Rev Esp Patol 1999; Vol. 32, N~ 3: 447-453

Short Course 11

Pigmented lesions of the skin

Chairperson **F** Contreras *Spain* **Ca-chairpersons** S McNutt *USA* and P McKee, *USA.*

Problematic melanocytic nevi

RH. McKee and F.R.C. Path

Brigham and Women's Hospital, Harvard Medical School, Boston, USA.

Whether the diagnosis of any particular nevus is problematic or not depends upon a variety of factors, including the experience and enthusiasm of the pathologist, the nature of the specimen (shave *vs.* punch *vs.* excisional), the quality of the sections (and their staining), the hour of the day or day of the week in addition to the problems relating to the ever-increasing range of histological variants that we are obliged to recognize. Reporting nevi, difficult or otherwise late on a Friday afternoon is probably always a mistake particularly if it follows rather than precedes the customary preweekend celebration (the TGIF club)! This presentation focuses on some of the more commonly misdiagnosed and problematic nevoid variants.

Neonatal and childhood congenital nevi

In the majority of cases, congenital nevi in neonates are not significantly different from similar lesions arising in children or adolescents. Rarely however, they may be characterized by extremely worrisome histological features including a junctional component (which may be lentiginous and nested) composed of pleomorphic epithelioid nevus cells with abundant cytoplasm and enlarged hyperchromatic or vesicular nuclei containing prominent eosinophilic nucleoli (1, 2). One or two mitoses may be seen. Particularly disturbing is the presence of pagetoid spread, (sometimes to the extent that it mimics *in situ* melanoma) and involvement of the appendage epithelium. The dermal component, when present, may contain similar cells or else be composed of more banal nevus cells showing maturation with depth and rendering the benignity of the lesion more obvious.

Similarly disturbing features may very occasionally be seen in congenital nevi excised from young children. Although the lesions appear clinically benign, their biological potential is as yet unknown. A modest re-excision, if the nevus cells approach anywhere near to the margins would be prudent.

Desmoolastic nevus

This nevus which was first described by Barr *et al.* (3) as a variant of Spitz nevus is still occasionally a source of diagnostic difficulty. It most often presents on the extremities of young adults. Many lesions are devoid of melanin pigment and clinically present as a flesh-colored to yellow or erythematous papule/nodule which may be misdiagnosed as a fibrous histiocytoma.

Histologically, the nevus presents as a symmetrical, dome-shaped dermal nodule covered by attenuated or acanthotic epidermis. Some lesions show small foci of residual junctional activity and melanin pigment is often evident. Frequently, however, the lesion is solely intradermal when it may be confused with a fibrohistiocytic tumor, particularly epithelioid cell fibrous histiocytoma (4). It is typically composed of epitheliold nevus cells with abundant eosinophilic cytoplasm and large, round, to oval vesicular nuclei containing prominent eosinophilic nucleoli. Intranuclear cytoplasmic pseudoinclusions are common and mitotic figures are occasionally present. The nevus cells which are embedded in a dense, sclerotic connective tissue stroma, usually show maturation with depth. Less frequently the nevus is composed solely of spindle cells which may result in confusion with atrophic fibrous histiocytoma. Desmoplastic nevus can be distinguished from epithelioid fibrous histiocytoma by its paucicellularity, absence of even a focal storiform growth pattern and SiQO protein/HMB 45 expression. Epithelioid fibrous histiocytoma often expresses smooth muscle actin and muscle-specific actin.

Recurrent nevus

A major diagnostic problem occasionally encountered following shave biopsy specimens, is the phenomenon of recurrent nevus (pseudomelanoma) (5). Re-excision specimens commonly show melanocytic hyperplasia particularly overlying the site of dermal scarring. If the nevus has been incompletely excised, regrowth of the junctional component may sometimes be accompanied by disturbing melanocyte cytology including nuclear pleomorphism, nucleolar prominence and occasional mitotic figures. Focal pagetoid spread may even be present. Clues to the benignity of the process include the presence of dense, horizontally orientated fibrous tissue in the superficial dermis and residual dermal nevus cells deep to the scar tissue. In those examples where the cytological changes are marked, review of the original biopsy specimen is always advisable. It is worth remembering that the original lesion may of course have been a dysplastic nevus or *in* situ/invasive melanoma.

Deen Denetratina nevus

This uncommon nevus variant is a common source of diagnostic difficulty. Particular problems relate to its precise histogenesis and biological potential. It presents as a densely pigmented papule or nodule on the face, neck or shoulder of young adults and as such may be clinically mistaken for melanoma (6).

Histologically the epidermis may be uninvolved although, not uncommonly, foci of lentiginous or nested junctional activity are seen (7). The nevus presents a wedge-shaped appearance with its broad base uppermost, extending into the deeper dermis or subcutaneous fat as one or more often bulbous extensions. Although in the original descriptions the nevus was said to be composed of a homogenous spindle cell population, in my own experience it more often consists of a superficial epithelioid nevus population which gradually merges with spindle cells in the deeper reaches. Cytoplasm is usually finely pigmented giving a dusty, and often gray appearance. Nuclei may be hyperchromatic and smudged or vesicular with prominent small nucleoli. Intranuclear cytoplasmic

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.

References

1. Silvers DN, Hewig EB. *Melanocytic nevi in neonates.* JAm Acad Dermatol 1981; 12: 39-44.
2. Lupton G~, Gagnier JM. *The recognition of recently described and potentially problematic melanocytic lesions of the skin.* Dermatologic Clinics 1992; 19: 161-187.
3. *Barr* RJ, Morales RV, Graham JH. *Desmoplastic nevus: A distinet histologic variant of mixed spindle cell and epithelioid cell nevus. Cancer* 1980; 46: 557-564.
4. Singh, Gbmez C, Calonie Fetal. *Epithelloid benign fibrous histiocytoma of skin: Clinicopathological analysis of 20 cases of a poorly known variant.* Histopathol 1994; 24: 123-129.
5. Kornberg R, Ackerman AB. *Pseudomelanoma.* Arch Derm 1975; 111: 1588-1590.
6. Seab JA, Graham JH, Helmig EB. *Deep pentrating nevus.* Am J Surg Pathol 1989; 13: 39-44.
7. Cooper PH. *Deep penetrating (plexiform spindle cell) nevus: A frequent participant in combined nevus.* J Cut Pathol 1992; 19: 172-180.
8. Graham J. *Malingnant deep penetrating nevus.* J Cut Pathol 1996; 23: 76 (abstract).

Spindle cell melanocytic tumors

W.J. Mooi

Dept. of Pathology Erasmus University Rotterdam, The Netherlands.

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-lOO 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-i 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 spindled 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-