

pseudoinclusions are sometimes evident and mild nuclear pleomorphism is typical. Mitoses are either absent or extremely infrequent. By definition dendritic cells are said not to be seen in this lesion.

The growth pattern often presents a plexiform appearance, fascicles of nevus cells following the dermal appendages and neurovascular bundles. Perineural or endoneural extension is a very common finding. Towards the base of the lesion the nevus often adopts a single cell infiltrative growth pattern dissecting between the collagen bundles. The nevus cell population is typically admixed with densely pigmented melanophages and lymphocytic infiltrates are not uncommon.

As originally described, deep penetrating nevus was not believed to be associated with any risk of recurrence or metastatic potential. The recent literature however casts some doubt on this viewpoint. Graham (8) presented one patient with a malignant variant and personal experience includes another in addition to evidence that there is a risk, albeit low of recurrence. Nuclear pleomorphism and multiple or deep mitoses are particularly worrying features.

The precise nature of this lesion is also somewhat problematic. It certainly shows some overlap with blue and cellular blue nevi. Although by strict definition dendritic cells are absent, the distinction is often far from easy. Some examples of this lesion appear to represent combined nevi and both banal and Spitz variants may be encountered. Whether the dermal component represents a blue nevus variant or a true deep penetrating nevus is as yet uncertain.

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Spindle cell melanocytic tumors

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Not uncommonly, the diagnosis of spindle cell melanocytic tumors presents problems to the diagnostic histopathologist (1). For practical purposes, these can be divided into two types, as follows: i) is the tumor melanocytic? ii) is the melanocytic tumor benign or malignant? Both of these questions will be briefly addressed in this presentation.

Are the (spindle-shaped) tumor cells melanocytes

It is fair to say that with few exceptions, this question of melanocytic vs. nonmelanocytic nature of a tumor is readily answerable: the main problems arise when the possibility of a melanocytic neoplasm is not considered at all.

The list of cutaneous spindle cell tumors is long and, apart from melanocytic tumors, includes neoplasms of fibroblasts, endothelium, smooth muscle cells, histiocytes, keratinocytes and various other cell types. The melanocytic nature of the tumor is generally obvious when a junctional component can be recognized or when melanin, produced by the tumor cells, is detected. However, even when these features are absent, the pathologist is well advised to consider the possibility of a melanocytic neoplasm, in order to avoid errors of diagnosis which may arise when the lesion is amelanotic and does not involve the dermoepidermal junction. Immunostaining for S-100 is usually of significant help but its usefulness obviously depends on the other entities relevant to the differential diagnosis under consideration. In addition, monoclonal antibodies HMB-45 and anti-MART-1 may be of help. We do not advocate the use of NKI-C3 since in our experience, this antibody lacks specificity. Finally, electron microscopy may be of help in problem cases, provided that lesional tissue has been specifically processed for ultrastructural investigation. The retrieval of tissue from paraffin blocks, which is very useful in some other areas of tumor pathology, often yields disappointing results when melanocytic differentiation (*i.e.*, the unequivocal establishment of the presence of premelanosomes) needs to be established.

The chance of an extracutaneous melanocytic tumor not being recognized as such is generally greater than in case of a cutaneous tumor, because as a group, extracutaneous melanocytic tumors are rare and mesenchymal spindle cell tumors are comparatively common. Again, an awareness of the possibility of a melanocytic tumor is very important.

Primary spindle cell melanocytic tumors of extracutaneous sites constitute a heterogeneous group of lesions. Melanocytic blue nevi have been described in a number of sites, including the subepithelial connective tissue of a variety of mucous membranes, the prostate, the uterine cervix, and (rarely) lymph nodes. Melanocytic tumors of the meninges, either of a localized (melanocytoma) or diffuse (melanocytosis) nature, may show histological features of blue nevus, although some examples exhibit a more plump cell type. Nevus cell aggregates of lymph nodes, which are much more common than nodal blue nevi, generally show small rounded or oval rather than spindle melanocytes. It should be borne in mind that not all brown pigment positive for melanin stains constitutes true melanosomal melanin, since some breakdown products show similar tinctorial features. In addition, not all melanin present in a tumor is necessarily produced by the tumor cells themselves: so-called colonization of tumors by accompanying non-neoplastic melanocytes occurs in some carcinomas of the skin, breast and other organs, in some benign epithelial skin tumors such as melanoacanthoma, and it may be the cause of pigmentation of the Bednar tumor (pigmented dermatofibrosarcoma protuberans).

A spindle cell metastasis of melanoma, the primary of which may hitherto have escaped clinical detection, should be considered especially in case of a spindle cell tumor of a lymph node. As a rule of thumb, it can be said that metastatic melanoma should be the first thought in every case where a malignant spindle cell tumor manifests itself for the first time in a lymph node draining the skin, even when a primary melanoma has not become clinically appar-

ent. Usually, the combination of morphology and immunohistochemistry will allow an unequivocal diagnosis.

