Spindle and Epithelioid Cell (Spitz) Nevus and Variants

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An important watershed in the pathology of pigmented lesions was the work of Sophie Spitz carried out that defined juvenile melanoma, the lesion that we now call spindle and/or epithelioid cell nevus of Spitz (Spitz 1948; Spatz and Barnhill 1999; Weedon and Little 1977; Paniago-Pereira et al. 1978). These observations resulted in a new understanding of childhood lesions and the resulting dramatic change in the management of these lesions. These seminal findings have allowed for the identification of a subset of lesions with rapid growth that have a characteristic spindle and epithelioid histologic appearance. The discovery of these lesions has also led to an understanding of variants of spindle and epithelioid cell tumor that do not show the maturation of the Spitz nevi but form expansile nodule (Barnhill et al. 1999; Ludgate et al. 2009). Some of these lesions that have been referred as atypical Spitz nevi can rarely metastasize (Busam et al. 2009; Smith et al. 1989). The impact of Sophie Spitz' discovery has far reaching consequences but also led to a revolution in the observation that these lesions can occur in children but also in adults (Weedon and Little 1977).

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Case 5A

Clinical History A ten-year-old female with a pigmented lesion on her trunk

Microscopic Description The epidermis shows marked epidermal hyperplasia in which there are multiple nests of cells and both lateral edges of the lesion are sharply circumscribed (Fig. 5.1). These nests are vertically oriented perpendicular to the long axis of the epidermis (Fig. 5.2). An interesting architectural feature is that at the edges of the lesion, which are also the edges of the nodule, the rete ridges as well as the nests are angular and outlining the inverted triangle characteristic of the Spitz nevus with the apex in the deep dermis. The cells infiltrate into the reticular dermis where they break up into small nests and single cells (Fig. 5.3). As they become smaller, they retain the appearance of the intraepidermal cells. The cytomorphology of the cells in the intraepidermal nests is spindle in appearance and contains oval nuclei with chromatin distribution in a delicate manner and small nucleoli (Fig. 5.4). Cells with similar morphology are present in the dermis in nests and as single cells (Fig. 5.5). Brightly eosinophilic globules are present within the upper portion of the epidermal nests (Fig. 5.4). These large Kamino bodies are characteristic of Spitz nevus (Kamino et al. 1979). A rare mitosis is noted within the intraepidermal nest (Fig. 5.6). The margins are free. We do not recommend any further treatment unless the lesion recurs.

Diagnosis Spindle and epithelioid cell (Spitz) nevus, compound type

Comment Approximately two thirds of patients with Spitz nevi are over 20 years of age with a female predominance in a recent series of 247 cases (Cesinaro et al. 2005). In a large series of 652 Spitz nevi, 30 % were located on the lower extremities, 26 % on the head and neck, and 25 % on the upper extremities (Gartmann and Ganser 1985). The most common presentation is an asymptomatic; pink-, red-, or flesh-colored; and dome-shaped nodule (Weedon and Little 1977), often less than 1 cm in size. Rarely, they can be multiple or agminated (Hamm et al. 1987).

The changes seen in this lesion are characteristic of Spitz nevus. It can be junctional, compound, or intradermal. The majority are compound. In 10–20 %, the Spitz nevi are intradermal, and these are seen mainly in adults (Weedon and Little 1977). Spitz nevi are characterized by architectural and cytologic symmetry. There is uniformity of cells and nuclei, especially from side to side in horizontal zones. The classic "raining-down" pattern of the cells is well shown in this lesion. Also excellent examples of Kamino bodies are present within the intraepidermal nests (Kamino et al. 1979). The lesion lacks the "consumption of the epidermis" (Hantschker et al. 2004) and is often associated with a hyperplastic epidermis (Scott et al. 1989). The cells show an excellent transition from nests of cells to single cells. This change along with the diminution in size of the cells from top to bottom is characteristic of Spitz nevus. Rare mitoses are often noted within the intraepidermal component of the lesion. The dermal component rarely shows mitotic activity. The absence of ulceration and partial regression are all features associated with benign Spitz nevus.

Key Histologic Features

Spindle and epithelioid cell (Spitz) nevus (Figs. 5.1, 5.2, 5.3, 5.4, 5.5, and 5.6)

- Marked epidermal hyperplasia.
- Circumscribed, wedge-shaped, or plaque growth pattern.
- Discrete nests of benign spindle cells with raining-down appearance infiltrate the dermis and exhibit maturation.

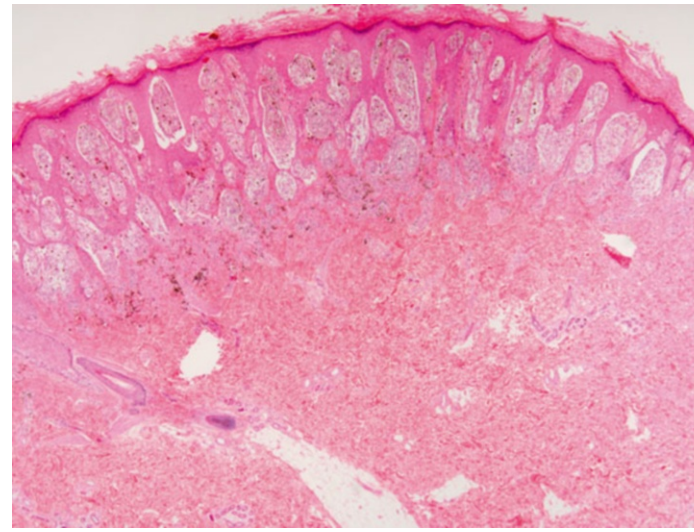

Fig. 5.1 Multiple large nests of melanocytes are seen in association with marked epidermal hyperplasia

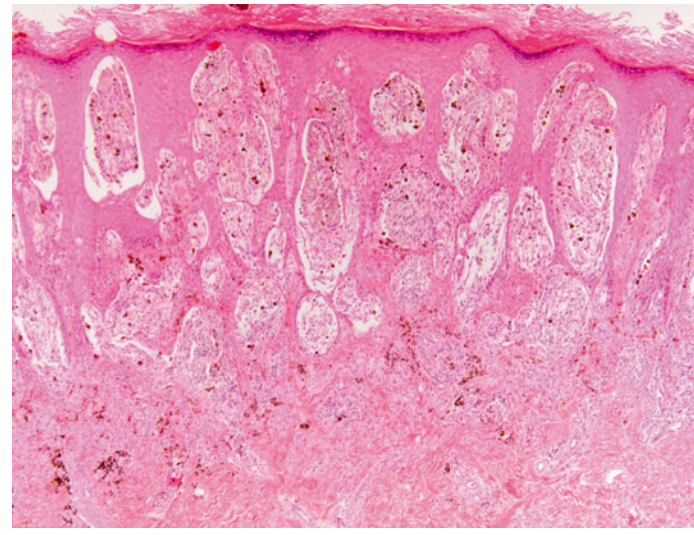

Fig. 5.2 The junctional nests are oriented perpendicular to the long axis of the epidermis

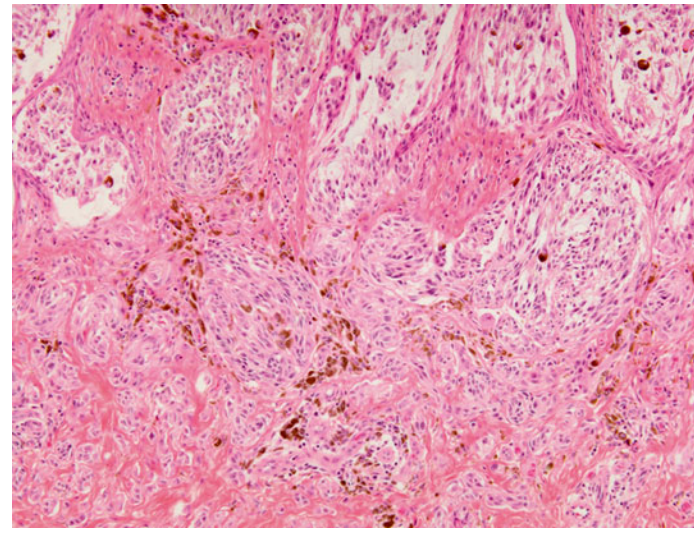

Fig. 5.3 As the melanocytes infiltrate into the reticular dermis, they exhibit maturation by breaking up into small nests and single cells

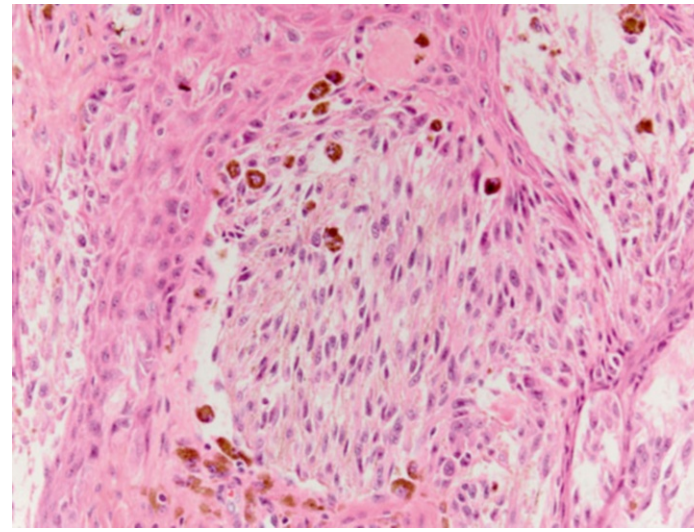

Fig. 5.4 The junctional melanocytes are spindle and with oval nuclei, small nucleoli, and delicate chromatin distribution

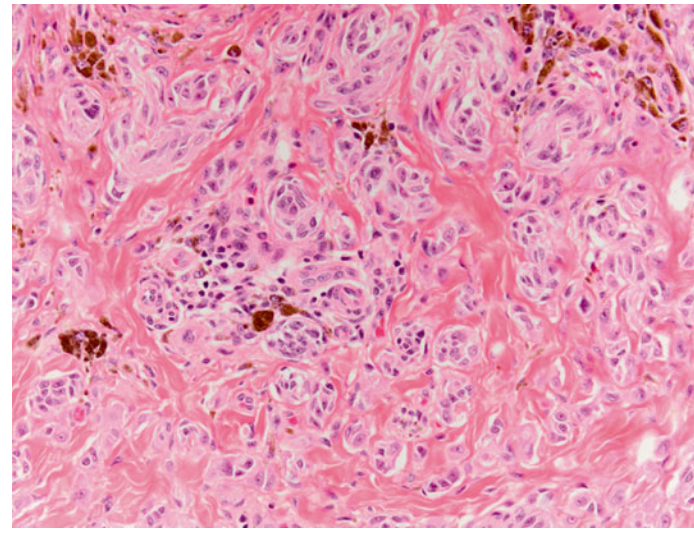

Fig. 5.5 Nested and single melanocytes with similar morphology are seen in the dermis

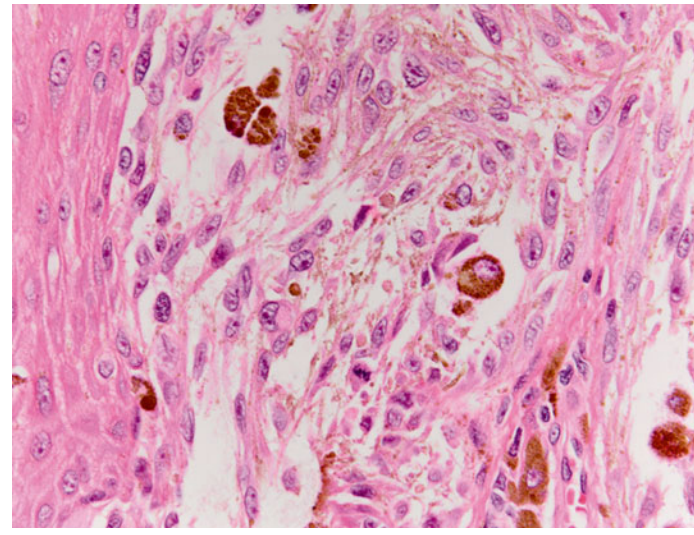

Fig. 5.6 A rare mitosis is noted within the intraepidermal nest

Case 5B

Clinical History A 40-year-old male with a pigmented lesion on his leg

Microscopic Description Low-power examination reveals a polypoid excrescence of the epidermis and dermis filled with a cellular infiltrate (Fig. 5.7). Higher-power examination shows effacement of the epidermis without evidence of an intraepidermal melanocytic proliferation (Fig. 5.8). The dermal cells are spindle in characteristic and are present in nests and in fascicles (Fig. 5.9). Toward the deeper dermis, the nests break up into single cells, but the cells maintain not only their size but also their nuclear characteristics. These cells are in a dense fibrotic dermis with small- to intermediate-sized collagen bundles that are separating the nests as well as surrounding the single cells (Fig. 5.9). Coursing through this dense matrix are quite prominent vessels with very thin walls and flattened endothelial cells. The fibrosing response delimits the lower edge of the lesion so that the entire lesion is a fibrocellular proliferation (Fig. 5.10). There are no mitoses and there is no evidence of host response or ulceration. The lesion presents at the margin. A conservative re-excision is recommended to prevent a recurrence. Alternatively, close follow-up of the patient is recommended, and a re-excision is performed if the lesion is recurred.

Diagnosis Desmoplastic Spitz nevus, intradermal type

Comment Spitz nevi can exhibit a wide spectrum of histologic appearance including myxoid (Hoang 2003), desmoplastic (Barr et al. 1980), hyalinizing (Suster 1994), angiomatoid (Diaz-Cascajo et al. 2000), pagetoid (Busam and Barnhill 1995), halo (Harvell et al. 1997), plexiform (Spatz et al. 1999b), heavily pigmented spindle cell (Barnhill et al. 1991), and combined variants.

Desmoplastic Spitz nevus typically presents as a firm dome-shaped papule or nodule on the extremities (Barr et al. 1980). The desmoplastic or sclerosing Spitz nevus is always a predominantly dermal lesion; however, in some cases, one may find rare junctional nests (Barr et al. 1980). It is important to recognize the fibrocellular lesion in which the fibrous response delimits the extent of the lesion. This type of response is characteristic of a benign proliferative lesion in contrast to desmoplastic melanoma in which there is infiltration in a highly irregular nature. In a desmoplastic Spitz nevus, the tumor is very well defined by the stroma, and the lesion is well demarcated from the adjacent dermis. The next important observation is the appreciation of the Spitzoid character of the nevus cells. Thus the cells have prominent nuclei with visible nucleoli and ample cytoplasm. Some are with cytoplasmic intranuclear pseudoinclusion. One of the more helpful clues in differentiating desmoplastic Spitz nevus from desmoplastic melanoma is the presence of epithelioid cells with often ample cytoplasm and round nuclei scattered throughout the lesion. In desmoplastic melanoma, the fibrosing area does not show scattered epithelioid cells. Also the absence of a radial growth phase equivalent or simple prominent melanocytic hyperplasia is distinct from desmoplastic Spitz nevus in which there are rare junctional nevus nests. Neurotropism can be seen with desmoplastic Spitz nevus. As far as the cell population in desmoplastic Spitz nevi is concerned, the epithelioid cells are predominantly seen in young adolescence, whereas lesions in later adolescence or adulthood are composed of spindle neoplastic cells. Our usual recommendation is conservative re-excision if the lesion extends to the edges of the lesion.

