# Desmoplastic malignant melanoma

## Case report, immunohistochemical observations and review of literature

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A case of malignant melanoma with a desmoplastic recurrence and local lymph node metastasis is reported. The local relapse and the axillary metastasis presented the desmoplastic variant without atypical melanocytes that were easily recognised in primary lesion. Histological slices were examined by light microscopy and immunohistochemically.

Melanin could not be demonstrated in either recurrence or metastasis by histochemical tehnique. Immunoperoxidase staining with anti S-100 protein antibody demonstrated diffuse positivity of spindle cells both in relapse and metastasis, allowing the assesment of the depth of invasion. All the sections were negative for vimentin, desmin and neuron-specific enolase.

Malignant melanoma may assume various histological and clinical patterns. One of them is known as desmoplastic malignant melanoma (DMM), first recognised in 1971 (1). Melanomas with this histological pattern can be easily confused with a large number of other spindle-cell reactions and neoplasms.

DMM shows a distinct propensity toward repeated local recurrence but may also give rise to systemic metastases and death. In this report, a case of DMM and the immunostain properties of the DMM tissue are described.

## CASE REPORT

A 62-year-old woman noticed that a mole on her left forearm had enlarged together with the nodule beneath the initial lesion. The excision was performed in April 1986. A pigmented lesion 6 mm in diameter overlying the grayish-white nodule of fibrous appearance was noted.

The centre of the pigmented lesion was ulcerated. Near the edges of ulceration, small groups of atypical melanocytes were observed both in epidermis and in the junctional zone. Toward the depth of the lesion, there was a slight transition between atypical melanocytes of spindle or epitheloid appearance and fibroblast-like cells with abundant collagen stroma performing the storiform pattern. The lesion was not sharply demarcated from the subcutaneous fat tissue. It was diagnosed as malignant melanoma (figure 1).

In July 1987 the same patient was readmitted to hospital because of a hard nodule arising at the site of previous excision. Wide excision was performed once again, revealing a grayish nodule 25 mm in diameter, infiltrating subcutaneous tissue extensively. A diagnosis of DMM was made on review of the previous biopsy (figure 2).

In October 1987 the patient palpated a hard nodule in her left axilla, and a smaller one on the site of the two earlier biopsies. Histological examination of a small nodule 4 mm in diameter revealed granulomatous inflamation with the multinucleated cells of the foreign-body type around the surgical material, with no tumour regrowth. However, axillary biopsy of a hard infiltrating grayish nodule 53 mm in diameter was diagnosed as a metastasis of the DMM. Histological appearance of the axillary lesion was that of the recurrence, with long spindle cells occasionally having enlarged hyperchromatic nuclei, with no melanin content, in a background of proliferating connective tissue with abundant collagen (figure 3). After a year, the patient was lost to follow-up.

**FIGURE 1.**
Biopsy of the primary lesion. Atypical melanocytes are present near the edges of ulceration. Haematoxylin-eosin, 8X
**SLIKA 1.**
Biopsija prve promjene. Atipični melanociti nalaze se uz rubove ulceracije. Hematoksilin-eozin, 8X
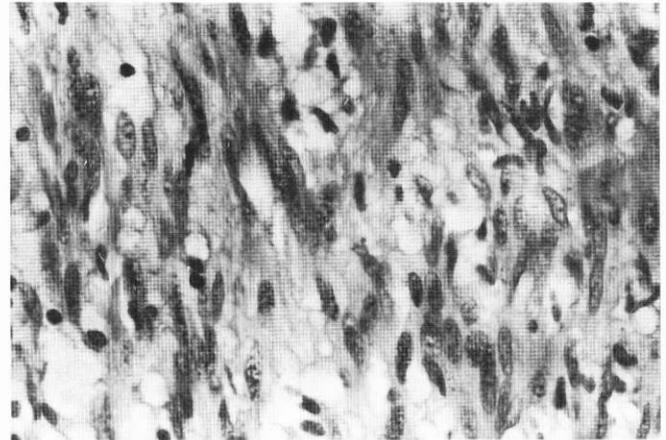


**FIGURE 3.**
Biopsy of the recurrence. Elongated to oval nuclei with coarse chromatin. Melanin pigment is not visible in the cytoplasm of the cells. Haematoxylin-eosin, 100X
**SLIKA 3.**
Biopsija recidivne promjene. Izdužene i ovalne jezgre s raspršenim kromatinom. Pigment melanin ne vidi se u citoplazmama stanica. Hematoksilin-eozin, 100X



**FIGURE 2.**
Biopsy of the recurrence. Elongated fibroblast-like cells surrounded by abundant collagen. Haematoxylin-eosin, 25X
**SLIKA 2.**
Biopsija recidivne promjene. Izdužene stanice nalik fibroblastima okružene su obilnim kolagenom. Hematoksilin-eozin, 25X

Reviewing the biopsies, paraffin sections of the tumour were stained by the Fontana method to delineate melanin granules. Additional paraffin sections of the tumour were stained for S-100 protein, vimentin, desmin and neuron-specific enolase (NSE). Melanin stains of all the examined sections were negative. Spindle cells both in relapse and metastasis were clearly positive with S-100 protein, and negative for vimentin, desmin and NSE. The S-100 protein immunostain proved to be useful in determining the depth of the lesion and the nature of fibroblast-like, elongated cells.

