Problems in Various Subtypes of Malignant Melanoma

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Malignant melanoma is one of the diseases that ranked high in the list of great imitators because of its many histologic variants. This characteristic applied to both radial and vertical growth phases of melanoma. Among the radial growth phase aspect certainly lentigo maligna melanoma must be considered. Because of the fact that in chronic sun damaged skin, the light effect causes not only melanocytic atypia but also changes in the adjacent keratinocytes. While the most characteristic feature of lentigo maligna is epidermal atrophy, the presence of epidermal hyperplasia can lead to confusion with a dysplastic nevus. Likewise, the additional presence of spindle cell nests in a dysplastic nevus can cause confusion with a Spitz nevus.

One of the most difficult discernment arises from the nevoid melanoma group of the lesions that can confound even the most experienced observers. These subtle tumors require very close attention to details to recognize them as malignant process. Only very careful inspection of these lesions will result in an appreciation of hyperchromatic abnormal nuclei and rare dermal mitotic figures in association with the lack of maturation (Table 8.1). Otherwise, the lesions can be misdiagnosed as a halo nevi or atypical dermal nevi.

Among the different types of vertical growth phases, the presence of epithelioid cells admixed with spindle cells and giant cells can lead to the misinterpretation of a fibrohistiocytic tumor. Similarly, the striking fibrotic response in desmoplastic melanoma can lead to the diagnosis of a fibromatosis or fibrosarcoma or even a spindle squamous cell carcinoma. Spindle cell melanomas that are poorly differentiated can present special problems in diagnosis since it can be confused with poorly differentiated tumors such as squamous cell carcinoma, atypical fibroxanthoma, and leiomyosarcoma.

Table 8.1 Comparison of histologic features of melanocytic nevus to nevoid melanoma

	Melanocytic nevus	Nevoid melanoma
Symmetry	Present	Usually absent
Circumscription	Present	Absent
Junctional component	Present	Minimal
Expansile nodule	Present	Absent
Maturation	Present	Impaired
Pleomorphism	Absent	Present
Mitotic figures	Absent	Present
Atypical mitotic figures	Absent	Present
HMB-45 expression in deep aspect	Absent	Present
MIB-1 proliferation index	Superficial	Superficial and deep

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Case 8A

Clinical History A 20-year-old female with back lesion

Microscopic Description A protuberant nodule of small epithelioid cells that form a cohesive sheet infiltrating into the upper reticular dermis (Fig. 8.1a, b). There is no evidence of maturation in the deep part of the lesion where it infiltrates the collagen bundles (Fig. 8.2). These cells exhibit high nuclear–cytoplasmic ratio and are very uniform in their appearance (Fig. 8.3). Rare dermal mitosis is noted (Fig. 8.4). There is no host response or ulceration or microscopic satellite or vascular invasion. Beside and overlying the peripheral part of the tumor is a dysplastic nevus (Fig. 8.5a, b). The cells toward the center of the lesion exhibit severe cytologic atypia (Fig. 8.4) and show some pagetoid spread. The dysplastic nevus otherwise shows moderate cytologic atypia of the intraepidermal and dermal components.

Diagnosis Nodular malignant melanoma with nevoid features, invasive to Clark level IV, and a measured thickness of 2.1 mm, arising in association with a compound dysplastic nevus

Comment Schmoeckel et al. (1985) were the first to coin the term "nevoid melanoma" which denotes a form of melanoma that mimics a melanocytic nevus (Wong et al. 1995; Blessing et al. 1993; Zembowicz et al. 2001). There are several histologic variants of nevoid melanomas reported in the literature: (1) the nodular or papular form (Schmoeckel et al. 1985; McNutt et al. 1995; Zembowicz et al. 2001), (2) the verrucous or papillomatous variants (Schmoeckel et al. 1985; Zembowicz et al. 2001), and (3) the lentiginous variants arising in sun-exposed skin of older individuals (Kossard and Wilkinson 1997).

In this particular case, one observes the evolution of a malignant melanoma in the center of a dysplastic nevus. This melanoma has very small epithelioid cells and qualifies for the designation of nevoid melanoma (McNutt et al. 1995; Schmoeckel et al. 1985; Wong et al. 1995). These lesions differ from nevi by the extensive sheet-like growth of the tumor, absence of maturation with very atypical cells present in the advancing front (pushing lower border) as it enters the reticular dermis. In this particular instance, the melanoma occurs in the center of the dysplastic nevus and one can observe progressive atypia of the melanocytes overlying the melanoma as it infiltrates into the center of the epidermis.

Key Histologic Features

Nodular malignant melanoma with nevoid features (Figs. 8.1, 8.2, 8.3, 8.4, and 8.5)

- Extensive sheet-like growth of the tumor.
- Absence of maturation with very atypical cells present in the advancing front as the lesion enters the reticular dermis.
- Rare dermal mitosis is noted.
- Minimal junctional or in situ component.

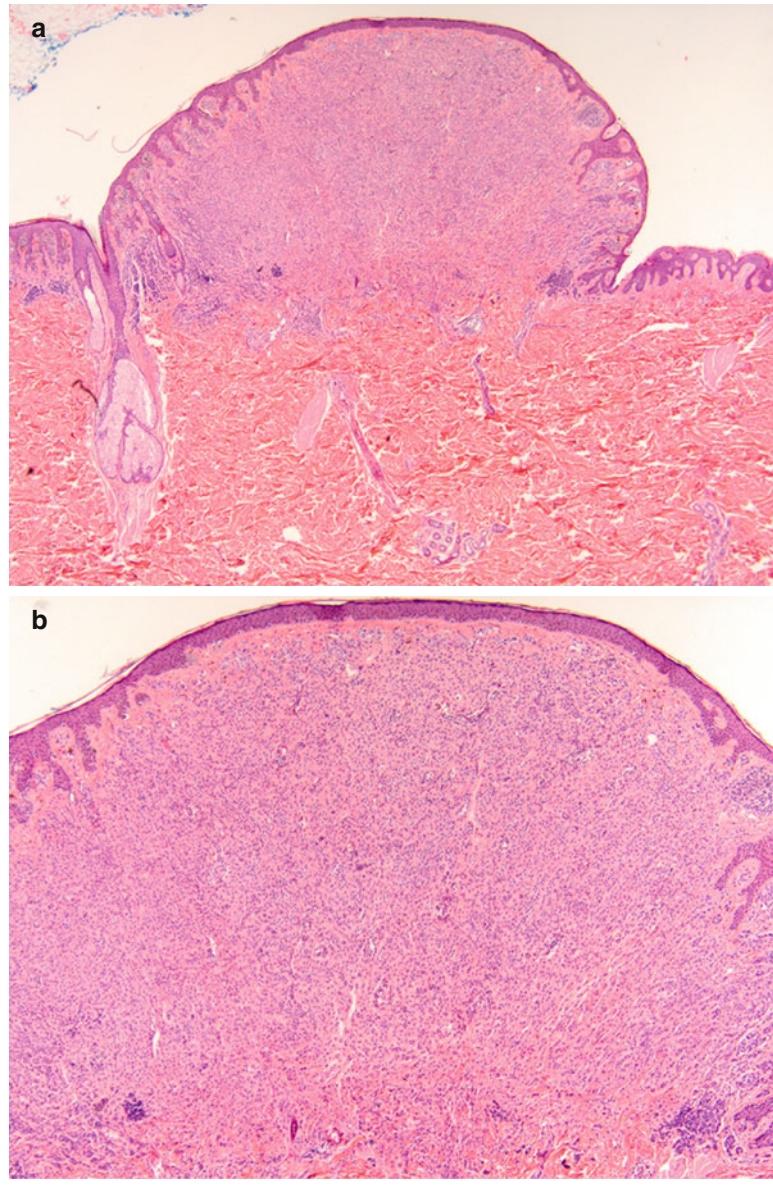


Fig. 8.1 (**a**, **b**) A protuberant nodule of epithelioid melanocytes is seen in the dermis

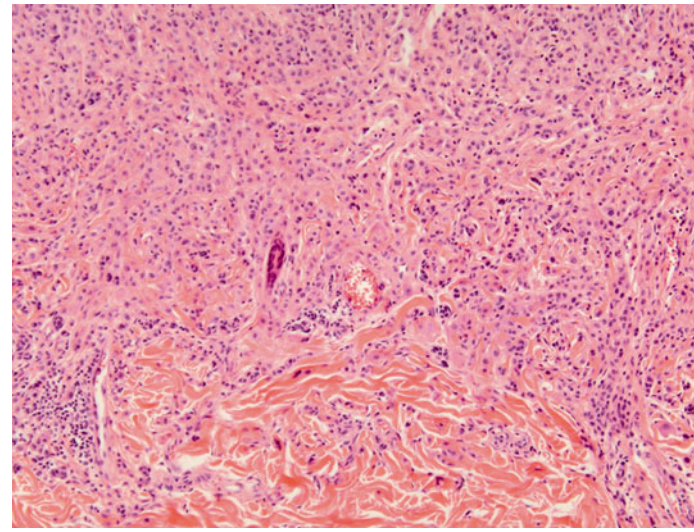


Fig. 8.2 The lesion exhibits no evidence of maturation in the deep aspect

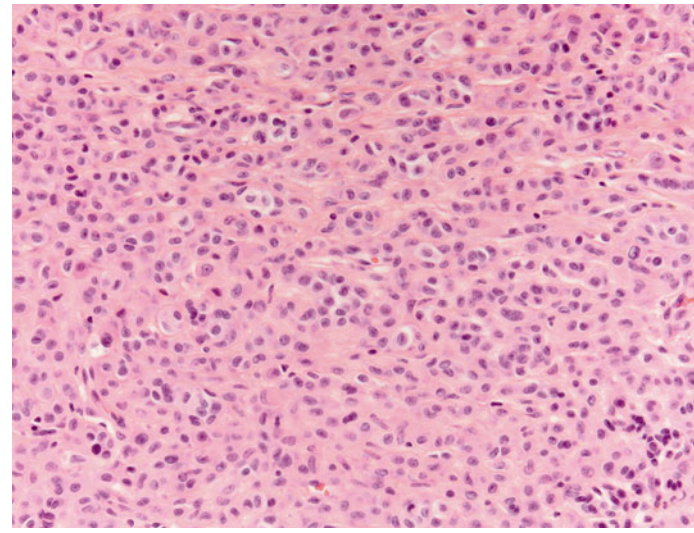


Fig. 8.3 The melanocytes are uniform and have large nuclear–cytoplasmic ratio

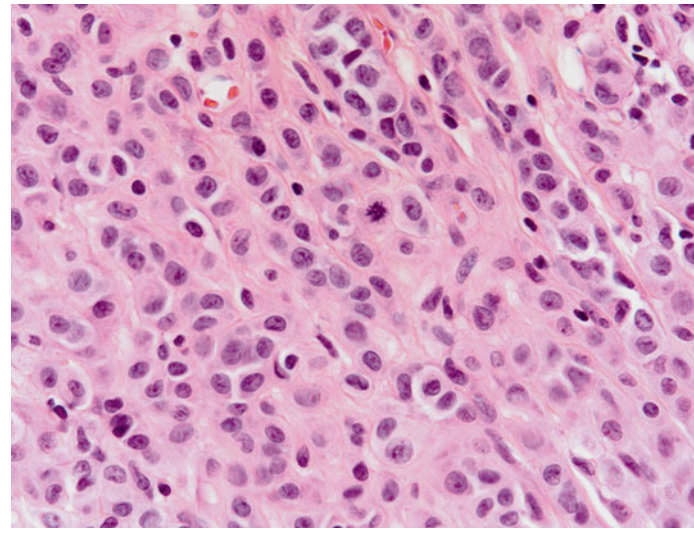


Fig. 8.4 Rare dermal mitosis is noted

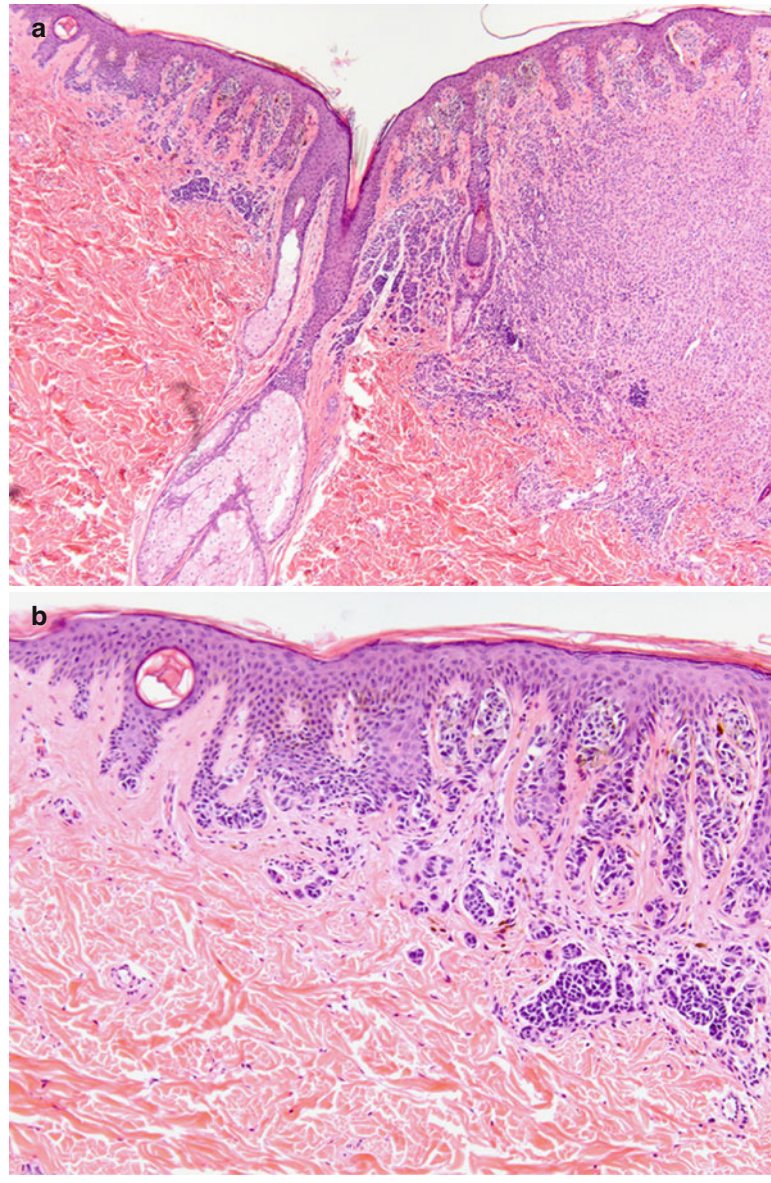


Fig. 8.5 (**a**, **b**) Beside and overlying the peripheral part of the nodule is a dysplastic nevus

Case 8B

Clinical History A 67-year-old male with right forearm lesion

Microscopic Description Forming a protuberant nodule below a relatively atrophic epidermis is a proliferation of small and hyperchromatic melanocytes with high nuclear–cytoplasmic ratio (Figs. 8.6a, b, 8.7, and 8.8). These cells are associated with a dermal nevus on one lateral side (Fig. 8.9). This benign dermal nevus shows an increase in hyperchromasia of cells in small nests as they progressively blend into the nevoid melanoma nodule (Fig. 8.9). The epidermis overlying the lesion shows no evidence of origin site. However, malignancy is evident when one observes that there is a progression of atypia from a benign lesion into a malignant lesion (Fig. 8.10a, b). Furthermore, to one edge of the biopsy, the lesion assumes a more spindled appearance with more pigmentation (Fig. 8.11). These cells gradually emerge from the area of small epithelioid cells and form large nests. There are rare mitoses (Fig. 8.12). We observe one mitotic figure per square millimeter. There is no vascular invasion or microscopic satellitosis.

Diagnosis Nevoid malignant melanoma, invasive to level IV, and Breslow thickness of 2.25 mm

Comment This lesion is a very straight example of nevoid malignant melanoma. As is often seen in these cases, the epidermal origin is not found. This leads to the hypothesis that these lesions represent intralesional malignant transformation. This type of transformation is more common in the head and neck region, especially around the eye when patients relate that lesions have been present for years and suddenly began to grow. This type of lesion, however, we treat as any other type of melanoma with excision and sentinel lymph node biopsy. If one is in doubt of the diagnosis, a Ki-67 immunostain can be performed which often shows a proliferation index greater than 10 % (McNutt et al. 1995). The differential diagnosis of this lesion includes metastatic melanoma and an atypical nevus. As far as metastatic melanoma is concerned, the presence of a mass of cells that form a protuberant nodule but with cells that have rather nevoid characteristic typically speaks against a metastasis which is often highly atypical and anaplastic. Metastases of small cell melanoma are often associated with numerous mitoses and hyperchromasia neither of which we see in nevoid melanoma. The atypical nevus can be distinguished from nevoid melanoma by which the atypical nevus cells do not have the high nuclear–cytoplasmic ratio. Furthermore, they do not show mitotic figures. Invariably, the nevus exhibits maturation characterized by type-C nevus cells as it infiltrates deep into the dermis. The dysplastic nevus with marked dermal atypia can often present a problem. The dermal change is composed of nests of cells with hyperchromatic nuclei. In the great majority of these dysplastic nests, even though they are hyperchromatic, they do show peripheral type-C cells that surround the nests. Also one does not see occasional malignant atypical cells in nevoid melanoma. Furthermore, they confine to the papillary dermis and do not form expansile nodule that destroy the dermal architecture.

Key Histologic Features

Nevoid malignant melanoma (Figs. 8.6, 8.7, 8.8, 8.9, 8.10, 8.11, and 8.12)

- Nodular proliferation of small hyperchromatic melanocytes with high nuclear–cytoplasmic ratio.
- The epidermis overlying the lesion shows no evidence of an in situ component.
- There are rare mitoses.
- The presence of a protuberant nodule but with cells that have rather nevoid characteristic typically speaks against a metastasis.

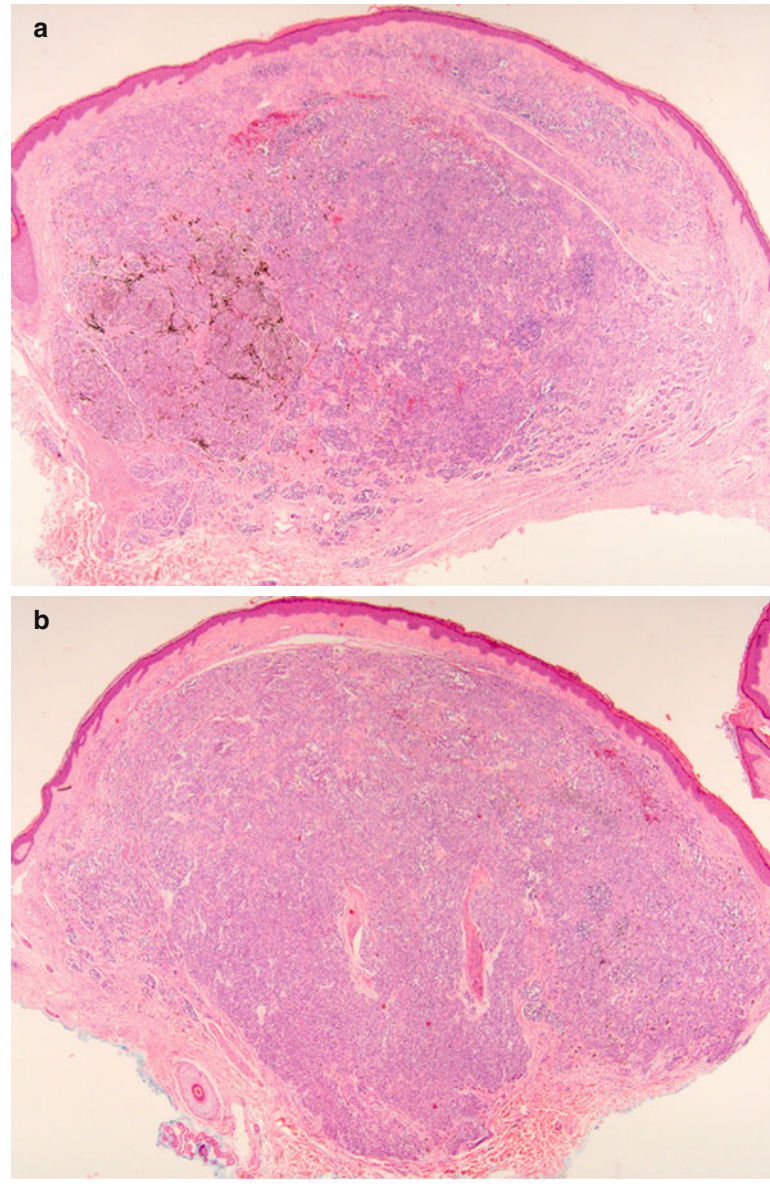


Fig. 8.6 (**a**, **b**) A protuberant nodule is seen below an atrophic epidermis

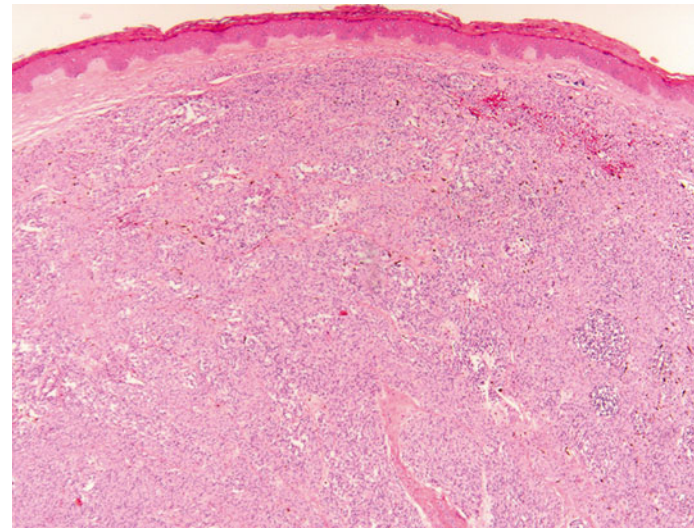


Fig. 8.7 The overlying epidermis appears uninvolved and is separated from the dermal nodule by a grenz zone

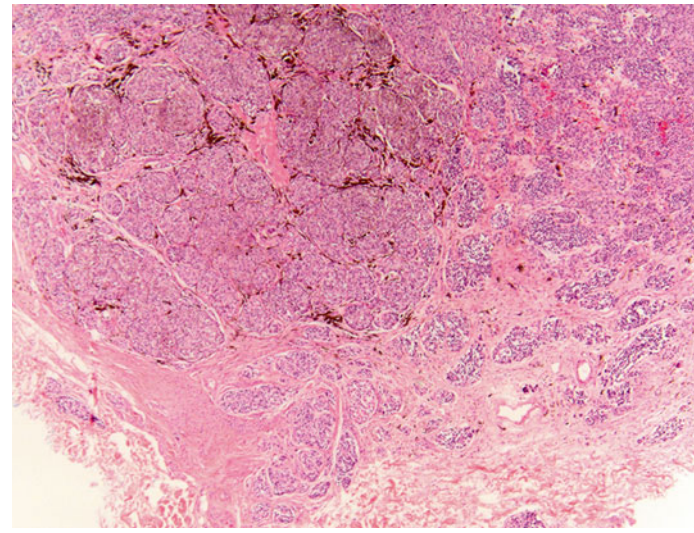


Fig. 8.8 The proliferation is comprised of small and hyperchromatic melanocytes with high nuclear–cytoplasmic ratio

