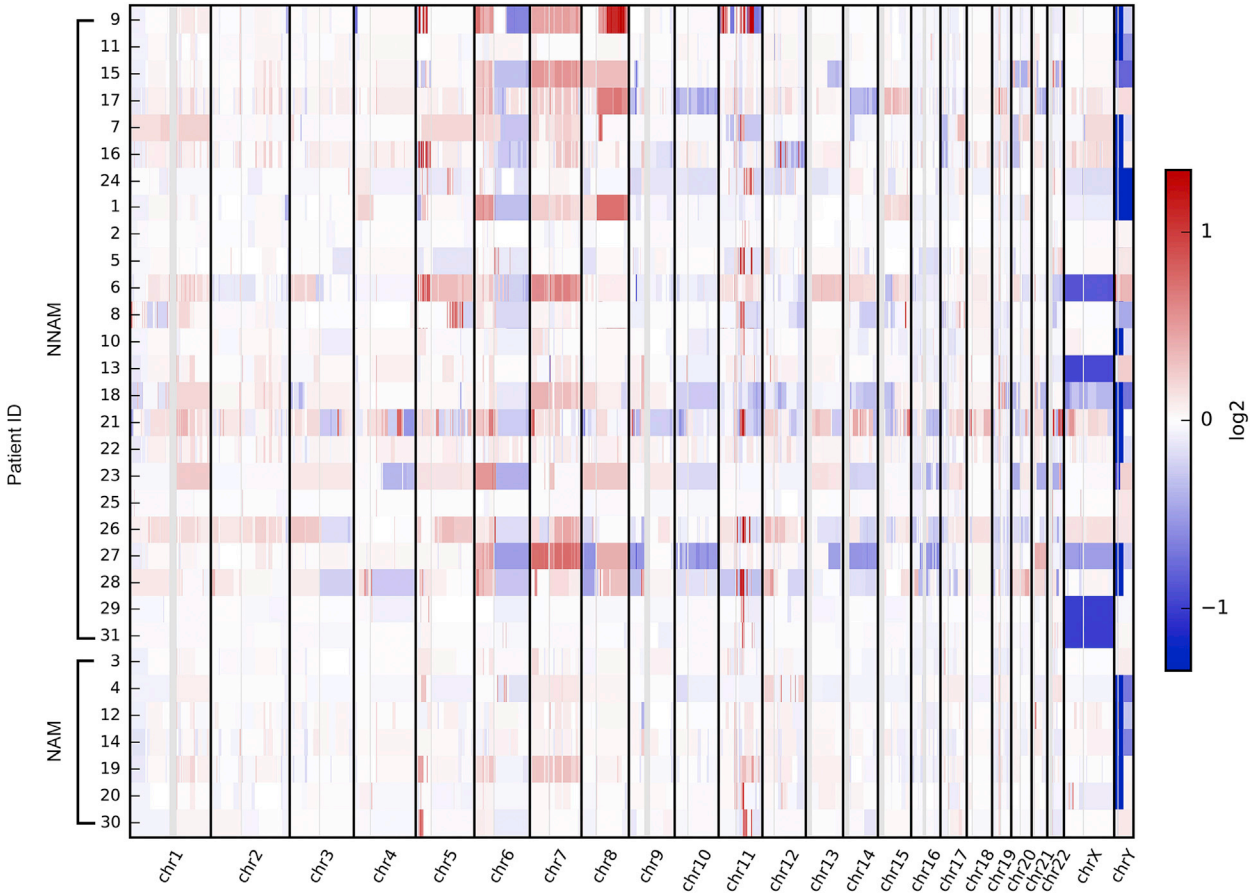

Fig 2. Heat map of copy number alterations detected in NNAM and nail apparatus melanoma NAM samples of patients. *ID*, Identification; *NAM*, nail apparatus melanoma; *NNAM*, nonnail acral melanoma.

