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## Management of a Patient With Calciphylaxis and Requiring Anticoagulant Therapy

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### To the Editor:

The different disorders associated with calciphylaxis include the possible relationship with oral anticoagulants,<sup>1</sup> nadroparin calcium,<sup>2</sup> and hypercoagulable states linked to lower concentrations of proteins S or C.<sup>1</sup> The disorder most commonly associated with calciphylaxis, however, is chronic renal failure,<sup>3,4</sup> with between 1% and 4% of these patients suffering from calciphylaxis.<sup>5</sup> Calciphylaxis has also been observed in association with neoplasia, hyperthyroidism, proteinuria,<sup>1</sup> rheumatoid arthritis,<sup>6</sup> and alcoholic cirrhosis.<sup>7</sup>

The pathogenesis remains obscure, although abnormal calcium and phosphorus metabolism (elevated calcium-phosphate product and high levels of parathyroid hormone),<sup>3,8</sup> inflammation,<sup>9</sup> and the presence of a hypercoagulable state<sup>3</sup> have been observed and may lead to vascular and extravascular calcification.

The foregoing leads us to ask several questions: what attitude should be adopted in the case of a patient with calciphylaxis who requires anticoagulation therapy? What are the available antithrombotic alternatives? Which is the most recommendable option?

We present the case of a 58-year-old man with calciphylaxis who was receiving anticoagulant treatment with acenocoumarol due to ischemic heart disease that had been treated with a double coronary artery bypass graft and who had severe pulmonary

hypertension, tricuspid insufficiency, and right ventricular dilation and hypokinesis. The patient visited the dermatology outpatient clinic with painful skin lesions on the legs that had appeared 10 days previously. The lesions were between 3 and 4 cm in diameter with a necrotic base and erythematous borders, and the patient was undergoing hemodialysis due to chronic renal failure. The patient presented secondary hyperthyroidism with high levels of aluminium (as a phosphorous chelating agent) but normal levels of calcium, phosphorous, and alkaline phosphates, along with anemia, high blood pressure, and dyslipidemia. The diagnosis of calciphylaxis was confirmed following a pathological study of the lesion biopsy.

In patients diagnosed with calciphylaxis, it is reasonable for both oral anticoagulant therapy and therapy with both unfractionated heparin and low-molecular-weight heparin calcium (nadroparin calcium) to be omitted as they may give rise to calcium deposits.<sup>10</sup> The following are proposed as recommendable alternative anticoagulant therapies: fondaparinux sodium and low-molecular-weight heparin sodium (preferably tinzaparin in patients who also present renal failure<sup>11</sup>), with the clear aim of avoiding exacerbation of the calciphylaxis and the instability inherent in oral anticoagulant therapy in patients with a poor clinical prognosis.

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## Melanotic Macules of the Penis

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### To the Editor:

After reading the article by Laguna et al,<sup>1</sup> published in this journal, we wished to contribute a new example, and to propose a series of considerations for improved management of these patients.

We present the case of a 29-year-old patient, with no relevant personal history, who consulted for multifocal pigmented macules of varying coloration on the penis; these were symptom free and had been present since the patient was 14 years old. The patient described the ongoing appearance of pigmented lesions with varying dark coloration (Figure 1). Histology revealed hyperpigmentation of the basal layer, with no increase in the number of

melanocytes or the frequency of atypical cells (Figure 2).

Melanotic macules on the penis—wrongly termed lentigines—are idiopathic and benign lesions, occasionally multifocal, of varying color, and irregular, which require differential diagnosis from mucosal melanoma.<sup>1</sup> Unlike melanoma, melanotic macules tend to appear in adulthood, not amongst the elderly, and they tend to remain stable for decades.

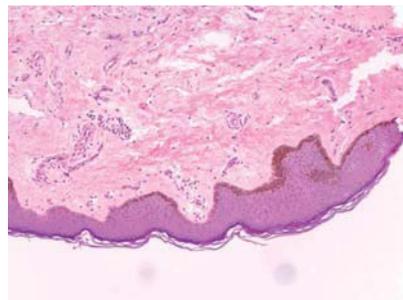
Histology confirms that the macules are benign. They are characterized by acanthosis with no elongation of the papillary ridges, hyperpigmentation of the basal layer with no increase in the number of melanocytes (hence they should not be termed lentigines), pigmentary incontinence, and the occasional presence of melanophages, all this with an absence of atypical melanocytes.<sup>2</sup>

When the lesions are irregular with varied coloration, or the patient reports changes or an increase in number of the same, ideally the entire macule would be surgically removed for a complete histological examination. In multifocal lesions, which are those that tend to necessitate differential diagnosis with melanoma, complete excision of the lesion is not usually feasible, and consequently several biopsies should be performed, choosing the sites carefully, in order to confirm if the case is benign. Dermoscopy may be a useful tool to identify the most suitable biopsy site.<sup>3</sup>

In spite of the fact that melanotic macules are not considered precursors of melanoma, a small number of publications describe the possibility of their becoming malignant.<sup>4,5</sup> Kahn et al<sup>4</sup> reported the case of a pigmented lesion on the palate that developed into mucosal melanoma. However, a significant clinical abnormality was observed in the initial lesion, and histology revealed melanocytic hyperplasia, and it can therefore be assumed that this was not a true melanotic macule. Taylor et al<sup>5</sup> do appear to have documented the development of a melanotic macule into an invasive melanoma. In this case, in the first biopsy—which included the entire lesion—increased pigmentation only occurred in the basal layer with neither hyperplasia nor atypical melanocytes, yet in biopsies performed 5 years later, nests of malignant melanocytes could be seen migrating through the mucosa.



**Figure 1.** Multifocal macules of varying coloration.



**Figure 2.** Hyperpigmentation of the basal layer, with no increase in number or atypical features of melanocytes (Hematoxylin-eosin, ×40).