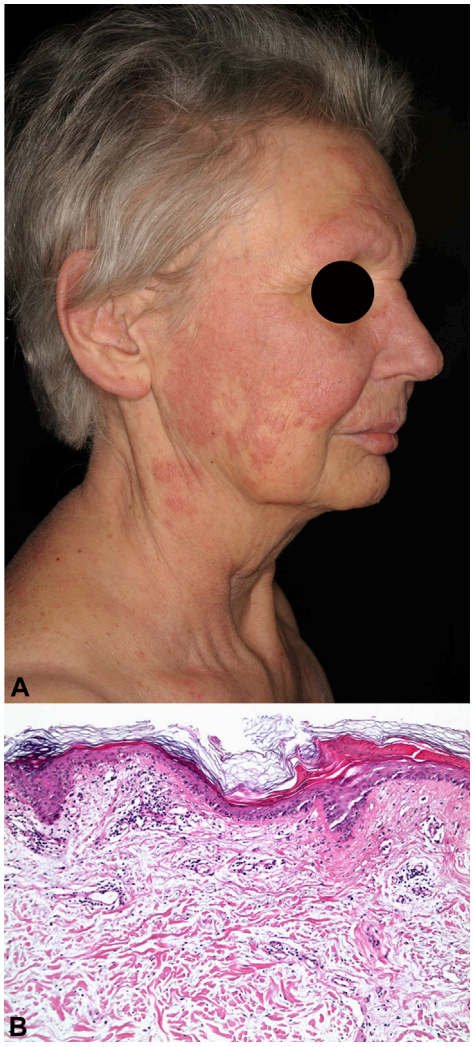

Fig 1. **A**, Sharply demarcated erythematous plaques in a 70-year-old woman developed in the context of vemurafenib melanoma therapy. **B**, Histology demonstrated interface dermatitis with follicular plugging and dermal mucin deposition consistent with lupus erythematosus–like eruption. (**B**, Hematoxylin-eosin stain; original magnification: ×20.)

erythematosus–like pattern (Fig 1, *B*). Indirect immunofluorescence showed elevated antinuclear antibody titers (1:320). Muscle creatine kinase was normal, which excluded the differential diagnosis of paraneoplastic dermatomyositis. There was no increased photosensitivity after 24 hours of ultraviolet A/B exposition. Moreover, photopatch testing also showed no sign of belated, increased photosensitivity after 4 weeks. Topical treatment of these lupus-like plaques was implemented with topical mometasone furoate cream that lead to gradual recovery within 4 weeks. In addition, the patient was instructed as to the careful use of sun blockers. Over the course of time the underlying disease progressed, with radiotherapy and chemotherapy needed.

The clinical and the histologic presentations of our patient are consistent with a lupus erythematosus–like skin eruption that was most likely associated with the vemurafenib therapy. A paraneoplastic reaction cannot totally be excluded but would be unusual in the context of malignant melanoma. Although the patient did not show increased photosensitivity we speculate that both the already well-known side effect of photosensitivity that can be an initial symptom of lupus erythematosus and the lupus erythematosus–like skin eruptions mark a spec-trum of vemurafenib-induced drug reactions. The pathomechanism behind this reaction pattern needs further investigations.

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Localized insulin-dependent amyloidosis with scar-tissue formation

To the Editor: The incidence and prevalence of diabetes mellitus has increased dramatically in the last few years as a result of increasing prevalence of

