Spitz Nevus Variants

13.1 Introduction

Spitz nevus has a huge number of morphological variants, which help make the differential diagnosis with melanoma a nightmare for many pathologists and a challenge for the most expert dermatopathologists.

Many of these variants are sufficiently distinctive that, with practice, general pathologists can learn to recognize them. Others raise issues that are at the edge of our current knowledge.

13.2 Desmoplastic Spitz Nevus

Desmoplastic Spitz nevus is a frequently encountered lesion, usually found on the limbs of young adults. The neoplasm is characterized by large epithelioid or spindled melanocytes distributed among thickened, rarely keloidal-appearing, collagen fibers (Figs. 13.1 and 13.2).

A substantial junctional component is usually lacking, although a few typical nests of epithelioid cells are found at the junction, especially if serial sections are performed.

Desmoplastic Spitz nevus is regularly misinterpreted as desmoplastic melanoma because of the atypia of the cells, its poor circumscription, and occasional neurotropism (Koc et al. 2011). The crucial aspects for the diagnosis of a desmoplastic Spitz nevus are:

- The base of the lesion is usually wedge shaped in desmoplastic Spitz nevus, and the lesion is symmetrical. While the cellularity diminishes toward the edge of a desmoplastic Spitz nevus, the most peripheral cells are often distributed along the two straight lines that define the edges of the wedge, while a line connecting those of desmoplastic melanoma would be jagged.
- The aggregations of melanocytes in a desmoplastic Spitz nevus, even though they may be small, diminish with descent, so that single cells are mostly present deeper in the lesion.
- The cells in the Spitz nevus are plump, and only rarely do they have the fibroblast-like features of those of a desmoplastic melanoma; their nuclei are usually vesicular. In desmoplastic melanoma, nuclei are often diffusely hyperchromatic.
- Fascicles of melanocytes in desmoplastic Spitz nevus are usually short and discrete; in desmoplastic melanoma, at least some are long.
- In desmoplastic Spitz nevus there are usually no signs of solar damage as in many desmoplastic malignant melanomas.
- In many desmoplastic malignant melanoma, there are nodular lymphocytic infiltrates, which are usually absent in a desmoplastic Spitz nevus. This may not reflect fundamental biology so much as the lesser depth of the lesion. A desmoplastic Spitz nevus can have lymphoid nodules if its cells reach the interface between the reticular dermis and subcutis, as many other fibrosing processes (e.g., dermatofibroma, morphea) do.
- The young age of the patient. In general, desmoplastic melanoma is rare before 50 years of age; the stereotypical patient with a desmoplastic Spitz nevus is usually a female of 30 years of age, but plenty of exceptions make this only a weak ancillary factor.
- The site of the lesion. Desmoplastic Spitz nevus is sited on the limbs and on the trunk. Pure desmoplastic melanomas (e.g., ones without a component of conventional melanoma) are rare outside the classic sites (face, head and neck, volar skin, and mucous membranes).
- Ki-67 proliferation rates are as a group lower in desmoplastic Spitz nevus than in desmoplastic melanoma. However, desmoplastic melanomas have a broad range, with exceptional cases lacking Ki-67-positive nuclei entirely.
- p16 immunostaining has been advocated in some studies for the differential diagnosis of desmoplastic Spitz nevus and desmoplastic melanoma. While one study found good discrimination, others have not been able to reproduce this (Hilliard et al. 2009).
- Spitz nevi with gains involving chromosome 11p and a mutation in HRAS exon3 have distinctive histopathologic findings that overlap with those of desmoplastic Spitz nevus. These lesions extend more deeply into the reticular dermis than most Spitz nevi, which is permeated by single cells or very small aggregations of melanocytes. In many cases, the lesional melanocytes have pale, almost
clear cytoplasm, and a thin pink line delineates cellular boundaries when groups of melanocytes are present (van Engen-van Grunsven et al. 2010).

13.3 Plexiform or “Granulomatous” Spitz Nevus

The Spitz nevus is usually a compact mass with a V-shaped or a cup-shaped silhouette. Rarely the neoplasm consists of distinct masses (Fig. 13.3) widely separated by dermal collagen; these masses have a vague similarity with sarcoidal granulomas. Assuming that these roundish or oval masses are connected, the lesion has also been dubbed as plexiform Spitz nevus. Large round aggregations of oval melanocytes simulating granulomas are also present in some atypical Spitz tumors, and this diagnosis is especially worth considering in large polypoid lesions.