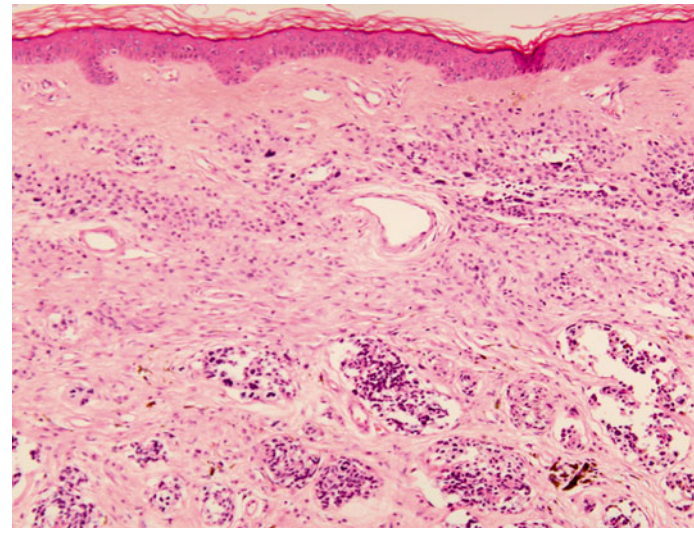


Fig. 8.9 There is an associated dermal nevus on one lateral side

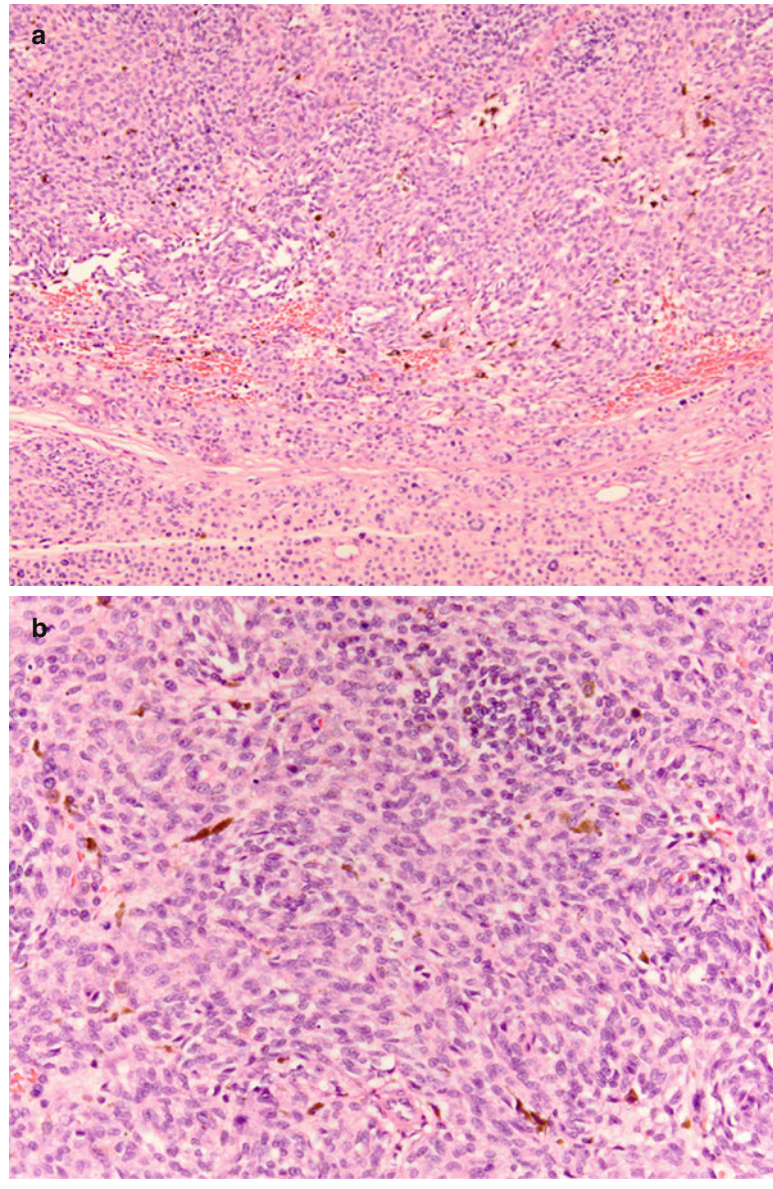


Fig. 8.10 (**a**, **b**) There is a progression of atypia from benign into a malignant lesion

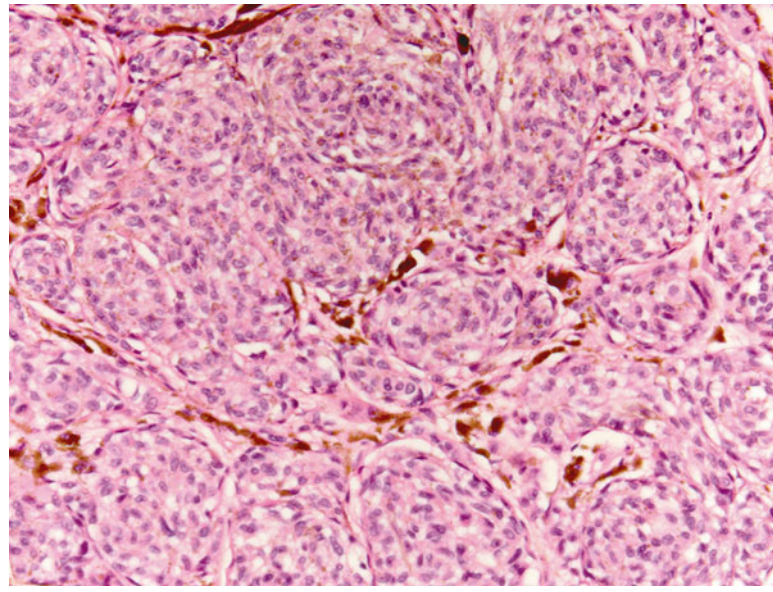


Fig. 8.11 In one edge of the biopsy the lesion assumes a more spindled appearance with more cytoplasmic pigmentation

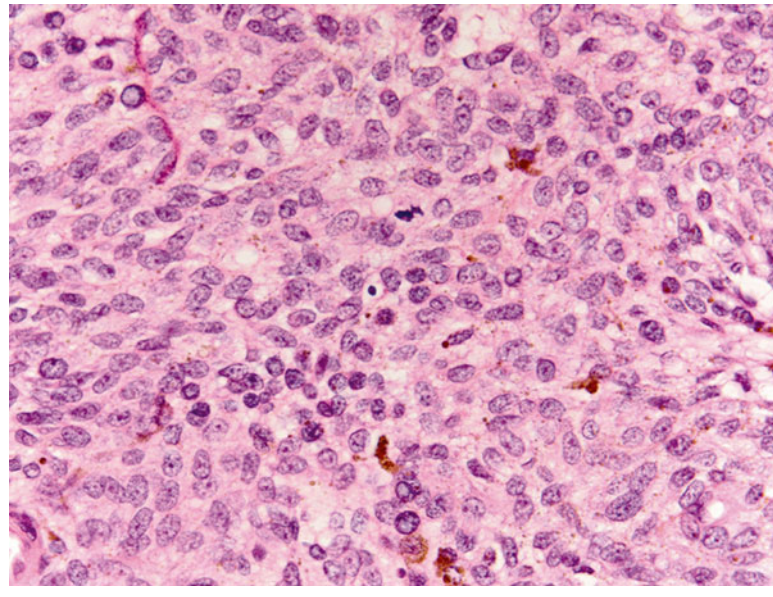


Fig. 8.12 Rare mitoses are identified

Case 8C

Clinical History A 53-year-old male with a pigmented lesion on his right trunk

Microscopic Description Low-power examination reveals a distinctive appearance of hyperchromatic cells forming a uniform and expansile nodule (Fig. 8.13). There is no evidence of epidermal origin (Fig. 8.13). High-power examination reveals a densely packed population of epithelioid-appearing cells with high nuclear to cytoplasmic ratio (Figs. 8.14 and 8.15). The nuclei have rather prominent nucleoli that vary from eosinophilic to basophilic. The nuclei are in overall oval to round in shape. The cells are closely packed that it is difficult to find collagen fibers between them. There is no maturation. At the base the cells have similar morphology with marked hyperchromasia and atypia at the advancing front (Fig. 8.16). A rare mitosis is noted (Fig. 8.15). There is no host response, no ulceration, no regression, nor vascular invasion.

Diagnosis Nodular melanoma, nevoid variant, at least Clark level IV, and a thickness of 1.5 mm

Comment This very excellent example of a nevoid melanoma is characterized by a striking uniform population of cells that form an expansile nodule. There are rare mitoses. The monotonous nature of the cells is the clue to the diagnosis. Lesions such as this with low number of mitoses in our experience will likely recur locally.

Key Histologic Features

Nodular melanoma, nevoid variant (Figs. 8.13, 8.14, 8.15, and 8.16)

- A uniform and expansile nodule with an advancing front composed of similar cells at the base.
- There is no evidence of epidermal origin.
- A densely packed population of epithelioid-appearing cells with high nuclear to cytoplasmic ratio.
- A rare mitosis is noted.

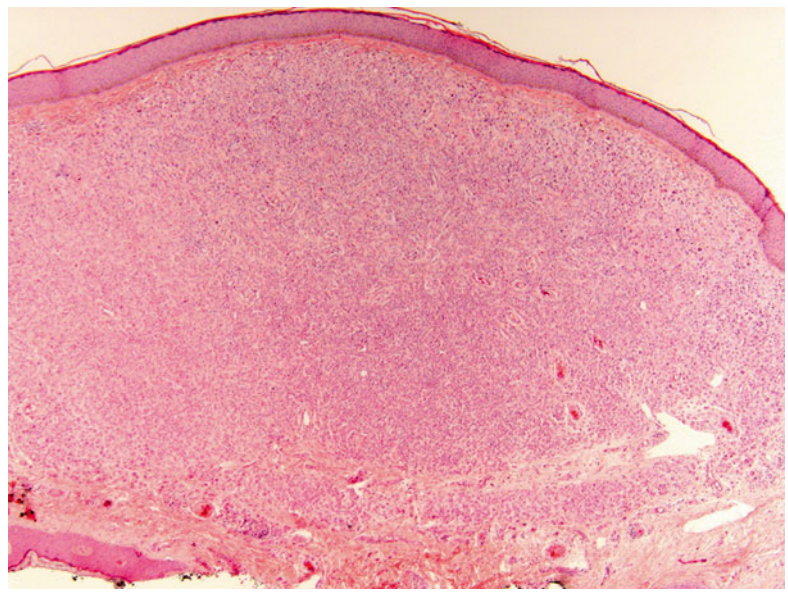


Fig. 8.13 An expansile nodule of uniform and hyperchromatic melanocytes is seen in the dermis

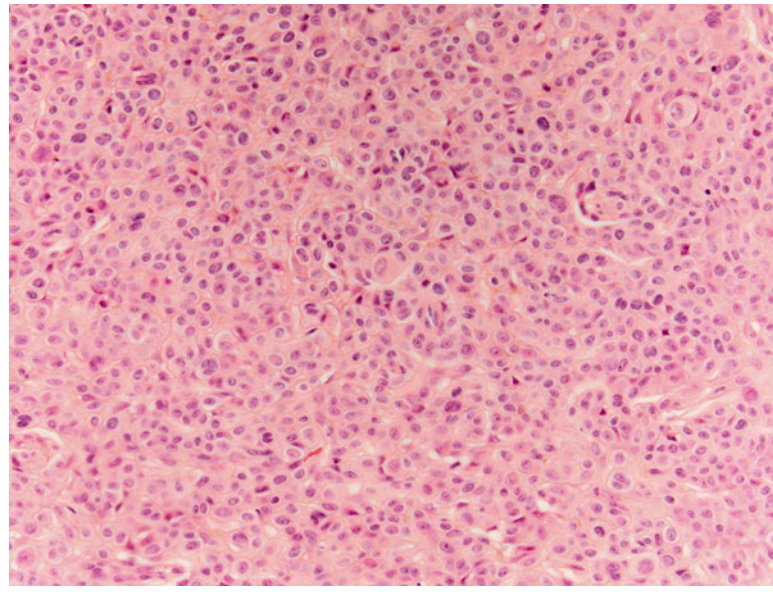


Fig. 8.14 These epithelioid melanocytes have high nuclear to cytoplasmic ratio

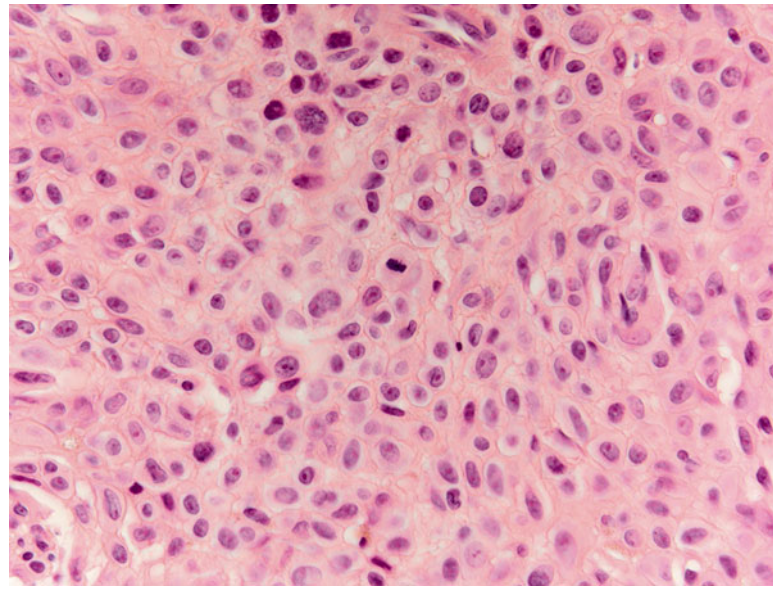


Fig. 8.15 A rare mitotic figure is identified

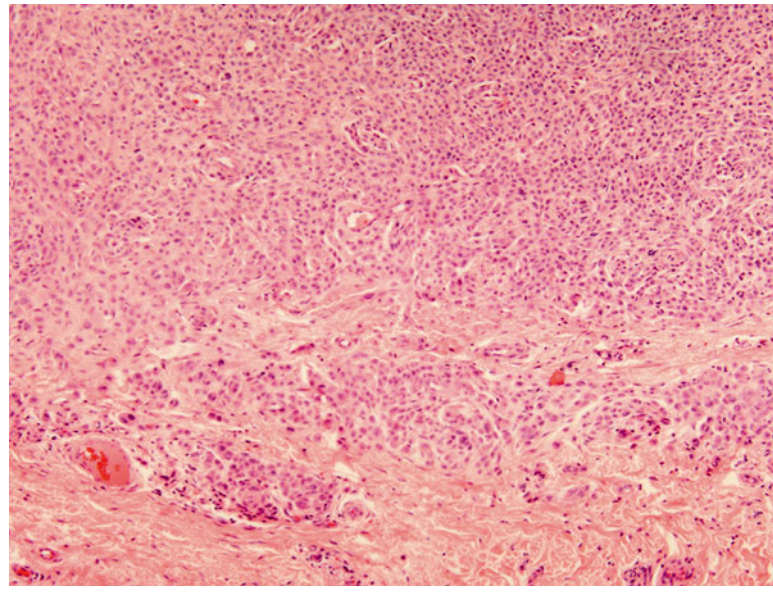


Fig. 8.16 There is no maturation with the melanocytes with similar morphology at the superficial as well at the advancing front in the deep dermis

Case 8D

Clinical History A 50-year-old male with a lesion on his scrotum

Microscopic Description The lesion exhibits a marked papillomatous epidermal hyperplasia associated with prominent pagetoid spread in the epidermis as well as involving the external root sheath of hair follicles (Fig. 8.17a, b). Between the areas of prominent pagetoid spread, there is a proliferation of epithelioid malignant cells resulting in involvement of the entire epidermis (Fig. 8.18). The lesion is multifocally invasive and forms expansile nodules filling and widening the papillary dermis (Fig. 8.19). Atypical mitoses are visible (Fig. 8.20). There is no evidence of regression or microscopic satellites. There is striking pigmentation within the lesion with areas of prominent single cells identified by the dendritic nature (Fig. 8.20). In addition, there are dermal melanophages. Multifocally, there are remnants of dermal congenital nevus beneath the lesion.

Diagnosis Malignant melanoma, superficial spreading type, with verrucous features, invasive to Clark level III, and a measured thickness of 0.7 mm, arising in association with a nevus with features of congenital onset, present close to the margin

Comment This very interesting lesion presents an unusual and distinctive problem, namely, how to measure the thickness of the lesion (Kamino et al. 1990; Reis-Filho et al. 2001). Because of the exuberant hyperplasia of the lesion, some of these lesions are only superficially invasive but measured more than 1 mm. In this particular case, there are obviously expansile nodules formed by the tumor, so the measured thickness is more representative of the tumor thickness. However, one must always be cautious in cases of verrucous melanoma to perform levels in order to assess the true thickness of the lesion. In some cases, the anatomic level may be a more accurate indicator of prognosis. In those cases having radial growth phase and no vertical growth phase, and with thick measured thickness, one must attempt to measure from the valley to the invasive cells rather than from an area of marked epidermal papillomatosis. Another aspect of this lesion worth mentioning is the marked involvement of the hair follicles. The pattern of follicular involvement is characteristic of verrucous melanoma. If there were invasion into the adjacent adventitial dermis, we would record the measured thickness. Once a vertical growth phase has been determined as in this case, then adequate re-excision and sentinel lymph node biopsy must be considered. Verrucous melanomas have been reported as verrucous and pseudo-nevoid melanoma (Steiner et al. 1988), verrucous-keratotic melanoma (Kuehnl-Petzoldt et al. 1982), and verrucous nevoid and keratotic melanoma (Blessing et al. 1993).

Key Histologic Features

Malignant melanoma, superficial spreading type, with verrucous features, arising in association with a nevus with features of congenital onset (Figs. 8.17, 8.18, 8.19, and 8.20)

- Marked papillary epidermal hyperplasia is associated with prominent pagetoid spread in the epidermis as well as involving the hair follicles.
- The pattern of follicular involvement is characteristic of verrucous melanoma.

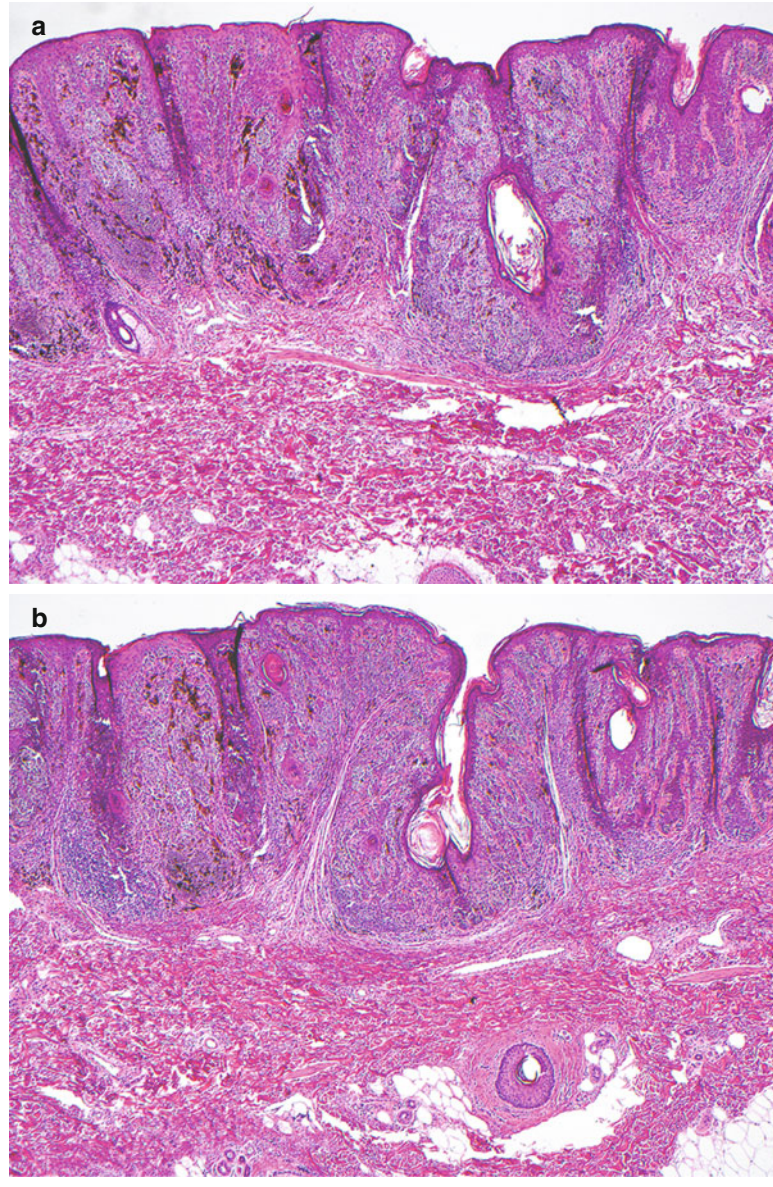


Fig. 8.17 (**a**, **b**) An atypical compound melanocytic proliferation is seen in association with marked papillomatous epidermal hyperplasia

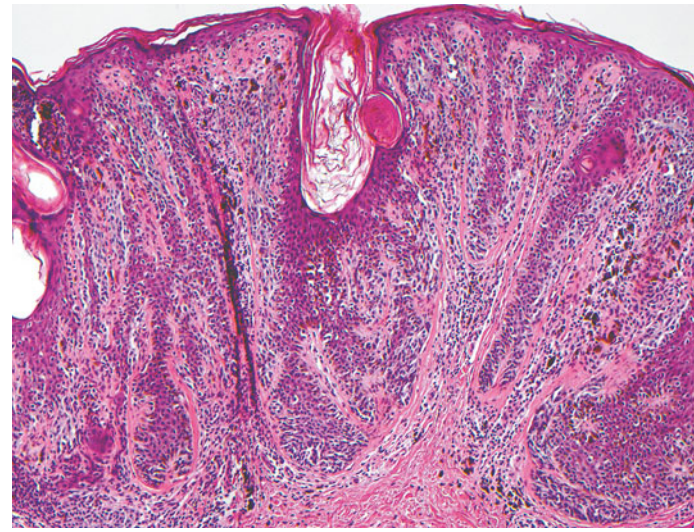


Fig. 8.18 There is a proliferation of atypical epithelioid melanocytes within the epidermis

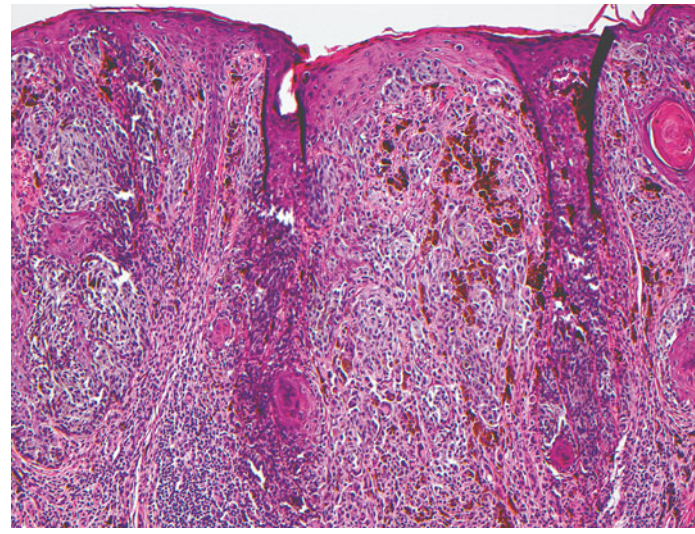


Fig. 8.19 The tumor is multifocally invasive and forms expansile nodules filling and widening the papillary dermis

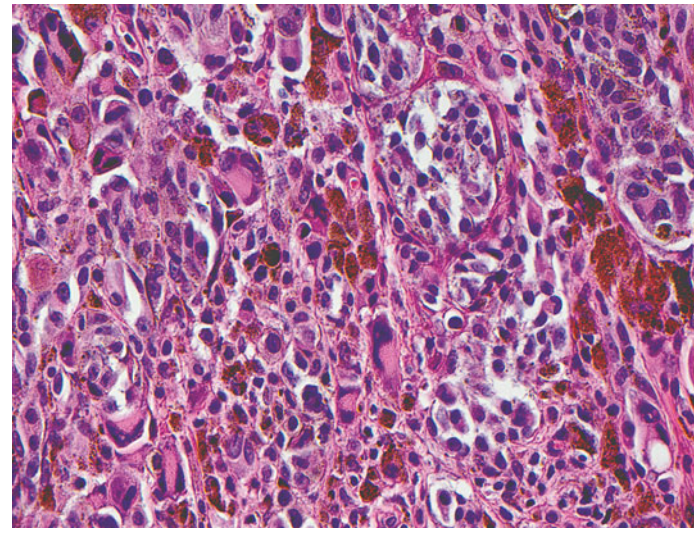


Fig. 8.20 Marked pleomorphism is noted

Case 8E

Clinical History A 65-year-old female with a lesion on her right lower leg

Microscopic Description This lesion is composed of a striking proliferation of inverted type-A cells (Fig. 8.21a). The overall architecture of this lesion is due to the plexiform nature of the lesion with extensive disposition of the cells along the neurovascular bundles (Fig. 8.21b). These cells are spindled and epithelioid in appearance and exhibit varying amount of pigment within the cytoplasm (Fig. 8.22). In this particular instance in contrast to the deep penetrating nevus cells, there is high nuclear–cytoplasmic ratio and true pleomorphism (Fig. 8.23). Likewise, there are two mitoses per squared millimeter and deep mitotic figure noted. Features that raise the possibility of the deep penetrating nevus are melanophages surrounding the melanocytic nests. There is no evidence of maturation.