Key Histologic Features

Desmoplastic Spitz nevus (Figs. 5.7, 5.8, 5.9, and 5.10)

- A dense eosinophilic fibrous response delimits the extent of the lesion.
- Neoplastic cells with a Spitzoid appearance – spindled or epithelioid cells, abundant cytoplasm, and vesicular nuclei.
- Little or no inflammation.

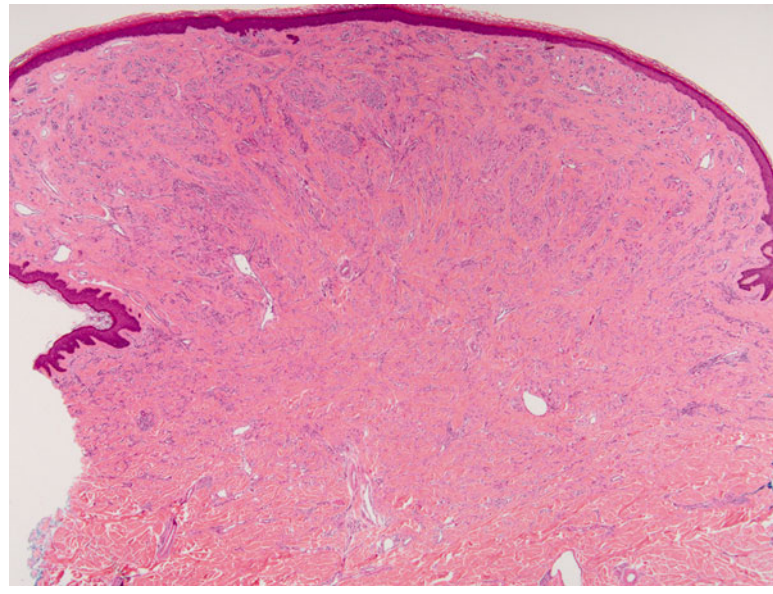

Fig. 5.7 A polypoid and cellular proliferation of spindle melanocytes is seen in the epidermis and dermis

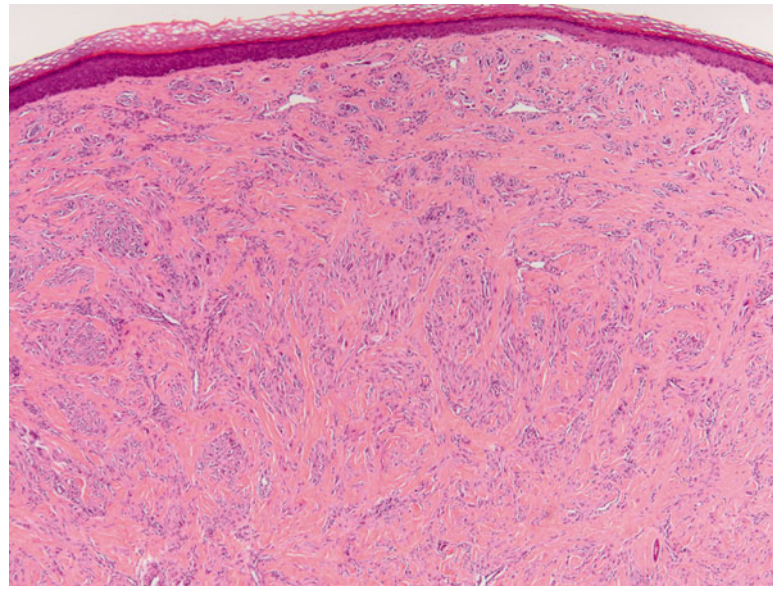

Fig. 5.8 There is no evidence of a junctional melanocytic proliferation

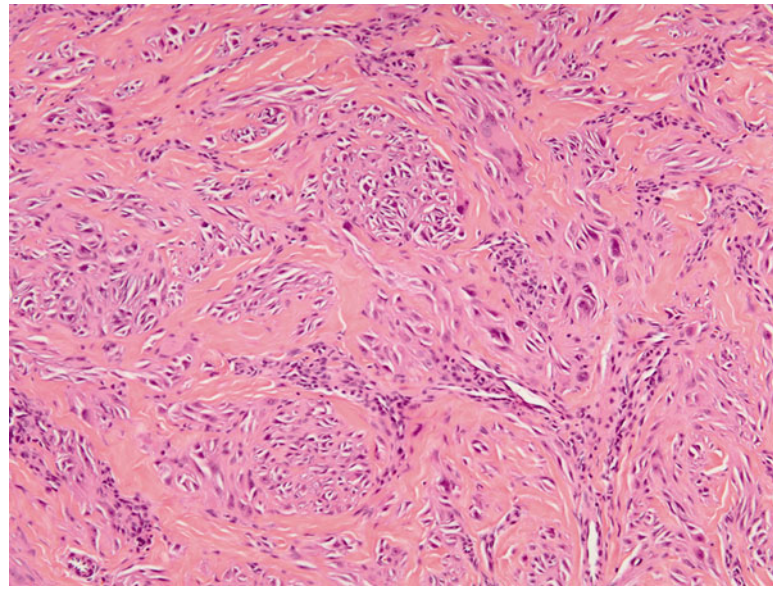

Fig. 5.9 Fascicles of spindle melanocytes are seen within a dense fibrotic dermis

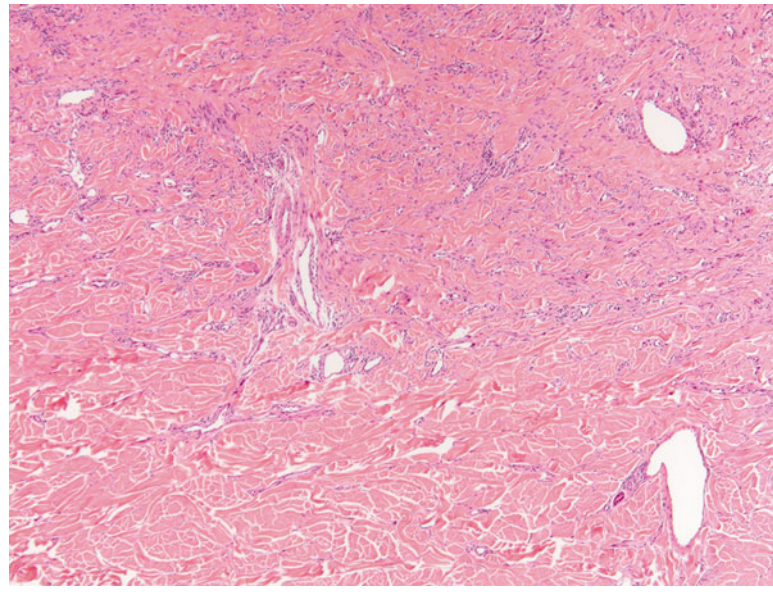

Fig. 5.10 Prominent vessels and fibrotic response outline the lower edge of the lesion

Case 5C

Clinical History A 24-year-old female with a right hip lesion

Microscopic Description Low-power magnification exhibits irregular epidermal hyperplasia with a prominent and dense dermal nevus component (Fig. 5.11). Eccentrically on both sides of the dermal component, there is elongation of rete ridges with fusion focally with proliferation of single melanocytes within the elongated rete ridges (Fig. 5.12). High-power examination reveals densely pigmented intraepidermal and dermal nests of spindle and epithelioid cells. The intraepidermal nests continue on both sides of the dermal component where they gradually merge with a proliferation of atypical epithelioid melanocytes within the hyperplastic rete ridges (Fig. 5.12). They are associated with fusion of the rete ridges by nests of melanocytes (Fig. 5.13). In addition, there is characteristic stromal proliferation of dysplastic nevus such as lamellar fibrosis, increased vascularity, and increased inflammatory infiltrate. The margins are free with the lesion extending to 0.5 mm from one tissue edge. Because of the marked cytologic atypia of the cells and the unusual appearance of the lesion, we recommend a re-excision with 5 mm margin.

Diagnosis Compound dysplastic nevus with Spitzoid features

Comment The current case is one that causes a great deal of confusion among clinicians and dermatopathologists (Ko et al. 2009). It is a combined lesion with focal Spitzoid features, but the majority of the lesion is a dysplastic nevus. We do not diagnose the lesion as "combined"; because there is merging of the spindle cells and the dysplastic cells so that the spindle cells appear to arise in an area of dysplasia. In addition in the area of both dysplasia and spindle cells, there are stromal and architecture features of dysplastic nevus. We recommend treatment of this lesion in the same manner as that for dysplastic nevi, and we grade the atypia accordingly.

Key Histologic Features

Compound dysplastic nevus with Spitzoid features (Figs. 5.11, 5.12, and 5.13)

- Eccentrically on both sides of the dermal component, there is elongation of rete ridges with fusion focally.
- Proliferation of single melanocytes in the elongated rete ridges with characteristic stromal changes.
- Scattered densely pigmented intraepidermal and dermal nests of spindle and epithelioid cells.

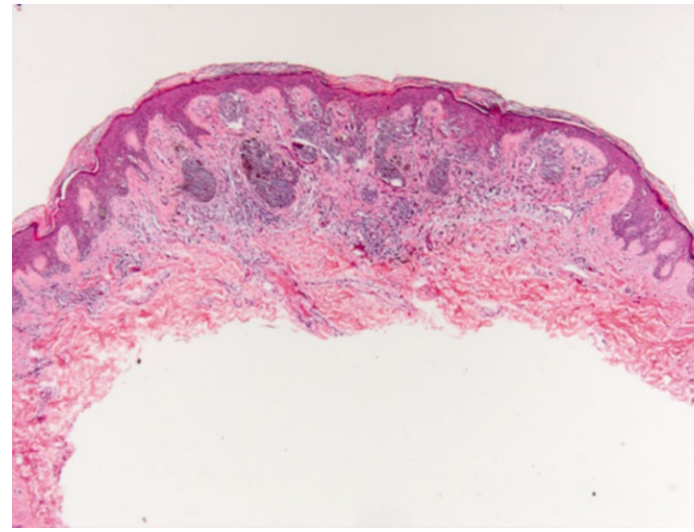

Fig. 5.11 A compound melanocytic proliferation is seen in association with irregular epidermal hyperplasia

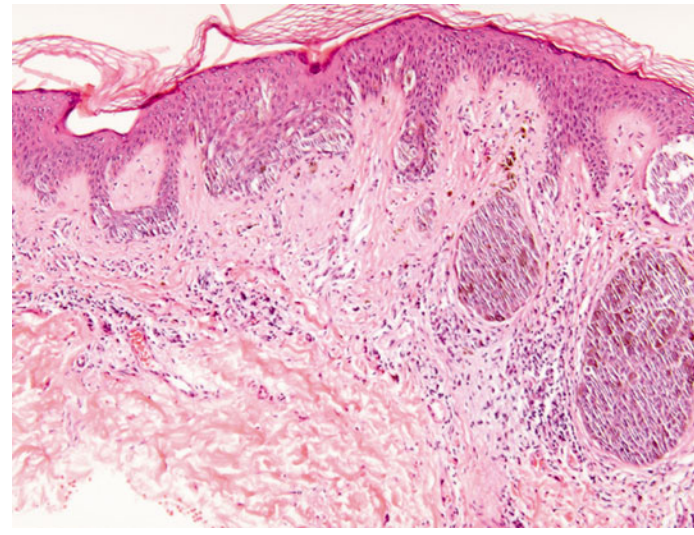

Fig. 5.12 Elongation of rete ridges and focal fusion of pigmented junctional nests of melanocytes are seen eccentrically on one side of the lesion

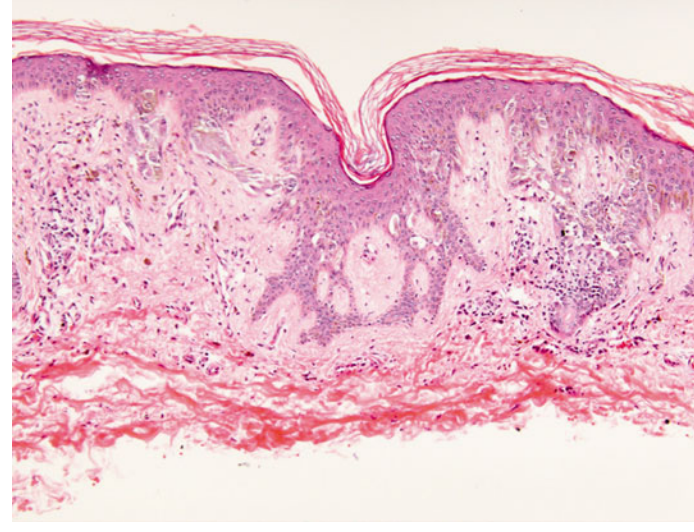

Fig. 5.13 Nests and single atypical melanocytes are seen within the epidermis

Case 5D

Clinical History A 24-year-old female with a lesion on her left cheek

Microscopic Description The epidermis shows characteristic elongation of rete ridges in which there are numerous melanocytes with variable degree of atypia scattered along the dermal-epidermal junction (Figs. 5.14 and 5.15). In addition, there are nests of pigmented atypical melanocytes irregularly disposed along the basilar area (Fig. 5.16). These changes are all present in a brightly eosinophilic dermis with lamellar fibroplasia and concentric fibrosis. In addition, the dermal vessels are prominent. There are foci of inflammation. In the lower papillary dermis, there are nests of ordinary type-B nevus cells (Fig. 5.16). Below the nevus is an oval zone of cells and fibrous tissue so that the inferior border is sharply demarcated from the reticular dermis (Fig. 5.17a). The cells comprising this areas are both spindle and epithelioid with classic Spitz-like characteristic (Fig. 5.17b). The eosinophilic collagen is composed of small bundles in contrast to the adjacent reticular dermis. This fibrocellular area is characteristic of a sclerosing Spitz nevus. There are no mitoses, no marked pleomorphism, and no inflammatory infiltrate.