13.4 Angiomatoid Spitz Nevus

A prominent vascular density, as result of neoangiogenesis, had already been noted in the past, and it is known that the Spitz nevus exhibits higher vessel counts and larger vessels than melanoma. Lesions with prominent diversely sized vessels that spread throughout the neoplasm have been called angiomatoid Spitz nevus, although the lesions seem less of a distinct entity than many of the other variants (Fig. 13.4). Clinically the neoplasm is usually sited on the extremities of third-decade women and clinically is a stable lesion. At dermoscopy, an atypical network with blurring of its center (manifest as a whitish area with telangiectases) is usually seen. The pigment is irregularly distributed.

Histologically, only sparse, epithelioid, ganglioid, or multinucleated melanocytes are present in this neoplasm, usually isolated in single units among thickened collagen bundles (Tetzlaff et al. 2009). Rarely small nests are discernible; a junctional component is lacking or inconspicuous. Vessels have a large patent round lumen and thick wall. Collagen bundles are thick and an inflammatory infiltrate is reported as frequent. Rete ridges are blunted or erased.

This peculiar variant can be easily mistaken for a hemangiomata or a regressing melanoma, in which a proliferation of small venules is a frequent finding. The differential diagnosis with a regressing melanoma is based upon the characteristics of the cells that are monomorphous and with spitzian features and upon their even distribution throughout the lesion. Most angiomatoid Spitz nevi have few melanophages, while they are generally abundant in regressing melanoma. Collagen is mature in angiomatoid Spitz nevus, usually fibrillar in melanoma.

A peculiar vascular or fibrohistiocytic lesion called multinucleate cell angiohistiocytoma is also in the differential diagnosis. This lesion has fibroctic stroma and dilated vessels and like Spitz nevus can be a dome-shaped papule or even slightly pedunculated and mushroom shaped. In multinucleate cell angiohistiocytoma, multinucleated cells with scalloped edges are present between vessels. These cells do not stain for S100 protein but are procollagen I positive.

13.5 Myxoid Spitz Nevus

Small amount of mucin can be seen in the nests of a Spitz nevus (Fig. 13.5). The deposits are Alcian blue and colloidal iron positive (and are composed of the so-called mesenchymal mucin) and are PAS negative (Hoang 2003). The Alcian deposits are susceptible to hyaluronidase digestion. These mucin deposits have been attributed to chronic trauma, but this seems unlikely to us.

Mucin can also be present in the connective tissue of the papillary dermis in superficial compound Spitz nevi. This may reflect recent remodeling of stroma, which in time is replaced by mature collagen, as it is in a wound healing reaction. This does not really qualify as a variant of Spitz nevus, so much as a variable morphological detail.

13.6 Hyperpigmented Spitz Nevus

The stereotypical Spitz nevus is an almost completely achromic or only scanty pigmented lesion. Rarely (Figs. 13.6 and 13.7), the neoplasm can be intensely pigmented (10% of all Spitz nevi according to Weedon, more frequent according to others), especially in dark-complexioned people. It has been said that this variant is more frequent in adults. The hyperpigmented Spitz nevus is quite alarming both clinically and histopathologically. It is worth remembering that melanoma (outside of acral sites and mucous membranes) is infrequent in dark-skinned people.

Aside from pigmentation, a finding peculiar to this type of Spitz nevus that needs to be noted is an occasional admixture of dendritic melanocytes and melanocytes with pale cytoplasm and dusty melanin. Irregular or even pseudocarcinomatous epithelial hyperplasia is more apt to be seen above hyperpigmented Spitz nevus. A common link to this finding, which is seen in Kamino compound blue nevi, in pigmented epithelioid melanocytoma and in hyperpigmented Spitz nevus is the finding of heavily pigmented dendritic melanocytes at the dermoeipidermal junction.

13.7 Spitz Nevus with Clark Dysplastic Nevus Features: So-Called SPARK Nevus

As noted by Hideko Kamino years ago, Spitz nevus (and other type of nevi) can have architectural features in common with dysplastic nevi. These lesions are frequently found on the thighs of women and are clinically atypical. Histologically (Fig. 13.8), the neoplasm is a “superficial spreading,” flat lesion, composed of fusiform spindle cells collected in elongated oblong nests parallel to the epidermal surface (Ko et al. 2009). Nests bridge adjacent rete ridges in the manner of a Clark nevus. The junctional melanocytes in ideal cases have homogeneous cytoplasm similar to that of classic Spitz cells, with clefts delimiting their borders. Within the papillary dermis, and usually in the center of the lesion, these cells mature to form small round melanocytes.

The differential diagnosis is with a form of severely atypical dysplastic nevus (for dermatopathologists who use these terms) or melanoma. Spitzoid Clark nevi tend to be