Diagnosis Plexiform and inverted type-A melanocytic lesion, borderline type, extending close to the margin

Comment This lesion obviously presents a difficulty in the differential diagnosis mainly the inverted type-A nevus. In this case there is an extensive plexiform tumor that forms a large expansile mass. The inverted type-A nevus is usually an inverted triangle in shape with diminution of cells at the base. Furthermore, this lesion is associated with mitotic activity even with deep mitotic figure noted. Another feature is the marked pleomorphism and absence of senescent changes. Marked senescent changes are typical of the inverted type-A nevus. These lesions in our experience may metastasize; however, the metastasis is mainly confined to the draining lymph node basin.

Key Histologic Features

Plexiform and inverted type-A melanocytic lesion, borderline type (Figs. 8.20, 8.21, 8.22, and 8.23)

- Expansile and plexiform proliferation of inverted type-A cells.
- Extensive disposition of the cells along the neurovascular bundles.
- There is high nuclear–cytoplasmic ratio and true pleomorphism.
- There are two mitoses per squared millimeters and deep mitotic figure noted.

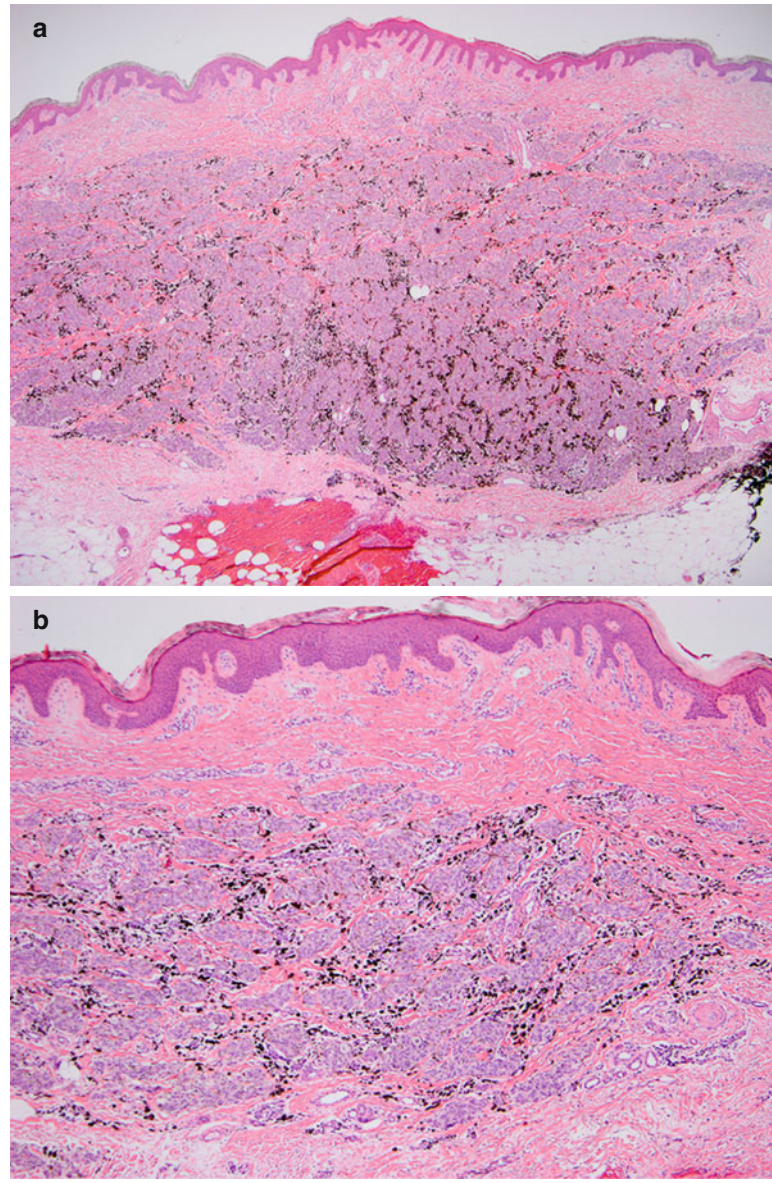


Fig. 8.21 (**a**, **b**) There is plexiform proliferation of inverted type-A cells in the dermis with deposition of melanocytes along the neurovascular bundles

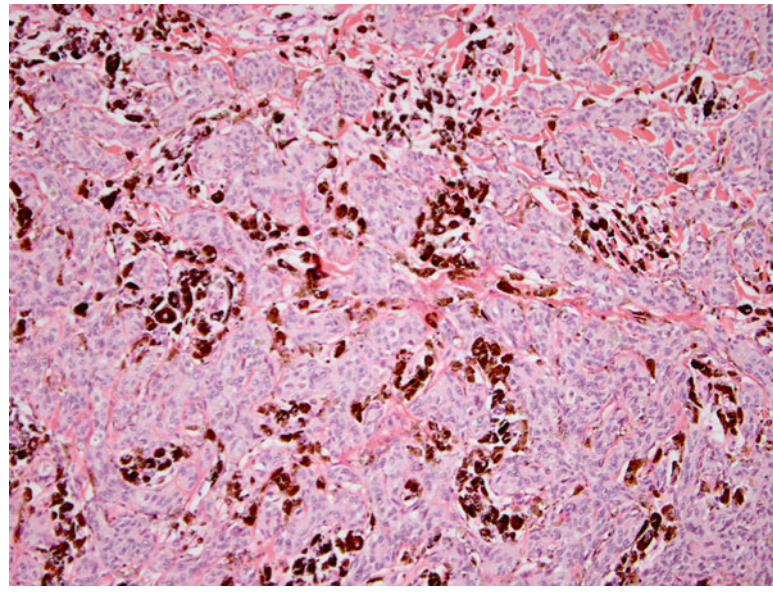


Fig. 8.22 These cells are spindled and epithelioid in appearance and exhibit varying amount of pigment within the cytoplasm

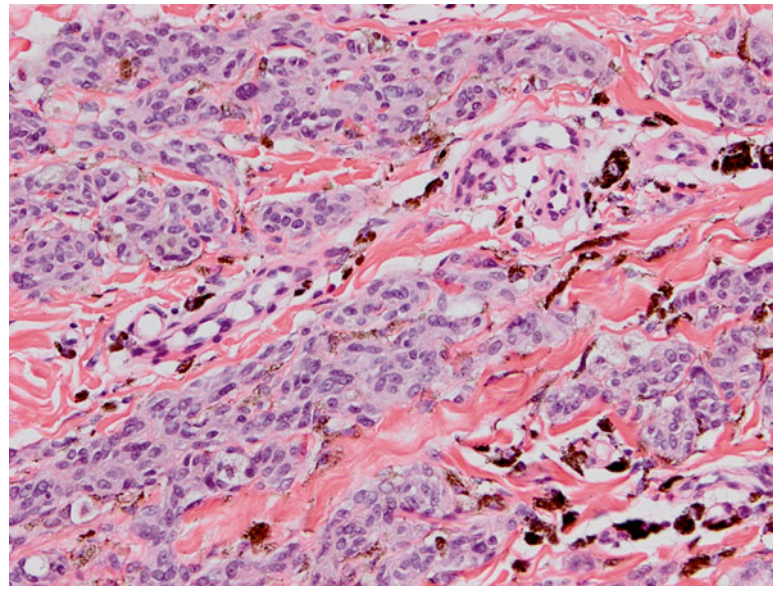


Fig. 8.23 High nuclear–cytoplasmic ratio and pleomorphism are noted

Case 8F

Clinical History A 74-year-old male with a left forehead lesion

Microscopic Description On low-power examination, there is striking epidermal atrophy associated with multiple nidi of chronic inflammation and prominent dermal fibrosis (Fig. 8.24). Higher-power examination exhibits an atrophic epidermis and a proliferation of markedly atypical melanocytes replacing the basal layer of the epidermis and extending to the hair follicular epithelium and along the eccrine basement membrane zone (Figs. 8.25 and 8.26). These changes are associated with a prominent proliferation of atypical and strikingly hyperchromatic fusiform nuclei with variable cytoplasm. These cells haphazardly infiltrate the reticular dermis and destroy the architecture and invade the adventitial dermis of appendages (Fig. 8.26). There are foci of neurotropism with perineural and endoneural proliferation of the fusiform atypical melanocytic cells. Throughout the base of the lesion extending to the junction of the dermis and subcutaneous fat, there are deposits of mucin scattered throughout the dermis (Fig. 8.27). The areas of chronic inflammation consist of nodules of lymphocytes as well as scattering of lymphocytes amidst the dermal collagen fibers. High-power examination reveals the constituent melanocytes are associated with marked hyperchromasia of fusiform nuclei with variable shape and sizes (Fig. 8.28). The cytoplasm of the affected melanocytes is sparse and often difficult to visualize. An occasional cell with hyperchromatic nuclei and densely eosinophilic cytoplasm is noted infiltrating the hyperchromatic fusiform cells. On higher examination of the affected nerve, one observes infiltration of the perineurium with dissection of the sheath by the malignant nuclei (Fig. 8.29). This invasion results in an almost onion skin appearance. The nerve itself is infiltrated by very hyperchromatic cells. Arrector pili are also infiltrated by the tumor cells and show focal mucinous degeneration.

Diagnosis Malignant melanoma, desmoplastic and neurotropic type, invasive to Clark level IV, and a measured thickness of 2.4 mm with associated lentigo maligna

Comment This lesion shows a classic example of a desmoplastic and neurotrophic melanoma (Busam et al. 2004; Quinn et al. 1998; Smithers et al. 1990; Posther et al. 2006). In this particular instance, the lesion arises in association with lentigo maligna, most usually arises with melanocytic hyperplasia within the overlying epidermis. Unquestionably there are rare cases of no associated junctional melanocytic component. These tumors have been referred as neurotropic melanoma, and these cases are quite rare (Reed and Leonard 1979; Kossard et al. 1987). Because most cases of desmoplastic melanoma have a lentiginous proliferation of melanocytes, they are found most commonly in sites of lentiginous melanoma. Mucosal lesions, chronic sun-exposed skin lesions, and lesions in the genitalia and in acral areas have all been described. However, desmoplastic melanoma can occur in association with congenital nevi, common acquired nevi, and solar lentigo; however, these later tumors are unusual. In this particular case, all of the features of desmoplastic melanoma are evident. There is a lentiginous proliferation of melanocytes in an atrophic epidermis. There is also the very striking dense fibrosis associated with the infiltrative tumor cells. The great majority of these cells have a fibroblast-like appearance with fusiform shape, dense hyperchromasia, and highly irregular nuclear contour. It is important to identify that these cells infiltrate the adventitial dermis and invade up to the basement membrane zone and deform the adnexal structures. This aggressive characteristic is used to differentiate desmoplastic melanoma from sclerosing Spitz or blue nevi which usually spare the adventitial structures. There are prominent neurotropism in this case. There are two stromal changes of importance. The first is the presence of nidi of inflammation in the collagen. These nodular aggregates of lymphocytes are seen even at low-power appreciation of the tumor. There is a sprinkling of lymphocytes throughout the entire neoplasm. The other important change is the deposition of mucin which can be striking and can resemble a myxoma or a mucin producing

tumor. It is very important to excise these lesions completely at the time of first diagnosis. If one leaves behind, for example, melanoma in the nerve tissues, the patient is destined to experience recurrence and even death in rare cases.

Desmoplastic melanoma was first described in 1971 by Conley et al. (1971). Reed and Leonard (1979) subsequently described neurotropic melanoma, a subset of desmoplastic melanomas with striking neural differentiation (Kossard and Wilkinson 1997). The most common histologic pattern of desmoplastic melanoma is the desmoplastic presentation (Jain and Allen 1989; Bruijn et al. 1992; Carlson et al. 1995). Desmoplastic neurotropic melanomas are associated with significantly reduced survival compared to desmoplastic melanomas without neurotropism (Baer et al. 1995).

Key Histologic Features

Malignant melanoma; desmoplastic and neurotropic type (Figs. 8.24, 8.25, 8.26, 8.27, 8.28, and 8.29)

- Epidermal atrophy associated with multiple nidi of chronic inflammation with prominent dermal fibrosis.
- Atypical and fusiform cells haphazardly infiltrate the reticular dermis, destroying the architecture and invading the adventitial dermis of appendages and deforming the adnexal structures.
- Foci of neurotropism with perineural and endoneural proliferation of the fusiform atypical melanocytic cells.
- Deposits of mucin scattered throughout the dermis.

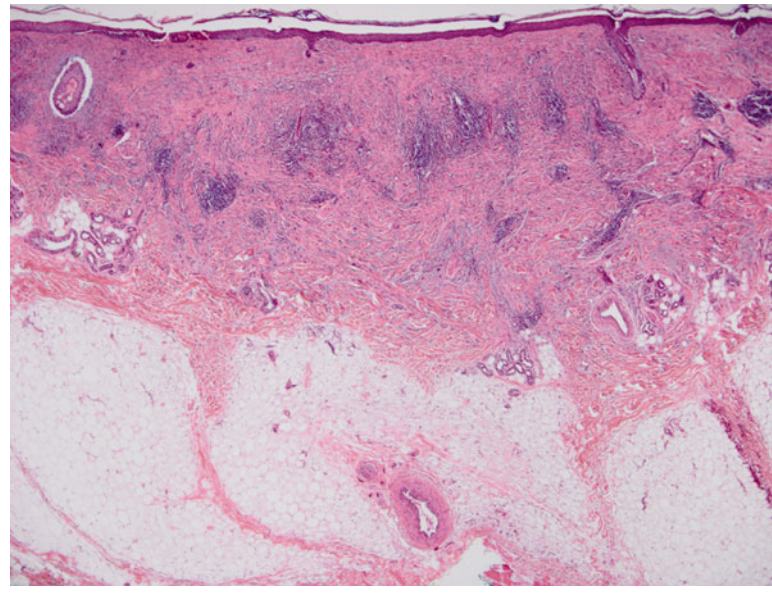


Fig. 8.24 At low magnification, there is striking epidermal atrophy associated with multiple nidi of chronic inflammation and prominent dermal fibrosis

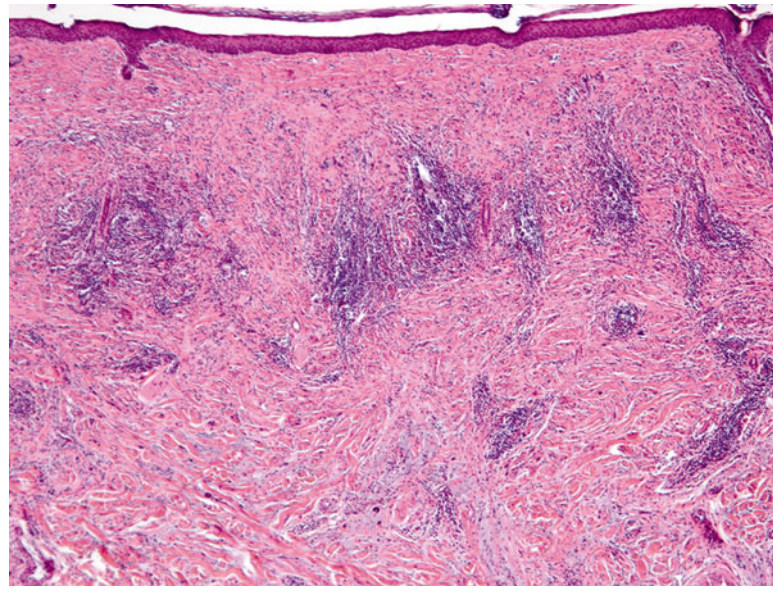


Fig. 8.25 Below an atrophic epidermis is a proliferation of markedly atypical melanocytes that haphazardly infiltrate the reticular dermis that extends along the hair follicles

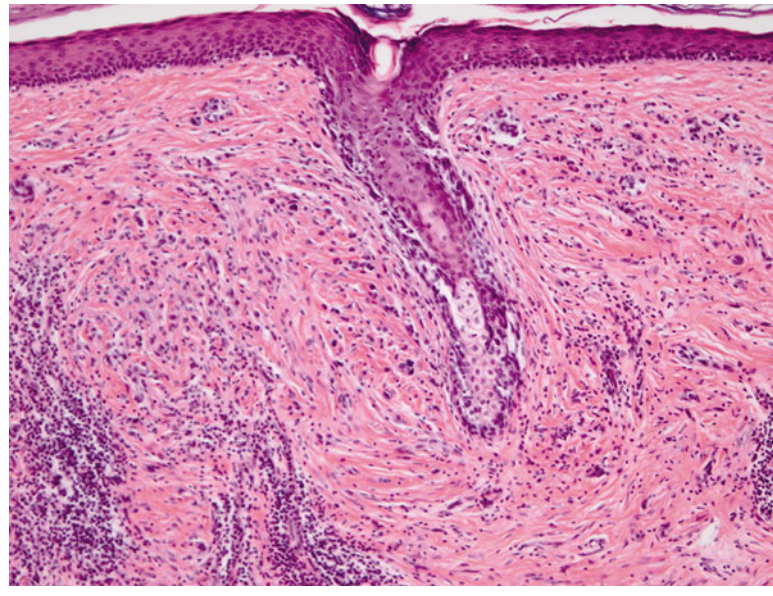


Fig. 8.26 Extension along hair follicles is noted

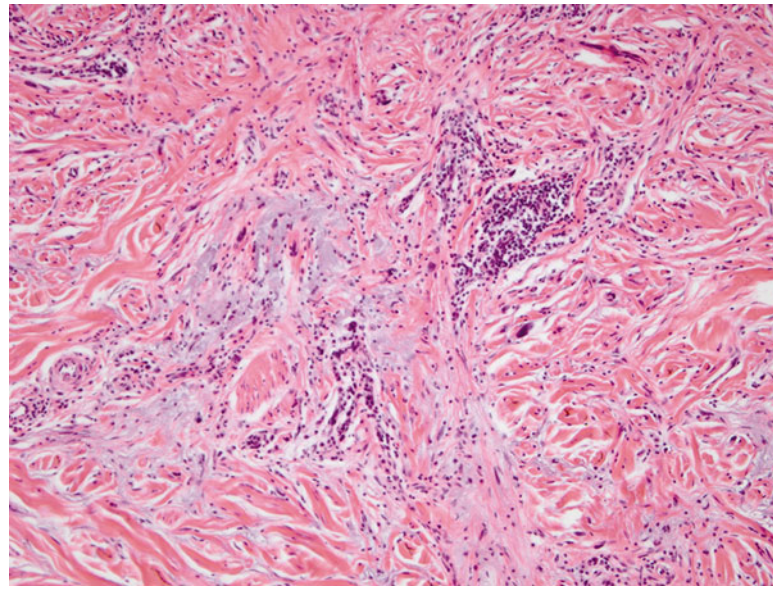


Fig. 8.27 Deposits of mucin is seen scattered throughout the dermis

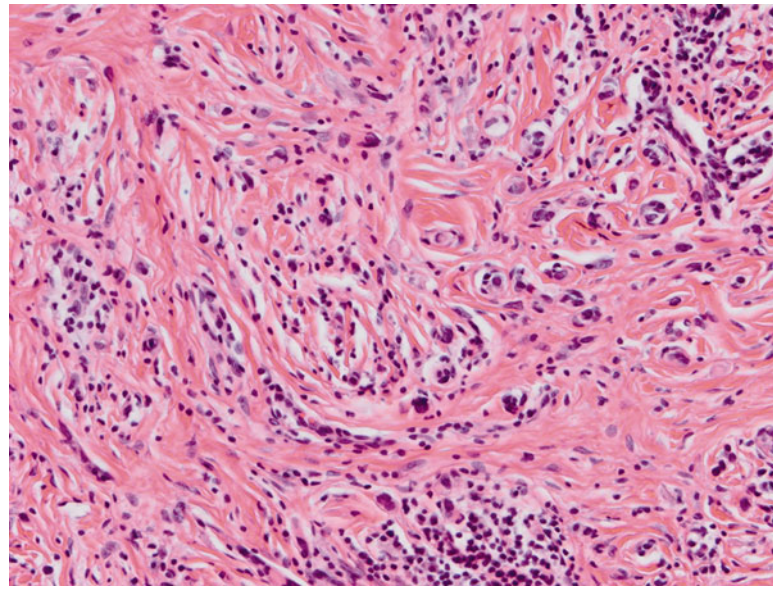


Fig. 8.28 The neoplastic melanocytes have hyperchromatic nuclei with variable size and shape

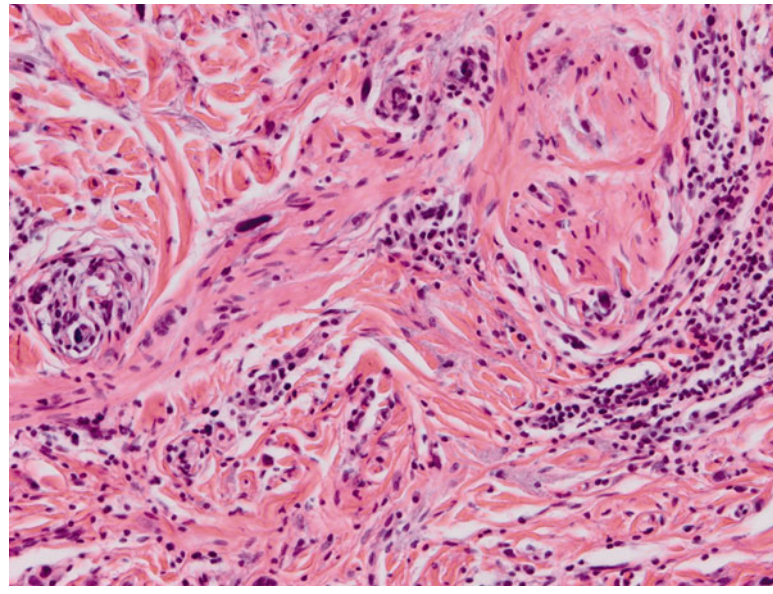


Fig. 8.29 Perineural invasion is identified

Case 8G

Clinical History A 69-year-old male with a lesion on his left temple

Microscopic Description Low-power examination reveals virtual replacement of the reticular dermis by a proliferation of cells in a background of pale-staining blue materials that extends to the subcutaneous fat (Fig. 8.30a, b). The papillary dermis is spared; however, there is a proliferation of atypical melanocytes within the epidermis and hair follicles (Fig. 8.31a). High-power examination reveals a striking proliferation of atypical melanocytes with variable nesting at the basal layer of the epidermis (Fig. 8.31b). In the lower portion of the papillary dermis focally and occupying the remainder of the reticular dermis is a proliferation of cells with prominent hyperchromatic nuclei (Fig. 8.32). These cells have eosinophilic cytoplasm with vacuoles, many of which contain the bluish materials that is present in the dermis as well (Fig. 8.33). There is high nuclear to cytoplasmic ratio and marked pleomorphism focally. Some cells exhibit intranuclear vacuoles representing intracytoplasmic invagination. Rare mitotic figures are noted; thus, there is one mitotic figure per squared millimeter (Fig. 8.33). There is invasion of both the septae and the lobules as the cells enter the subcutaneous fat (Fig. 8.34). Perineural invasion is noted (Fig. 8.35). In addition to pale blue matrix, there is focal fibrosis of the affected area. Mucin stain reveals extensive mucopolysaccharide throughout the tumor extending into the affected nerves. There is no ulceration, no regression, no microscopic satellite, and no inflammatory host response. The melanocytic proliferation colonizes the hair follicle extensively and even extending deep down the fibrous sheath. The neoplastic cells stain for S100 and MART-1 immunostains.

