

Supplemental Online Content

Dupré A, Morel N, Yelnik C, et al. Cutaneous involvement in catastrophic antiphospholipid syndrome in a multicenter cohort of 65 patients. *JAMA Dermatol*. Published online December 7, 2022. doi:10.1001/jamadermatol.2022.5221

eMethods. Supplementary methodological details

eResults. Pathology findings

eTable. Comparison of cutaneous involvement between patients with catastrophic antiphospholipid syndrome (CAPS) in or outside pregnancy

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Supplementary methodological details

Thirteen centers participated in our study (Hôpital Cochin (APHP, Paris), Hôpital Huriez (Lille), Hôpital Bichat (APHP, Paris), Hôpital Montpied (Clermont-Ferrand), Hôpital Brabois (Nancy), Hôpital Charles-Nicolle (Rouen), Hôpital Saint Antoine (APHP, Paris), Hôpital La Pitié Salpêtrière (APHP, Paris), Hôpital Mondor (APHP, Paris), Hôpital Foch (Suresnes), Hôpital Saint André (Bordeaux), Hôpital de Caen (Caen), Hôpital de la Timone (Marseille)). The international criteria for CAPS require the involvement of three or more organs, development of manifestations simultaneously or within less than a week, confirmed by histopathology with small-vessel occlusions, and/or laboratory confirmation of the presence of aPL. The clinical features used to identify the group with cutaneous involvement included new onset or worsening of livedo racemosa, necrotic and/or ulcerated lesions, distal (hands, feet, face) bilateral inflammatory edema, and isolated vascular purpura.

eResults. Pathology findings

Eighteen patients (28%) had a skin biopsy during their CAPS episode, and 16 (89%) biopsies were centralized and reviewed. The histological studies showed microthrombi in 15/16 patients (94%), affecting dermal capillaries. Five patients had a severe histologic presentation with thrombosis of all skin vessels biopsied, with hypodermal or dermal venule and arteriole involvement. Isolated hypodermal capillary involvement was observed in only one case. Periodic acid-Schiff-positive thrombotic material was surrounded by plump endothelial cells and occasionally dissociated by inflammatory cells, in a reflection of the organization of mural thrombi. Microthrombi were usually accompanied by purpura, mild pericapillary lymphohistiocytic and/or neutrophilic infiltrate. No vasculitis was observed. Ischemic epidermal necrosis with possible junctional bullous detachment was observed in severe cases

when superficial dermal capillaries were damaged (n=5). Necrosis of interstitial dermal tissue and sweat glands was seen in one severe case. Solitary sweat gland ischemic necrosis, with no epidermal or dermal involvement, was found in one case with deep dermal and hypodermal capillary occlusion. Only one patient's skin biopsy did not provide useful CAPS-related information; this biopsy of an ecchymotic lesion on the leg showed a nonspecific dermal pericapillary hemorrhagic focus mixed with neutrophils, without thrombosis or necrosis; it suggested a possible capillary occlusion up- or downstream. Twenty-one patients had a definite CAPS (meeting all criteria for CAPS), including 12 patients for whom the skin biopsy was the only pathological criterion available. Thus, for 12 patients, the skin biopsy allowed us to classify the CAPS as definite instead of probable.

Five patients had biopsies defined as histologically severe. It is, however, difficult to correlate histologic presentation and clinical severity, given the heterogeneity of the clinical lesions, with individual patients often having several types.

eTable. Comparison of cutaneous involvement between patients with catastrophic antiphospholipid syndrome (CAPS) in or outside pregnancy

	CAPS during pregnancy (n=16)	CAPS without pregnancy (n=49)	p
Type of cutaneous involvement			
- Livedo racemosa	2 (13)	27 (55)	< .01
- Necrotic and/or ulcerated lesions	8 (50)	19 (39)	.56
- Distal inflammatory edema	5 (31)	10 (20)	.50
- Vascular purpura	3 (19)	6 (12)	.68
- Subungual splinter hemorrhages	4 (25)	15 (31)	.76
Anatomic site of lesions (except subungual splinter hemorrhages)			
- Superior limb	3/12 (25)	15/31 (48)	.19
- Inferior limb	2/12 (17)	17/31 (55)	.04
- Face	8/12 (67)	6/31 (19)	< .01
- Including ears	8/12 (67)	5/31 (16)	< .01