Cholesterol Crystal Embolization Presenting as Erythema Induratum of Bazin

Sir,

In patients affected with severe abdominal aortitis, cholesterol microembolization may occur from an atheromatous plaque, with ensuing skin lesions in the lower extremities (1). The most frequent cutaneous signs include livedo reticularis, purple toes, ulcerations and distal gangrenes. They are frequently associated with systemic symptoms due to the involvement of other organs. Histopathologic study is required for diagnosis, showing biconvex needle-shaped clefts, corresponding to the cholesterol crystal dissolved by the fixation procedure (2). We report a case of cholesterol crystal embolization (CCE) which presented clinically and histopathologically as erythema induratum of Bazin (EIB) without classical cutaneous signs or systemic manifestation.

CASE REPORT

A 70-year-old woman was investigated for painful leg ulcerations that had developed on inflammatory nodules. She had no past medical history except for recurrent thrombophlebitis, leading to an antithrombotic therapy with fluindione (an oral vitamin K antagonist derived from indanedione) initiated 2 years earlier. Subsequently, she had developed persistent nodules on the back of both legs. These lesions remained indolent until spontaneous ulcerations occurred on the right calf 6 months later. Physical examination revealed multiple and confluent violaceous subcutaneous nodules, forming two large plaques on the posterior aspect of the lower part of both legs. Their size was 10×15 cm. A solitary non-ulcerated violaceous plaque was also found near the left knee (Fig. 1). Two ulcerations were seen over the plaque of the right leg with a fibrous and necrotic center. A violaceous and livedoid discoloration was seen over the plaques. All pulses were bilaterally palpable, and the remainder of the examination was unremarkable. The patient denied a personal or family history of active tuberculosis.

Results of the following laboratory investigations were negative or normal: blood cell count, cholesterol level, immunoelectrophoresis, hepatic and renal function, antinuclear antibodies, rheumatoid factor, complement level, chest X-ray film, abdominal ultrasonography. The only laboratory abnormality was an elevated erythrocyte sedimentation rate of 50 mm/h. Purified protein derivative 5 tuberculin units produced induration 2.5×2 cm at 48 h. Cultures for acid-fast bacilli from sputum and urine were negative. A skin biopsy from inflammatory ulcerative and non-ulcerative lesions (left knee and calf) revealed a diffuse inflammatory cell infiltrate in the subcutis and thickening of septa. Multiple small granulomas were present, composed of epithelioid and giant cells, sometimes with fibrinoid necrosis. Small dermal arteries showed thrombosis. One vessel had a lumen partially occluded by biconvex spear-shaped (Fig. 1). Direct immunofluorescent studies, gram and Ziehl-Nielsen stain were negative. Abdominal and chest computed tomographic scans failed to show features of severe atherosclerosis and aortic aneurysmal dilatation. The only abnormality was mild wall calcifications of infrarenal aorta. A fundoscopic examination showed no chlosterol emboli in retinal vessels. Because of CCE anticoagulant therapy was discontinued and the patient was treated with platelet aggregation inhibitors (250 mg/day acetosalicylic acid treatment). The inflammatory skin lesions gradually improved and the pain disappeared within 1 month. Six months later there was still a moderate infiltration of both calves, with superficial ulcerations. Complete healing was obtained within 9 months. A mild inflammatory aspect still persisted.

DISCUSSION

In our patient, the clinical presentation associated with high tuberculin sensitivity and histologic features such as inflammatory infiltrate in the subcutis, epithelioid granulomas and vascular alterations fulfilled the criteria for EIB (3–5). However, one vessel was shown to contain cholesterol clefts and was detected only after multiple were made.

As illustrated by this case, the diagnosis of CCE may be difficult, based on careful histologic examination. A difficulty in assessing histopathologic changes in lesions arises from the variation in histologic appearance depending on their age. Lesions examined by biopsy early in their course will demonstrate "negative" pictures of cholesterol crystals in vascular lumen, but older lesions will show extensive inflammation of vessels with macrophagic granuloma (8). These features can explain the histologic appearance of EIB.

Embolization occurs spontaneously or after angiographic procedures, aortic surgery, anticoagulant or streptokinase therapies (6, 7). Generally, patients have extensive and severe atherosclerosis (1, 6). Since multiple organs can be affected, the cutaneous lesions are often helpful in suggesting the diagnosis. Skin manifestations are present in one third of the cases. The most frequent cutaneous signs include (8): livedo (49%), purples toes (38%), distal gangrene (35%) and ulcerations (17%). Nodular lesions or indurated plaques are only rarely found and could be seen in about 10% of cases according to two series (2, 8). They are firm, violaceous, painful and necrotic in their center, occurring on the calves or thighs. Such lesions are usually accompanied by other manifestations of CCE, particularly livedo reticularis, or other visceral manifestations mimicking polyarteritis nodosa (9). Three atypical cases of isolated nodular lesions due to cholesterol emboli have been described in the literature. Chesney (10) reported a nodule of an ear, without predisposing factors except local surgical trauma, which recovered completely after excision. Several dermis arterioles were occluded by thrombi that contained cholesterol clefts. The case related by Day & Aterman (11) concerned a red and painful swelling of the chest, without precipitating cause, treated by excision. Microscopic examination showed a hemorrhagic panniculitis and extensive inflammatory response in the subcutis and dermis. Several vessels showed thrombotic blockage, but only one con-

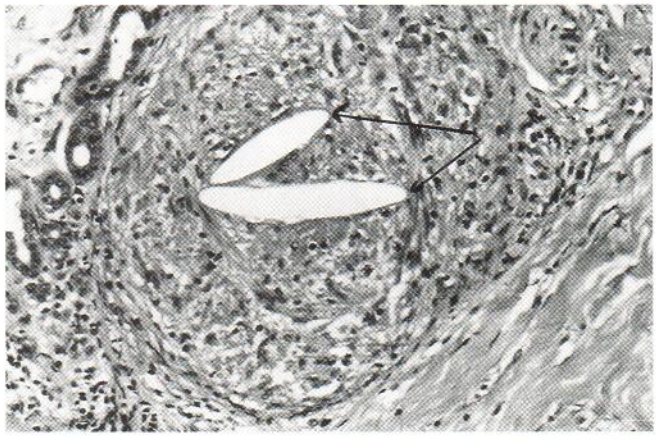

Fig. 1. Biopsy taken from a non-ulcerated lesion. Cholesterol clefts in a dermal artery (H.&E. $\times 250$).

tained cholesterol needles. Recently, an observation of pseudolymphoma with inflammatory nodule on a foot and plaques on both wrists was reported by Castell et al. (12). The lesions occurred after transient antithrombotic therapy and persisted for 4 years until an ultimate biopsy discovered cholesterol crystals in only one vessel.

Our case emphasizes the possibility of uncommon clinical and pathologic manifestations such as the features of EIB in CCE. Moreover, it shows that cholesterol emboli can occur without plurisystemic features, poor prognosis or symptomatic atherosclerosis. Finally, it underlines that cholesterol clefts may easily be missed and that the diagnosis of CCE needs serial sections and careful examination of specimens of skin or other organs when biopsies are available.

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