## DISCUSSION

In 1971, Conley et al. (6) described an uncommon variant of malignant melanoma they termed »desmoplastic melanoma«. Those were seven subcutaneous non-pigmented, collagenizing, fibrosarcoma-like tumours that were associated with overlying inconspicuous, intraepidermal aggregations of atypical malenocytes. Desmoplasia may be defined as fibroconnective tissue proliferation of variable degree often found associated with highly invasive epithelial tumours (such as carcinomas of the breast, pancreas and linitis plastica of the stomach (13,25)), in which it has been implicated in the benign host reaction to the malignant cells (18).

Desmoplastic malignant melanomas were later subdivided into three groups on the basis of the clinicopathological features at the time of the first biopsy (14) : 1) desmoplastic melanoma with an atypical intraepidermal melanocytic component – classical DMM, 2) desmoplastic melanomas without a demonstrated atypical intraepidermal melanocytic component – de novo DMM, and 3) nerve-centered DMM, either with or without an intraepidermal melanocytic component. While the latter were histologically indistinguishable from the classical DMM, the clinically apparent and grossly visible nerve enlargement created the impession of a primary nerve tumour (14).

Conley's concept was extended by Reed and Leonard (21), who observed schwannian appearance of the amelanotic spindled melanocytes and described it under the term »neurotropic« melanoma. This type of melanoma

usually occurs on the face, particculary the lips, and exhibits a marked tendency for peripheral nerve invasion (7,21).

DMM are usually located in the head and neck area (6,9,14,17), including the eye-lid (24). The anatomical locations less frequently involved are limbs, trunk and anus (1,6,27).

The reported patients' ages vary from 13 to 91 years, with the peak in the seventh decade (6,9,14). The male patients are affected slightly more frequently – an approximate male to female ratio is 1.5:1 (9,14).

The relationship of the superficial, melanocytic, precursor lesion (lentigo maligna, acral-lentiginous melanoma), at least in most cases, including our own, with a deeper, amelanotic spindled component has been stressed (6,9,17,21,22,27). It has been suspected that tumour growth is triggered by the sun exposure (4,5). An association with ionizing radiation has also been reported (14). Jain and Allen (1989) (14) believed thet the observed clinicopathological features of DMM occured as a result of the following chain of events: sunlight or ionizing radiation produce lentigo maligna or melanocytic dysplasia in epidermis. Some of these, over the years, may develop nodular, epitheloid or spindle cell malignant melanomas, with or without melanin production. A very small minority proceed along different growth pathways – after developing the malignant potential in the epidermis, the neoplastic nevus cells change their appearance so they resemble light microscopical features of fibroblastic, histiocytic, smooth muscle, Schwann's, endothelial or epithelial cells.

The desmoplastic response and the nature of the spindle cells were believed by some authors to be the host reaction to the growth of the tumour (17), analogous to the atypical but otherwise benign fibroblasts seen in the inflammatory pseudosarcomatous lesion after ionizing radiation (20), trauma (15), squamous cell carcinoma (18), or other cutaneous injury. A similar explanation has been proposed to account for the spindle cells in desmoplastic nevus (3). Fibrosis and collagenization of the stroma have also been mentioned in connection with benign nevi in older age groups (2,3), or as a feature of the cellular and of the malignant blue nevus (8,11,16,19,23).

However, ultrastructural and immunohistochemical findings indicate that the spindle cells of the DMM possess some melanocytic features. These are the occasional presence of premelanosomes (6,13), melanosomes (13), and macular desmosomes (26), observed earlier in both melanotic and amelanotic melanomas (10, 12), as well as the S-100 protein (9,13,14,22,24,28), and desmin (22) positive stain. All these findings, together with observations of neuroma-like qualities in DMM (21), neurosarcomatous transformation (7), simulated Schwann's cell (7,21,27) fibroblastic and myofibrobla-

stic differentiation (13,26,27), suggest that melanoma cells may undergo a transformation or metaplasia (4) and differentiate along alternate pathways, so producing the desmoplastic component. Such metaplasia in malignant melanoma is expected, considering the neutral crest derivation of nevus cells (7,14,28).