Diagnosis Combined compound dysplastic nevus and desmoplastic Spitz nevus

Comment The term "combined nevus" is used to describe the combination of any two histologic patterns of nevi, congenital or acquired, found in the same lesion (Pulitzer et al. 1991). This lesion represents an unusual presentation of a dysplastic nevus with a sclerosing spindle and epithelioid cell. Although uncommon, the lesion is not rare, and it is usually sent in consultation as myxoid or desmoplastic melanoma arising in association with a compound dysplastic nevus. The clue to the diagnosis is the very sharp demarcation of the lesion and the underlying stroma. Furthermore, the cells upon careful inspection show epithelioid appearance with wispy cytoplasm admixed with spindle cells. The diagnosis is successfully made when one appreciates the overall banal appearance of the infiltrating cells. It is important to emphasize that as in the compound nevus of Spitz the reticulin stain will demonstrate reticulin fibers investing single cells within the nests – a feature of benignity. We usually recommend excision if the lesion extends to the margins.

Key Histologic Features

Combined compound dysplastic nevus and desmoplastic Spitz nevus (Figs. 5.14, 5.15, 5.16, and 5.17)

- Nests of pigmented atypical melanocytes irregularly disposed along the basal aspect of the epidermis, associated with lamellar fibrosis.
- Below the nevus is an oval zone of dense fibrous tissue containing cells that are both spindle and epithelioid with classic Spitz-like characteristic.

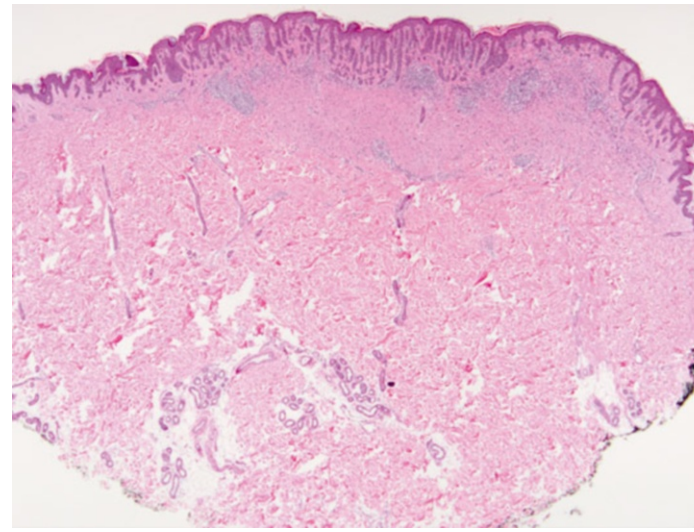

Fig. 5.14 A compound melanocytic proliferation is seen in association with prominent elongation of rete ridges

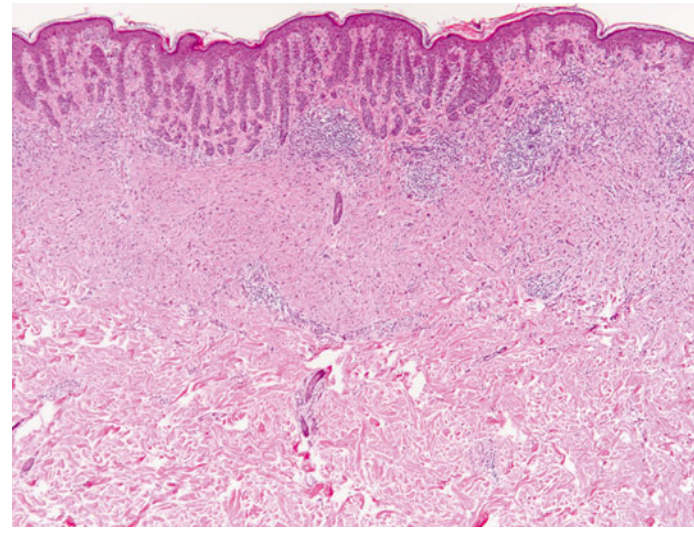

Fig. 5.15 Nests of pigmented atypical melanocytes are seen irregularly disposed along the basilar area

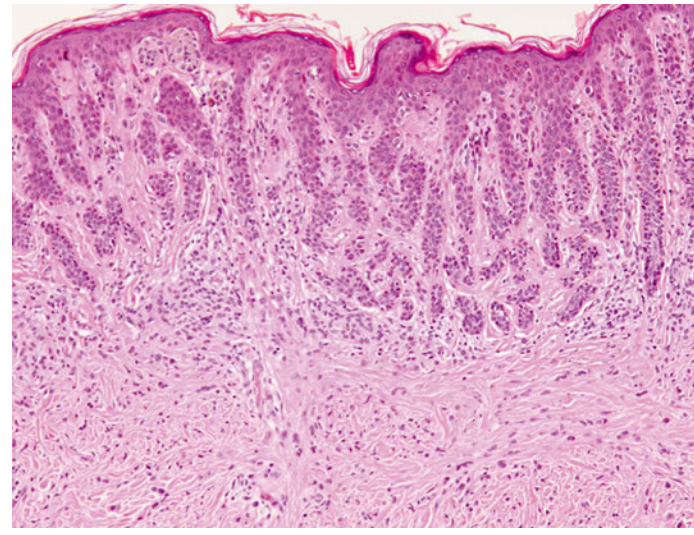

Fig. 5.16 Nests of ordinary type-B nevus cells, lamellar fibroplasia, and concentric fibrosis are seen in the papillary dermis

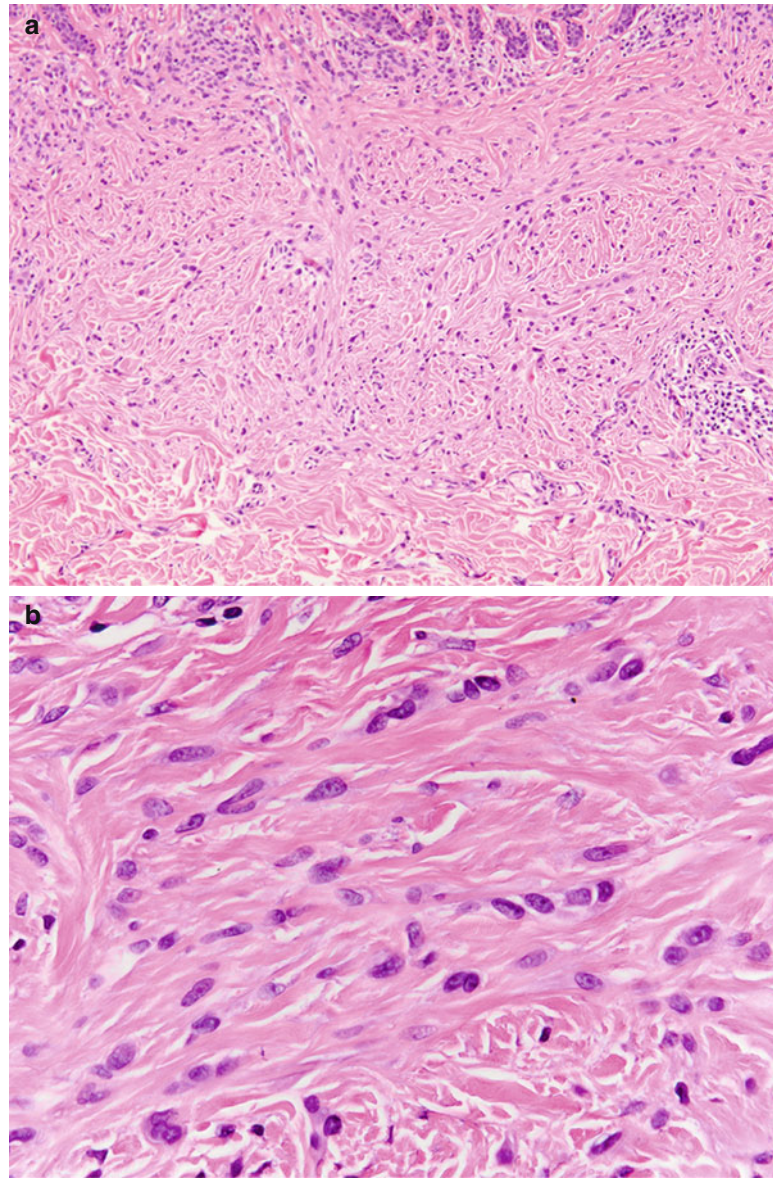

Fig. 5.17 (**a**, **b**) Spindle and epithelioid melanocytes are seen in the underlying fibrotic dermis

Case 5E

Clinical History A 46-year-old female with an atypical nevus on her left thigh

Microscopic Description Low-power examination reveals an area of epidermal hyperplasia in which there are numerous nests of pigmented melanocytes (Figs. 5.18 and 5.19). Together with the changes of epidermis, these changes form a plaque-like lesion. High-power examination reveals nests composed of uniform cells (Fig. 5.20). These nests are sharply demarcated from both sides of the lesion. The spindle cells within these nests run perpendicular to the long axis. In several areas, one sees separation of the cohesive nests from the adjacent epidermis by spaces. These spaces often cap the nests (Fig. 5.20). They throw in the contrast and emphasize the striking cohesion of the nests of spindle cells of this lesion. In the dermis, there are scattered nests of spindle cells numbering from 3 to 5 cells with the exact appearance of the intraepidermal cells (Fig. 5.21). The margins are free, and we do not recommend further therapy.

Diagnosis Pigmented spindle cell nevus of Reed, compound type

Comment Considered as a distinct entity and not a variant of Spitz nevus, pigmented spindle cell nevus (Reed nevus) is a well-circumscribed dark papule that is frequently located on the thigh of young adults (Barnhill and Mihm 1989; Smith 1987; Sagebiel et al. 1984). Pigmented spindle cell nevus of Reed differs from the Spitz nevus in that it is a lesion of the epidermis and papillary dermis and thus often forms a plaque-like lesion rather than a nodule (Smith 1987). The Spitz nevus on the other hand is a lesion of the reticular dermis, and it is associated with deep infiltration of cells into the lower reticular dermis. The features that are immediately helpful in diagnosing the pigmented spindle cell nevus of Reed are the sharply circumscribed nests of nevomelanocytes with sharp borders. Secondly, the cohesion of the cells and nests with often a space separating the epidermis from the nevus nests is very characteristic (Sau et al. 1993). The cells in the nests are oriented predominantly in a 90° angle perpendicular to the long axis but may also form concentric arrangement or horizontally. There is quite variation in the pigmentation of the cells, but the appellation of pigmented spindle cell nevus of Reed applies to all lesions including those with intracorneal pigmentation even though there is no prominent pigmentation of the nests. There is often a collection of small nests of cells in the papillary dermis that are widely scattered. Kamino bodies can usually be demonstrated with deeper sections (Sau et al. 1993). As in Spitz nevus, extension along adnexal structures is common. An inflammatory infiltrate that usually contains variable amount of lymphocytes and melanophages is present. Mitotic figures are rare and do not affect the dermal component. Occasionally, there is a halo of pigment occurring around pigmented spindle cell nevus of Reed when it undergoes the halo phenomenon. In the latter, the entire lesion is involved, whereas focal regression is worrisome for a malignant process.

Key Histologic Features

Pigmented spindle cell nevus of Reed, compound type (Figs. 5.18, 5.19, 5.20, and 5.21)

- A lesion of the epidermis and papillary dermis
- Symmetrical predominantly intraepidermal arrangement of discrete nests of spindle cells with raining-down appearance

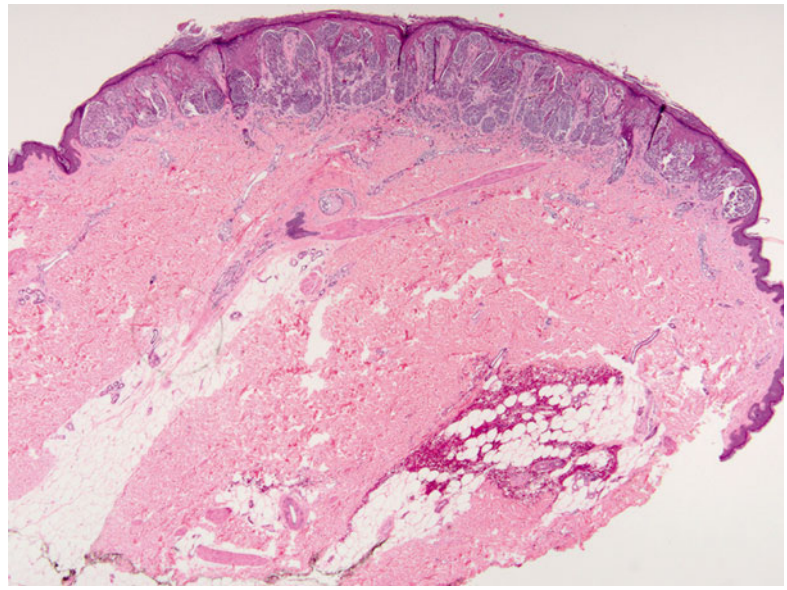

Fig. 5.18 A proliferation of spindle and pigmented melanocytes are seen within a hyperplastic epidermis and in the superficial dermis

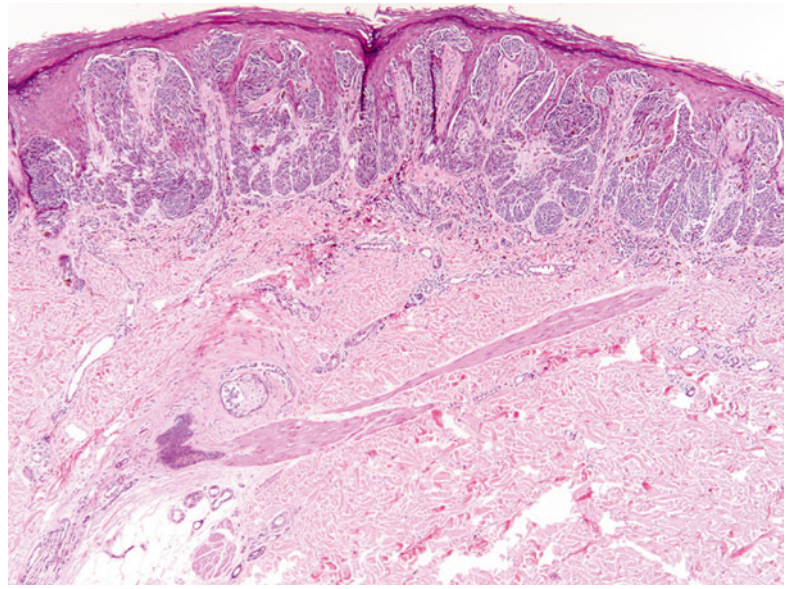

Fig. 5.19 The large junctional nests are cohesive and arranged perpendicular to the epidermis