Diagnosis Lentigo maligna melanoma with myxoid features

Comment This lesion represents a fascinating example of the rare variant of vertical growth phase melanoma, namely, the myxoid type (Hitchcock et al. 1999; Patel et al. 2002). It arises in the background of lentigo maligna melanoma best appreciated very focally in the epidermis but more prominently along the follicular epithelium. There is invasion directly from the follicle into the dermis. The entire vertical growth phase is composed of a mixture of predominantly epithelioid cells that are embedded in a matrix of mucin. The appearance of the lesion is changed somewhat in that in addition to the mucin there is fibrosis in the background. Myxoid melanoma can occur de novo as a variant of nodular melanoma, but they are more commonly associated with vertical growth phase melanoma. The content of the mucinous areas varied from very prominent epithelioid cells to very sparse spindled cells. The differential diagnosis includes the benign and malignant mucin-producing tumors. The lesion is too cellular to be a benign myxoma. Among the atypical cellular lesions, one must consider acral fibromyxoma in which there is no atypia in the cells and the quantity of mucin is usually much greater. The fibromyxoid sarcoma enters into the differential diagnosis. The staining of the melanocytes for S100 and the presence of an in situ component exclude the possibility of fibromyxoid sarcoma, myxoid dermatofibrosarcoma protuberans, and myxoid liposarcoma. In a series by Hitchcock et al. (1999), the authors found no prognostic difference in myxoid melanoma compared with melanoma with similar depth and with other characteristics. One of the most important caveat that we can cite is in myxoid lesion of any sites especially the digit; if there is cellularity, one must evaluate the overlying epidermis for any atypical melanocytic proliferation. We have seen melanocytic lesions of the nasal sinus and mucosa given the diagnosis of sarcoma in which the overlying atypical melanocytic proliferation was not appreciated.

Key Histologic Features

Lentigo maligna melanoma with myxoid features (Figs. 8.30, 8.31, 8.32, 8.33, 8.34, and 8.35)

- There is a proliferation of atypical melanocytes within the epidermis and dermis embedded in a mucinous matrix.
- Atypical melanocytes with variable nesting at the basal layer of the epidermis.
- Neoplastic cells with prominent hyperchromatic nuclei.
- Rare mitotic figures and perineural invasion are noted.

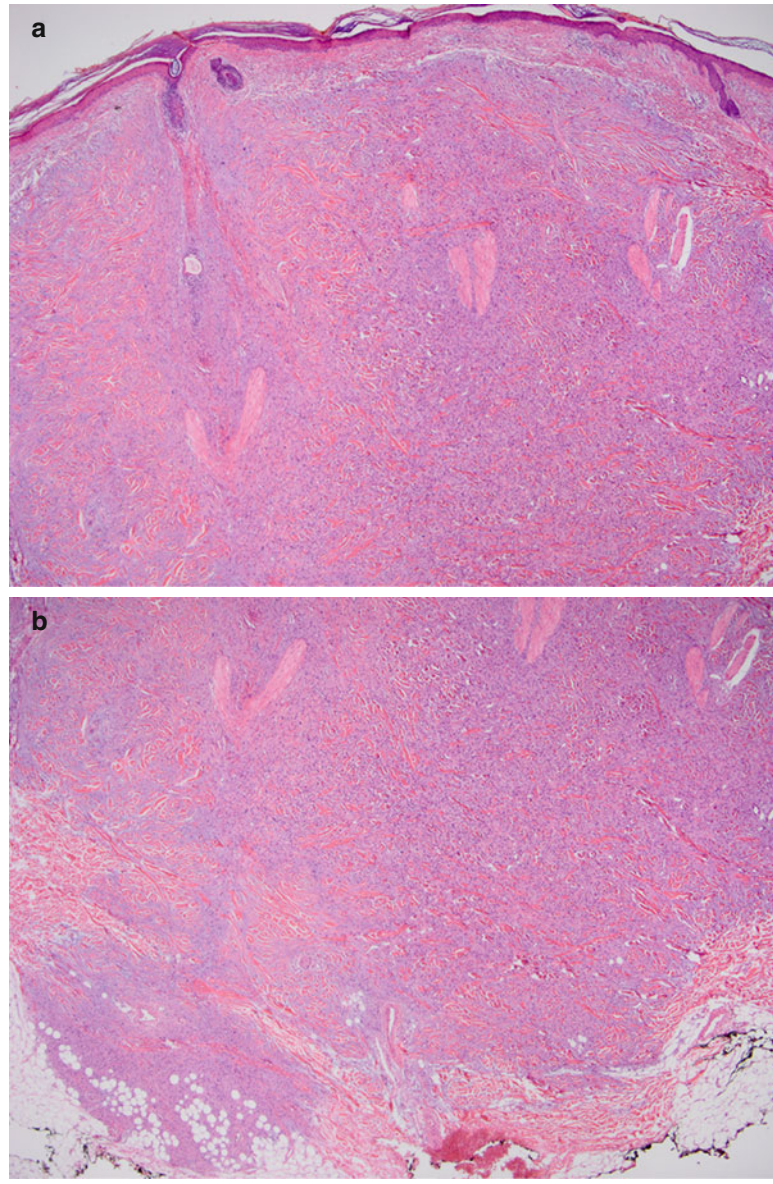


Fig. 8.30 (**a**, **b**) An expansile proliferation of atypical melanocytes is seen extending to the subcutaneous fat

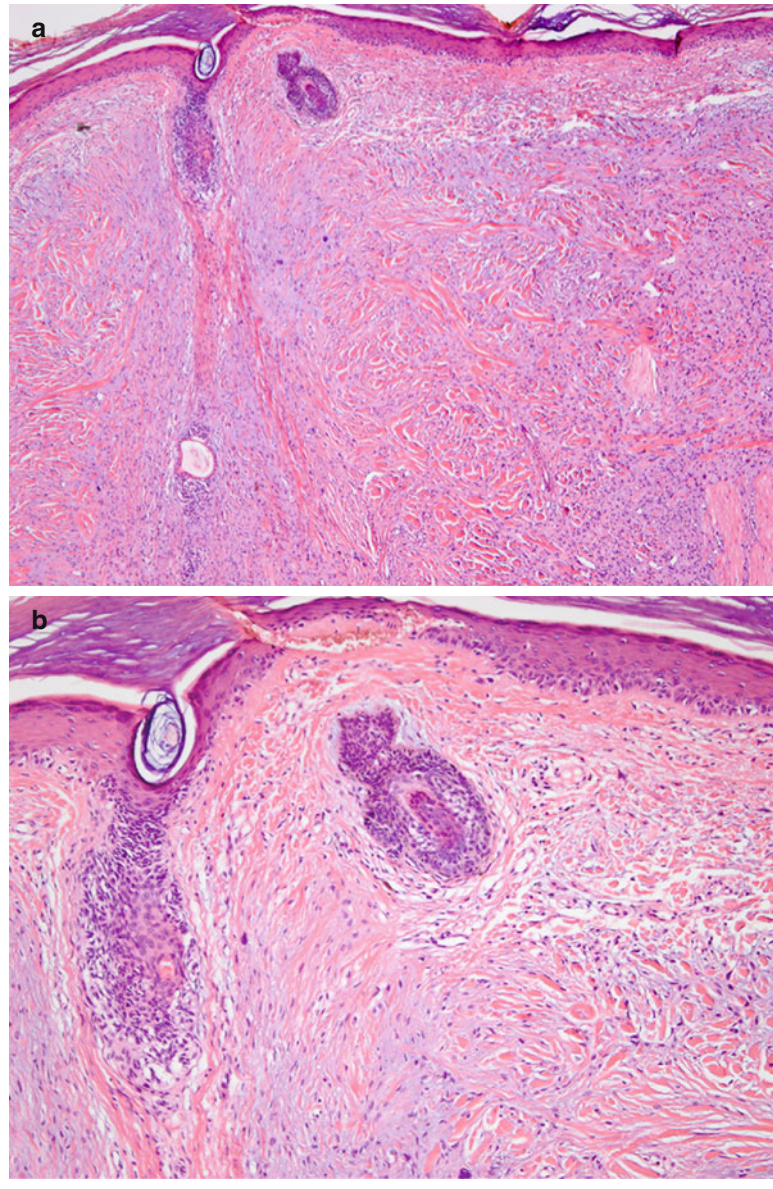


Fig. 8.31 (**a**, **b**) A proliferation of atypical melanocytes is seen within the epidermis and hair follicles

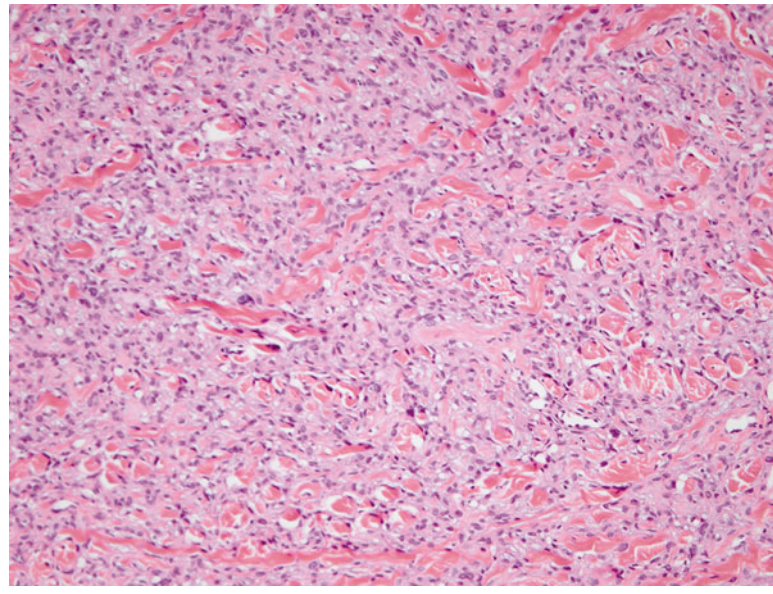


Fig. 8.32 A proliferation of atypical melanocytes with prominent hyperchromatic nuclei is seen in the dermis

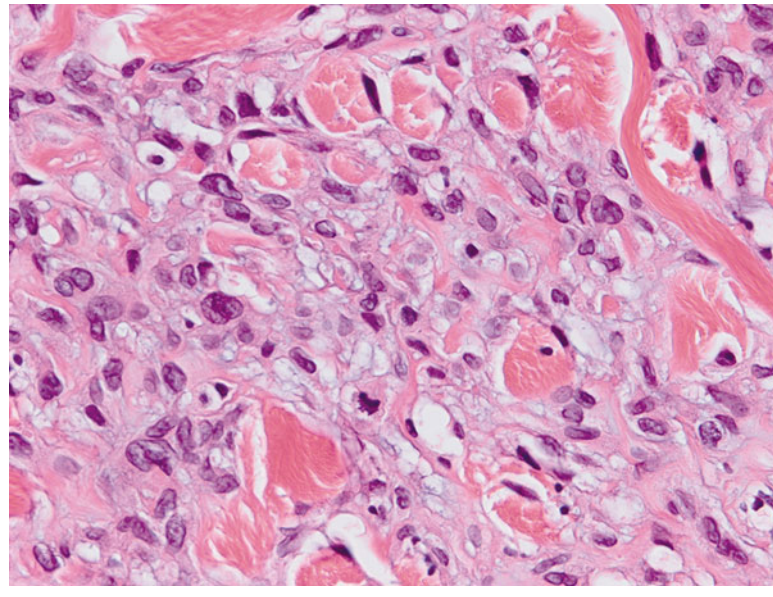


Fig. 8.33 The tumor cells have eosinophilic cytoplasm and some with vacuoles

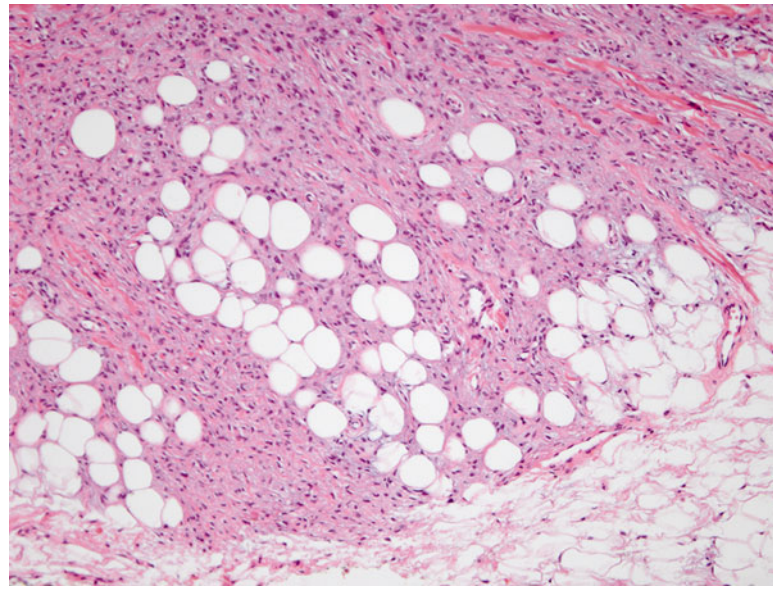


Fig. 8.34 There is invasion of both the septae and the lobules as the cells enter the subcutaneous fat

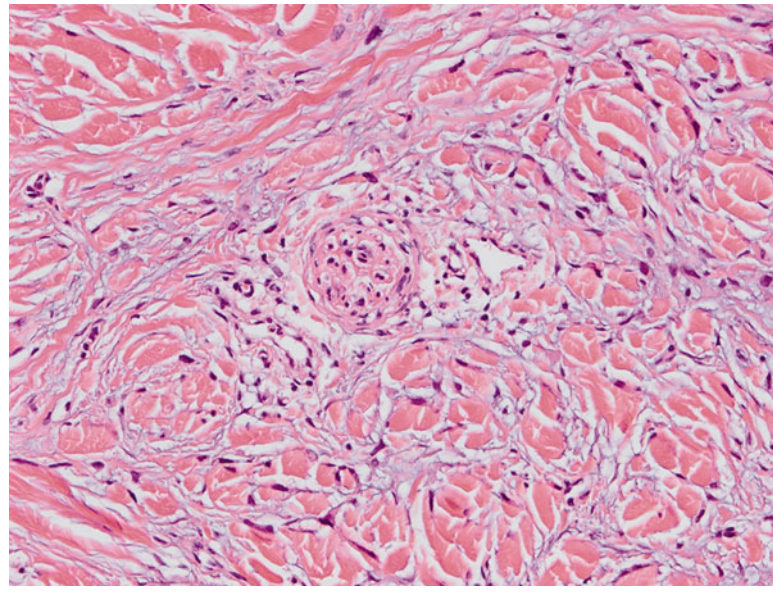


Fig. 8.35 Perineural invasion is noted

Case 8H

Clinical History A 73-year-old male with a left forearm lesion

Microscopic Description Low power reveals a large expansile nodule of tumor cells at the edge of which there is a radial growth phase composed of epithelioid cells replacing the basal layer of the epidermis (Fig. 8.36a, b). Rare pagetoid spread is noted (Fig. 8.37). The radial growth phase is pigmented (Fig. 8.38). In contrast, the vertical growth phase shows little or no pigment (Fig. 8.39). It is composed of spindle-shaped cells arranging in prominent fascicles (Fig. 8.39). The principal type of cells has fusiform nucleus with prominent nucleoli, many of which are eosinophilic (Fig. 8.40). Interspersed are highly atypical multinucleated giant cells with nuclear convolution with eosinophilic nucleoli. The cells abut and invade vessels wall. There is no visible pigmentation. There are as many as 14 mitoses per squared millimeter (Fig. 8.40). There is no evidence of ulceration, regression, or neurovascular invasion. Microscopic satellites cannot be evaluated due to the superficial nature of the biopsy. There is a non-brisk host response.

Diagnosis Malignant melanoma, superficial spreading with spindle and amelanotic vertical growth phase, Clark level IV, and Breslow depth of 4.3 mm

Comment This lesion is a very good example of amelanotic melanoma arising in association with a pigmented radial growth phase (Gualandri et al. 2009). 1.8 % of 2,881 melanomas in the series by Giuliano et al. (1982) have no associated pigmentation. It demonstrates that the clonality of the intraepidermal growth phase is different. The spindle cell melanoma is characterized by cells with prominent nucleus, marked irregular chromatin, and prominent nucleolus. The nucleus is surrounded by mass of fusiform cytoplasm in which there are no pigment granules. Furthermore, there is an amphophilic appearance to the cytoplasm. The cells are organized in fascicles with the nuclei abutting each other resembling a "school of fish." In benign melanocytic lesion such as spindle cell or Spitz nevus, the nuclei are separated by ample cytoplasm. The orientation of the cells abutting the blood vessels is very characteristic of melanoma resembling the picture seen in glioblastoma multiforme. There is no maturation. There is individual cell necrosis. There are many mitoses and many of which are atypical.

Key Histologic Features

Malignant melanoma, superficial spreading with spindle and amelanotic vertical growth phase (Figs. 8.36, 8.37, 8.38, 8.39, and 8.40)

- A large expansile nodule of tumor cells at the edge of which there is a radial growth phase composed of epithelioid cells replacing the basal layer.
- The radial growth phase is pigmented.
- The vertical growth phase shows little or no pigment and is composed of spindle shaped cells arranging in prominent fascicles.

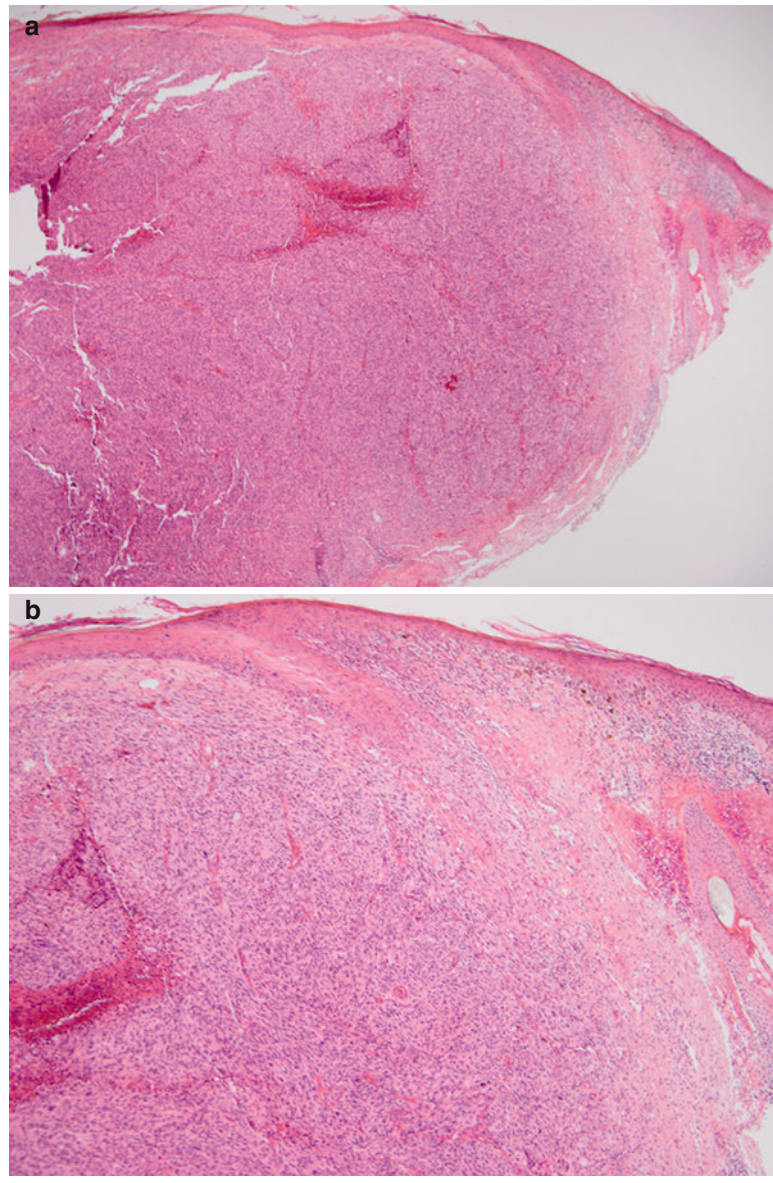


Fig. 8.36 (**a**, **b**) An expansile nodule of invasive tumor with an in situ component at the basal layer of the epidermis is seen