Clear cell sarcoma, which most commonly arises from deep soft tissues of distal sites of the extremities, is the most important malignant melanocytic tumor arising outside the skin. Histological features include confluent nests and strands of usually oval cells with somewhat vesicular nuclei and a low mitotic rate, lying between paucicellular bands of stroma. Multinucleated tumor giant cells are a helpful diagnostic feature. S-100 and HMB-45 immunostains are eminently useful. In our hands, melanin stains have been negative in the majority of cases. Cytogenetic demonstration of the characteristic t(1 2;22) translocation is diagnostically useful in problem cases (2). Clinically, the tumor is characterized by a usually slow progression and long disease-free intervals after treatment but ultimately, over half of the patients succumb to recurrent disease.

Is the melanocytic spindle cell tumor benign or malignant

Again, it is useful to consider cutaneous and extracutaneous lesions separately.

Cutaneous lesions

In cutaneous lesions the main entities entering the differential diagnosis are Spitz nevus (3), pigmented spindle cell nevus (Reed), (cellular) blue nevus, combined nevus and, of course, primary cutaneous spindle cell melanoma (1). There are no general rules of universal applicability in differentiating benign from malignant lesions: this requires a detailed knowledge of the histological features of each of these entities. For the present purpose, some practical remarks can be made, but these are by no means intended to substitute a more comprehensive discussion, which is outside the scope of this brief text.

Spindle cell melanoma

There are five main points, as follows:

- i) Spindle-cell melanocytic tumors arising in sun-damaged skin in the elderly should be regarded with much suspicion.
- ii) Thick spindle cell melanoma often does not exhibit the architectural and cytological variability and the inflammatory and fibrosing host response evident in most thick melanomas of epithelioid cell type. In thick spindle cell melanocytic tumors, their absence should, therefore, not be taken as evidence against malignancy.
- iii) In thick spindle cell melanocytic tumors, important evidence of malignancy is often present, should be sought after, in the deep part of the tumor (a compact architecture, mitotic activity, hyperchromasia of elongated (not just oval) nuclei and an absence of biphasic architecture) rather than in the epidermal and subepidermal portions of the tumor. In such cases, a superficial shave biopsy, which does not contain this part of the lesion, constitutes inadequate material for diagnosis.
- iv) Spindle-cell melanoma appears to grow within and along nerves more commonly than melanomas of other cell types. A diligent search for intra- and perineural growth is in order in (re) excision specimens of spindle cell melanoma.
- v) Cellular blue nevus is a main differential diagnostic consideration: this lesion may occur in various sites, but the larger and richly cellular examples are surprisingly commonly located in the coccygeal-gluteal area, where spindle cell melanoma is rare. Distinguishing features include presence of pigmented dendritic melanocytes, biphasic architecture (not always pre-

sent), absence of high numbers of mitoses and of atypical mitotic figures, absence of coagulation necrosis. It should be borne in mind that very rarely, cellular blue nevi develop into tumors behaving in a locally aggressive way and some may metastasize (4). From the relatively small number reported and from personal experience, it appears that this may perhaps be more common in lesions of the cranial half of the body.

Pigmented spindle cell nevus (Reed nevus)

This lesion, which is most common on extremities of young adult females, not uncommonly gives rise to some concern because of the jet-black color of this usually sharply circumscribed lesion. The unnecessary suspicion may be compounded by the histology which shows a richly cellular melanocytic tumor with often mitotic activity and the presence of ascending melanocytes within the epidermis. Many features are of help in the distinction from melanoma (5) and a few are listed below:

- i) compact and richly cellular junctional component, which includes many confluent large melanocytic nests;
- ii) spindle-cell type with preferential vertical orientation of some nests (although horizontal and oblique orientation of some nests is often also present);
- iii) sharp borders, symmetry in most cases;
- iv) hyperplastic epidermal reactive changes (especially rete ridge proliferation) and absence of epidermal flattening above the centre of the lesion;
- v) absence of abrupt changes in cell type or architectural pattern within the lesion.

Extracutaneous melanocytic tumors may be benign or malignant. Since this is a heterogeneous group of tumors, there are no useful general guidelines to the diagnosis: the diagnosis should rest on a good knowledge of the various entities relevant to the differential diagnosis of the individual case. As a word of caution, it could be said that not all brown stains, positive for melanin stains, are melanin (counter-example: neuromelanin in some neural tumors); not all melanin present within tumors is derived from tumor cells (counter-examples: melanocyte colonization); not all mitotically active melanocytic tumors are malignant (counter-example: some extracutaneous blue nevi and melanocytomas); not all melanocytic lesions of lymph nodes constitute lymph node metastases of melanoma (counter-examples: nevus cell aggregates of lymph nodes, nodal blue naevi); not all HMB-45 positive lesions and tumors are melanocytic in origin (counter-examples: lymphangio-lipomatosis, angiomyolipoma).

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