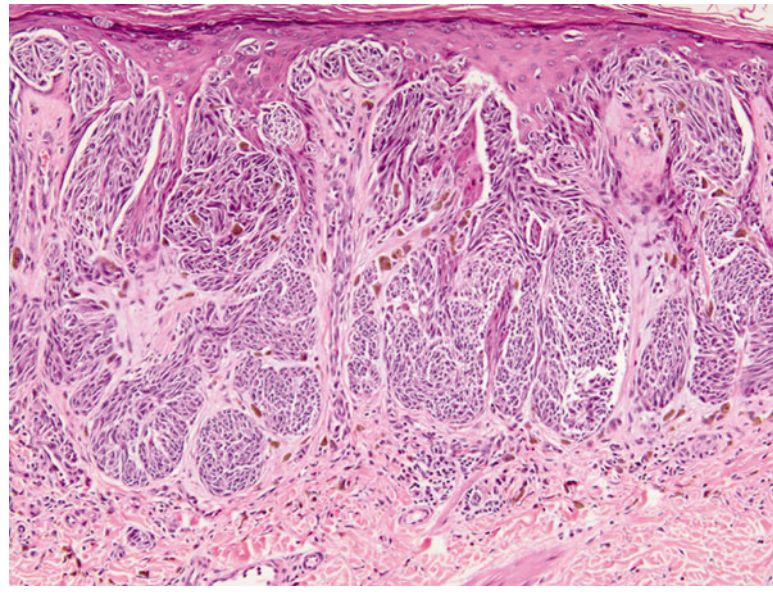

Fig. 5.20 The melanocytes are uniformly spindle and pigmented

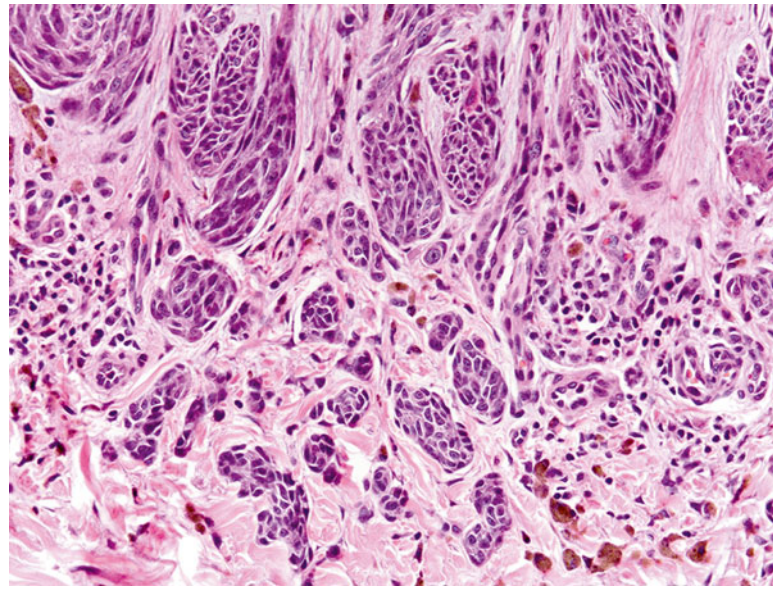

Fig. 5.21 Scattered small nests of spindle cells with similar appearance to the intraepidermal ones are seen in the superficial dermis

Case 5F

Clinical History A 34-year-old female with a lesion on her left inner knee

Microscopic Description This lesion consists of multiple aggregates of spindle cells present within the intraepidermal and dermal nests (Figs. 5.22 and 5.23). The intraepidermal nests show some upward migration to the granular layer of the epidermis with some "consumption" of the epidermis. The cells are sharply demarcated from the adjacent epidermis (Fig. 5.24). Between the nests, there is some evidence of melanocytic atypia where the cells are present as single cells within the basilar region of the epidermis (Fig. 5.24). Furthermore, there are dermal nests with variable size and degree of hyperchromasia. There are no mitoses. There is indeed a striking host response with fibrosis separating the nodules (Fig. 5.25). There is no evidence of regression. The lesion is present at the margin and should be re-excised with a 5–10 mm margin.

Diagnosis Pigmented spindle cell nevus of Reed with moderate cytologic atypia of both the dermal and intraepidermal components

Comment The pigmented spindle cell nevus of Reed can have atypical features including pagetoid spread (Barnhill et al. 1991). This type of spread, however, is common in nevi especially in children below 5 years of age. In other aspects, this lesion shows a prominent dermal component that is unusual for a Reed nevus. This type of diffuse proliferation of nests within the papillary dermis is associated with an atypical Reed nevus. In the typical or conventional Reed nevus, there is usually only a rare nest within the papillary dermis. This pattern of growth leads to the diagnosis of atypical Reed nevus, and we would recommend a conservative re-excision.

Key Histologic Features

Pigmented spindle cell nevus of Reed with moderate cytologic atypia of both the dermal and intraepidermal components (Figs. 5.22, 5.23, 5.24, and 5.25)

- Symmetrical arrangement of discrete nests of spindle cells with raining-down appearance with atypical features of expansile nests in the dermis and cytologic atypia

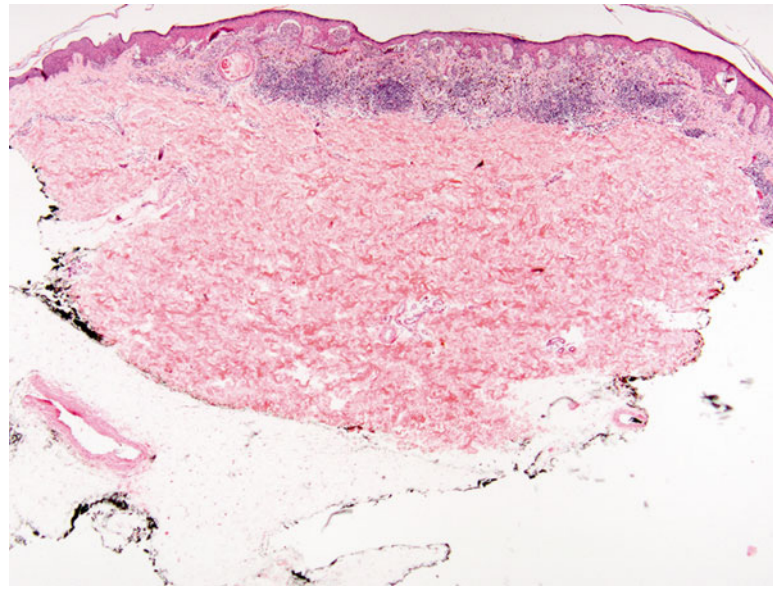

Fig. 5.22 The intraepidermal and dermal nests are comprised of pigmented and spindle melanocytes

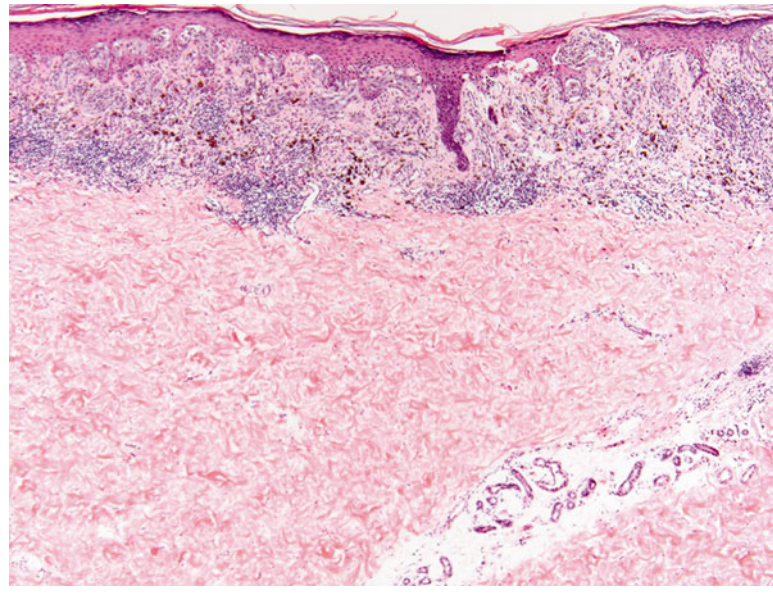

Fig. 5.23 The junctional nests are irregular, distort the architecture of the epidermis, and migrate toward the granular layer

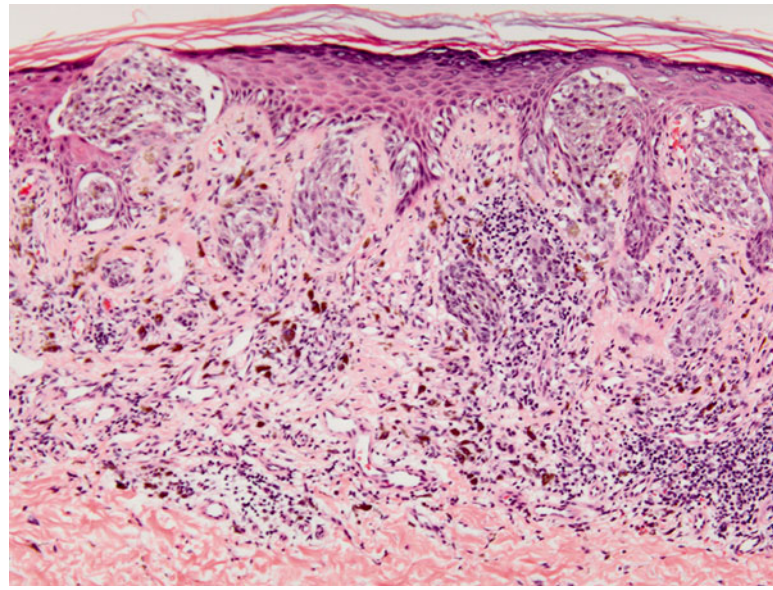

Fig. 5.24 The junctional nests of melanocytes are sharply demarcated from the adjacent epidermis

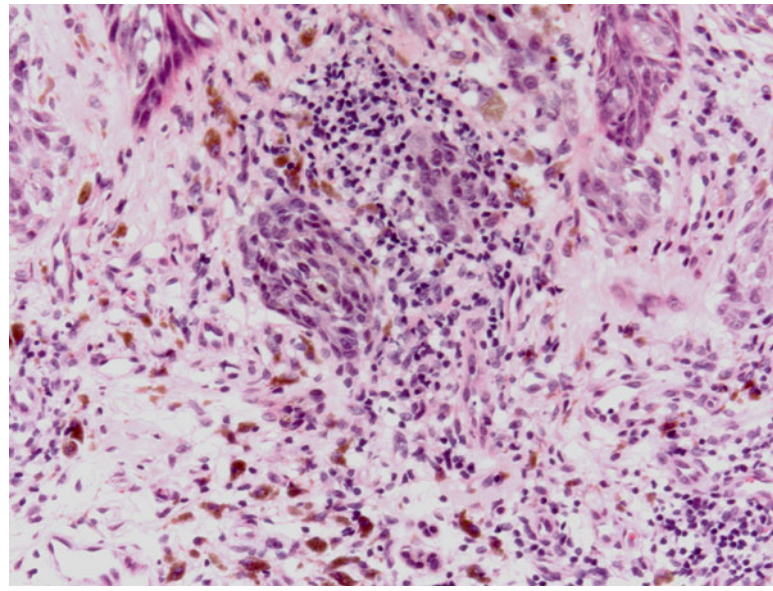

Fig. 5.25 Variably sized dermal nests are seen associated with inflammatory infiltrate of lymphocytes and melanophages

Case 5G

Clinical History A 15-year-old male with a pigmented lesion on his back

Microscopic Description This lesion exhibits a striking intraepidermal component and dermal component (Figs. 5.26 and 5.27). The intraepidermal component is composed predominantly of nests of cells scattered along the basilar region (Fig. 5.28). The other aspect is the striking dermal proliferation that even at low power shows pleomorphism (Fig. 5.27). Higher inspection of the intraepidermal component reveals discreet nests of benign spindle cells in the lower half of the epidermis (Fig. 5.29). The spindle cells tend to arrange perpendicular to the epidermis. In addition, there is a striking proliferation of single epithelioid cells exhibiting prominent pagetoid spread (Fig. 5.29). These cells are confined to the nested area – an important criterion of Haupt and Stern (1995). In this article, they described the frequency of pagetoid spread in benign as well as malignant melanocytic lesions. The dermal component shows pleomorphism at all levels, and the pleomorphic cells are similar throughout the entire lesion (Figs. 5.30 and 5.31). In addition, these cells become smaller and break up into single cells at the base of the lesion – a characteristic of an atypical Spitz nevus in which the pattern of maturation is preserved (Fig. 5.30). Because this lesion approaches the deep margin, we recommend at least a 5 mm margin on re-excision.

Diagnosis Atypical Spitz nevus

Comment Atypical Spitz nevus is used to designate a lesion with atypical histologic features that are not commonly associated with Spitz nevus (Barnhill et al. 1999). We designate a lesion as an atypical Spitz nevus when there are sufficient characteristics that allow exclusion of an aggressive Spitz tumor. These characteristics include the absence of ulceration and dermal mitotic activity. The presence of large intraepidermal nests of spindle and epithelioid cells leads to the expansion of epidermis and papillary dermis and expansile growth of dermal component. However, the expansile nests do not replace the dermis in sheetlike fashion but infiltrate amidst the collagen bundles. Usually, atypical Spitz nevus does not assume a thickness greater than 2 mm. Evidence of maturation is always a reassuring sign. The atypical Spitz nevus has characteristics of an ordinary Spitz nevus, but they are exaggerated. Most of the benign lesions are not associated with partial involvement by inflammation. When there is inflammation in an atypical Spitz nevus, there is involvement of the entire lesion as seen in a halo nevus.