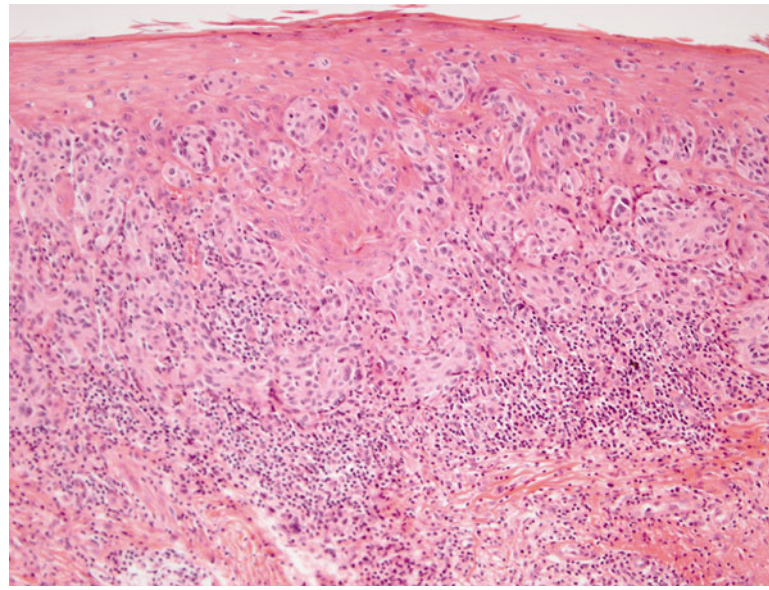


Fig. 8.37 Pagetoid spread of atypical melanocytes is noted

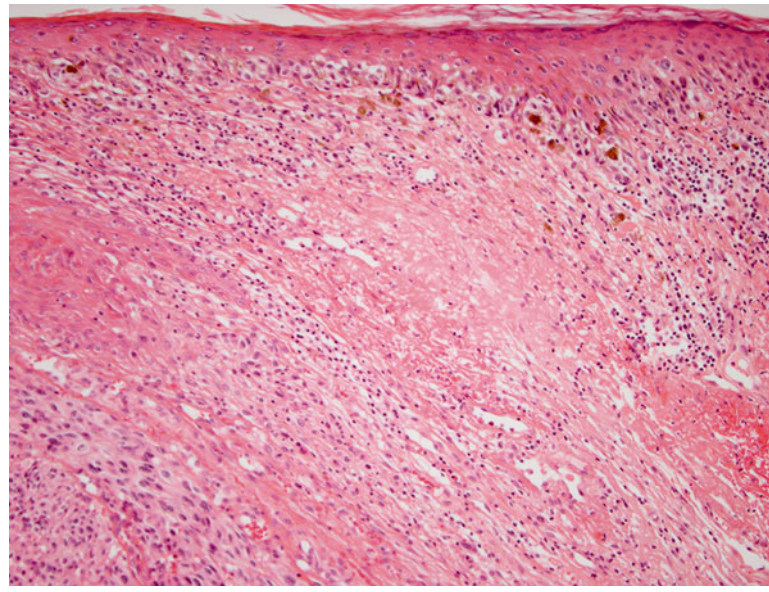


Fig. 8.38 The in situ component is pigmented

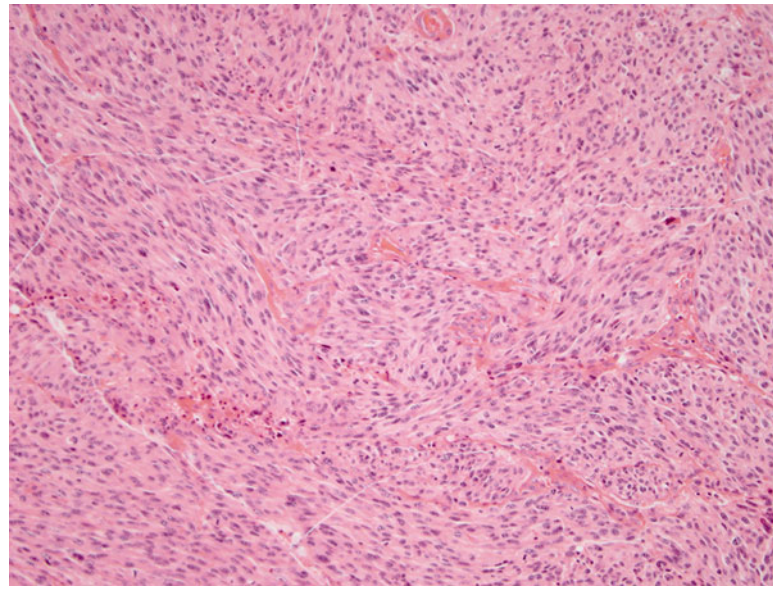


Fig. 8.39 The vertical growth phase is composed of fascicles of spindle-shaped cells

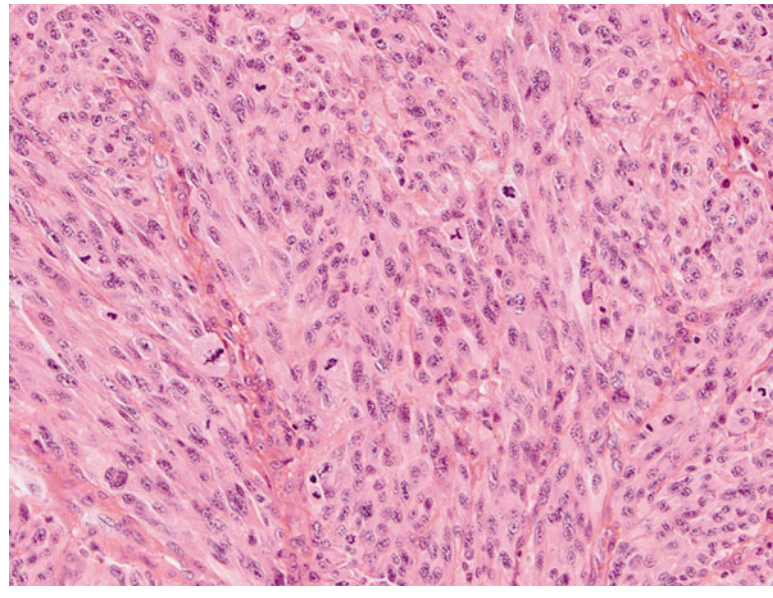


Fig. 8.40 Fusiform nuclei with prominent nucleoli and prominent mitotic figure are seen

Case 8I

Clinical History A 52-year-old male with a right posterior shoulder lesion

Microscopic Description This lesion is a nodular melanoma composed of spindle cells (Fig. 8.41a, b). There is no evidence of pigmentation. The spindle cells exhibit very prominent nuclear to cytoplasmic ratio so that the nuclei are very closely apposed (Fig. 8.42). The cytoplasm has a slightly eosinophilic appearance. The interesting aspect of the lesion is the pattern of the spindle cell. For example, there are areas of storiform appearance. In other areas, a pattern of intersecting bundles is noted. There are numerous mitoses with 13 mitoses seen per squared millimeter (Fig. 8.42). There is marked ulceration greater than 8 mm in extent (Fig. 8.41a). There is a non-brisk host response. There is no evidence of vascular invasion although there are many dilated lymphatics (Fig. 8.43). There is no evidence of micro-satellites or regression.

Diagnosis Nodular malignant melanoma, predominantly amelanotic type, invasive, level IV, and measured thickness of 5.3 mm

Comment This lesion presents one of the real problems arising when one has a predominantly spindle cell lesion. The issue becomes more difficult when the cells become amelanotic. For example, in this lesion, there are storiform and fascicular areas resembling a fibrohistiocytic lesion. Some of the helpful features are the nuclei of the cells which have very prominent nucleoli. This change always raises the possibility of malignant melanoma. The cytoplasm of the cells has a very distinctive appearance, eosinophilic, resembling Spitz nevus cells. However, in all such cases, the use of immunohistochemistry results in a conclusive diagnosis. The S100 stain is usually positive. The Melan A/MART-1 stain, however, may be negative. The HMB-45 stain is usually negative. The use of MiTF stain is helpful because it is a product visualized in the nucleus. In a study by Granter et al. (2001b), MiTF can be positive in spindle cell lesion; thus, its specificity is low. Another interesting aspect of this lesion is the presence of dilated lymphatics. Multiple dilated lymphatics at the periphery are seen as well. Of course, the issue of a spindle cell nevus also enters the differential diagnosis with a spindle cell malignant melanoma. The features favoring malignant melanoma include ulceration, necrosis, multiple mitoses especially in the deep aspect of the lesion, and expansile nature of the tumor nodule. The cytologic features of malignancy include very high nuclear–cytoplasmic ratio consisting of prominent nucleoli. The presence of striking dilated lymphatics is not seen at the base of the lesion, and the lack of maturation of the cells is not usually seen in Spitz nevus. Finally, evidence of regression in adjacent papillary dermis is present. In contrast, the Spitz nevus has very prominent nuclear–cytoplasmic ratio, usually does not show ulceration even though it has mitoses, and lacks any evidence of regression.

Key Histologic Features

Nodular malignant melanoma, predominantly amelanotic type (Figs. 8.41, 8.42, and 8.43)

- A nodular melanoma composed of spindle cells with no evidence of pigmentation
- Storiform and fascicular areas resembling a fibrohistiocytic lesion

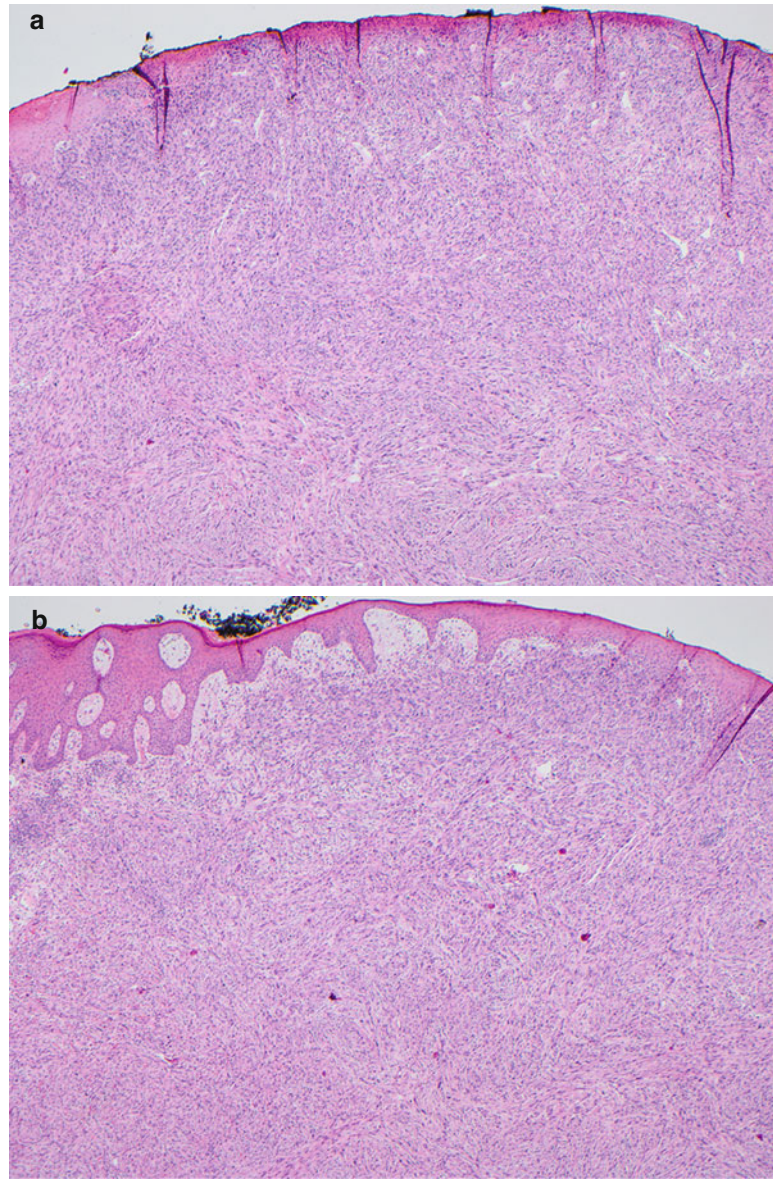


Fig. 8.41 (**a**, **b**) A nodular and ulcerated melanoma composed of spindle cells is seen

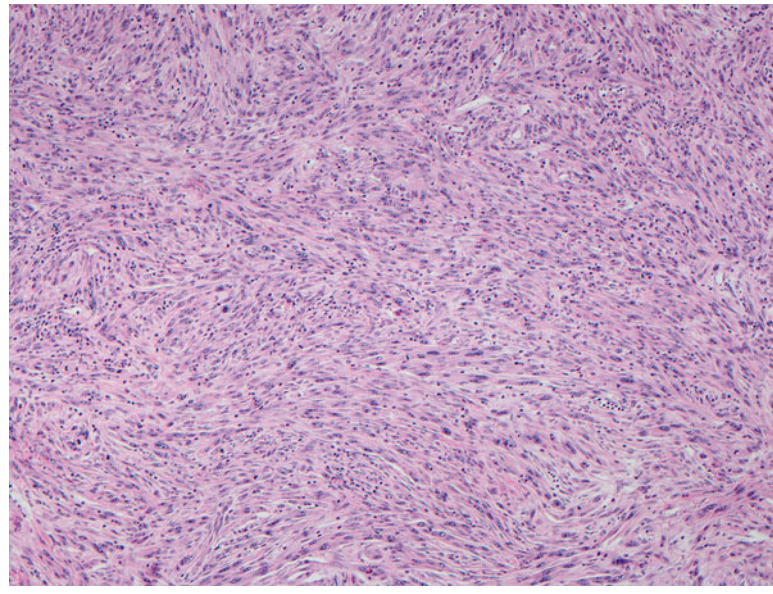


Fig. 8.42 The spindle cells exhibit high nuclear to cytoplasmic ratio

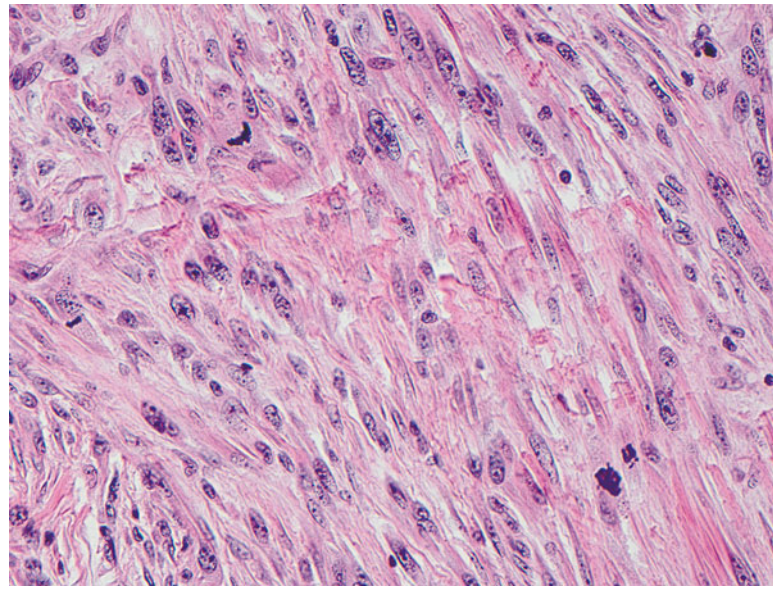


Fig. 8.43 Atypical mitotic figures are readily identified

Case 8J

Clinical History A 45-year-old male with a right temple lesion

Microscopic Description This malignant melanoma exhibits a pure vertical growth phase. It has several foci of origin within the epidermis and proliferates as clusters of spindle-shaped nests that expand the papillary dermis forming an expansile nodule (Fig. 8.44a–c). There is no evidence of maturation. The cells show mild pleomorphism and predominantly spindled. They resemble the Spitz nevus cells in that they exhibit prominent nuclear–cytoplasmic ratio but have ample cytoplasm (Fig. 8.45). The cytoplasm has a pale and vacuolated appearance but no pigment granules observed in the more typical type of malignant melanoma cells. There is a brisk host response. There is no ulceration, microscopic satellite, or vascular invasion. There is no evidence of a precursor lesion, but the skin shows severe solar elastosis.

Diagnosis Malignant melanoma, nodular, invasive, Clark level III and measured thickness of 1.3 mm, and with Spitzoid features

Comment This lesion falls into the general rubric of melanoma with Spitz-like features and included the so-called Spitzoid melanoma (Okun 1979). The Spitzoid group of tumor is predominantly dermal based with small foci of in situ component. They can be composed of Spitzoid cells as in this case. In the extremely atypical variant, there is severe pleomorphism of the cells that are usually epithelioid and can have monster cells. The current case does not have this degree of pleomorphism, but it is clearly malignant on the basis of the high nuclear-cytoplasmic ratio and the formation of expansile nodule. This lesion differs from the atypical Spitzoid tumor in which sheets of spindle cells are found but without significant cytologic atypia. Also the lesion does not exhibit the type of host response that infiltrates the nests in a manner that we associated with malignant melanoma. The paucity of mitotic activity in addition to the brisk host response and absence of ulceration all speak for a lesion with good prognosis.

Key Histologic Features

Malignant melanoma, nodular type, and with Spitzoid features (Figs. 8.44 and 8.45)

- Clusters of spindle-shaped nests present within the epidermis and papillary dermis forming an expansile nodule.
- The cells resemble the Spitz nevus cells.

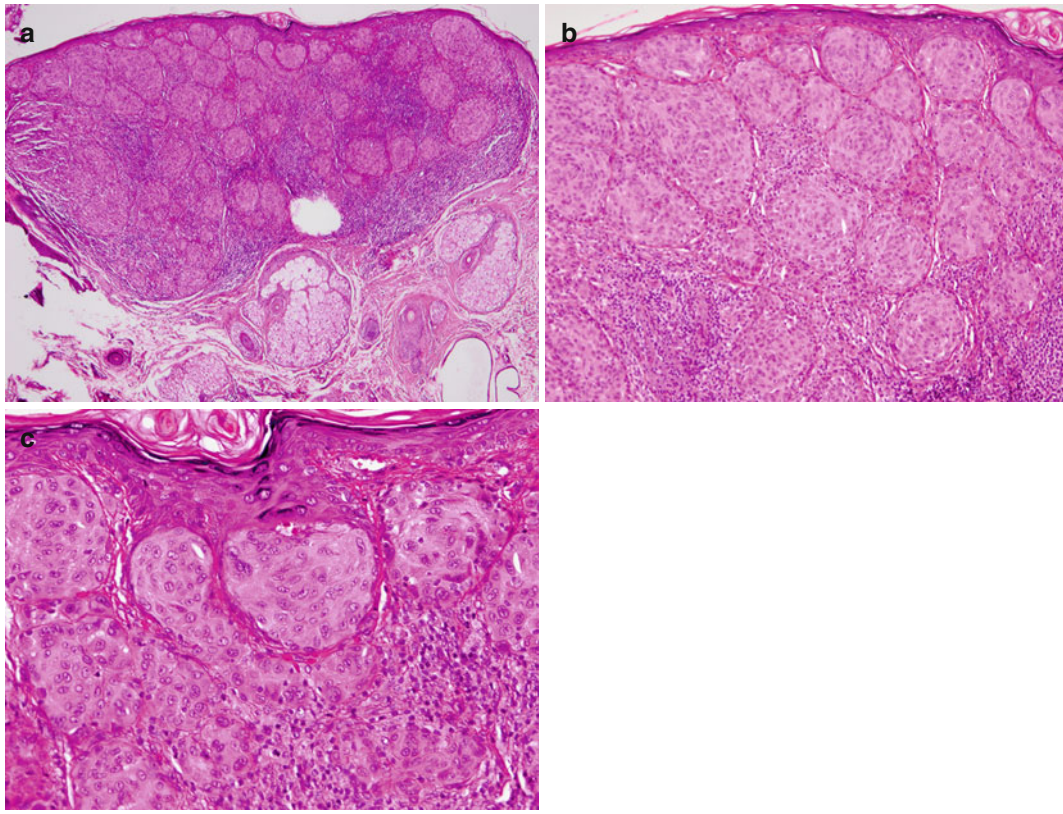


Fig. 8.44 (**a**–**c**) An expansile nodule comprised of clusters of spindle-shaped nests of melanocytes is seen in the dermis

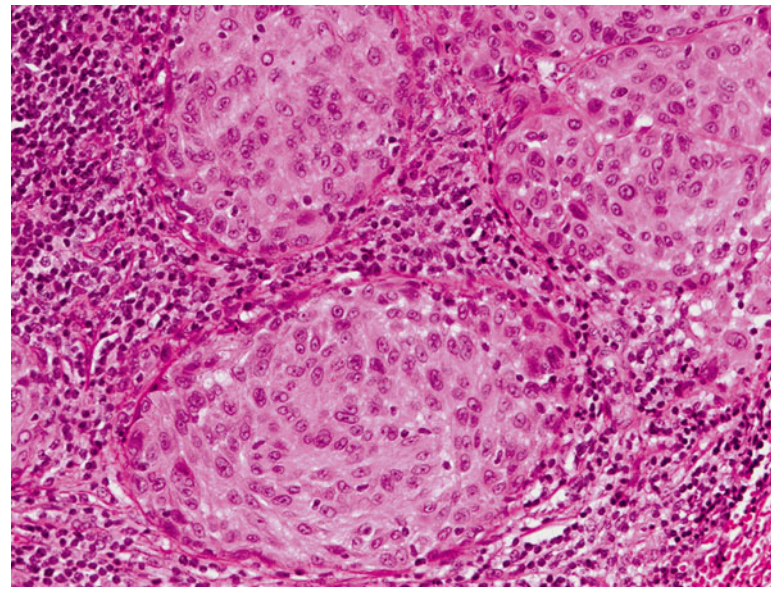


Fig. 8.45 The melanocytes resemble the Spitz nevus cells in that they exhibit ample eosinophilic cytoplasm

Case 8K

Clinical History A 72-year-old male with a lesion on his scalp

Microscopic Description In chronically damaged scalp skin, there is a characteristic cellular blue nevus composed of ordinary blue nevus alternating with classic cellular blue nevus (Fig. 8.46a–c). The latter areas are large nodules composed of small cells with clear cytoplasm (Fig. 8.47a, b). As seen in typical cellular blue nevus there are small nests of these cells in these nodules. As one observes the mid dermis, one sees a rather abrupt change in the cell characteristic (Fig. 8.48a). Extending downward from mid dermis, there are nests and sheets of cells now assuming spindle morphology with cells with epithelioid characteristic (Fig. 8.48a–d). One observes a transition from characteristic blue nevus to cellular blue nevus to a nodule of melanoma. The nodule of melanoma in the deep dermis is comprised of severely atypical neoplastic cells with prominent nucleoli. The remainder of the lesion is a malignant melanoma with large zone of necrosis extending to the deep aspect of the specimen and the subcutaneous tissue (Fig. 8.49). The lesion is present at the margin.

Diagnosis Malignant blue nevus, invasive to level IV, and a measured thickness of 16 mm or 1.6 cm, arising in cellular blue nevus

Comment Allen and Spitz were the first to propose the term malignant blue nevus (1953). Malignant blue nevi often present as blue or blue-black nodules on the scalp (Connelly and Smith 1991; Ozgur et al. 1997; Mehregan et al. 1992). They are considered by many to be highly aggressive with a metastatic rate of 82 % (Connelly and Smith 1991). Rare case of malignant blue nevus has been documented in the vulva and in children (Spatz et al. 1998; Aloi et al. 1996). There have been rare reports of melanoma arising in association with nevus of Ota and nevus of Ito (Connelly and Smith 1991). This lesion is a classic example of malignant blue nevus arising in a setting of a cellular blue nevus (Granter et al. 2001a; Connelly and Smith 1991). In our experience this is the most common example of malignant transformation in a setting of cellular blue nevus. In this case, one can observe unquestionable transformation from the cellular blue nevus to malignant melanoma. We have also seen on one occasion transformation in an ordinary blue nevus to a malignant blue nevus. One other characteristic of malignant blue nevus is multifocal and deep infiltration into deep subcutaneous fat but not as multifocal tongues. Another characteristic is true tumor necrosis not a degenerative or liquefactive change one commonly seen in cellular blue nevus especially on the scalp and buttock. In the latter process, one will find lacunae with aggregates of clear cells free in the lacuna cavity. This change we believe is due to the pressure inducing mild ischemia in contrast to the marked ischemia seen in tumor necrosis.

Key Histologic Features

Malignant blue nevus arising in cellular blue nevus (Figs. 8.46, 8.47, 8.48, and 8.49)

- Cellular blue nevus composed of large nodules of small cells with clear cytoplasm.
- Nests and sheets of cells now assuming spindle morphology with cells with epithelioid characteristic.
- A transition from characteristic blue nevus to cellular nevus to a nodule of melanoma.
- The nodule of melanoma in the deep dermis is comprised of severely atypical neoplastic cells with prominent nucleoli.

