis, described that "vasculitis, usually lymphohistiocytic, involves venules, veins, and even arterioles and small arteries in the pannicular septae."

In a recent series of 20 patients with erythema induratum of Bazin-nodular vasculitis, the lesions were histopathologically classified into two types: focal panniculitis (type I) and diffuse panniculitis (type II). In type I erythema induratum of Bazin-nodular vasculitis, only one artery or a small blood vessel within the fat lobule was involved by neutrophilic vasculitis. In type II erythema induratum of Bazin-nodular vasculitis, several blood vessels of different sizes both in the septa and the fat lobule showed features of neutrophilic vasculitis. Necrosis of the adipocytes and inflammatory response were more intense in type II. In our opinion, this classification is difficult to apply in a particular case, because the intensity of inflammation of the fat lobules often varies from one lobule to another within the same biopsy specimen. Furthermore, in our experience this system of classification is not of practical use, because in the cases that we are reporting in this series we did not find correlation between the intensity of inflammatory infiltrate within the fat lobule and the number, size, nature, and location of the involved blood vessels of the subcutis. Moreover, in some cases of erythema induratum of Bazin with all the stereotypical clinicopathologic features of erythema induratum of Bazin-nodular vasculitis, serial sections throughout the block of a subcutaneous nodule did not demonstrate findings of vasculitis. Therefore, we do not consider vasculitis as a sine qua non criterion to establish the diagnosis of erythema induratum of Bazin when other characteristic findings are present.

Another major problem in dealing with small blood vessel vasculitis in the context of neutrophilic
lobular panniculitis is the question of whether or not the vascular injury is primary. Cutaneous vasculitis can be classified into primary, secondary, or incidental. Primary vasculitis is idiopathic and implies that the vascular insult is the predominant pathogenic factor in the process. Examples of primary cutaneous vasculitis include most cases of cutaneous leukocytoclastic vasculitis, polyarteritis nodosa, giant cell arteritis, and antineutrophilic cytoplasmic antibody–positive vasculitis syndromes, including Wegener granulomatosis, Churg-Strauss syndrome, and microscopic polyangiitis. In contrast, secondary vasculitis is caused by and part of a known disease, and although inflammation is also directed at vessel wall constituents, there is one more process in wider, often inflammatory syndromes. Secondary cutaneous vasculitic syndromes include lupus erythematosus vasculitis, rheumatoid vasculitis, malignancy-induced vasculitis, infection-induced vasculitis, and drug-induced vasculitis. Finally, incidental vasculitis refers to focal vasculitis found within a predominantly neutrophilic infiltrate, such as in venous ulcers of the lower legs or in early lesions of herpes simplex and herpes zoster, and it is accepted that this incidental vasculitis has no pathogenic role in the process and the vascular collateral damage is caused by a nonvasculitic insult to the vessels. Inflammation is not directed at the vessel, but the vessels are damaged because they are in the vicinity of the insult. In this sense, it might be interpreted that the leukocytoclastic vasculitis involving the small blood vessels of the fat lobule seen in early lesions of erythema induratum of Bazin with a mostly neutrophilic infiltrate within the fat lobule was a secondary infective vasculitis as a result of *M. tuberculosis* or even an incidental vasculitis within a neutrophilic infiltrate. However, there are several features that militate against these possibilities. Concerning infective vasculitis, *M. tuberculosis* has been demonstrated by polymerase chain reaction techniques in cases of erythema induratum of Bazin of some countries, but not in cases from other geographic areas and, if the process is the same in all areas, another pathogenic factor besides *M. tuberculosis* must be involved in the process. Finally, the vasculitic process involving the small blood vessels of the fat lobules in most of our cases of erythema induratum of Bazin can not be interpreted as an incidental vasculitis. First of all, necrotizing leukocytoclastic vasculitis of the small blood vessels

Fig 9. Early lesion of erythema induratum of Bazin. Serial sections failed to demonstrate vasculitis. **A**, Scanning power. **B**, Higher magnification showing mostly lobular panniculitis. **C**, Inflammatory infiltrate of fat lobule was mostly composed of neutrophils. **D**, Still higher magnification showing neutrophils and some nuclear dust, but no evidence of vasculitis. (**A** to **D**, Hematoxylin-eosin stain; original magnifications: **A**, ×10; **B**, ×40; **C**, ×200; **D**, ×400.)
was seen not only in early lesions of our series, but also in many biopsy specimens from fully developed lesions with a predominantly granulomatous infiltrate involving the fat lobule. Second, besides erythema induratum of Bazin, there are several other panniculitic processes with a predominantly neutrophilic infiltrate within the fat lobule, such as neutrophilic lobular panniculitis or subcutaneous Sweet syndrome, pancreatic panniculitis, alpha-1-antitrypsin deficiency—associated panniculitis, infective panniculitis, and factitial panniculitis, which do no show leukocytoclastic vasculitis of the small blood vessels of the fat lobule. Therefore, we think that the most common type of vasculitis seen in biopsy specimens of erythema induratum of Bazin has pathogenic significance and it must be considered as primary vasculitis.

In conclusion, although there is no consensus about the nature, size, and location of the involved vessels in erythema induratum of Bazin, on the basis of the findings of this series, we consider vasculitis as almost always present in lesions of erythema induratum of Bazin, and the nature, location, and size of the involved vessels is, from more to less frequent, as follows: (1) small venules of the fat lobule; (2) both veins of the connective tissue septa and venules of the

Table I. Type of involved vessels in vasculitis in 101 biopsy specimens from 86 patients with erythema induratum of Bazin

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<thead>
<tr>
<th>Lobular venules</th>
<th>Lobular venules + septal veins</th>
<th>Septal veins</th>
<th>Lobular venules + septal veins + septal arteries</th>
<th>Septal veins + septal arteries</th>
<th>No vasculitis</th>
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<tr>
<td>47 Cases (46.5%)</td>
<td>13 Cases (12.8%)</td>
<td>12 Cases (11.8%)</td>
<td>10 Cases (9.9%) (All cases were EL)</td>
<td>9 Cases (8.9%)</td>
<td>10 Cases (9.9%)</td>
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<td>- EL: 23 cases</td>
<td>- EL: 5 cases (4.9%)</td>
<td>- EL: 2 cases (1.9%)</td>
<td>- EL: 8 cases (7.9%)</td>
<td>- EL: 2 cases (1.9%)</td>
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<td>(22.7%)</td>
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<td>(7.9%)</td>
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<td>- FDL: 24 cases</td>
<td>- FDL: 8 cases (7.9%)</td>
<td>- FDL: 10 cases (9.9%)</td>
<td>- FDL: 1 case (0.9%)</td>
<td>- FDL: 8 cases (7.9%)</td>
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<td>(23.7%)</td>
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EL, Early lesions (mostly neutrophilic infiltrate); FDL, fully developed lesions (mostly histiocytic infiltrate).
fat lobule; (3) only veins of the connective tissue septa; (4) veins and arteries of the connective tissue septa and venules of the fat lobule; and (5) veins and arteries of the connective tissue septa. Because some type of vasculitis is seen both in early and fully developed lesions and because vasculitis is more consistently present in lesions of erythema induratum of Bazin than in other mostly lobular panniculitis, we think that vasculitis plays an important role in the pathogenesis of this process. However, vasculitis should not be considered as a criterion sine qua non for histopathologic diagnosis of erythema induratum of Bazin when all other clinicopathologic features of the process are consistent with that diagnosis.

REFERENCES
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