Key Histologic Features

Atypical Spitz nevus (Figs. 5.26, 5.27, 5.28, 5.29, 5.30, and 5.31)

- A proliferation of large expansile nests of spindle and epithelioid melanocytes in the dermis and at the dermal-epidermal junction
- Spindle cells with similar pleomorphism throughout the entire lesion
- Absence of ulceration and dermal mitotic activity
- Evidence of maturation

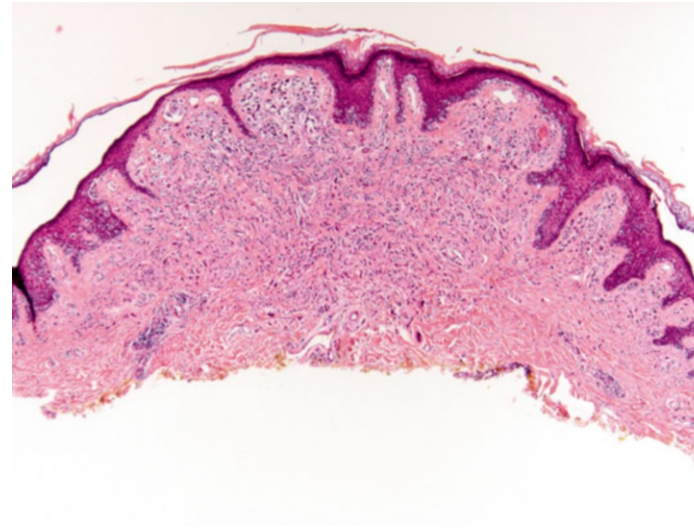

Fig. 5.26 A proliferation of epithelioid melanocytes is seen within the epidermis and in the dermis

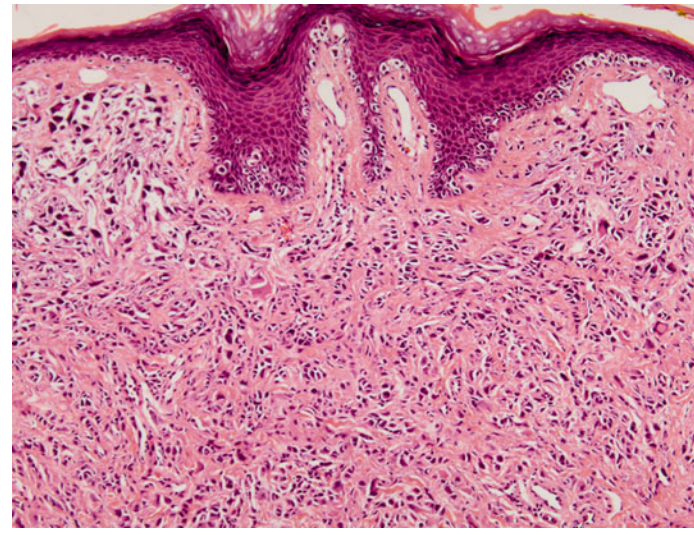

Fig. 5.27 The dermal melanocytes show striking pleomorphism

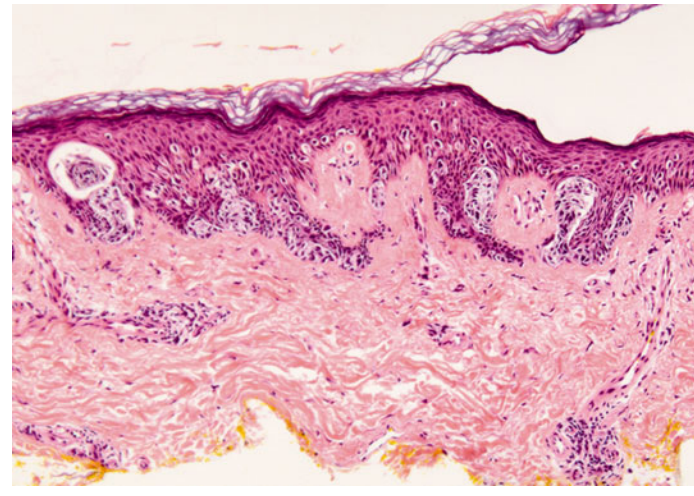

Fig. 5.28 Single and nested epithelioid melanocytes are seen scattered along the basilar region of the epidermis

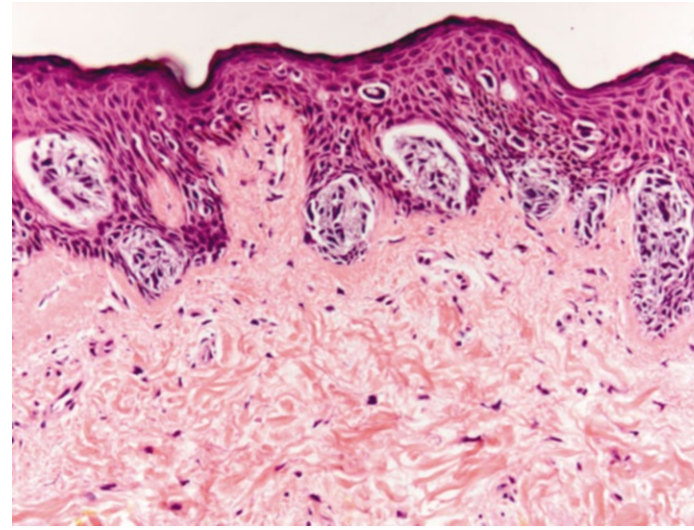

Fig. 5.29 Nests of spindle and epithelioid melanocytes are seen in the lower half of the epidermis

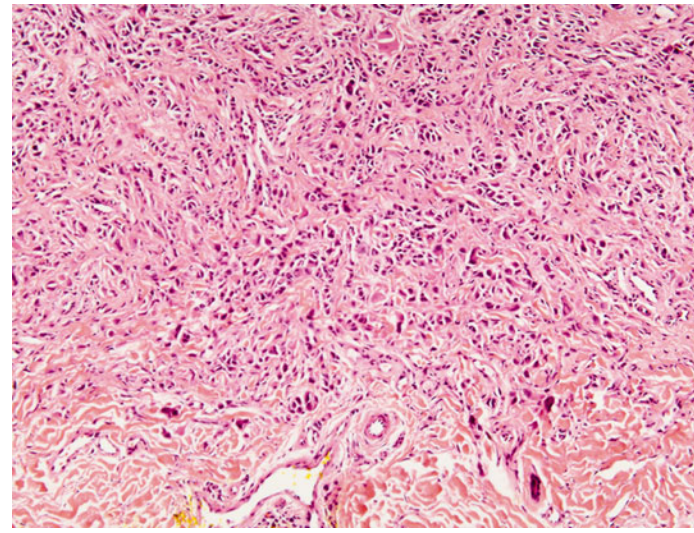

Fig. 5.30 Maturation is evident by the breaking up of the dermal nests into single cells at the base of the lesion

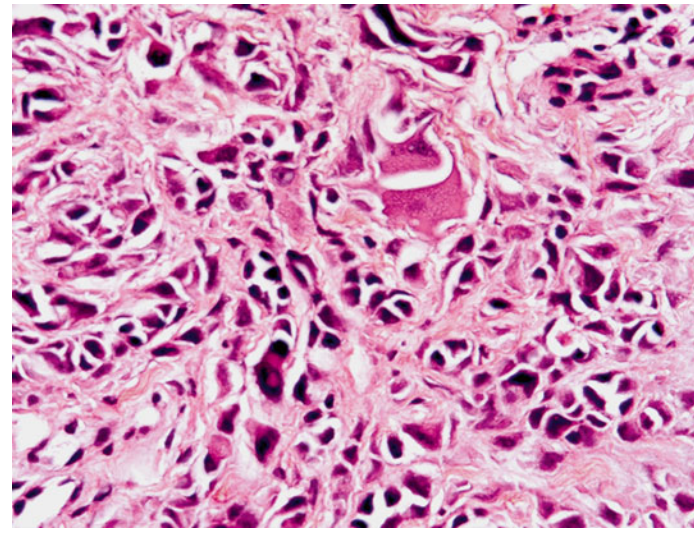

Fig. 5.31 The dermal melanocytes exhibit pleomorphism throughout the entire lesion

Case 5H

Clinical History A two-year-old male with a pigmented lesion on his posterior ear

Microscopic Description This lesion consists of a strikingly polypoid excrescence filled with nests of spindle-shaped melanocytes (Figs. 5.32 and 5.33). These cells are present in large fascicles superficially. The fascicles arrange haphazardly in relation to the epidermis (Fig. 5.34). There are focal intraepidermal nests obviously at the site of origin of the tumor (Fig. 5.35). The fascicles in the nodules do not appear to break up into smaller nests and single cells. Vascular ectasia is present. These cells in the reticular dermis below show definite maturation as the large nests become smaller and the cells within them become smaller as well (Fig. 5.36). The measured thickness of the lesion is 6 mm. Mitotic figures are extremely rare (Fig. 5.37). There is protrusion of cells lined by spindle endothelium; however, we do not see any intralymphatic invasion (Fig. 5.38). There is a focal host response, especially toward the base of the lesion. A conservative re-excision is recommended.

Diagnosis Polypoid Spitz nevus with atypical features, present at margin

Comment This lesion exhibits the very common appearance of polypoid Spitz nevi in the first decade of life (Fabrizi and Massi 2000). These nevi often occur on or near the face and even on the hairline. The polypoid configuration is completely benign in our opinion. What becomes problematic is the presence of cells in large fascicles almost replacing the dermis. A reassuring sign is the absence of mitoses. The abrupt transition from nests to single cells is very characteristic of Spitz nevi in children and helps the pathologists to identify the lesions as benign as oppose to those without maturation. The paucity of mitosis, the absence of ulceration, and the absence of severe cytologic atypia all support the diagnosis of benignancy. Because the lesion is very close to the margin, a conservative re-excision is recommended.

Key Histologic Features

Polypoid and atypical Spitz nevus (Figs. 5.32, 5.33, 5.34, 5.35, 5.36, 5.37, and 5.38)

- A polypoid excrescence filled with nests of spindle-shaped melanocytes present in large fascicles superficially.
- These cells in the reticular dermis show definite maturation as the large nests as well as the cells within them become smaller.
- Rare mitotic figure seen.
- Absence of ulceration and severe cytologic atypia.

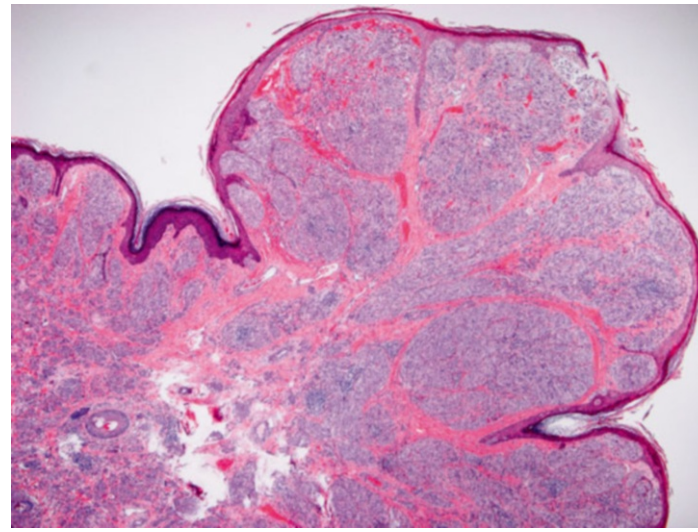

Fig. 5.32 A polypoid proliferation of spindle-shaped melanocytes is seen predominantly in the dermis

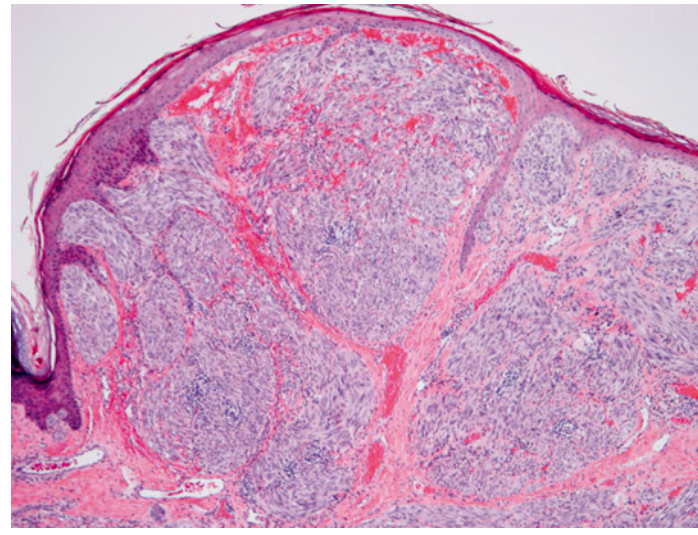

Fig. 5.33 Large fascicles of spindle melanocytes are seen in the superficially dermis

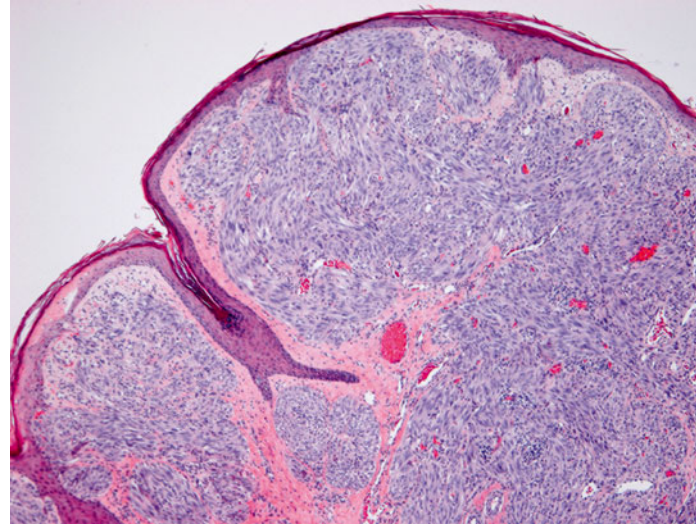

Fig. 5.34 These fascicles arrange haphazardly in relation to the epidermis

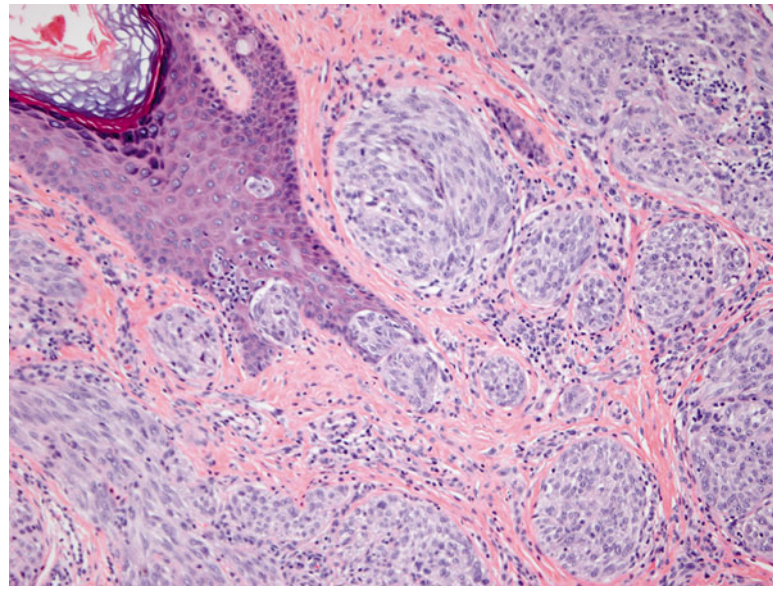

Fig. 5.35 Intraepidermal nests are focally seen

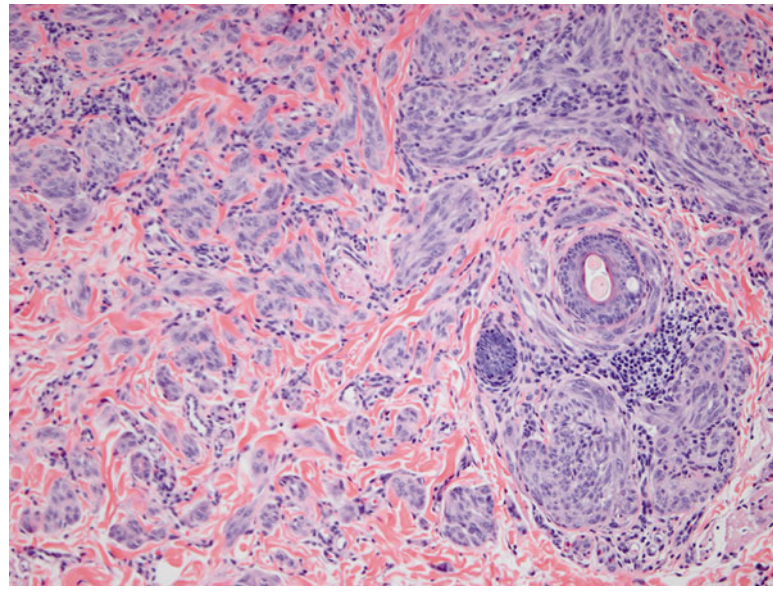

Fig. 5.36 As the lesion extends into the reticular dermis, both the size of the nests and the individual melanocytes become smaller