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Clinical and pathological dermatological features of deficiency of adenosine deaminase 2: A multicenter, retrospective, observational study

To the Editor: Adenosine deaminase 2 deficiency (DADA2) is a monogenic autoinflammatory disease associated with *ADA2* mutations.[1]

Diagnosis of DADA2 remains difficult given its variable clinical presentation.[2] Although no tests are commercially available, serum ADA2 activity measurement can help secure the diagnosis, which is confirmed by *ADA2* sequencing. Recently, Rama et al[2] proposed a decision tree for the genetic diagnosis of DADA2 based on prerequisites including, among others, cutaneous manifestations. However, to our knowledge, no study has specifically described DADA2's dermatologic spectrum. Furthermore, pathologic findings on skin biopsy samples have rarely been reported,[1,3] and specific histologic features remain to be determined. We conducted a multicenter, retrospective study with

Table I. Main clinical and pathologic skin features of the 8 French patients with DADA2

Patient/ number of biopsies	Skin manifestations	Extracutaneous manifestations	Site of biopsy	Thrombosis	Type of vessels	Vasculitis*	Type of vessels	Other findings
1/1	Livedo racemosa Perimalleolar ulcers Raynaud phenomenon Atrophie blanche	Recurrent fever, increased CRP level, abdominal pain, peripheral neuropathy	Leg ulcer	No	—	No	—	Pyogenic granuloma
2/1	Livedo racemosa	Recurrent fever, arthralgia, myalgia, hepatitis	Livedo on the leg	No	—	No	—	Slight perivenular lymphocytic infiltrate in hypodermis
3/1	Livedo racemosa	Anemia, increased CRP level	Nodule on the leg	Yes	Hypodermal capillaries	No	—	Nonspecific inflammation
3/2	Leg nodules		Livedo on an ankle	Yes	Dermal capillaries	No	—	
3/3	Perimalleolar ulcers		Livedo on the trunk	No	—	No	—	
3/4	Atrophie blanche		Nodule on an ankle	Yes	Dermal and hypodermal capillaries	No	—	
3/5			Nodule on the leg	Yes	Dermal and hypodermal capillaries	No	—	
4/1	Livedo racemosa Leg nodules Digital necrosis Raynaud phenomenon Erythematous feet papules	Recurrent fever, recurrent ENT infections, cerebral infarct, hypogammaglobulinemia	Livedo on the thigh (infiltrated zone)	Yes	Dermal and hypodermal capillaries	Subacute cPAN	Deep dermis medium-sized artery	—
5/1	Livedo racemosa Ulcerated leg nodules Leg nodules Psoriasis	Recurrent fever, increased CRP level, pericarditis, myocarditis, intestinal vasculitis, renal microaneurysm, peripheral neuropathy, death from visceral complications	Nodule on the leg	Yes	Deep dermis medium-sized artery	Acute cPAN	Deep dermis medium-sized artery	—
6	Livedo reticularis	Increased CRP level, ischemic strokes, hepatosplenomegaly, low IgM level, negative vaccinal serology results	No biopsy	—	—	—	—	—

Continued

Table I. Cont'd

Patient/ number of biopsies	Skin manifestations	Extracutaneous manifestations	Site of biopsy	Thrombosis	Type of vessels	Vasculitis*	Type of vessels	Other findings
7/1	Livedo racemosa Leg nodules	Recurrent fever, increased CRP level, arthralgia, abdominal pain, hepatosplenomegaly, epilepsy	Nodule on the leg	No	—	Reparative cPAN	Deep dermis medium-sized artery	Septal panniculitis
7/2			Nodule on the leg	No	—	No	—	
8/1	Livedo racemosa Digital necrosis Leg nodules	Recurrent fever, increased CRP level, ischemic stroke, abdominal pain, psychosis, pericarditis	Nodule on the leg	No	—	Subacute cPAN	Deep dermis medium-sized artery	—

cPAN, Cutaneous periarteritis nodosa; *CRP*, C-reactive protein; *ENT*, ear, nose, and throat; *TIA*, transient ischemic attack.
*Definitions of the cPAN stages by Ishibashi and Chen[4] are as follows. Acute: endothelial loss and fibrin thrombi with neutrophil infiltration without obvious internal elastic lamina disruption and medial fibrinoid necrosis. Subacute: mixed-cell infiltrates showing a unique intimal target-like fibrinoid necrosis with fibrinoid leakage extending through the disrupted sites of the internal elastic lamina to the media. Reparative: intimal fibroblastic proliferation and perivascular neovascularization with predominant infiltrates of histiocytes and lymphocytes. Healed: minimal cellular inflammation with occlusive intimal thickening. Thrombosis was defined as complete occlusion of the vascular lumen by a cluster of fibrin.

assessment of clinical and pathologic dermatologic findings among 8 French patients with DADA2.

