CASE REPORT

Melanoma with rhabdomyosarcomatous differentiation

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SUMMARY

Melanoma with rhabdomyosarcomatous differentiation is an extremely rare observation with a review of the literature revealing fewer than 15 previously identified cases. The authors describe a case of a 72-year-old man with a cutaneous lesion of the left scalp that was diagnosed as malignant melanoma on biopsy and wide excision. One month later, a punch biopsy of the excisional area revealed rhabdomyosarcomatous proliferation. Re-examination of the wide-excision specimen with muscle markers revealed areas of neoplastic melanoma cells consistent with rhabdomyosarcomatous differentiation.

BACKGROUND

Divergent differentiation is a rare phenomenon in melanomas which has been defined as the development of morphologically, immunochemically and/or ultrastructurally recognisable non-melanocytic cell or tissue components in melanomas.¹ Types of divergent differentiation reported include smooth muscle, fibroblastic/myofibroblastic, Schwannian and perineural, osteocartilaginous, ganglionic and ganglioneuroblastic, neuroendocrine and epithelial.¹ Melanoma with rhabdomyosarcomatous differentiation, in which tumour cells exhibit rhabdomyoblastic morphology and express striated muscle-specific immunohistochemical markers, is extremely rare.² In our case, as in three of seven previously reported cases, the rhabdomyosarcomatous differentiation was initially overlooked only to be found on retrospective review. This highlights the importance of considering this rare subtype in patients with a history of malignant melanoma and a new diagnosis of rhabdomyosarcoma. All cases reviewed were associated with poor prognosis and resistance to conventional chemotherapy.

CASE PRESENTATION

A 72-year-old man with a medical history of type 2 diabetes mellitus, coronary artery disease, myocardial infarction with stenting, atrial fibrillation and chronic obstructive pulmonary disease who presented to his dermatologist with a pigmented lesion on his left lateral scalp that his wife noticed while she was cutting his hair. A biopsy revealed superficial spreading malignant melanoma with a depth of invasion of at least 1.2 mm. At that point, the patient was referred to our institution for wide local excision with sentinel lymph node dissection. Preoperative imaging identified two sentinel lymph

nodes: one in the left preauricular region and the other in the left neck at the level of the mandible. A wide local excision and skin grafting without sentinel lymph node dissection showed malignant melanoma with a maximal thickness of 3.1 mm without ulceration. There was no evidence of lymphovascular or perineural invasion. The staging was pT3a pNx.

At his 4-month postoperative visit, the patient presented with severe itching at the surgical site. On physical examination, the graft site was notably hypervascular with thickened, violaceous edges and a region of erythema extending 4 inches circumferentially beyond the surgical border (figure 1). It was non-tender to palpation and without evidence of induration, fluctuance or palpable adenopathy. He was started on topical diphenhydramine cream and a course of topical triamcinolone. Several weeks later, he reported persistent itching with increased erythema. At that time, he was admitted for intravenous antibiotics for presumed cellulitis. A CT scan of the head and neck was performed which demonstrated non-specific skin thickening and subcutaneous soft tissue enhancement of the left scalp without adenopathy. A punch biopsy just beyond the surgical margin was also obtained with results consistent with rhabdomyosarcomatous differentiation of melanoma.

INVESTIGATIONS

The primary lesion was biopsied with histopathological examination showing infiltrative nests of epithelioid cells extending from the dermal-epidermal junction downward into the reticular dermis and involving the full thickness of the specimen (figure 2). The findings were consistent with malignant melanoma with at least a Clark level of IV and a maximum thickness of 1.2 mm.

Subsequent wide local excision of the left scalp was performed. Gross examination revealed a 6.5×6×0.3 cm specimen with a centrally located, brown-black variegated circular lesion measuring 1.5 cm in greatest diameter. Histopathological examination revealed a proliferation of infiltrating atypical epithelioid cells with a mitotic count of 3/mm² and a maximum thickness of 3.1 mm. The radial margin was 10 mm away, and the deep margin was 4 mm away. No perineural or lymphovascular invasion was identified. Immunohistochemical stains for melan-A and HMB-45 were noted to be diffusely and strongly positive in the neoplastic cells. A diagnosis of superficial spreading melanoma was made with stage pT3a, pNx.