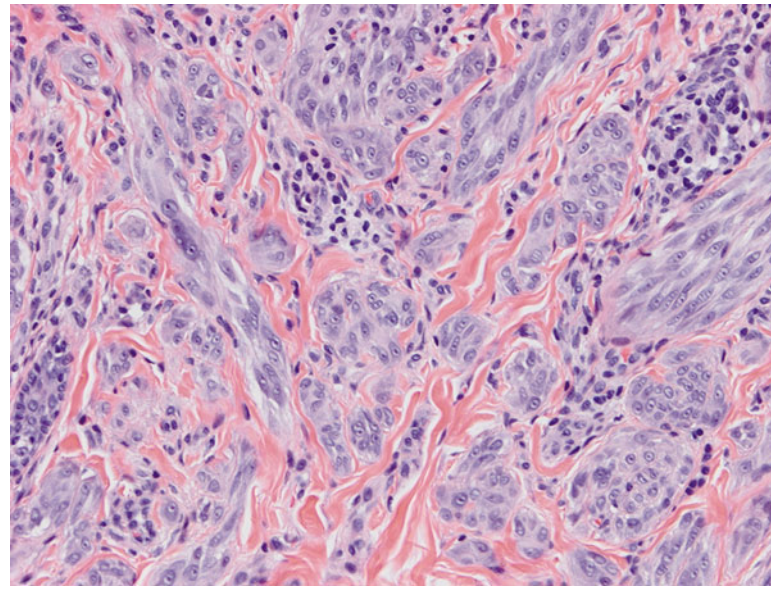

Fig. 5.37 Mitotic figures are not readily identified

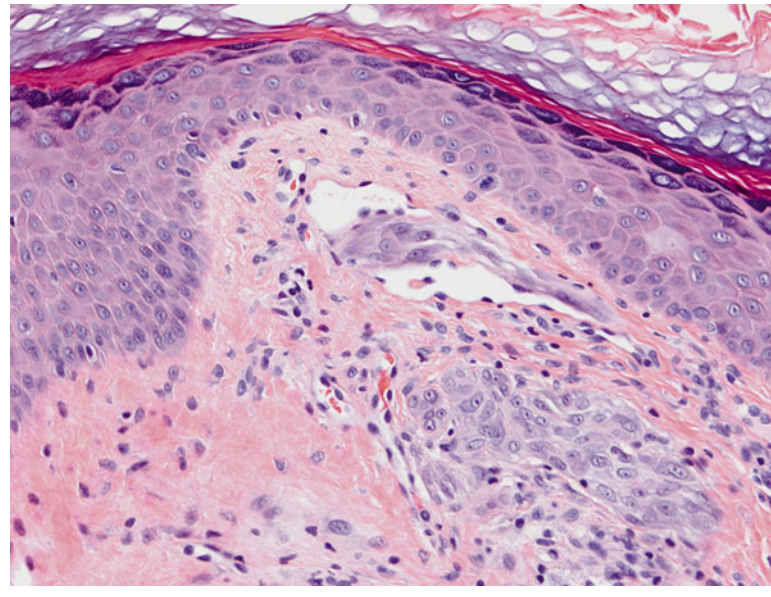

Fig. 5.38 Protrusion of tumor cells into a vascular space is focally seen

Case 5I

Clinical History A nine-year-old female with a pigmented lesion on her right buttock

Microscopic Description Low-power examination exhibits a melanocytic proliferation that virtually and completely replaced the reticular dermis, and at the base there is an expansile nodule that abuts the subcutaneous fat (Figs. 5.39 and 5.40). High-power examination reveals multiple nests of cells; some are intraepidermal and some are present predominantly in the papillary and upper reticular dermis (Fig. 5.41). These nests contain cells that are spindle in character. Superficially, they have a "raining-down" appearance in the papillary dermis but change to horizontal arrangement in the deeper dermis (Fig. 5.42). The cells extend into the deep dermis without any evidence of maturation and give rise to an expansile nodule replacing the dermis that abuts the subcutaneous fat (Fig. 5.43). High-power examination reveals that the cells do not show marked pleomorphism but rather resemble each other even in the deep nodule (Fig. 5.44). Superficially, the lesion exhibits approximately three mitoses per ten high-power fields (HPFs), but in the deep nodule, there are four mitoses per 10 HPFs (Figs. 5.44 and 5.45). Another sign of atypia is the infiltration by cords of cells into the adjacent mid reticular dermis. Thus cells intermingle with dermal collagen bundles in an "intersecting" pattern disrupting the dermal architecture (Fig. 5.46). This lesion measures 6.8 mm in size. We definitely recommend re-excision with a 1–1.5 cm margin.

Diagnosis Atypical Spitz tumor

Comment STUMP (Spitzoid tumors of uncertain malignant potential) has been used to designate lesions such as this case whose malignant potential is uncertain (Ludgate et al. 2009). The atypical Spitz tumor is a highly distinctive tumor that is opposite to the Spitz nevus that exhibits no maturation and extends deep into the subcutaneous fat as in this case. There is an inverse maturation. Rather than breaking into cells and nests, the cells form an expansile nodule deeply. As in this case, the large nodule exhibits high mitotic counts. In addition, marginal mitoses, i.e., mitoses within a zone of one high-power field around the periphery of the entire lesion, are highly significant for recurrence or metastases. Atypical Spitz tumor may ulcerate. They do not show any significant necrosis.

Histologic distinction between metastasizing and nonmetastasizing Spitzoid lesions currently cannot be done; thus the term "atypical Spitz tumor" has been proposed (Barnhill 2006; Urso et al. 2006). There is a lack of consensus in the classification of atypical Spitz tumor and Spitzoid melanoma in the pediatric population (Gerami et al. 2013a, b). Proposed criteria for diagnosing "atypical Spitz tumor" include age greater than 10 years, greater than 10 mm in diameter, presence of ulceration, subcutaneous tissue involvement, and at least six mitoses per squared millimeters (Spatz et al. 1999a, b) (Table 5.1). Recent detailed criteria encompassed architectural (tumor diameter, depth of invasion, ulceration, circumscription, asymmetry, cellularity, confluent growth, pagetoid spread, Kamino bodies, and maturation) and cytologic (mitosis, marginal mitosis, nuclear size and shape, chromatin pattern, nucleolar characteristics, and cytoplasm) features (Luo et al. 2011; Crotty et al. 2002). An atypical Spitz tumor with positive sentinel lymph node does not correlate with poor prognosis as seen in conventional melanoma (Ludgate et al. 2009; Hung et al. 2013). In addition, death as a result of malignant melanoma is uncommon in children (Paradela et al. 2010).

Atypical Spitz nevi/tumors appear to have a different immunoprofile and molecular alterations than those observed in malignant melanoma. Overexpression of cyclin D1, p16, and p21 in Spitz nevi was seen in comparison to non-Spitzoid melanoma (Garrido-Ruiz et al. 2010; Kapur et al. 2005; Al Dhaybi et al. 2011). Spitz nevi often demonstrate *HRAS* gene amplification and a lack of *BRAF*V600E mutation (Bastian et al. 2000; Palmedo et al. 2004), whereas *BRAF*

and *NRAS* mutations are seen in Spitzoid melanoma but absent in Spitz nevi (van Dijk et al. 2005). There appears to be genetic differences by comparative genomic hybridization between atypical Spitz tumors and malignant melanomas (Bastian et al. 2003). Spitzoid melanomas in children have shown frequent homozygous 9p21 deletion (Gerami et al. 2013a). In addition, atypical Spitz tumor with homozygous 9p21 deletions has a significant correlation with aggressive behavior, whereas those with 6p23 deletions or no copy number aberrations have significantly less risk (Gerami et al. 2013a; Shen et al. 2013). Cases with 6p25 or 11q13 gain have an intermediate risk (Gerami et al. 2013a, b). It has been suggested that atypical Spitz nevi are borderline lesions with biologic behavior lying between Spitz nevi and malignant melanoma (Kapur et al. 2005). The role of fluorescence in situ hybridization (FISH) in the distinction of atypical Spitzoid neoplasms from melanoma remains uncertain (Massi et al. 2011; Gerami et al. 2013a, b; Gammon et al. 2012).

Key Histologic Features

Atypical Spitz tumor (Figs. 5.39, 5.40, 5.41, 5.42, 5.43, 5.44, 5.45, and 5.46)

- An asymmetric and expansile nodule in the dermis and subcutaneous fat.
- Lack of maturation and presence of deep pigmentation.
- Monomorphic tumor cells without marked pleomorphism.
- Infiltration of cords of cells into the reticular dermis.
- Superficially, the lesion exhibits approximately 3 mitoses/10 HPFs, but in the deep nodule there are 4/10 HPFs.

Table 5.1 Histologic features of Spitz nevus, atypical Spitz nevus, and Spitz tumor

	Spitz nevus	Atypical Spitz nevus	Spitz tumor
Size	<1 cm	<1 cm	>1 cm
Symmetry	Symmetrical	Symmetrical	Asymmetrical
Shape	Inverted triangle	Square or rectangle	Irregular shape including oval, round, and irregularly expansile nodule
Expansile nodule	Absent	Absent	Present
Deep extension	Unusual	Sometimes	Present
Ulceration	Rare	Rare	Often
Maturation	Present	Present	Absent
Cytologic atypia	Rare, background benign nevus cells	Mild to moderate	Pleomorphic
Deep mitoses	Absent	Rare	Present
Marginal mitoses	Absent	Absent	Present
Multinucleated tumor cells	Rare	Scattered	Sometimes present with irregular nuclear sizes
Inflammation	Rare	Scattered	Often, patchy
Lymphatic invasion	Present, protrusion with endothelial lining	Present, protrusion with endothelial lining	Maybe present but without endothelial lining

Data from Kapur et al. (2005), Barnhill et al. (1999), and Spatz et al. (1999a, b)

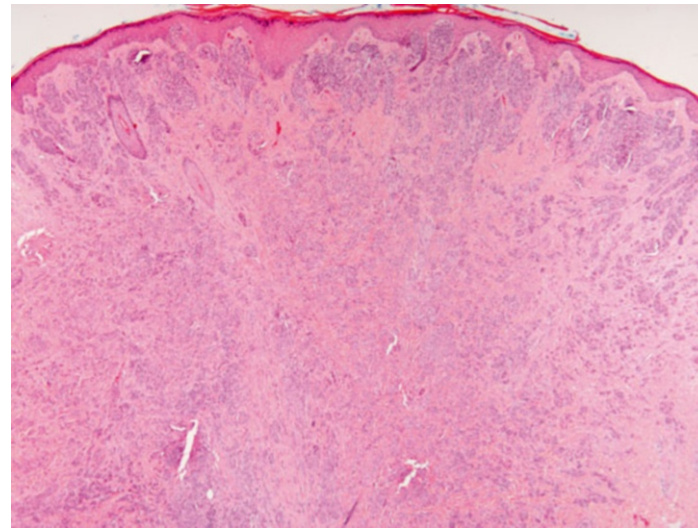

Fig. 5.39 An expansile proliferation of atypical melanocytes is seen replacing the reticular dermis

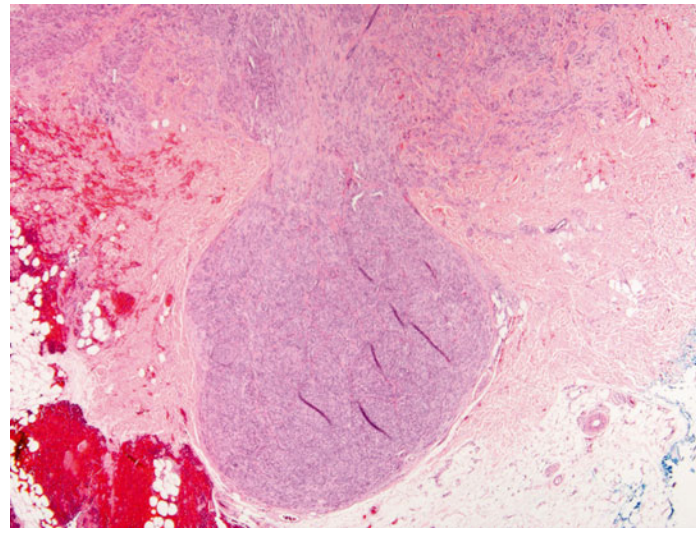

Fig. 5.40 An expansile nodule is seen in the deep aspect of the lesion

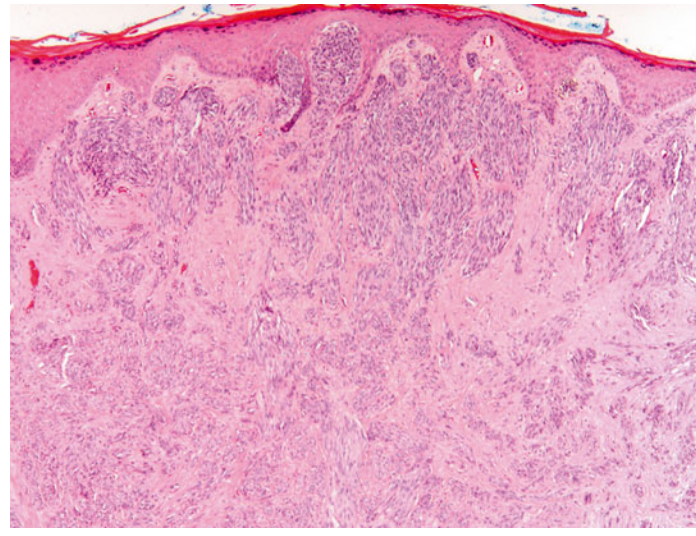

Fig. 5.41 Nests of spindle melanocytes are seen predominantly in the papillary and upper reticular dermis and only focally within the epidermis