Cutaneous polyarteritis nodosa (cPAN) was defined as fibrinoid necrotizing vasculitis affecting the small arteries and arterioles (≥300 μm) in the panniculus and dermal-subcutaneous junction as described by Ishibashi and Chen[4] in a 4-stage process with exclusion after clinicopathologic correlation of differential diagnoses, particularly antineutrophil cytoplasmic antibody–associated vasculitis.

DADA2's main clinical features are presented in Table I and detailed in Supplemental Table I (available at Mendeley via https://data.mendeley.com/datasets/xd9mp9tn3x/draft?a=a2c80a86-9920-4422-b2a2-16d9e5aca560). Median age at first symptom was 9.5 years (range, 0.5-29 years), whereas median age at diagnosis was 25.5 years (range, 6-38 years.

Cutaneous manifestations (Fig 1) were the first symptoms of DADA2 in 3 of 8 patients. Livedo was observed in all cases and was of the racemosa subtype in 7 of 8 patients, with mostly a large pattern (6/8). It involved both legs and arms in all patients, extending to the abdomen or trunk in 3 patients. It was palpable in 1 patient. Other cutaneous manifestations included leg nodules (n = 7, nonspecific or erythema nodosum–like lesions), leg ulcers (n = 3), Raynaud phenomenon (n = 2), atrophie blanche (n = 2), digital necrosis (n = 2), erythematous foot papules (n = 1), and psoriasis (n = 1).

Overall, 12 skin biopsy samples from 7 patients were reviewed (Table I and Fig 1). cPAN was identified in 4 of 7 patients. In patients 3 and 4, skin biopsy samples showed thrombosis of dermal and/or hypodermal capillaries, without vasculitis. Although subacute cPAN was also observed in a skin biopsy sample from patient 4, patient 3 had only isolated thrombosis.

Here, we portrayed the dermatologic spectrum of patients with DADA2, thus contributing to its better recognition. Livedo was observed in all cases and was mostly racemosa, extensive, and with a large reticular pattern. Differentiating between DADA2 and antiphospholipid-negative Sneddon syndrome (as in patient 4) may be challenging because both may present with livedo and stroke.[5] Although skin biopsy samples of patients with DADA2 most frequently showed vasculitis, 2 patients in our series showed capillary thrombosis, such as in Sneddon syndrome.[5]

Importantly, 3 of 7 patients did not have vasculitis on skin biopsy. The site and depth of biopsy is probably important. Indeed, although we found nonspecific features in 2 superficial biopsies of livedo without analyzable hypodermis, cPAN was more frequently identified in biopsy samples taken from nodules.