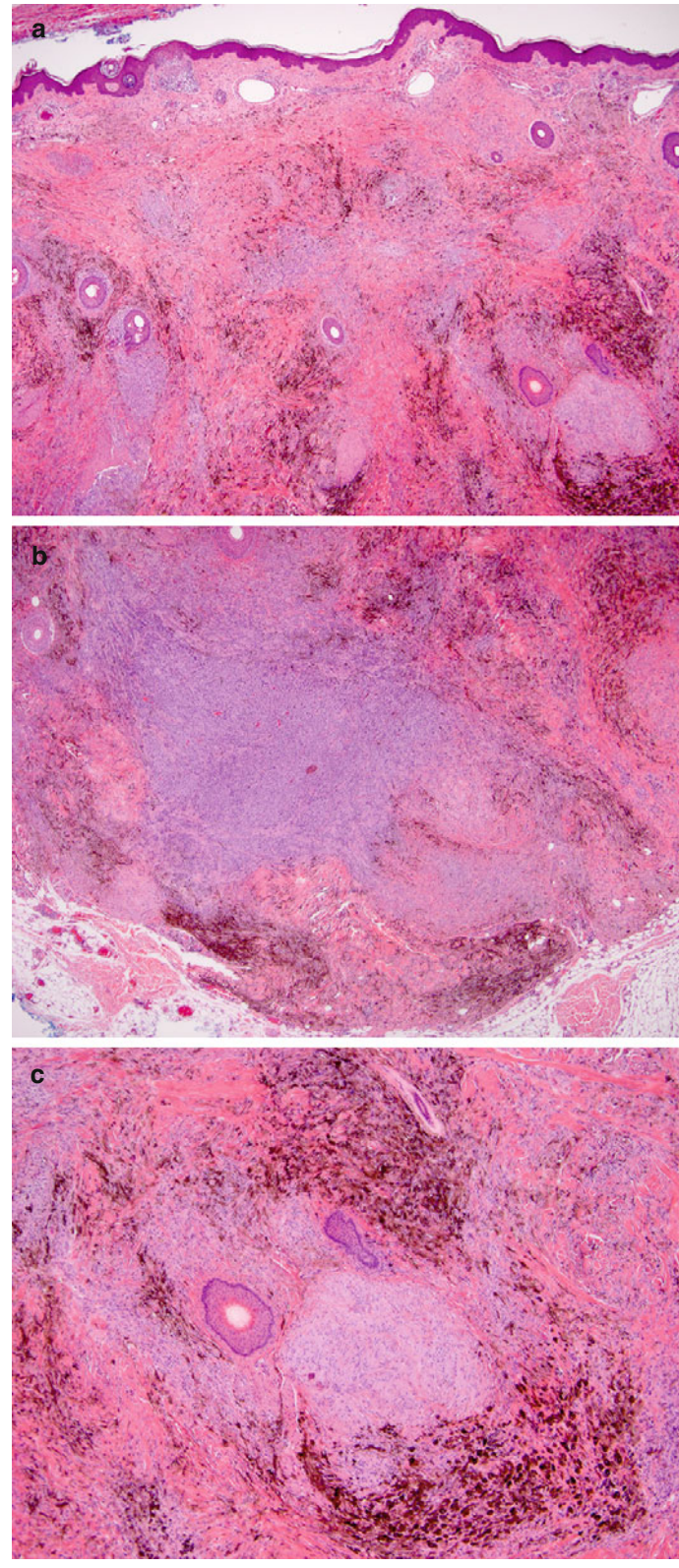


Fig. 8.46 (**a**–**c**) A proliferation composed of areas of ordinary blue nevus alternating with those of classic cellular blue nevus

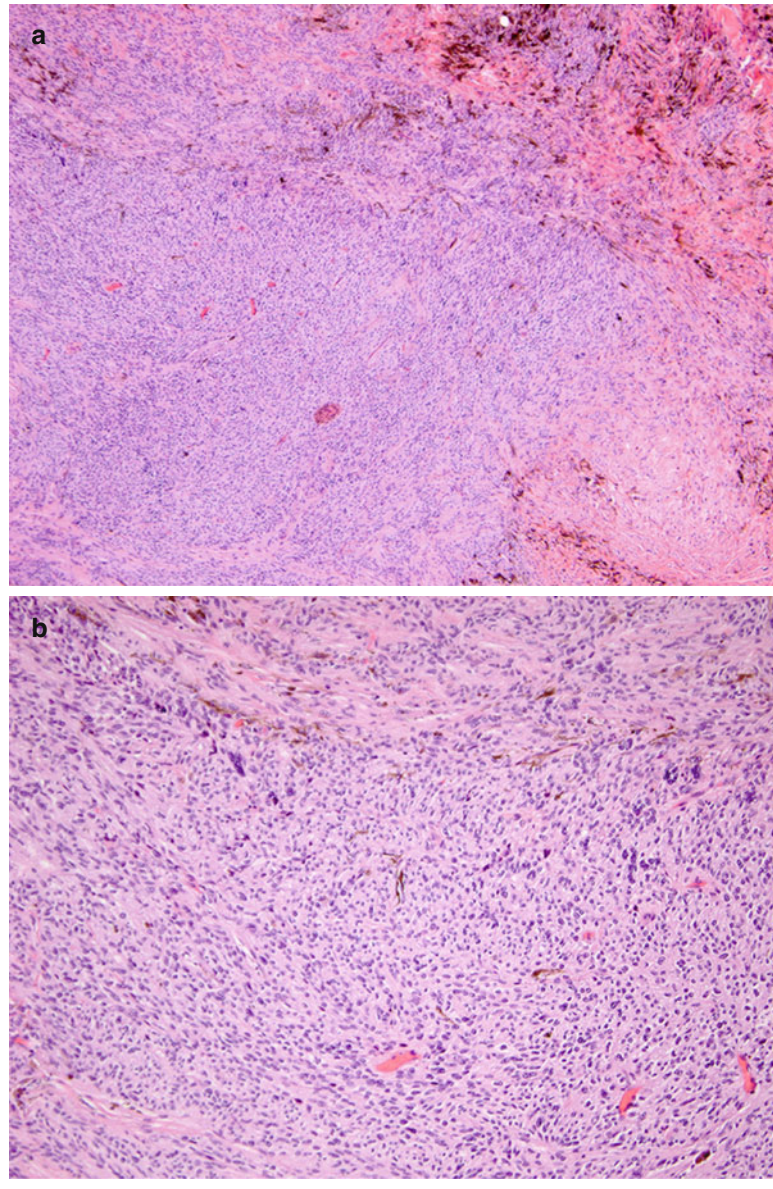


Fig. 8.47 (**a**, **b**) The large nodules are composed of small cells with clear cytoplasm

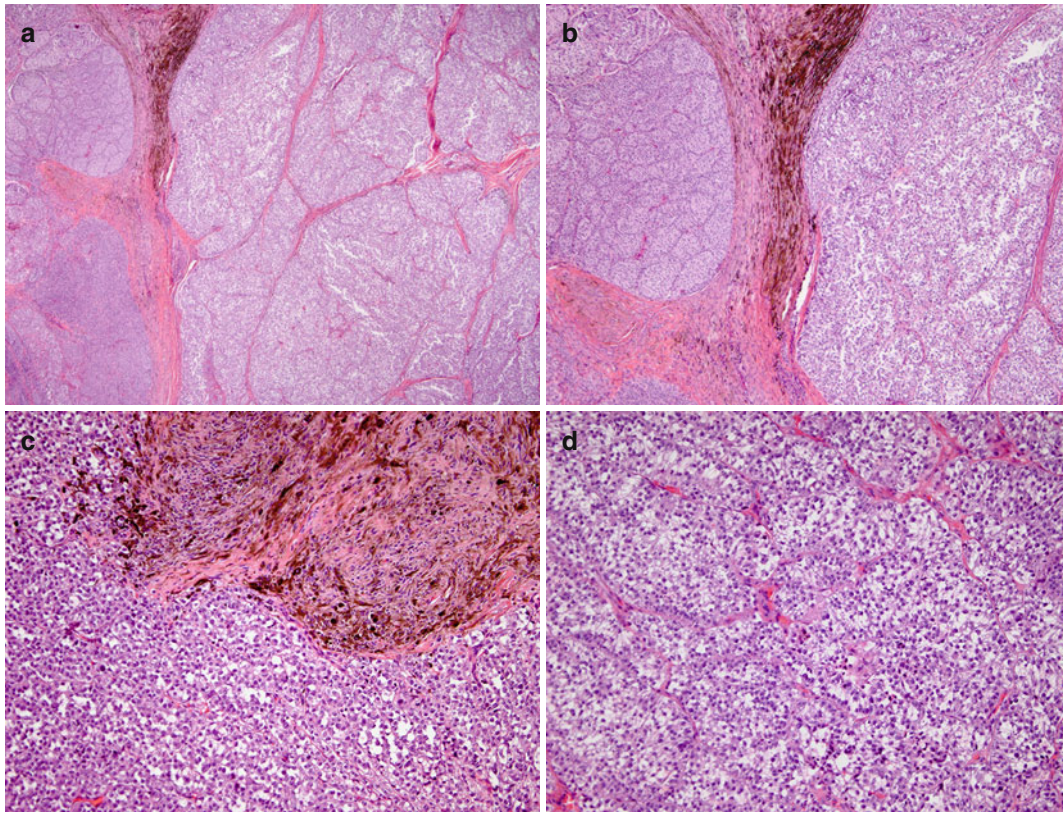


Fig. 8.48 (**a**–**d**) At the base of the lesion, nests and sheets of atypical melanocytes now assuming spindle morphology and some with epithelioid characteristic are seen

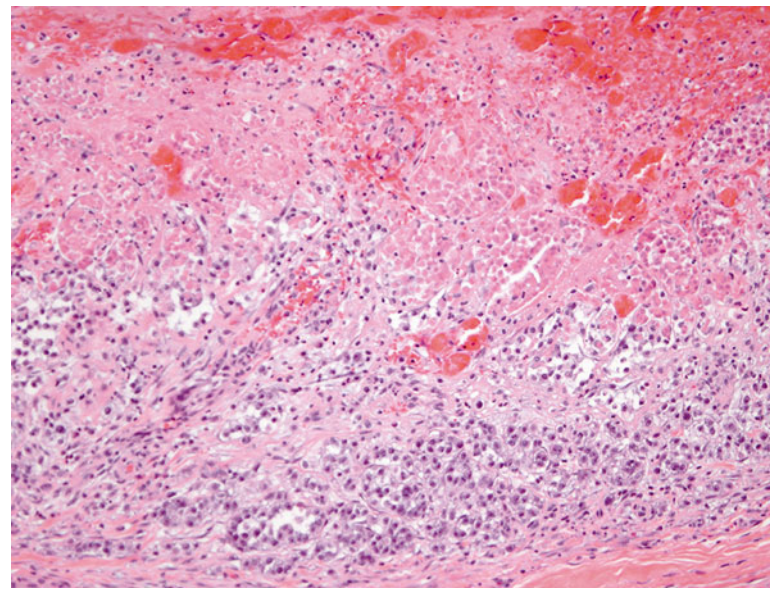


Fig. 8.49 Large zone of necrosis is seen extending to the deep aspect of the specimen and the subcutaneous tissue

Case 8L

Clinical History A 57-year-old male with a lesion on his right anterior chest wall

Microscopic Description A tumor nodule composed of very prominent cells with nevus-like appearance is completely surrounded by a heavily pigmented melanocytic proliferation (Figs. 8.50a, b and 8.51a). The cells within these nodules have high nuclear to cytoplasmic ratio (Fig. 8.51b). They are associated with prominent nucleoli and a rather coarsely scattered chromatin. Some cells show evidence of pigmentation in their cytoplasm (Fig. 8.51b). The great majority shows little pigmentation. The large nodule appears to be infiltrated by vascular spaces and in some areas there appear to be vascular mimicry (Fig. 8.52). However, other areas appear to be lined by true endothelial cells. Despite the prominent vascularity, there appears to be no evidence of vascular invasion. One other important aspect is that there are foci of differentiation in the tumor that resulted in whorl of tumor zones suggestive of Schwannian-type changes. This entire huge nodule is surrounded by heavily pigmented cells that alternate with spindle cell proliferation that has minimal pigmentation (Fig. 8.53a, b). In addition, there are small nidi of epithelioid cells that suggest possible Schwannian differentiation. The pigmented cells are both epithelioid and spindle-shaped forms and are associated with prominent peri-appendageal location. There are also present small oval islands of tumors scattered throughout the subcutaneous fat.

Diagnosis Severely atypical proliferative nodule consistent with borderline malignant melanoma, arising in a neurocristic hamartoma

Comment This lesion represents an interesting example of borderline melanocytic tumor that arises in a setting of a hamartomatous melanocytic proliferation, specifically neurocristic hamartoma (Pearson et al. 1996; Denlinger et al. 2007). Neurocristic hamartoma is characteristically associated with a proclivity to surround dermal appendages especially hair follicles. In addition, there are multiple islands of proliferative tumor scattered throughout the subcutaneous fat. Clinically, these lesions are bluish plaque. In this instance, the plaque extends from the neck to the pelvic area. The tumor is composed of small epithelioid cells that are not pigmented in many areas. In other areas, there is fine pigmentation within the cells and the cells are associated with nodules of spindle cells and at times epithelioid cells that contrast strikingly with the nonpigmented cuboidal cells. There are rare mitoses in the lesion. In this particular case a re-excision was performed and the patient was carefully followed.

Key Histologic Features

Severely atypical proliferative nodule consistent with borderline malignant melanoma, arising in a neurocristic hamartoma (Figs. 8.50, 8.51, 8.52, and 8.53)

- In the midst of a heavily pigmented melanocytic proliferation is a tumor nodule composed of very prominent cells with nevus-like appearance.
- These cells have large nuclear to cytoplasmic ratio, prominent nucleoli, and focal cytoplasmic pigmentation.

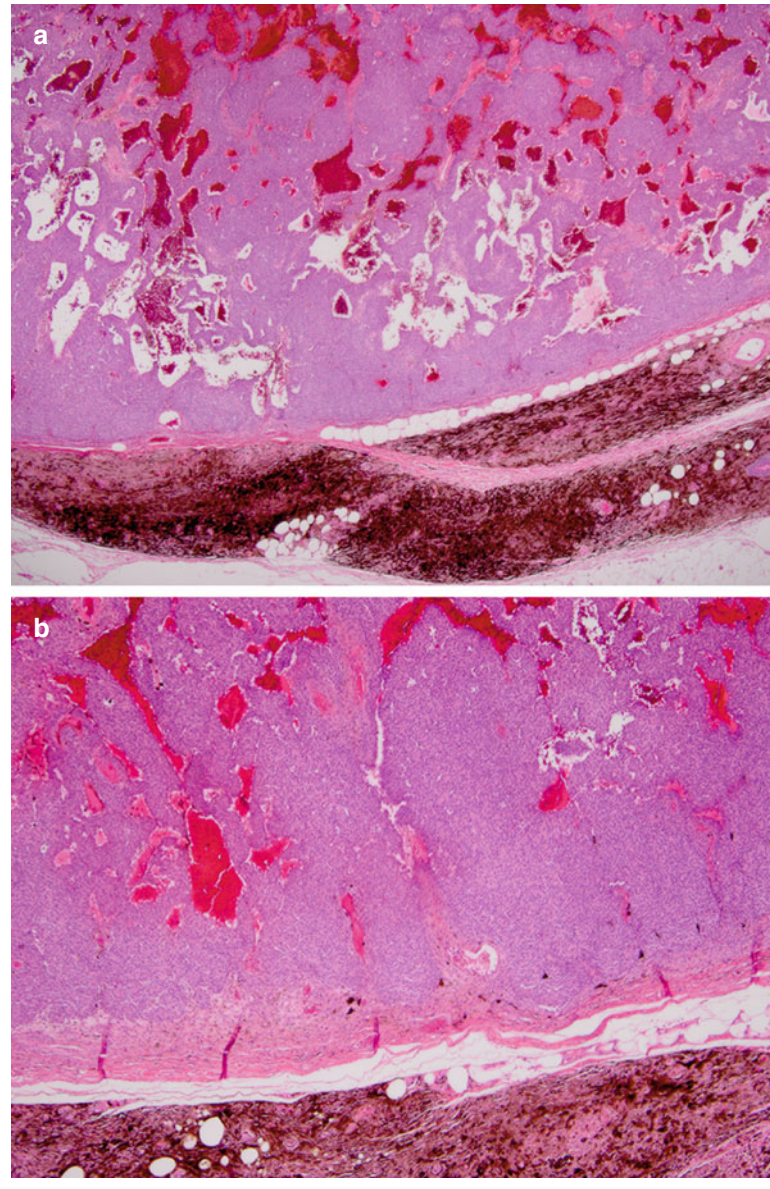


Fig. 8.50 (**a**, **b**) A tumor nodule composed of uniform cells with nevus-like appearance is completely surrounded by heavily pigmented melanocytes

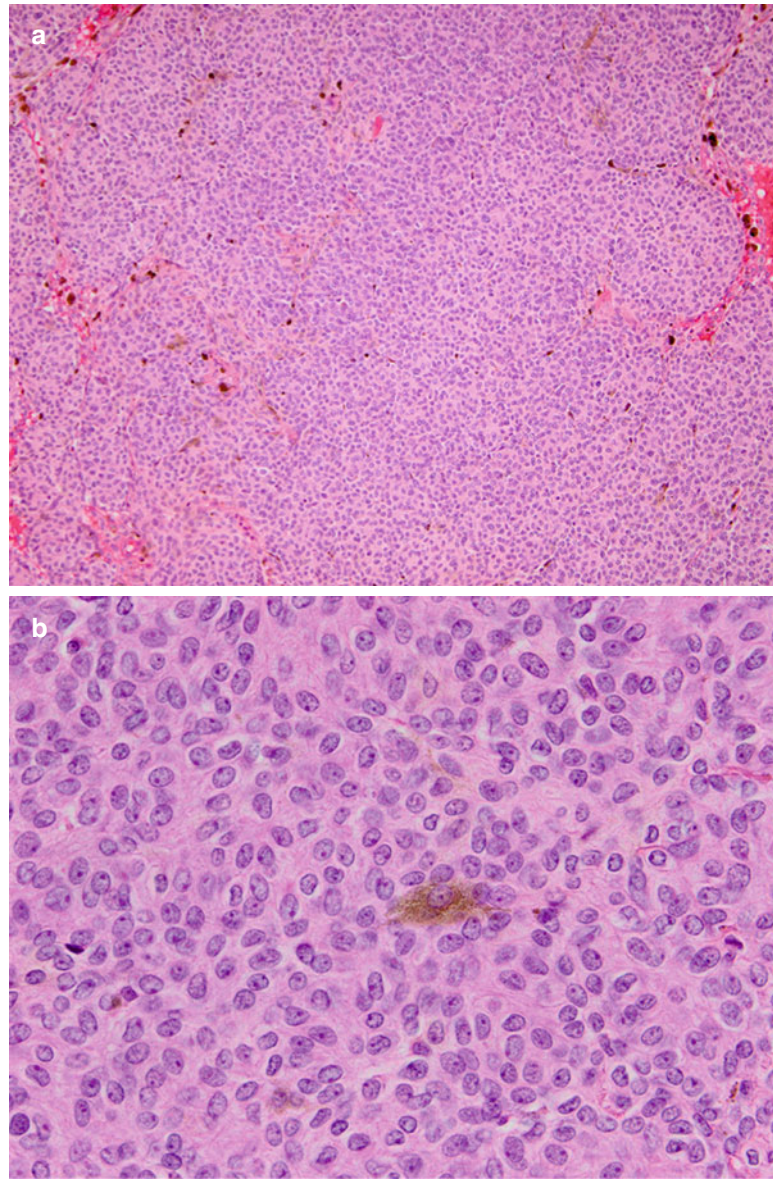


Fig. 8.51 (**a**, **b**) The cells within the nodule have prominent nucleoli, coarsely scattered chromatin, and focal cytoplasmic pigmentation

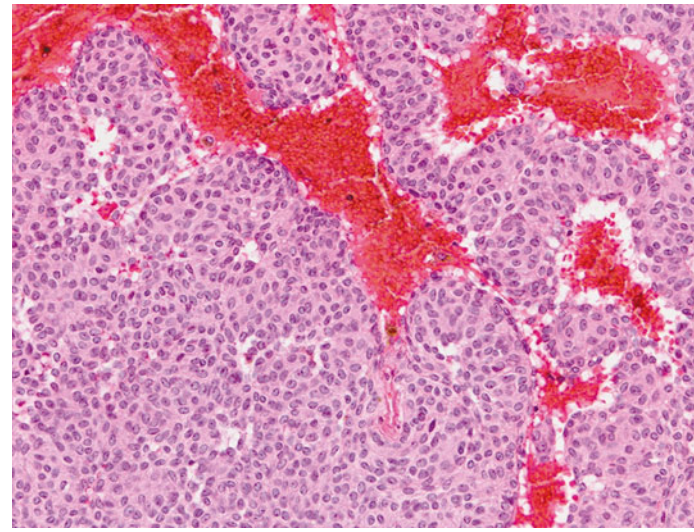


Fig. 8.52 Irregular vascular spaces are seen within the nodule

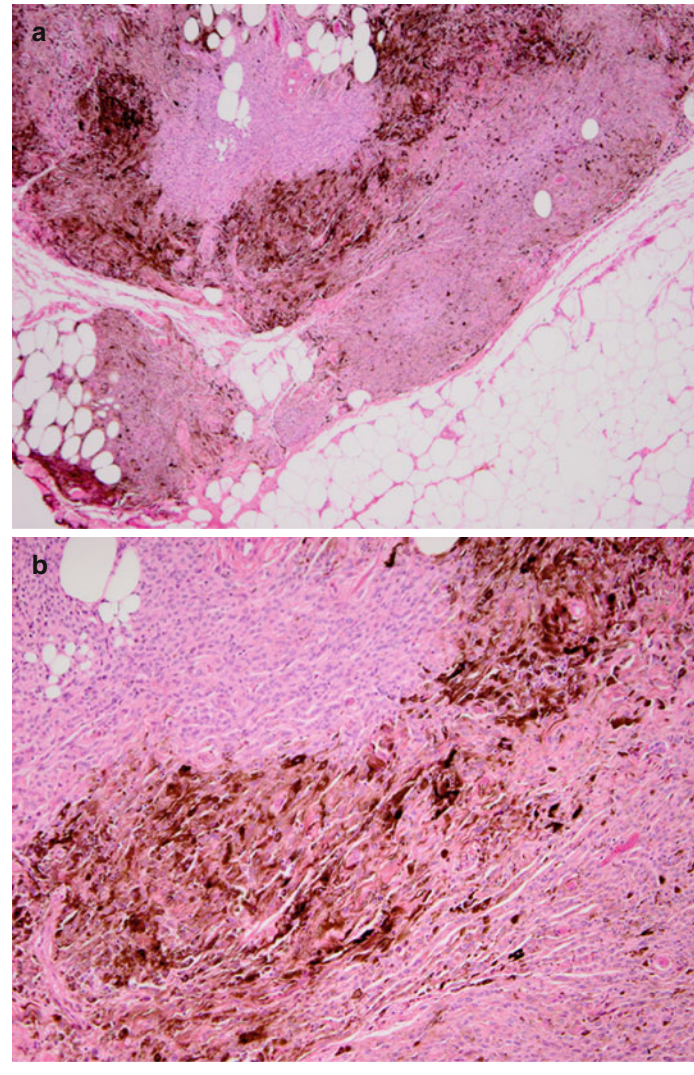


Fig. 8.53 (**a**, **b**) Heavily pigmented cells that alternate with nonpigmented spindle cells are seen surrounding the nodule

Case 8M

Clinical History A 32-year-old male with a scalp lesion

Microscopic Description In the deeper portion of scalp skin there is a folliculocentric proliferation of pigmented dendritic cells that are more striking in the aponeurotic galea in which one finds characteristic dendritic blue nevus cells but also complex neurotization with organoid structures (Fig. 8.54a–d). Some of these latter areas resemble Schwannian differentiation (Fig. 8.55). For example, there are areas of pigmented cells that resemble Antony A and B areas seen in schwannoma. In the deep portion there are clear cells that resemble blue nevus cells admixed with the peculiar characteristics (Fig. 8.56a, b). These cells give rise to the more hyperchromatic cells and result in a mixed epithelioid and spindle malignant melanoma (Figs. 8.57a, b and 8.58). The lesion is present at margins.