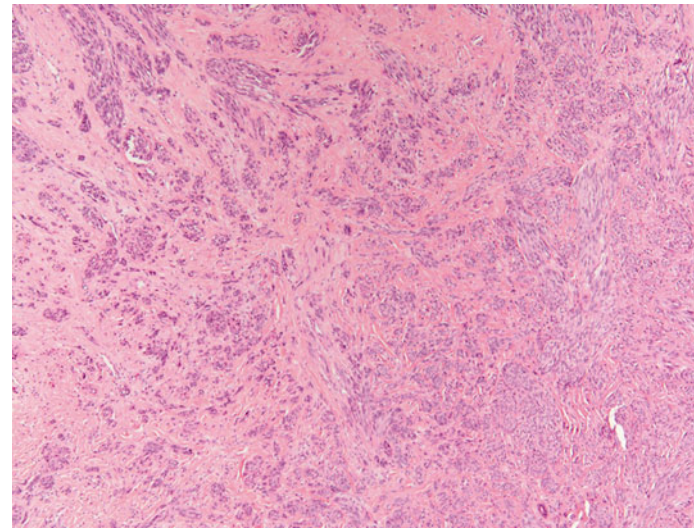

Fig. 5.42 The dermal nests have a "raining-down" appearance in the superficial dermis, but they change to a horizontal arrangement in the reticular dermis

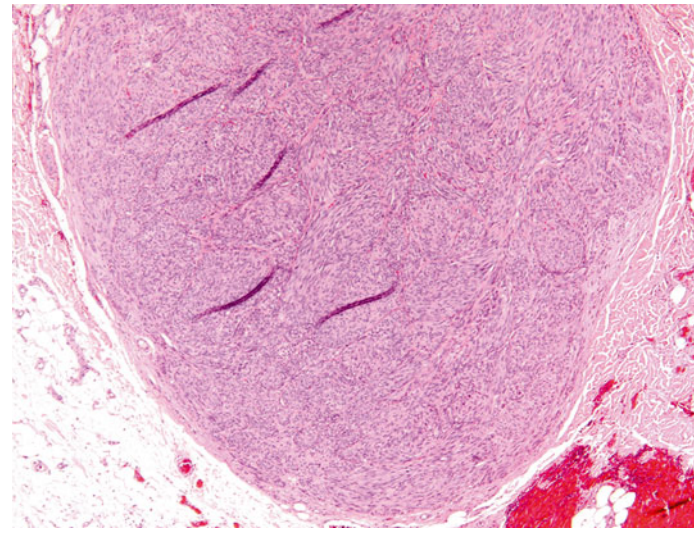

Fig. 5.43 The tumor cells extend into the deep dermis as an expansile nodule that abuts the subcutaneous fat

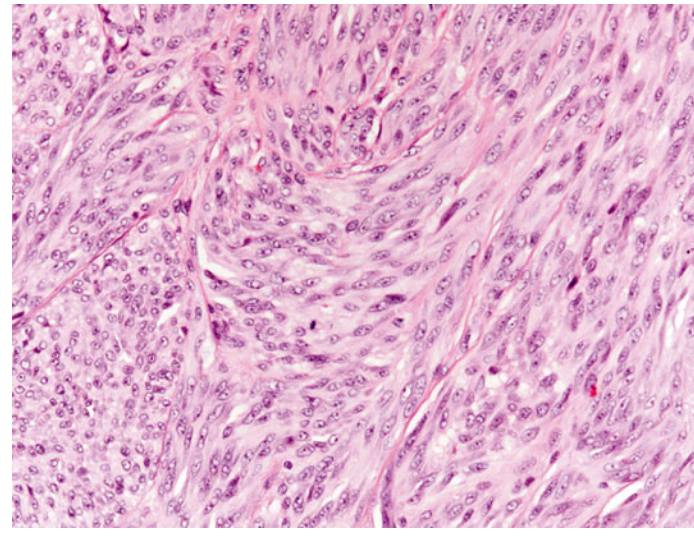

Fig. 5.44 These atypical melanocytes are uniform in appearance even in the deep nodule

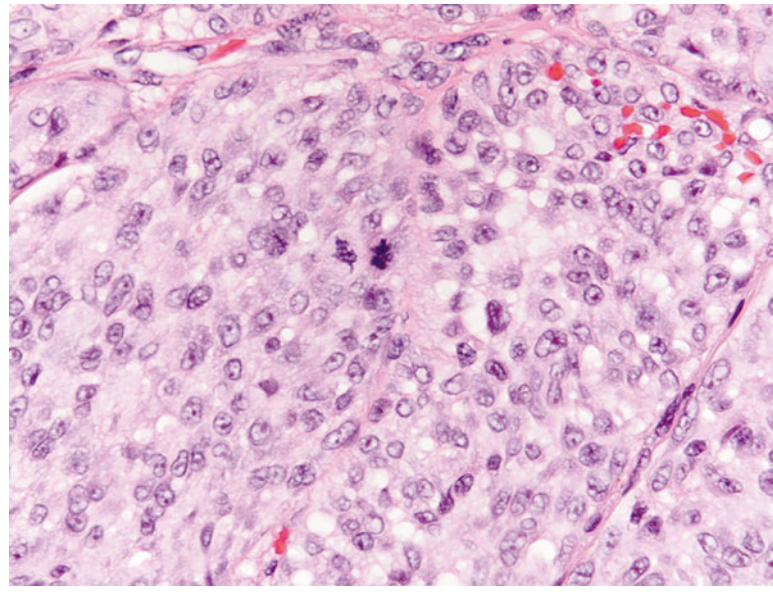

Fig. 5.45 Mitotic figures including atypical ones are readily identified

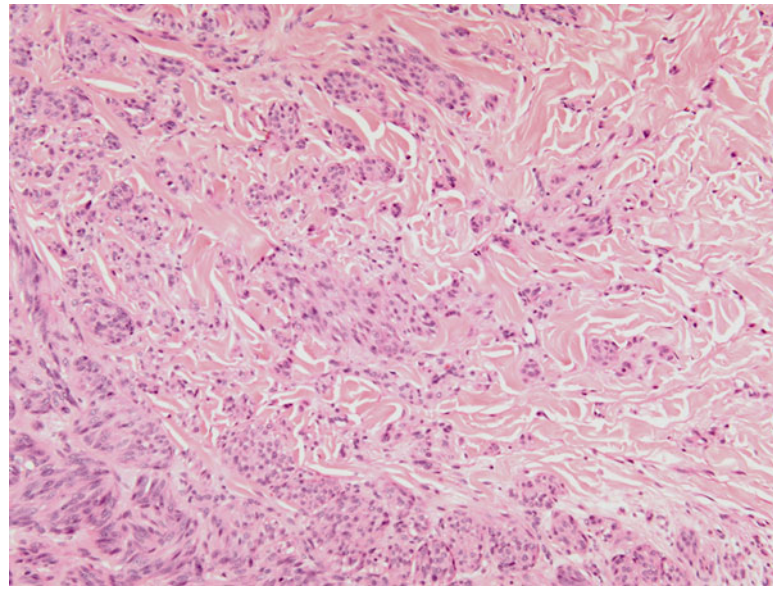

Fig. 5.46 The atypical melanocytes infiltrate the dermal collagen bundles in an "intersecting" pattern

Case 5J

Clinical History An 11-year-old male with a lesion on his left upper back

Microscopic Description A wedge-shaped lesion is formed by a proliferation of spindle-shaped nevomelanocytes arranged in fascicles extending to the lower reticular dermis and focally into the subcutaneous tissue (Figs. 5.47 and 5.48). The measured thickness is 6.0 mm, and the lesion is 12.0 mm in width. There is an area of ulceration (Fig. 5.49). The lesion is composed of multiple fascicles of predominantly spindle-shaped cells that infiltrate into the deep dermis and focally into the subcutaneous tissue (Figs. 5.48 and 5.50). There is no evidence of maturation. What is most troubling is the frequency of mitosis with 7 seen per mm^2 (Fig. 5.51). In addition, there is focal pigmentation in some of the deeper nests (Fig. 5.52). Re-excision is recommended as well as consideration of sentinel lymph node biopsy.

Diagnosis Atypical Spitz tumor with borderline features

Comment This lesion is an example of borderline tumor that can occur at any age in life, but it is more common in children. This lesion exhibits the following features of concern: width >1 cm, depth >1 mm, level V, mitotic activity 7/mm^2, deep pigmentation, and ulceration. These features have been associated with high risk for metastasis (Spatz et al. 1999a, b). However, as in these lesions, one must appreciate that the disease will not progress further even if the metastasis occurs (Hung et al. 2013). All series of these borderline lesions have at most 2–3-year follow-up (Barnhill et al. 1999; Urso 2005, 2006; Spatz et al. 1999a, b). Nevertheless, some recommend re-excision and sentinel lymph node sampling of these lesions (Ludgate et al. 2009; Busam et al. 2009; Murali et al. 2008).

Key Histologic Features

Atypical Spitz tumor with borderline features (Figs. 5.47, 5.48, 5.49, 5.50, 5.51, and 5.52)

- A proliferation of spindle-shaped nevomelanocytes arranged in fascicles extending to the lower reticular dermis and subcutaneous tissue with no evidence of maturation
- Deep pigmentation
- Ulceration and high mitotic rate

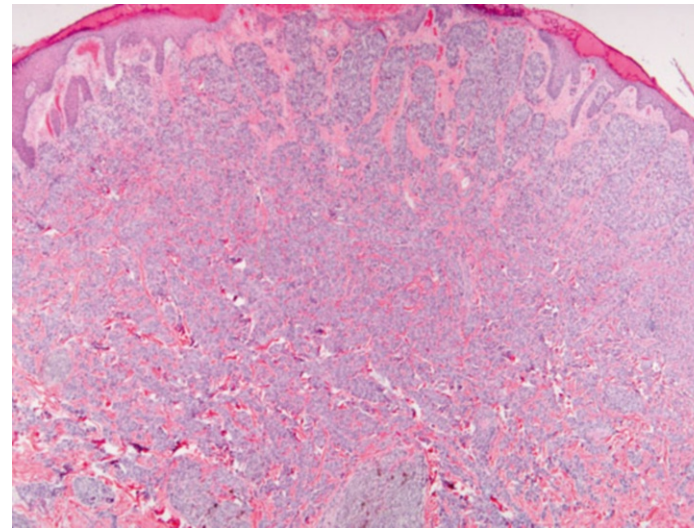

Fig. 5.47 A wedge-shaped proliferation of spindle-shaped melanocytes is seen in the dermis

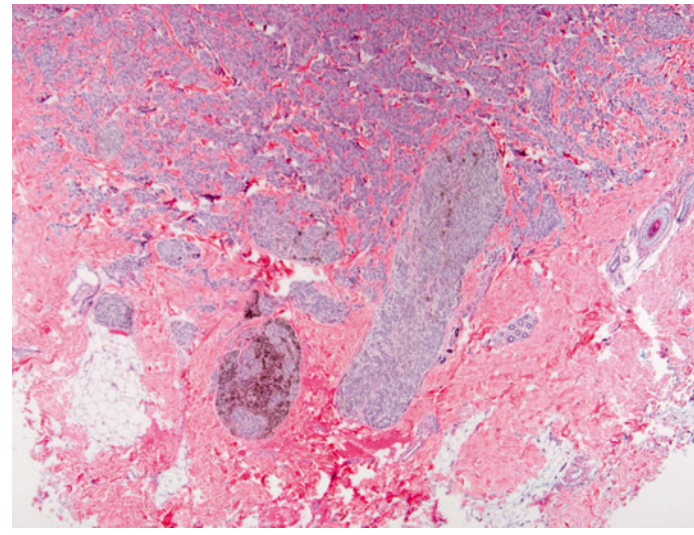

Fig. 5.48 Multiple fascicles of spindle-shaped melanocytes extend focally into the subcutaneous tissue

