

Animal-type melanoma: an unusual variant of human melanoma with prominent pigment synthesis and unpredictable course

Hayvansal tip melanom: belirgin pigment sentezi ve öngörülemez seyir ile insan melanomunun olağandışı bir çeşidi

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Described for centuries in the horses under the terminology of 'equine melanotic disease' and, subsequently recognized in non-equine animal models and in humans, animal-type melanoma, also known as pigmented epithelioid melanocytoma (PEM), is characterized by nodules and fascicles of epithelioid transformed melanocytes with pleomorphic nuclei and striking pigmentation, dendritic cells, numerous melanophages and, sometimes, lymphocytic infiltrate¹. Up to day, only small series have been reported in humans and, therefore, its biological behavior remains unclear. Recently, some authors have supported that the tumor follows an indolent clinical course, with very low risk of spread beyond regional lymph nodes². Given the complexity of the matter, Elder and Murphy proposed a histological categorization of PEM and PEM-like lesions, with distinctive clinicopathological and biologic features³. Herein this entity was highlighted and revisited in brief.

- *Epithelioid blue nevus resembling PEM*: it is a hyperpigmented, poorly circumscribed, dermal lesion, which shows heavily pigmented

globular melanocytes, intermingled with hypopigmented spindle melanocytes. Commonly misinterpreted as classical blue nevus, cellular blue nevus or PEM, its exact identification is important because it is strongly associated with the Carney complex⁴. Conservative excision is generally recommended; moreover, affected patients (and their relatives) should be considered at risk for other pathologies of the complex, especially cardiac myxoma⁴.

- *PEM*: not associated with the Carney complex, is quite similar to epithelioid blue nevus at scanning magnification, but cytologic atypia and sparse low mitogenicity are encountered during a careful histological inspection, exactly as observable in melanocytic tumors of uncertain malignant potential (MELTUMP)^{3,5,6}. When epidermal pagetoid diffusion and overtly anaplastic nuclei are present, diagnosis of malignant melanoma with prominent pigment synthesis can be also made¹. In fact, Magro et al. have reported one case of disease-related

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death¹ and Robledo-Sánchez et al. an aggressive clinical course in a 79-year-old male patient^{1,7}; therefore, although the tumor can be lethal given the depth of invasion according to Magro and colleagues, it seems to be less lethal than other usual or unusual vertical growth phase melanomas^{1,2}. Local lymph nodes are often involved by metastases. Lymph node sentinel biopsy is recommended and a wide re-excision (1-2 cm margins) must be performed¹. Follow-up, as in any case of invasive malignant melanoma, should be conducted¹.

- *Tumoral melanosis mimicking PEM*: it is a nodular cluster of melanophages and it may represent a complete regression of a vertical growth phase melanoma or of a pigmented basal cell carcinoma³. In the radial and vertical growth phases, the regression has negative impact on the prognosis^{8,9}; therefore, the follow-up should be very accurate, because the lesion could be the result of a preceding, completely regressed melanoma¹⁰.

The genetic and molecular investigations have a limited value in helping to distinguish PEM from PEM-like lesions, and a good histology in the hands of an expert dermatopathologist remains to be the most reliable diagnostic approach in these controversial cases.

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