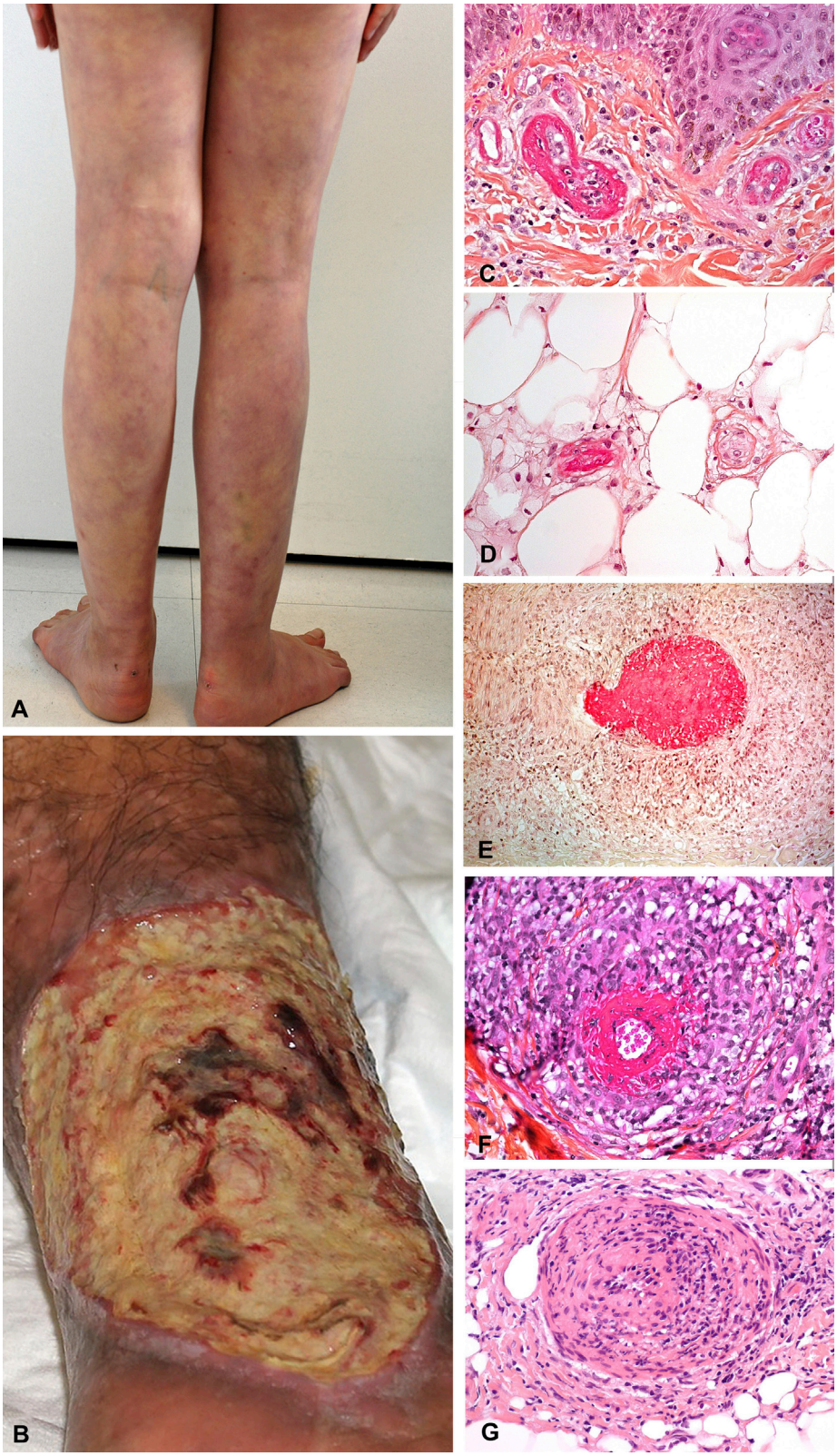

Fig 1. **A**, Livedo racemosa with large branch-pattern involving the leg. **B**, Fibrino-necrotic large perimalleolar ulceration with necrotic borders. **C-G**, Hematoxylin-eosin-saffron stained (original magnification ×400): dermal (C) and hypodermal (D) capillary thrombosis. Dermo-hypodermal cPAN lesions: acute stage with intraluminal thrombosis (E), subacute stage (F), and reparative stage (G).

Overall, livedo racemosa with a large branch pattern, nodules, or ulcerations in a context of neurovascular events, recurrent fever, low immunoglobulin M levels, and pediatric onset is suggestive of DADA2. Although cPAN on skin biopsy is suggestive of DADA2, its absence or the presence of thrombotic features does not exclude the diagnosis.

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Characteristics of dermatologists sanctioned by the Office of Inspector General: A cross-sectional database analysis

To the Editor: Sanctions such as medical license suspension are a distant yet ominous threat to physicians. Given that few data exist, we analyzed the nature of serious action against dermatologists and the characteristics of disciplined dermatologists.

Dermatologists subject to significant disciplinary action were identified by using the Office of Inspector General (OIG)'s List of Excluded Individuals and Entities (LEIE).[1] This is a list of individuals barred from receiving payment from federally funded health care programs subsequent to disciplinary action pursuant to sections 1128 and 1156 of the Social Security Act. Data on medical license termination or suspension must be reported by state medical licensing boards, and this information is relayed to the OIG. Additionally, individuals