DMM may be misdiagnosed as some mesenchymal proliferations (fibromatosis (6,14), hypertrophied scar and keloid fibroma (6,25,26), desmoplastic nevus (3,27), benign and malignant fibrous histiocytoma (6,9, 26), atypical fibroxantoma (13,14,17,27), dermatofibrosarcoma protuberans (13,17), fibrosarcoma (6,9,13,14,17), leiomyoma and leiomyosarcoma (9,13)) as well as benign and malignant neurinoma, (9,13,14) neurofibroma (9,13,14) neurofibrosarcoma (9,13) and, finally, malignant nerve-sheat tumours (9). Additional malignant lesions within the differntial diagnosis are spindle cell squamous carcinoma (6,13,27) and renal cell carcinoma metastases (9).

All these lesions may be impossible to differentiate from non-pigmented DMM by light microscopy diagnostic. In the absence of an obvious associated melanoma, careful attention to the basal layer of the epidermis may reveal melanocytic dysplasia (27). We succededin assessing the right diagnosis only according to the first biopsy with clearly visible melanocytic atypia. Staining with S-100 is helpful in assessment of the level of invasion (13), and is used to exclude fibrohistiocytic and epitheloid lesions (9,13,22). However, tumours of the neural origin cannot be excluded in this way (13,22). Clinically, DMM are deeply invasive lesions that frequently recur and metastasize. Relapses and metastases may have histological appearance of both classical and desmoplastic (our case) MM (6). Walsh et al. concluded that with desmoplasia comes a more favourable pattern of biological behaviour (27). in contrast to others who stated that DMM is a highly malignant lesion (9,24). Although there were occasional »unexpectedly good responses to radiotherapy and chemotherapy« (14), radical surgical excision appears to offer the best results. The mortality rates are reported to be 36% (14) up to 66% (22).

As a conclusion, it is most important for the pathologist and clinical to be aware of this rare variant of malignant melanoma.

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# Sažetak

## DEZMOPLASTIČNI MALIGNI MELANOM
### Prikaz bolesnika, imunohistokemijske analize i pregled literature

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Prikazana je 62-godišnja bolesnica kojoj je s lijeve podlaktice odstranjen maligni melanom s izraženom dezmoplastičnom komponentom. Tumor je na površini bio ulceriran, uz rubove ulceracije opažene su nakupine atipičnih melanocita, dok su u dubljim dijelovima vretenaste tumorske stanice nalikovale benignim fibroblastima. 15 mjeseci nakon prethodne ekscizije odstranjen je recidiv koji je bio građen od vretenastih stanica nalik benignim fibroblastima, a nije pronađen ni jedan atipični melanocit »klasičnog izgleda«. Ispravna dijagnoza postavljena je jedino na osnovi nalaza prethodne biopsije. Poslije 3 mjeseca bolesnica je napipala povećan limfni čvor u lijevom pazuhu koji je kirurški odstranjen. Histološkim pregledom opaženo je tkivo identičnog izgleda poput onoga u recidivu, koje je izbrisalo normalnu građu limfnog čvora, s očitim znakovima invazije okolnog masnog tkiva. Histokemijskim metodama u recidivu i metastazi nije se mogao dokazati melanin. Vretenaste tumorske stanice prikazale su difuznu reaktivnost nakon primjene antitijela na S-100 protein, a nakon primjene antitijela na vimentin, desmin i neuron-specifičnu enolazu (NSE), pozitivna imunohistokemijska reakcija nije opažena.

Dezmoplastični maligni melanom (DMM) opisan je kao zaseban entitet 1971. godine. Dok se u uobičajenim okolnostima iz prekursorskih kožnih melanocitnih lezija (lentigo maligna, melanocitna displazija) mogu razviti maligni melanomi dobro poznatog, »klasičnog«, histološkog izgleda, u malom broju slučajeva neoplastične stanice mijenjaju svoj izgled nalikujući fibroblastima, histiocitima, glatkim mišićnim stanicama ili Švanovim stanicama.
DMM histološkim izgledom sliči brojnim mezenhimskim proliferacijama (fibromatoze, hipertrofični ožiljak, fibrom, dezmoplastični nevus, benigni i maligni fibrozni histiocitom-dermatofibrom, atipični fibroksantom, dermatofibrosarkoma protuberans, fibrosarkom, leiomiom i leiomiosarkom), benignom i malignom neurinomu, neurofibromu, neurofibrosarkomu, pa i vretensto-staničnim oblicima pločastog karcinoma ili metastazama karcinoma bubrežnih stanica.
Diferencijalna dijagnoza DMM izuzetno je teška. Primjena imunohistokemijske reakcije s antitijelima na S-100 protein može biti od pomoći prilikom procjene dubine i porijekla lezije (isključuju se fibrohistiocitne i epitelne neoplazije).