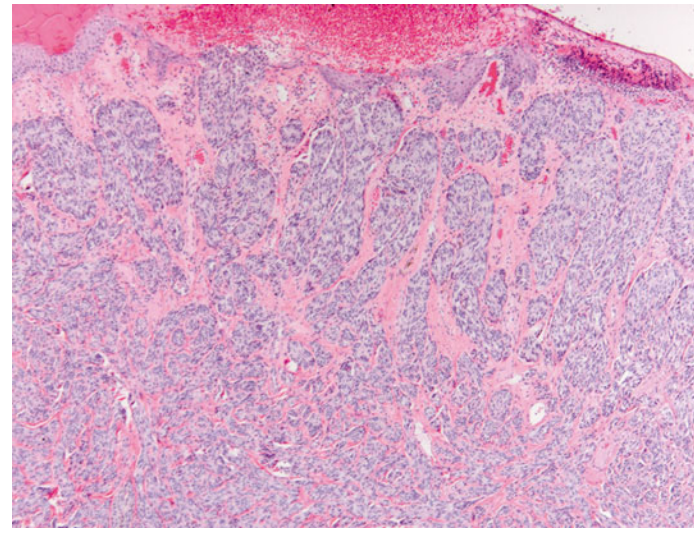

Fig. 5.49 Focally, an area of ulceration is noted

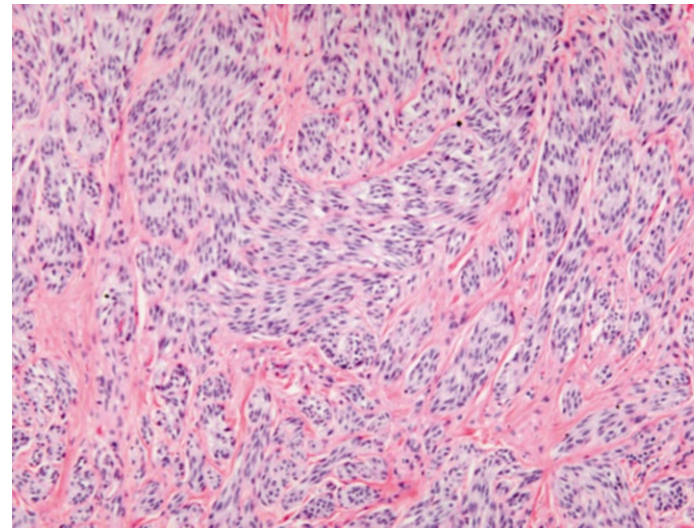

Fig. 5.50 The tumor cells are spindle in shape

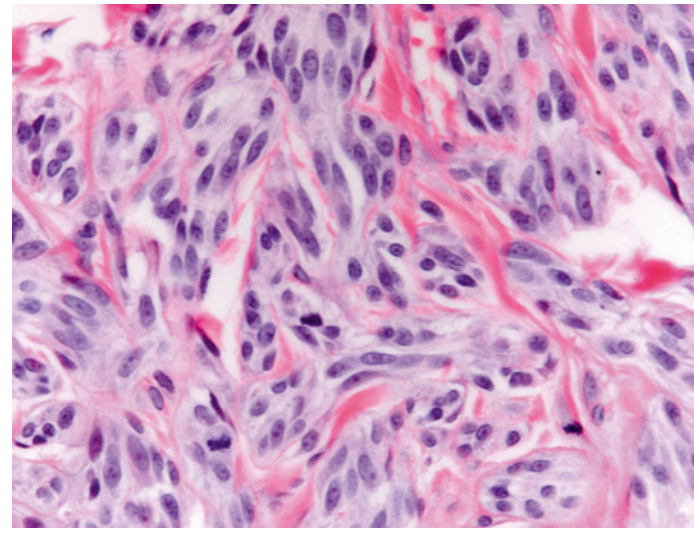

Fig. 5.51 Mitotic figures are readily identified

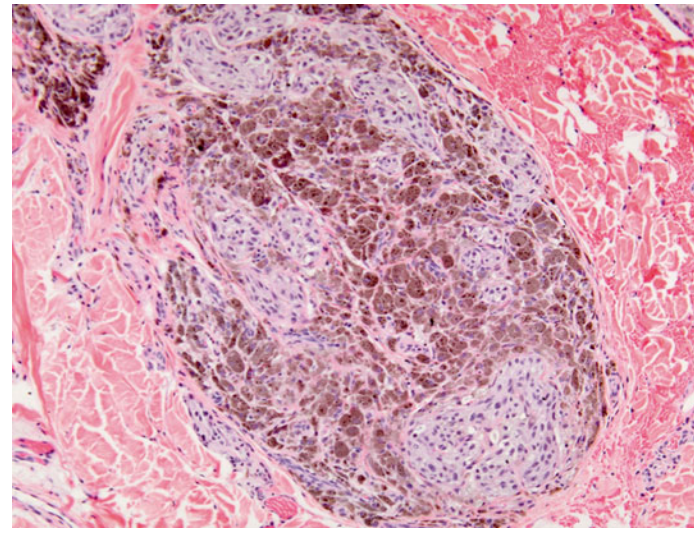

Fig. 5.52 Focal pigmentation is noted in some of the deeper nests

References

Al Dhaybi R, Agoumi M, Gagne I, McCuaig C, Powell J, Kokta V. p16 expression: a marker of differentiation between childhood malignant melanomas and Spitz nevi. J Am Acad Dermatol. 2011;65(2):357–63.

Barnhill RL. The Spitzoid lesion: rethinking Spitz tumors, atypical variants, 'Spitzoid melanoma' and risk assessment. Mod Pathol. 2006;19 Suppl 2:S21–33.

Barnhill RL, Mihm Jr MC. Pigmented spindle cell naevus and its variants: distinction from melanoma. Br J Dermatol. 1989;121(6):717–25.

Barnhill RL, Barnhill MA, Berwick M, Mihm Jr MC. The histologic spectrum of pigmented spindle cell nevus: a review of 120 cases with emphasis on atypical variants. Hum Pathol. 1991;22(1):52–8.

Barnhill RL, Argenyi ZB, From L, Glass LF, Maize JC, Mihm Jr MC, et al. Atypical Spitz nevi/tumors: lack of consensus for diagnosis, discrimination from melanoma, and prediction of outcome. Hum Pathol. 1999;30(5):513–20.

Barr RJ, Morales RV, Graham JH. Desmoplastic nevus: a distinct histologic variant of mixed spindle cell and epithelioid cell nevus. Cancer. 1980;46(3):557–64.

Bastian BC, LeBoit PE, Pinkel D. Mutations and copy number increase of *HRAS* in Spitz nevi with distinctive histopathologic features. Am J Pathol. 2000;157:967–72.

Bastian BC, Olshen AB, LeBoit PE, Pinkel D. Classifying melanocytic tumors based on DNA copy number changes. Am J Pathol. 2003;163(5):1765–70.

Busam KJ, Barnhill RL. Pagetoid Spitz nevus: intraepidermal Spitz nevus with prominent pagetoid spread. Am J Surg Pathol. 1995;19(9):1061–7.

Busam JK, Murali M, Pulitzer M, McCarthy SW, Thompson JF, Shaw HM, et al. Atypical Spitzoid melanocytic tumors with positive sentinel lymph nodes in children and teenagers, and comparison with histologically unambiguous and lethal melanomas. Am J Surg Pathol. 2009;33(9):1386–95. doi:10.1097/PAS.0b013e3181ac1927.

Cesinaro AM, Foroni M, Sighinolfi P, Migaldi M, Trentini GP. Spitz nevus is relatively frequent in adults. A clinico-pathologic study of 247 cases related to patient's age. Am J Dermatopathol. 2005;27(6):469–75.

Crotty KA, Scoyler RA, Li L, Palmer AA, Wang L, McCarthy SW. Spitz naevus versus Spitzoid melanoma: when and how can they be distinguished? Pathology. 2002;34(1):6–12.

Diaz-Cascajo C, Borhi S, Weyers W. Angiomatoid Spitz nevus: a distinct variant of desmoplastic Spitz nevus with prominent vasculature. Am J Dermatopathol. 2000;22(2):135–9.

Fabrizi G, Massi G. Polypoid Spitz naevus: the benign counterpart of polypoid malignant melanoma. Br J Dermatol. 2000;142(1):128–32.

Gammon B, Beilfuss B, Guitart J, Gerami P. Enhanced detection of spitzoid melanomas using fluorescence in situ hybridization with 9p21 as an adjunctive probe. Am J Surg Pathol. 2012;36(1):81–8. doi:10.1097/PAS.0b013e31822d5ff8.

Garrido-Ruiz MC, Requena L, Ortiz P, Perez-Gomez B, Alonso SR, Peralto JL. The immunohistochemical profile of Spitz nevi and conventional (non-Spitzoid) melanomas: a baseline study. Mod Pathol. 2010;23(9):1215–24. doi:10.1038/modpathol.2010.102.

Gartmann H, Ganser M. The Spitz nevus. Spindle cell and/or epithelioid cell nevus – a histological analysis of 652 tumors. Z Hautkr. 1985;60(1–2):29–30, 34–6, 39–42.

Gerami P, Cooper C, Bajaj S, Wagner A, Fullen D, Busam K, et al. Outcomes of atypical Spitz tumors with chromosomal copy number aberrations and conventional melanomas in children. Am J Surg Pathol. 2013a;37(9):1387–94. doi:10.1097/PAS.0b013e31828fc283.

Gerami P, Scoyler RA, Xu X, Elder DE, Abraham RM, Fullen D, et al. Risk assessment for atypical spitzoid melanocytic neoplasms using FISH to identify chromosomal copy number aberrations. Am J Surg Pathol. 2013b;37(5):676–84. doi:10.1097/PAS.0b013e3182753de6.

Hamm H, Happle R, Broecker EB. Multiple agminate Spitz nevi: review of the literature and report of a case with distinctive immunohistological features. Br J Dermatol. 1987;117(4):511–22.

Hantschker M, Bastian BC, LeBoit PE. Consumption of the epidermis: a diagnostic criterion for the differential diagnosis of melanoma and Spitz nevus. Am J Surg Pathol. 2004;18(12):1621–5.

Harvell JD, Meehan SA, LeBoit PE. Spitz's nevi with halo reaction: a histopathologic study of 17 cases. J Cutan Pathol. 1997;24(10):611–9.

Haupt HM, Stern JB. Pagetoid melanocytosis: histologic features in benign and malignant lesions. Am J Surg Pathol. 1995;19(7):792–7.

Hoang MP. Myxoid Spitz nevus. J Cutan Pathol. 2003;30(9):566–8.

Hung T, Piris A, Lobo A, Mihm Jr MC, Sober AJ, Tsao H, et al. Sentinel lymph node metastasis is not predictive of poor outcome in patients with problematic spitzoid melanocytic tumors. Hum Pathol. 2013;44(1):87–94. doi:10.1016/j.humpath.2012.04.019.

Kamino H, Flotte TJ, Misheloff E, Greco MA, Ackerman AB. Eosinophilic globules in Spitz's nevi. New findings and a diagnostic sign. Am J Dermatopathol. 1979;1(4):319–24.

Kapur P, Selim MA, Roy LC, Yegappan M, Weinberg AG, Hoang MP. Spitz nevi and atypical Spitz nevi/tumors: a histologic and immunohistochemical analysis. Mod Pathol. 2005;18(2):197–204.

Ko CJ, McNiff JM, Glusac EJ. Melanocytic nevi with features of Spitz nevi and Clark's/dysplastic nevi ("Spark's" nevi). J Cutan Pathol. 2009;36(10):1063–8. doi:10.1111/j.1600-0560.2008.01221.x.

Ludgate MW, Fullen DR, Lee J, Lowe L, Bradford C, Geiger J, Schwartz J, Johnson TM. The atypical Spitz tumor of uncertain biologic potential: a series of 67 patients from a single institution. Cancer. 2009;115(3):631–41. doi:10.1002/cncr.24047.

Luo S, Sepehr A, Tsao H. Spitz nevi and other Spitzoid lesions. Part I. Background and diagnoses. J Am Acad Dermatol. 2011;65(6):1073–84. doi:10.1016/j.jaad.2011.04.040.

Massi D, Cesinaro AM, Tomasini C, Paglierani M, Bettelli S, Dal Maso L, et al. Atypical Spitzoid melanocytic tumors: a morphological, mutational, and FISH analysis. J Am Acad Dermatol. 2011;64(5):919–35. doi:10.1016/j.jaad.2010.05.043.

Murali R, Sharma RN, Thompson JF, Stretch JR, Lee CS, McCarthy SW, Scoyler RA. Sentinel lymph node biopsy in histologically ambiguous melanocytic tumors with spitzoid features (so-called atypical Spitzoid tumors). Ann Surg Oncol. 2008;15(1):302–9.

Palmedo G, Hantschke M, Rutten A, Mentzel T, Hugel H, Flaig MJ, et al. The T1796A mutation of the BRAF gene is absent in Spitz nevi. J Cutan Pathol. 2004;31(3):266–70.

Paniago-Pereira C, Maize J, Ackerman A. Nevus of large spindle and/or epithelioid cells (Spitz' nevus). Arch Dermatol. 1978;114(12):1811–23.

Paradela S, Fonseca E, Pita-Fernandez S, Kantrow SM, Diwan AH, Herzog C, Prieto VG. Prognostic factors for melanoma in children and adolescents: a clinicopathologic, single-center study of 137 patients. Cancer. 2010;116:4334–44. doi:10.1002/cncr.25222.

Pulitzer DR, Martin PC, Cohen AP, Reed RJ. Histologic classification of the combined nevus. Analysis of the variable expression of melanocytic nevi. Am J Surg Pathol. 1991;15(12):1111–22.

Sagebiel RW, Chinn EK, Egbert BM. Pigmented spindle cell nevus. Clinical and histologic review of 90 cases. Am J Surg Pathol. 1984;8(9):645–53.

Sau P, Graham JH, Helwig EB. Pigmented spindle cell nevus: a clinicopathologic analysis of ninety-five cases. J Am Acad Dermatol. 1993;28(4):565–71.

Scott G, Chen KT, Rosai J. Pseudoepitheliomatous hyperplasia in Spitz nevi: a potential source of confusion with squamous cell carcinoma. Arch Pathol Lab Med. 1989;113(1):61–3.

Shen L, Cooper C, Bajaj S, Liu P, Pestova E, Guitart J, Gerami P. Atypical Spitz tumors with 6q23 deletions: a clinical, histological, and molecular study. Am J Dermatopathol. 2013;35(8):804–12. doi:10.1097/DAD.0b013e31828671bf.

Smith NP. The pigmented spindle cell tumor of reed: an under-diagnosed lesion. Semin Diagn Pathol. 1987;4(1):75–87.

Smith K, Barrett TL, Skelton 3rd HG, Lupton GP, Graham JH. Spindle cell and epithelioid cell nevi with atypia and metastasis (malignant Spitz nevus). Am J Surg Pathol. 1989;13(11):931–9.

Spatz A, Barnhill RL. The Spitz tumor 50 years later: revisiting a landmark contribution and unresolved controversy. J Am Acad Dermatol. 1999;40(2 Pt 1):223–8.

Spatz A, Calonje E, Handfield-Jones S, Barnhill RL. Spitz tumors in children. A grading system for risk stratification. Arch Dermatol. 1999a;135(3):282–5.

Spatz A, Peterse S, Fletcher CD, Barnhill RL. Plexiform Spitz nevus: an intradermal Spitz nevus with plexiform growth pattern. Am J Dermatopathol. 1999b;21(6):542–6.

Spitz S. Melanomas of childhood. Am J Pathol. 1948;24(3):591–609.

Suster S. Hyalinizing spindle and epithelioid cell nevus: a study of five cases of a distinctive histologic variant of Spitz's nevus. Am J Dermatopathol. 1994;16(6):593–8.

Urso C. A new perspective for Spitz tumors? Am J Dermatopathol. 2005;27(4):364–6.

Urso C, Borgognoni L, Saieva C, Ferrara G, Tinacci G, Begliomini B, Reali UM. Sentinel lymph node biopsy in patients with 'atypical Spitz tumors'. A report on 12 cases. Hum Pathol. 2006;37(7):816–23.

Van Dijk MC, Bernsen MR, Ruiter DJ. Analysis of mutations in B-RAF, N-RAS, and H-RAS genes in the differential diagnosis of Spitz nevus and spitzoid melanoma. Am J Surg Pathol. 2005;29(9):1145–51.

Weedon D, Little J. Spindle and epithelioid cell nevi in children and adults. A review of 211 cases of the Spitz nevus. Cancer. 1977;40(1):217–25.