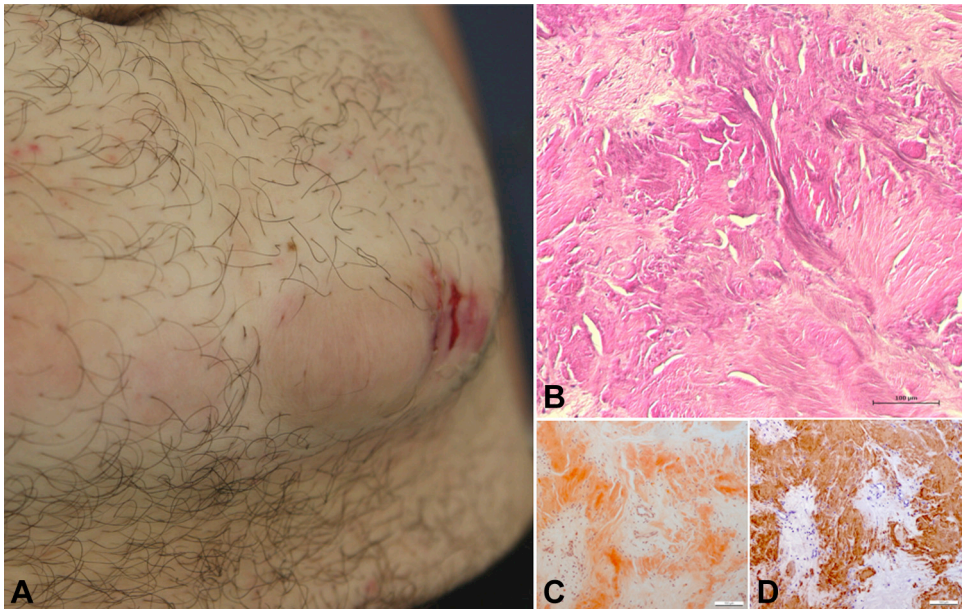

Fig 1. Insulin-induced localized amyloidosis. **A**, Indurated erythematous subcutaneous lumps on the lower abdominal quadrants. **B**, Hematoxylin and eosin–stained skin biopsy specimen of the subcutaneous mass showing fibrocollagenous scar tissue. **C**, Congo-red staining of the fibrocollagenous scar tissue. **D**, Immunohistochemical staining for insulin of the fibrocollagenous scar tissue. Bars = 100 μm.

obesity, physical inactivity, and aging. In the course of the disease nearly all patients develop skin complications caused by the long-term effects of diabetes mellitus.[1] Sequelae can, however, also be caused by the treatment regimen.

Here we describe the case of a 26-year-old male patient with a 24-year history of type 1 diabetes mellitus, who presented with 2 relocatable, indurated subcutaneous lumps below his navel (Fig 1, *A*). His treatment regimen included regular subcutaneous administration of insulin detemir and insulin lispro, which he had habitually injected into these nodules for 2 to 3 years. His diabetic control was moderate (hemoglobin A1c 8.0%) and he had no diabetic long-term complications. For diagnostic purposes, 1 nodule was excised. Histologic examination showed a highly homogenized connective tissue with a depletion of cells and vessels in the tumor area accompanied by foci of necrobiosis and calcification (Fig 1, *B*). Congo-red staining revealed the brick-red coloration of amyloid within the subcutaneous nodule (Fig 1, *C*). Immunohistochemical staining for insulin demonstrated that the amyloid fibrils originated from insulin deposits (Fig 1, *D*).

Insulin-induced localized amyloidosis combined with scar tissue is an underdiagnosed complication of regular insulin injections in patients with insulin-dependent diabetes. Only a few cases of localized insulin-derived amyloidosis have been described in the literature[2] and even fewer cases of insulin-induced amyloid deposits were associated with scar-tissue formation.[3] In 1 case, insulin injections caused scar-tissue formation without amyloid depositions. Here, the authors suggested that the scar tissue might be caused traumatically by the repeated subcutaneous injections.[4]

The mechanism underlying insulin-derived amyloid formation is not entirely clear. It has been shown that insulin in the absence of its C-peptide can assemble into fibrils and that an acidic environment frequently found in scar tissue in combination with high insulin concentrations can accelerate this process.[5]

Compared with the well-known insulin-induced lipohypertrophy, the nodules form more solid and firm lesions, which do not resolve quickly after rotation of the insulin injection site.[3]

Dermatologists should think of this differential diagnosis when diabetic patients present with firm nodes at the injection site, as regular insulin injections in these subcutaneous nodules can be associated with poor diabetic control. In addition, the presence of scar tissue in localized insulin-induced amyloidosis is worth mentioning as the low pH present in this environment might trigger insulin-derived amyloid formation.

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