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Figure 1 Postoperative photograph of hypervascularity with thickened, violaceous edges and a region of erythema surrounding surgical site.

Histopathological examination of the postoperative punch biopsy revealed a proliferation of markedly pleomorphic, spindled-to-polygonal cells in the dermis that spared the epidermis and adnexal structures. Some of the neoplastic cells showed tapered cytoplasmic processes that varied from amphophilic to brightly eosinophilic (figure 3). Features suggestive of cross-striations were focally identified. Myogenin was focally positive in these cells (figure 3). Brisk mitotic activity was identified numbering up to 5 per 10 high-power fields although no atypical mitosis was detected. The lesion was accompanied by an associated mild chronic inflammatory infiltrate consisting predominantly of lymphocytes. Immunohistochemical stains for CK903, HMB-45, melan-A, SOX10 and S100 were performed and found to be negative in the lesional cells, while vimentin and desmin showed strong positivity in the lesional cells. Immunohistochemical stains for CD68 demonstrated patchy staining, while smooth muscle actin highlighted vasculature. The morphological and immunohistochemical findings were consistent with rhabdomyosarcomatous differentiation. This finding

Figure 2 Skin biopsy from initial pigmented scalp lesion. There are infiltrating epithelioid neoplastic cells extending from the epidermal-dermal junction down through the full thickness of the biopsy specimen consistent with invasive melanoma.

Figure 3 Punch biopsy after wide local excision. There is a diffuse infiltration of neoplastic cells in the dermis with amphophilic to brightly eosinophilic cytoplasm consistent with rhabdomyoblastic differentiation. Myogenin is focally positive.

prompted a re-examination of the previously received wide-excision specimen.

Re-examination of the wide-excision specimen revealed distinct small foci of rhabdomyosarcomatous differentiation concentrated at the advancing front of the infiltrating neoplastic melanoma cells. Immunohistochemical stain for desmin was performed and showed strong positivity while stains for myogenin showed focal positivity in the areas suspected of rhabdomyosarcomatous differentiation (figure 4).

A second postoperative punch biopsy was received from the posterior aspect of the scalp that revealed additional tumour with rhabdomyosarcomatous differentiation (figure 5). Clinical follow-up revealed increased nodularity, hypervascularity and violaceous discoloration at the surgical site (figure 6). Immunohistochemical stains for HMB-45 and melan-A were found to be negative while desmin was found to be strongly and diffusely positive in the lesional cells confirming the diagnosis of rhabdomyosarcomatous differentiation.

OUTCOME AND FOLLOW-UP

Previously described cases of melanoma with rhabdomyosarcomatous differentiation describe what appears to be an aggressive form of malignancy that responds poorly to standard chemotherapeutic interventions. For example, Gattenlöhner *et al*³ described a patient with malignant melanoma with metastatic rhabdomyosarcomatoid transdifferentiation, who was treated with dacarbazine and 56 Gy of cobalt 60 gamma rays. The patient died after developing distant metastases to the lung, mediastinum and abdominal organs with malignant ascites within 6 months after primary diagnosis.⁴ Our patient is being evaluated using genomic profiling to identify potential targeted therapy for systemic therapy. The patient was also referred to radiation oncology for consideration of external beam radiation therapy.