Diagnosis Malignant melanoma arising in a neurocristic hamartoma, present at the margin

Comment This lesion exhibits features of neurocristic hamartoma. These include the presence of folliculotropic distribution of dendritic cells that extend into the fascia. How this lesion differed from the blue nevus is based on the areas with Schwannian differentiation. In this particular case there are structures resembling Antony A area in addition to the peculiar neurotization. There is a progressive transformation of the cells into heavily pigmented atypical cells with hyperchromatic nuclei that give rise to fully evolved malignant melanoma. In our experience, one can observe proliferative nodule, borderline nodule, and as in this case malignant melanoma in the setting of neurocristic hamartoma (Linskey et al. 2011). These lesions are treated with wide excision and sentinel lymph node biopsy.

Key Histologic Features

Malignant melanoma arising in a neurocristic hamartoma (Figs. 8.54, 8.55, 8.56, 8.57, and 8.58).

- Background neurocristic hamartoma is characterized by proliferation of folliculocentric pigmented dendritic cells that are more striking in the aponeurotic galea.
- In the deep portion there are clear cells that resemble blue nevus cells.
- A mixed epithelioid and spindle malignant melanoma.

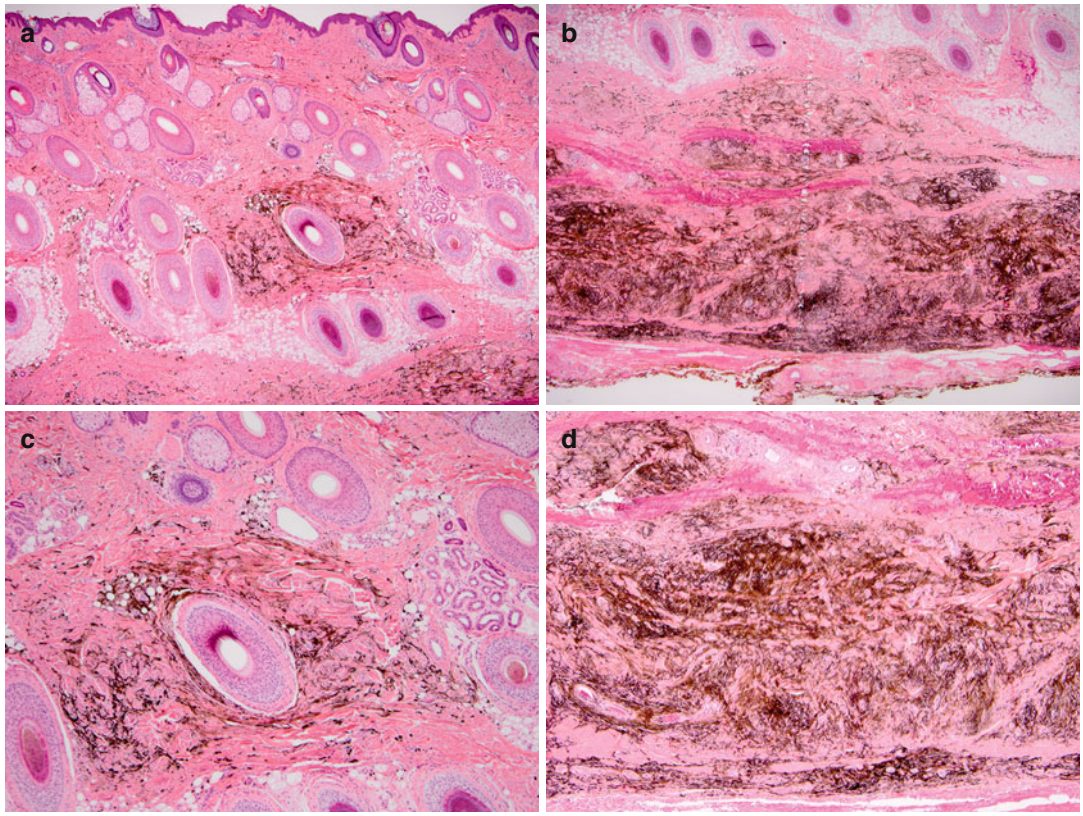


Fig. 8.54 (**a**–**d**) A proliferation of dendritic blue nevus cells with neurotization is seen in the dermis extending to the subcutaneous fat and fascia

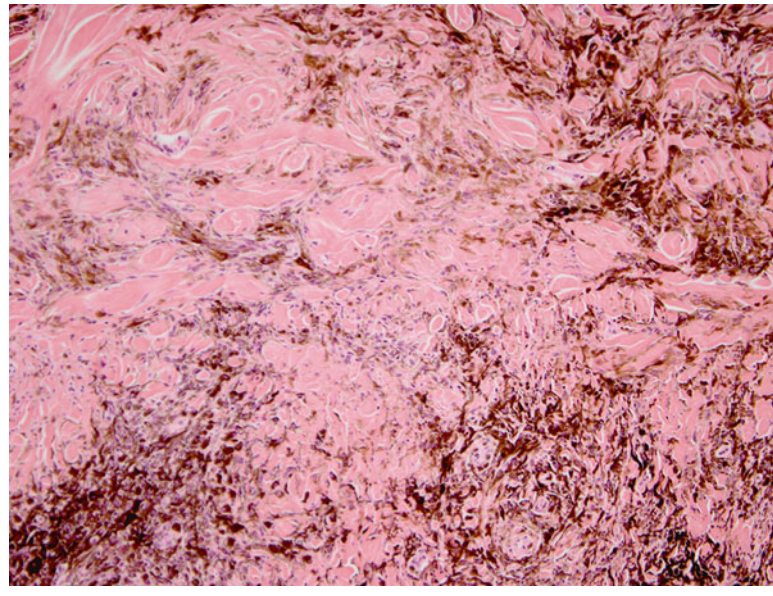


Fig. 8.55 In areas the tumor cells exhibit Schwannian differentiation

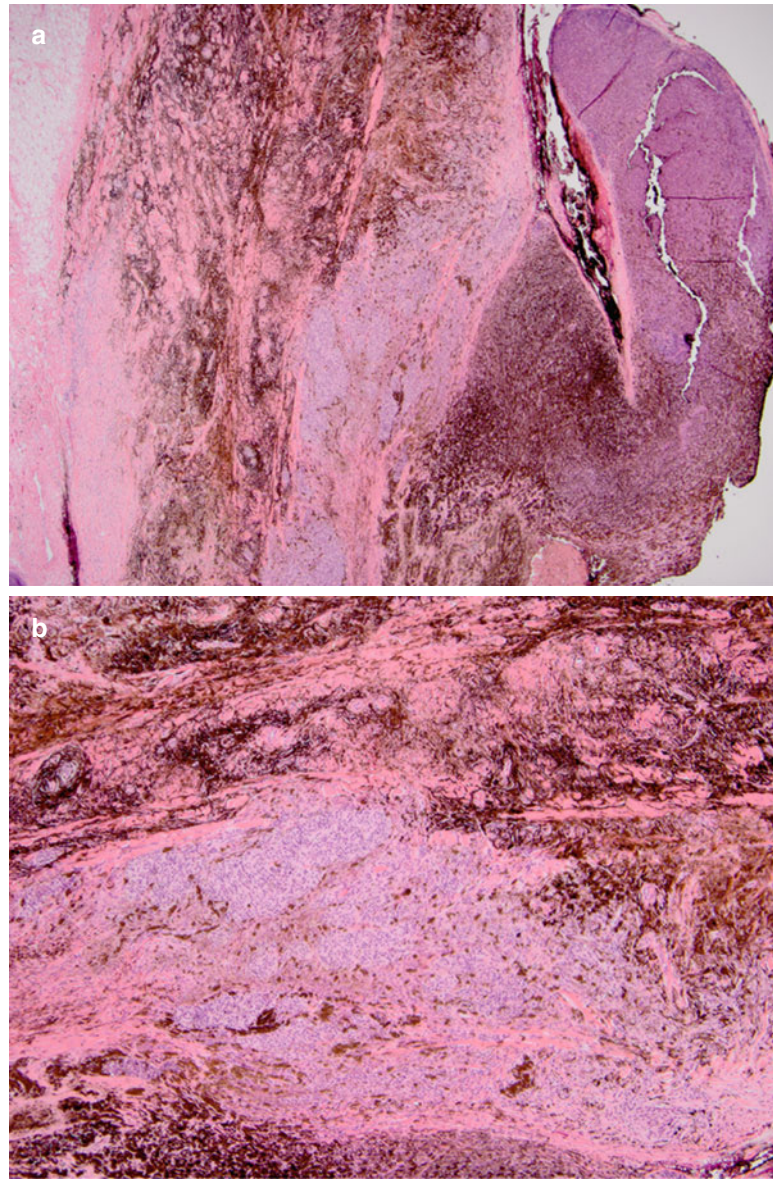
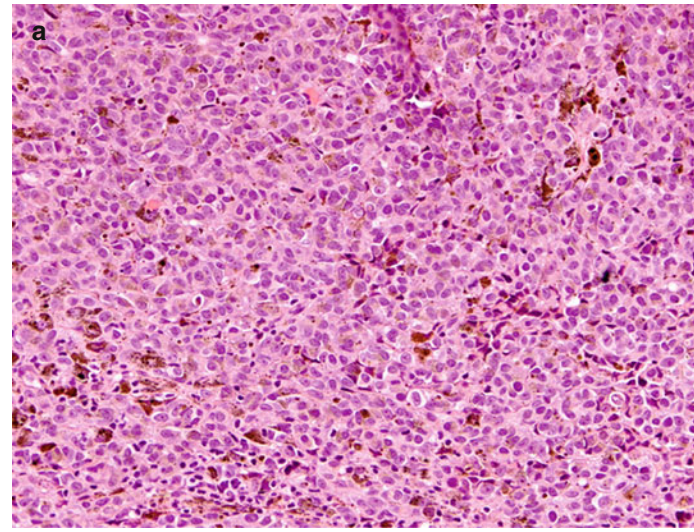


Fig. 8.56 (**a**, **b**) In the deep portion there are clear cells that resemble blue nevus cells



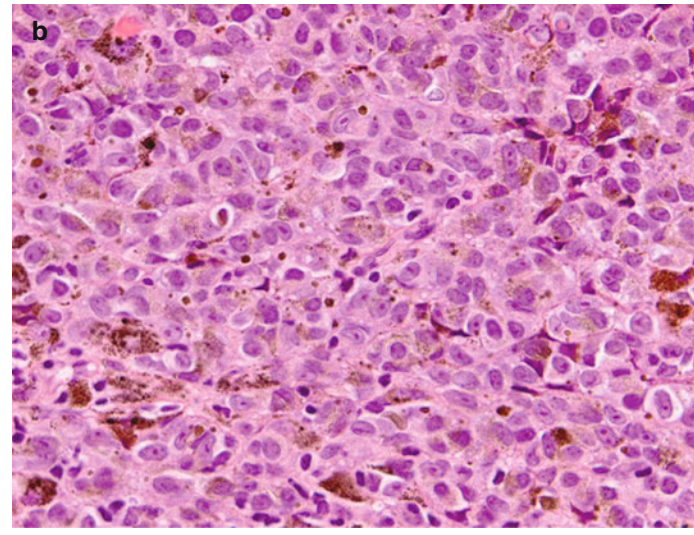


Fig. 8.57 (**a**, **b**) A proliferation of epithelioid atypical cells with prominent nucleoli is seen

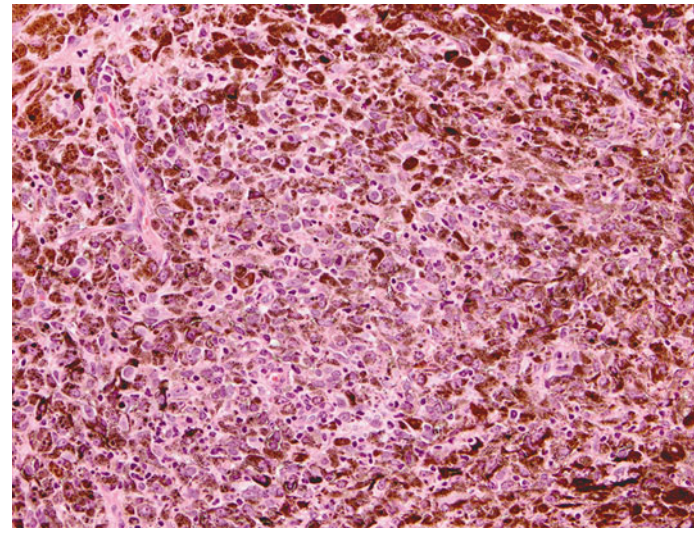


Fig. 8.58 In areas, the tumor cells are heavily pigmented

Case 8N

Clinical History A 91-year-old female with a lesion on the first toe of her left foot

Microscopic Description This case exhibits an ulceration that is greater than 6 mm in width associated with radial and vertical growth phases of spindle cells and desmoplastic response (Figs. 8.59, 8.60, and 8.61a, b). The lesion is composed of spindle cells with marked fibrosis and perineural and perivascular invasion (Figs. 8.62 and 8.63). There are two mitoses per squared millimeter. There is no evidence of regression. Microscopic satellites cannot be evaluated due to the superficial nature of the biopsy. The radial growth phase is associated with a prominent proliferation of atypical melanocytes at the dermal-epidermal junction with foci of pagetoid spread (Fig. 8.64). There are foci in which the tumor extends from the dermal-epidermal junction to the stratum corneum (Fig. 8.64). There are numerous mitoses in the radial growth phase (Fig. 8.65). The tumor is present at the margin.

Diagnosis Acral lentiginous malignant melanoma, invasive to at least level IV, and Breslow depth of 4.45 mm with desmoplastic response and ulceration

Comment Acral melanoma is the most frequent form of melanoma among Asians, Africans, and other dark-skinned individuals (Krementz et al. 1982). Acral melanomas may involve glabrous skin and the nail apparatus of the hand and feet. The distributions of acral melanoma are as follows: 68–71 %, soles; 11 %, toes; 9–10 %, subungual area of the feet; 4–10 %, palms; 2 %, fingers; and 6–10 %, subungual areas of the hands (Krementz et al. 1982).

Acral lentiginous melanoma exhibits a striking proliferation of variably atypical to fully malignant melanocytes along the dermal-epidermal junction with prominent large nuclear to cytoplasmic ratio (Arrington et al. 1977; Phan et al. 2007). The lesion is associated with epidermal hyperplasia in most instances, and there is often rather extensive pagetoid spread where there is full invasion of the dermis by the tumor. This particular lesion exhibits the classics pattern associated with prominent pagetoid spread. In accordance with the clinical picture, malignant melanocytes intraepidermally tend to affect the areas of the acrosyringium as well as the other area ascribable to the valley in the skin. Appendageal involvement often accounts for frequent recurrence. The dermal component in this case shows superficial invasion by spindle melanocytes that quite abruptly transformed to highly atypical nuclei with desmoplastic response. Desmoplastic melanoma as we have stated previously often arises in lesion with lentiginous radial growth phase as seen in this case. In almost all desmoplastic melanomas, one must carefully searched for perineural and vascular invasion which is present in this case. Dermal mitoses in these lesions are few in number as seen in this case. Mitoses are difficult to find in desmoplastic melanoma but do occur. Treatment for this case is re-excision and careful examination for any residual melanoma within the vascular or neurovascular bundles. In this particular case, there is no preexisting precursor lesion.

Key Histologic Features

Acral lentiginous malignant melanoma with desmoplastic response (Figs. 8.59, 8.60, 8.61, 8.62, 8.63, 8.64, and 8.65)

- A characteristic acral lentiginous radial growth with vertical growth phases of spindle cells and desmoplastic response.
- The lesion is composed of spindle cells with marked fibrosis and perineural and perivascular invasion.

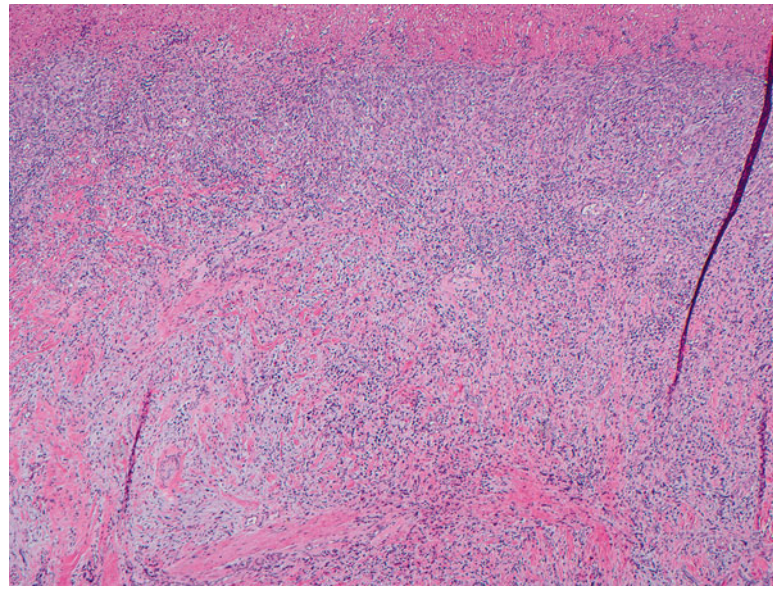


Fig. 8.59 A tumor with extensive ulceration is noted

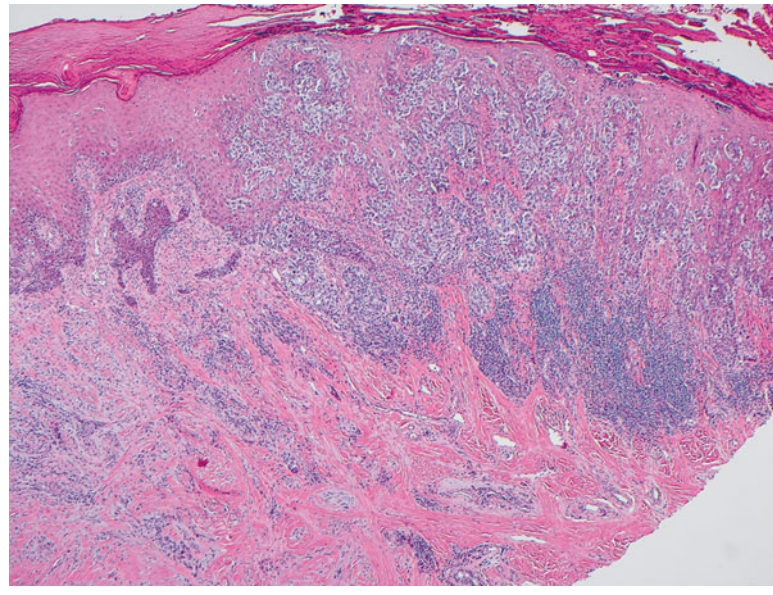


Fig. 8.60 Proliferation of atypical melanocytes exhibiting prominent pagetoid spread is seen within the epidermis

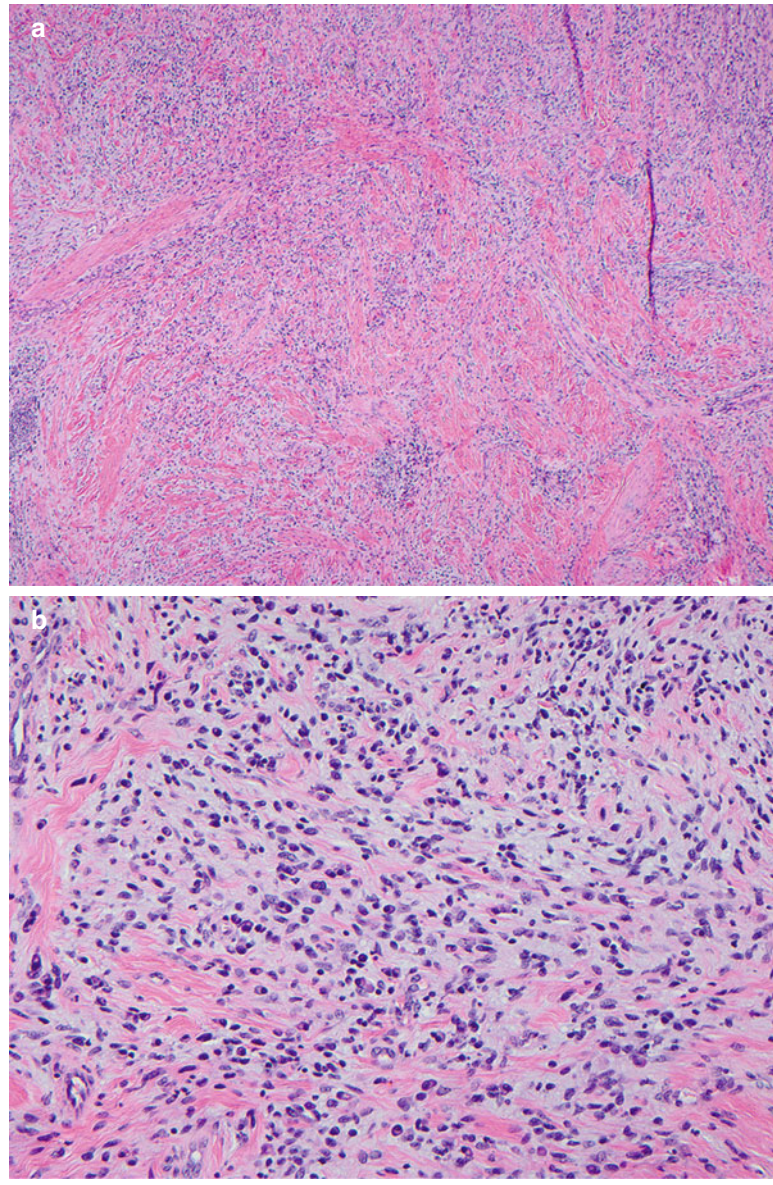


Fig. 8.61 (**a**, **b**) A vertical growth phase composed of spindle cells and desmoplastic response is seen in the dermis

