An HIV-Positive Man with Slowly Enlarging Nodules on the Extremities
(See page 976 for the Photo Quiz)

Figure 1. Nodular erythema elevatum diutinum with multiple acral nodules (A, B). Histological examination revealed a circumscribed dermal nodule (C) composed of histiocytes, spindle cells, and neutrophils displaying areas (D) with heavy neutrophilic infiltrations (arrow), fibrinoid necrosis (circle), and nuclear dust (triangle), as well as areas with prominent tissue fibrosis (detail in C).

Diagnosis: Nodular erythema elevatum diutinum (nEED).

The development of disseminated, dark, purpuric skin nodules in HIV-infected patients is usually suspicious for Kaposi sarcoma or bacillary angiomatosis [1, 2]. In the present case, a diagnosis of nEED was made on the basis of the clinical presentation and histological findings characteristic for nEED—namely, a nodular accumulation of histiocytes, spindle cells, and neutrophils displaying areas of heavy neutrophilic infiltration with fibrinoid necrosis and nuclear dust adjacent to areas with marked tissue fibrosis (figure 1)—in conjunction with the failure to detect any infectious agents, such as human herpesvirus 8 or Bartonella henselae.

nEED is an extremely rare cause of HIV-associated skin nodules and can, therefore, be easily missed in the differential diagnosis [3]. To the best of our knowledge, ~20 cases of nEED in association with HIV infection have been published [3–9]. Erythema elevatum diutinum is a rare, chronic vasculitis of unknown etiology that promotes tissue fibrosis. The nodular variant is even rarer, but it evolves most often in HIV-positive individuals [10]. Although the pathophysiology of erythema elevatum diutinum is unclear, it has been reported several times in association with IgA hypergammopathy [11], which is also a common finding in HIV infection. One may speculate that the hemorrhagic macules were initially caused by an IgA-associated vasculitis. Because of the induced leakage of the vessel walls, lipid droplets (which were markedly elevated in the serum after ritonavir intake) poured into the perivascular tissue and became phagocytosed by histiocytes. The ongoing inflammation finally induced fibrotic tissue remodeling.

Treatment options for nEED are limited and disappointing. Dapsone might be beneficial in preventing new lesions [6, 9], whereas late-stage fibrotic nodules do not respond to this treatment [3, 4, 7]. Colchicine has been favored in 2 cases [8], and surgical excision may be an option for large, disturbing lesions [4]. Decreasing hypertriglyceridemia may be important for the general health of the patient, but it has no impact on the lesions.

In conclusion, disseminated skin nodules in HIV-infected patients may belong to a peculiar spectrum of tumors, ranging from the common appearance of Kaposi sarcoma and bacillary angiomatosis to the very rare occurrence of nEED. The latter may occur, in particular, in patients with hyper IgA gammopathy promoting chronic vasculitis and with hypertriglyceridemia stimulating histiocytic phagocytosis of lipids.

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