DISCUSSION

Malignant melanoma can exhibit a wide range of divergent differentiation defined as morphological, immunohistochemical and ultrastructural characteristics that deviate from typical melanocytic components.^{2 5} Previously described divergent

Figure 4 Wide local excision with infiltrating malignant melanoma. Immunohistochemical staining reveals diffuse, strong positivity for desmin and myogenin at the advancing front.

differentiations include smooth muscle, fibroblastic, perineural, osteocartilaginous, neuroendocrine, epithelial and rhabdomyosarcomatous.⁵ Rhabdomyosarcomatous differentiation of melanoma represents an extremely rare observation with a review of the literature revealing fewer than 10 previously described confirmed cases.² In this case report, we describe an additional case of melanoma with rhabdomyosarcomatous differentiation.

The original skin biopsy in our case showed melanoma, and the postexcisional punch biopsy exclusively showed a rhabdomyosarcomatous neoplasm. Similar to the case described by Antonov and Niedt in 2016, the discordant morphological findings from the two biopsies taken from the same lesional area warranted careful revisiting of our case.² Retrospective review of the wide local excision for melanoma revealed numerous small foci of rhabdomyosarcomatous differentiation with associated desmin positivity at the advancing edge. The linkage of the melanoma with the rhabdomyosarcomatous cells was further supported by the clinical course and the infrequency of primary rhabdomyosarcoma at the site.

Figure 5 Punch biopsy of the posterior scalp revealing melanoma with rhabdomyosarcomatous differentiation. Immunohistochemical staining for desmin is strongly and diffusely positive.

Figure 6 Clinical photograph of surgical site on follow-up examination.

Previously identified cases of melanoma with rhabdomyosarcomatous differentiation have been confirmed by light microscopy, immunohistochemistry and electron microscopy.² In 2007, Gharpuray-Pandit *et al* described two cases of tumour cells with concurrent melanocytic and rhabdoid features.⁴ The first case stained positively for desmin, myogenin and Myo-D1 with an electronic microscopic finding of melanosomes. The second case showed an identical staining pattern with electron microscopic features of rhabdomyoblastic differentiation.⁴ In 2014, Senjere *et al* described two cases of rhabdomyosarcomatous differentiation in melanoma by desmin and myogenin positivity and electronic microscopic findings of irregularly arranged sarcomeres.¹ Our case represents an addition to these previously described cases of melanoma with rhabdomyosarcomatous differentiation by confirmation with light microscopy and immunohistochemical staining pattern.

Melanoma with rhabdomyosarcomatous differentiation tends to occur in middle-aged to older adults with an average age at diagnosis of 58 years.² A wide age range of cases has been described with the youngest reported a 21-year-old woman and the oldest reported a 90-year-old man.² All described cases were associated with a poor prognosis, and lesions with complete rhabdomyosarcomatous differentiation have previously been noted to be unresponsive to conventional chemotherapy.³ Six prior cases showed distant metastases, and three died between a period of 6 and 10 months after initial presentation.^{1–5}

The case we describe represents an addition to this unique differentiation of melanoma that can easily be missed on initial

Learning points

- ▶ Melanoma with rhabdomyosarcomatous differentiation is a unique subtype that can easily be missed on initial biopsy.
- ▶ Melanoma with rhabdomyosarcomatous differentiation should be considered in a patient with a known history of malignant melanoma and new diagnosis of rhabdomyosarcoma.
- ▶ Review of previously described cases all showed poor prognosis; three patients died within 6–10 months.
- ▶ Comprehensive genomic profile testing has the potential to identify target therapies to treat patients with this rare and aggressive disease.

approach. Of note, three previously described cases were discovered on a retrospective review after the patient developed a rhabdomyosarcomatous neoplasm.³ As such, rhabdomyosarcomatous differentiation of melanoma should enter the differential diagnosis in a patient with a known history of melanoma and a new diagnosis of rhabdomyosarcoma.

Contributors AK was pathology resident and the principal author and contributed to the majority of the research and text. JA was the surgical resident on the case who wrote the clinical findings and follow-up. MD was the pathologist who originally recognised and diagnosed the case and contributed to the histopathological description of the tumour. FS was the general surgeon who performed multiple biopsies and resection on the scalp tumour, as well as clinical follow-up of the patient.

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