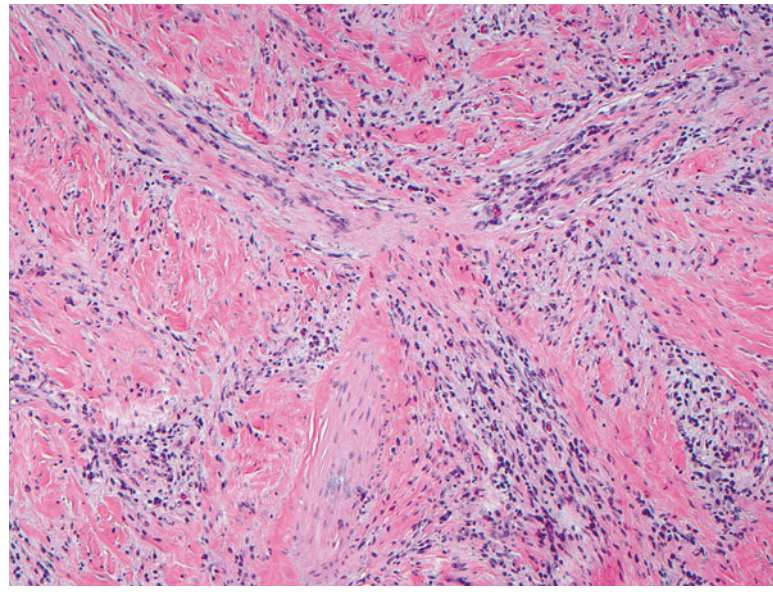


Fig. 8.62 The spindle tumor cells are associated with marked fibrosis

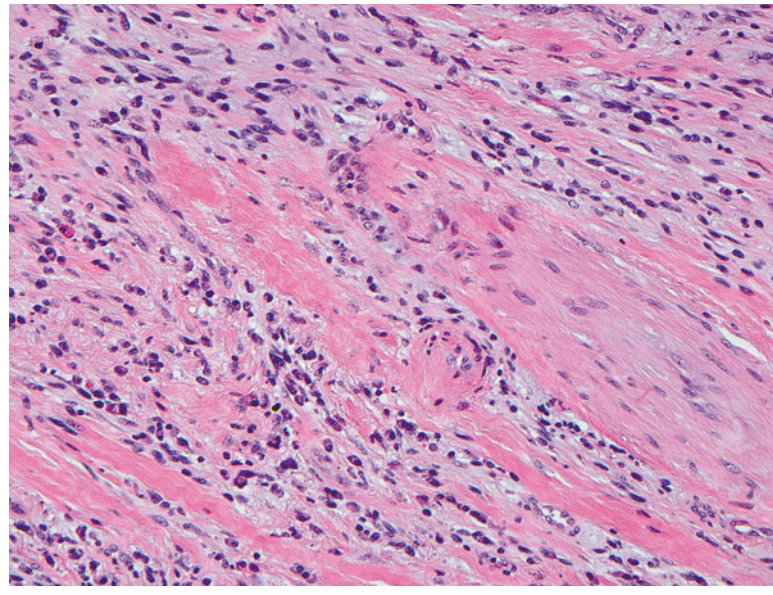


Fig. 8.63 Perineural invasion is noted

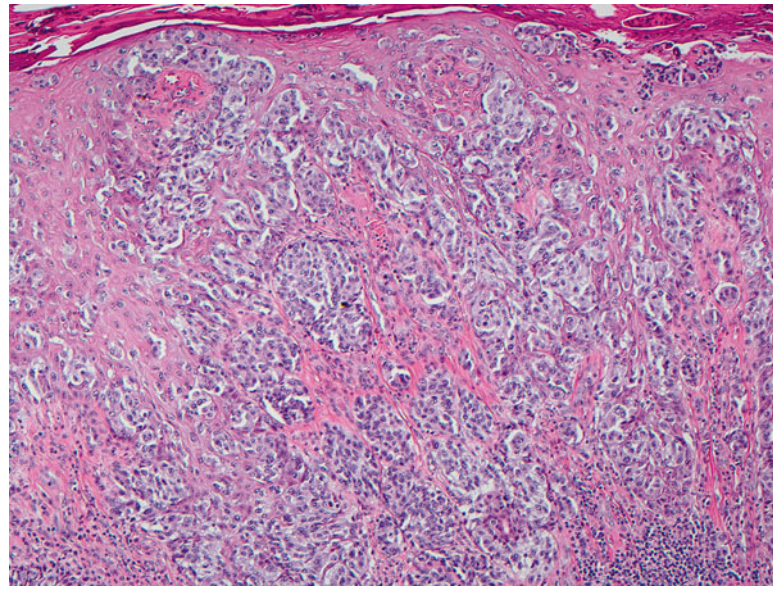


Fig. 8.64 The intraepidermal component is comprised of atypical epithelioid melanocytes with foci of pagetoid spread

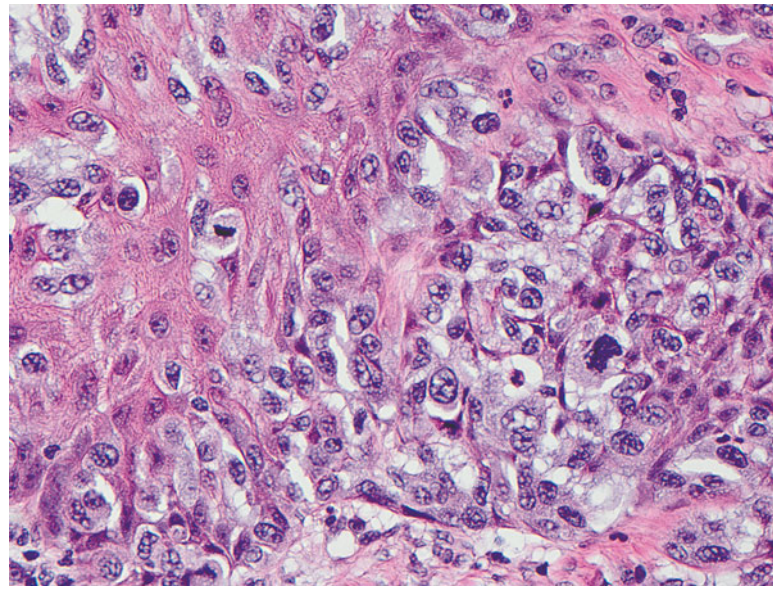


Fig. 8.65 Numerous mitoses are readily identified

Case 80

Clinical History A 52-year-old male with a right shoulder lesion

Microscopic Description A malignant melanoma, superficial spreading type, focally invasive to Clark level III, has a pigmented epithelioid radial growth phase with pagetoid spread (Figs. 8.66 and 8.67a, b). The invasive component is formed by expansile nodule that widens the papillary dermis (Fig. 8.68). There is a non-brisk host response. There are no mitoses or evidence of ulceration or regression. Adjacent to the melanoma there is quite striking junctional dysplastic nevus with prominent nests, many of which exhibit fusion of the rete ridges (Fig. 8.69). There is dense eosinophilic fibrosis around the rete ridges (Fig. 8.70). The nests of the dysplastic nevus reach a very large magnitude with one large nest fusing rete ridges. Relatively abruptly there is a pigmented epithelioid cell proliferation that marks the onset of the malignant melanoma component. This transition occurs over a few rete ridges.

Diagnosis Malignant melanoma, invasive, Clark level III, and depth of 0.50 mm arising in a preexisting dysplastic nevus

Comment This very striking case exhibits a dysplastic nevus that focally transform into a malignant melanoma. There is a marked difference between the nevus cells and the melanoma. The nevus cells have little pigment in contrast to the melanoma cells with marked cytoplasmic pigment. The vertical growth phase is composed of epithelioid cells with no mitotic figures. Re-excision with 1–1.5 cm is recommended.

Because tumor thickness is the most important prognostic factor, it is important to accurately determine the extent of dermal involvement by melanoma cells. The coexistence of nevi and melanomas is often seen in superficial spreading melanomas (Sagebiel 1993). The associated nevi can be dysplastic nevi (5–56 %), congenital nevi (3–38 %), junctional nevi, compound nevi, or dermal nevi (Sagebiel 1993; Kaddu et al. 2002; Smolle et al. 1999). Study has suggested that the benign dermal nests might be the precursor lesion (Dadzie et al. 2009).

Key Histologic Features

Malignant melanoma arising in a preexisting dysplastic nevus (Figs. 8.66, 8.67, 8.68, 8.69, and 8.70)

- A malignant melanoma, superficial spreading type, with a pigmented epithelioid radial growth phase.
- Adjacent to the melanoma there is a junctional dysplastic nevus with prominent nests, fusion of the rete ridges, and dense eosinophilic fibrosis.

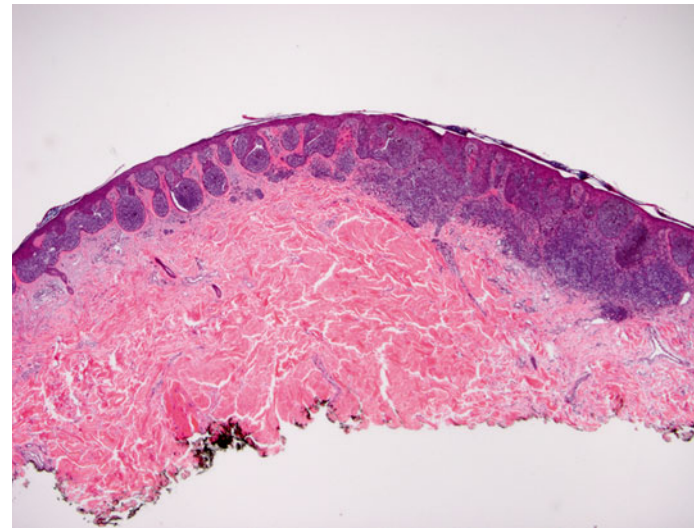
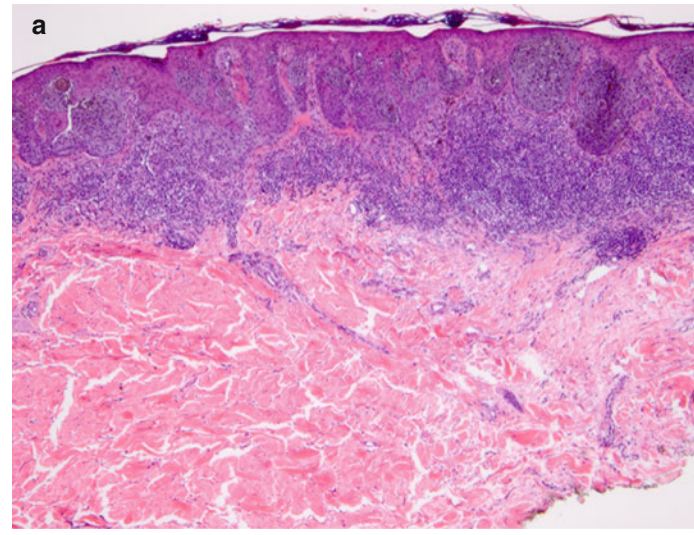


Fig. 8.66 An asymmetrical and compound melanocytic proliferation is noted



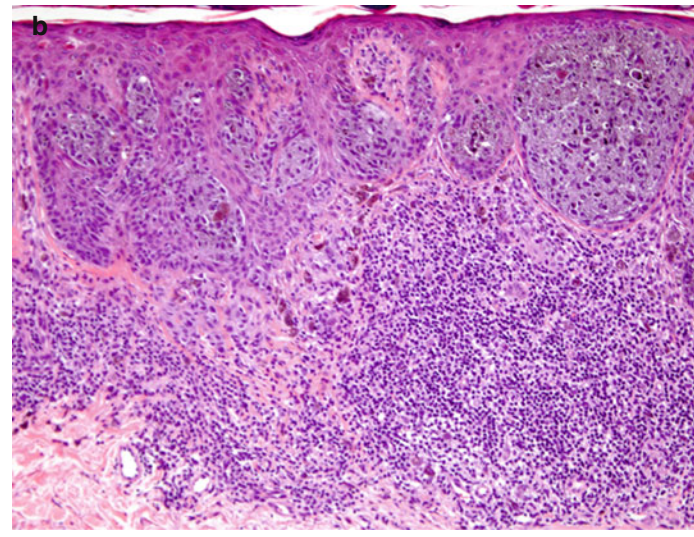


Fig. 8.67 (**a**, **b**) The intraepidermal component is comprised of pigmented epithelioid atypical melanocytes

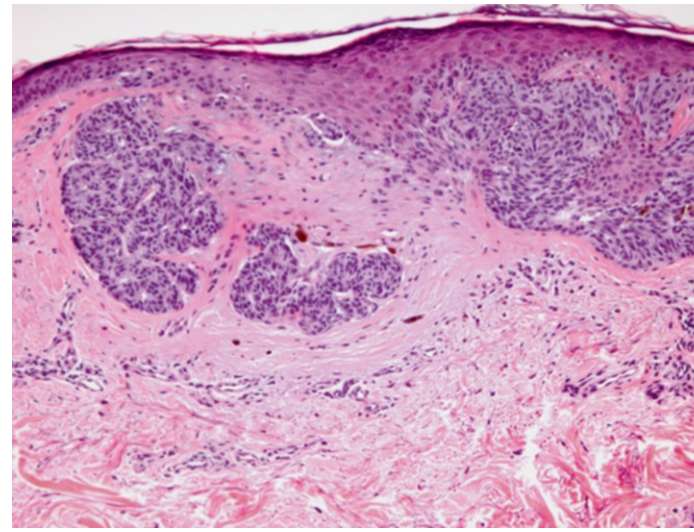


Fig. 8.68 The invasive component is formed by expansile nodule that widens the papillary dermis

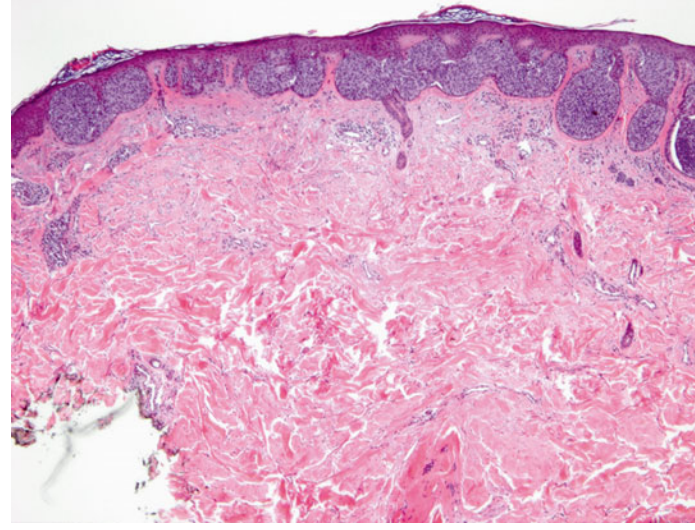


Fig. 8.69 To the edge of the lesion, a junctional dysplastic nevus with prominent nests and fusion of the rete ridges is seen

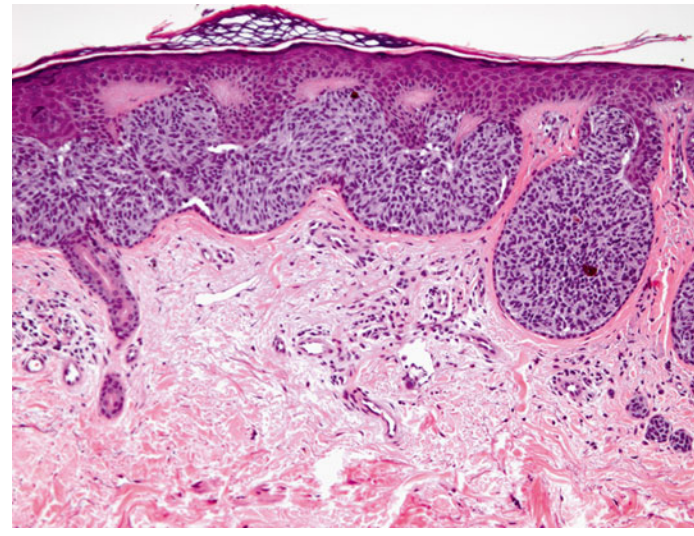


Fig. 8.70 Dense eosinophilic fibrosis is seen around the rete ridges

References

Allen AC, Spitz S. Malignant melanoma. A clinicopathological analysis of the criteria for diagnosis and prognosis. Cancer. 1953;6(1):1–45.

Aloi F, Pich A, Pippione M. Malignant cellular blue nevus: a clinicopathological study of 6 cases. Dermatology. 1996;192(1):36–40.

Arrington 3rd JH, Reed RJ, Ichinose H, Krementz ET. Plantar lentiginous melanoma: a distinctive variant of human cutaneous malignant melanoma. Am J Surg Pathol. 1977;1(2):131–43.

Baer SC, Schultz D, Synnestvedt M, Elder DE. Desmoplasia and neurotropism: prognostic variables in patients with stage I melanoma. Cancer. 1995;76(11): 2242–7.

Blessing K, Evans AT, al-Nafussi A. Verrucous nevoid and keratotic malignant melanoma: a clinico-pathological study of 20 cases. Histopathology. 1993;23(5): 453–8.

Bruijn JA, Mihm Jr MC, Barnhill RL. Desmoplastic melanoma. Histopathology. 1992;20(3):197–205.

Busam KJ, Mujumdar U, Hummer AJ, Nobrega J, Hawkins WG, Coit DG, et al. Cutaneous desmoplastic melanoma: reappraisal of morphologic heterogeneity and prognostic factors. Am J Surg Pathol. 2004;28(11): 1518–25.

Carlson JA, Dickerson GR, Sober AJ, Barnhill RL. Desmoplastic neurotropic malignant melanoma: a clinicopathologic analysis of 28 cases. Cancer. 1995; 75(2):478–94.

Conley J, Lattes R, Orr W. Desmoplastic malignant melanoma (a rare variant of spindle cell melanoma). Cancer. 1971;28(4):914–36.

Connelly J, Smith Jr JL. Malignant blue nevus. Cancer. 1991;67(10):2653–7.

Dadzie OE, Yang S, Emley A, Keady M, Bhawan J, Mahalingam M. RAS and RAF mutations in banal melancytic aggregates contiguous with primary cutaneous melanoma: clues to melanomagenesis. Br J Dermatol. 2009;160(2):368–75.

Denlinger CE, Slingluff Jr CL, Mihm Jr MC, Patterson JW. Extensive neurocristic hamartoma with skeletal muscle involvement. J Cutan Pathol. 2007;34(8):634–9.

Granter SR, McKee PH, Calonje E, Mihm Jr MC, Busam K. Melanoma associated with blue nevus and melanoma mimicking cellular blue nevus. A clinicopathologic study of 10 cases on the spectrum of so-called 'malignant blue nevus'. Am J Surg Pathol. 2001a;25(3):316–23.

Granter SR, Weilbaecher KN, Quigley C, Fletcher CD, Fisher DE. Microphthalmia transcription factor: not a sensitive or specific marker for the diagnosis of desmoplastic melanoma and spindle cell (non-desmoplastic) melanoma. Am J Dermatopathol. 2001b;23(3):185–9.

Gualandri L, Betti R, Crosti C. Clinical features of 36 cases of amelanotic melanomas and considerations about the relationship between histologic subtypes and diagnostic delay. J Eur Acad Dermatol Venereol. 2009;23(3):283–7.

Guiliano AE, Cochran AJ, Morton DL. Melanoma from unknown primary site and amelanotic melanoma. Semin Oncol. 1982;9(4):442–7.

Hitchcock MG, McCalmont TH, White WL. Cutaneous melanoma with myxoid features. Twelve cases with differential diagnosis. Am J Surg Pathol. 1999;23(12): 1506–13.

Jain S, Allen PW. Desmoplastic malignant melanoma and its variants. A study of 45 cases. Am J Surg Pathol. 1989;13(5):358–73.

Kaddu S, Smolle J, Zenahlik P, Hofmann-Wellenhof R, Kerl H. Melanoma with benign melanocytic naevus components: reappraisal of clinicopathological features and prognosis. Melanoma Res. 2002;12(3):271–8.

Kamino H, Tam ST, Alvarez L. Malignant melanoma with pseudocarcinomatous hyperplasia – an entity that can simulate squamous cell carcinoma. A light-microscopic and immunohistochemical study of four cases. Am J Dermatopathol. 1990;12(5):446–51.

Kossard S, Wilkinson B. Small cell (naevoid) melanoma: a clinicopathologic study of 131 cases. Aust J Dermatol. 1997;38 Suppl 1:S54–8.

Kossard S, Dohertly E, Murray E. Neurotropic melanoma. A variant of desmoplastic melanoma. Arch Dermatol. 1987;123(7):907–12.

Krementz ET, Feed RJ, Coleman 3rd WP, Sutherland CM, Carter RD, Campell M. Acral lentiginous melanoma. A clinicopathologic entity. Ann Surg. 1982;195(5): 632–45.

Kuehnl-Petzoldt C, Berger H, Wiebelt H. Verrucous-keratotic variations of malignant melanoma. A clinicopathological study. Am J Dermatopathol. 1982;4(5): 403–10.

Linskey KR, Dias-Santagata D, Nazarian RM, Le LP, Lam Q, et al. Malignant neurocristic hamartoma: a tumor distinct from conventional melanoma and malignant blue nevus. Am J Surg Pathol. 2011;35(10):1570–7.

McNutt NS, Urmacher C, Hakimian J, Hoss DM, Lugo J. Nevoid malignant melanoma: morphologic patterns and immunohistochemical reactivity. J Cutan Pathol. 1995;22(6):502–17.

Mehregan DA, Gibson LE, Mehregan AH. Malignant blue nevus: report of eight cases. J Dermatol Sci. 1992;4(3): 185–92.

Okun MR. Melanoma resembling spindle and epithelioid cell nevus. Arch Dermatol. 1979;115(12):1416–20.

Ozgur F, Akyurek M, Kayikcioglu A, Barista I, Gokoz A. Metastatic malignant blue nevus: a case report. Ann Plast Surg. 1997;39(4):411–5.

Patel P, Levin K, Waltz K, Helm KF. Myxoid melanoma: immunohistochemical studies and a review of the literature. J Am Acad Dermatol. 2002;46(2):264–70.

Pearson JP, Weiss SW, Headington JT. Cutaneous malignant melanotic neurocristic tumors arising in neurocristic hamartomas. Am J Surg Pathol. 1996;20(6):665–77.

Phan A, Touzet S, Dalle S, Ronger-Savle S, Balme B, Thomas L. Acral lentiginous melanoma: histopathological prognostic features of 121 cases. Br J Dermatol. 2007;157(2):311–8.

Posther KE, Selim MA, Mosca PJ, Stanley WE, Johnson JL, Tyler DS, et al. Histopathologic characteristics, recurrence patterns, and survival of 129 patients with desmoplastic melanoma. Ann Surg Oncol. 2006;13(5): 728–39.

Quinn MJ, Crotty KA, Thompson JF, Coates AS, O'Brien CK, McCarthy WH. Desmoplastic and desmoplastic neurotropic melanoma. Cancer. 1998; 83(6):1128–35.

Reed RJ, Leonard DD. Neurotropic melanoma: a variant of desmoplastic melanoma. Am J Surg Pathol. 1979; 3(4):301–11.

Reis-Filho JS, Gasparetto EL, Schmitt FC, Fillus-Neto J. Pseudoepitheliomatous hyperplasia in cutaneous malignant melanoma: a rare and misleading feature. J Cutan Pathol. 2001;28(9):496–7.

Sagebiel RW. Melanocytic nevi in histologic association with primary cutaneous melanoma of superficial spreading and nodular types: effect of tumor thickness. J Invest Dermatol. 1993;100(3):322S–5.

Schmoeckel C, Castro CE, Braun-Falco O. Nevoid malignant melanoma. Arch Dermatol Res. 1985;277(5): 362–9.

Smithers BM, McLeod GR, Little JH. Desmoplastic, neural transforming and neurotropic melanoma: a clinicopathologic analysis of 28 cases. Aust N Z J Surg. 1990;60(12):967–72.

Smolle J, Kaddu S, Kerl H. Non-random spatial association of melanoma and naevi – a morphometric analysis. Melanoma Res. 1999;9(4):407–12.

Spatz A, Zimmermann U, Bachollet B, Pautier P, Michel G, Duvillard P. Malignant blue nevus of the vulva with late ovarian metastasis. Am J Dermatopathol. 1998;20(4): 408–12.

Steiner A, Konrad K, Pehamberger H, Wolff K. Verrucous malignant melanoma. Arch Dermatol. 1988;124(10): 1534–7.

Wong T-Y, Suster S, Duncan LM, Mihm Jr MC. Nevoid melanoma: a clinicopathological study of seven cases of malignant melanoma mimicking spindle and epithelioid cell nevus and verrucous dermal nevus. Hum Pathol. 1995;26(2):171–9.

Zembowicz A, McCusker M, Chiarelli C, Dei Tos AP, Granter SR, Calonje E. Morphological analysis of nevoid melanoma: a study of 20 cases with a review of the literature. Am J Dermatopathol. 2001;23(3):167–75.