

Malignant melanoma with a rhabdoid phenotype exhibiting numerous solid tumor masses: A case report

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Abstract. We present a case of malignant melanoma with a rhabdoid phenotype in a 44-year-old female with a quite unique and aggressive clinical course. Rhabdoid features are defined by characteristics such as sheets or solid trabeculae of neoplastic cells with large, vesicular, round to bean-shaped nuclei, prominent centrally located nucleoli, and abundant eccentric cytoplasm. Although various histological differential diagnoses were cited for the present case that showed 'rhabdoid features', most of them were excluded on the basis of the clinical history, tumor location, clinical behavior, and a broad panel of immunohistochemical stains. In the present case, the immunohistochemical findings were positive for vimentin, S-100 protein, melan-A, and EMA, but negative for HMB45, cytokeratin, CD34 and desmin. In addition, the positive expression of BAF47 was also recognized. These findings lead to the conclusion that this quite unique aggressive soft tissue tumor should therefore be diagnosed as malignant melanoma with a rhabdoid phenotype.

Introduction

Malignant melanoma is known to display tremendous histologic diversity (1,2). Rare cases of malignant melanoma with a rhabdoid phenotype have been reported (3-7). We present a case of malignant melanoma with a rhabdoid phenotype which has a quite unique and aggressive clinical course.

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Patients and methods

Clinical history. A 44-year-old female attended the hospital because of multiple subcutaneous tumor masses which were initially noticed 2 months earlier and were continuously increasing in number and size. Numerous masses were distributed throughout the body (Fig. 1). The tumor masses were elastic hard, well-circumscribed with smooth surfaces, and fixed to the deep fascia. The patient's laboratory examination revealed decreased hemoglobin, total protein and albumin (9.2, 6.3 and 3.1 g/dl, respectively) and increased LDH, C-reactive protein and soluble-IL2 receptor (1179 IU/l, 3.39 mg/dl and 864.2 U/ml, respectively). Other tumor makers including CEA, AFP and CA125 were within the normal range. Fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed numerous positive lesions throughout the body (Fig. 2). Most of the tumors were in the subcutaneous tissue partially involving the deep fascia of the muscle. Magnetic resonance imaging (MRI) indicated that the tumors located at right anterior shoulder, left sterno-clavicular joint and left axilla, showed an iso-signal intensity on T1-weighted images and heterogeneously high-signal intensity on T2-weighted images. After gadolinium contrast medium administration, the tumors were heterogeneously enhanced (Fig. 2). An excision biopsy was performed on the lesions of the right anterior shoulder and abdominal wall, both of which were causing severe pain.

Tissue was fixed in 10% neutral-buffered formalin, embedded in paraffin, and stained with hematoxylin and eosin. For the immunohistochemical analysis, the primary antibodies listed in Table I were used.

Results

The tumor masses had a yellowish, homogeneous cut surface with small areas of hemorrhage and necrosis. Microscopic findings showed a proliferation of round or polygonal cells with vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm, arranged in sheets or alveolar patterns, accompanied by necrosis. Rhabdoid cells with cytoplasmic inclusion

Table I. Immunohistochemical stain.

Antibody	Dilution	source	Pretreatment
S-100 protein	1:100	Dako Corporation, Tokyo, Japan	
Vimentin	1:100	Dako	10 min Microwave
Melan-A (A103)	1:25	Dako	10 min Microwave
BAF47 (25)	1:250	BD Transduction Laboratories, San Diego, CA, USA	20 min Microwave
EMA (E29)	1:100	Dako	10 min Microwave
HMB-45	1:75	Dako	10 min Microwave
Pan-CK (5D3)	1:100	Novocastra Laboratories, Newcastle, UK	10 min Microwave
CK (CAM5.2)	1:100	Dako	10 min Microwave
LCA (CD45)	1:50	Dako	10 min Microwave
Smooth muscle actin (IA4)	1:400	Dako	10 min Microwave
κ light chain	1:50	Dako	10 min Microwave
λ light chain	1:50	Dako	10 min Microwave
CD34 (QBEnd 10)	1:40	Dako	10 min Microwave
Desmin (D33)	1:200	Dako	10 min Microwave

EMA, epithelial membrane antigen; Pan-CK, pan-cytokeratine; CK, cytokeratine; LCA, leukocyte common antigen.

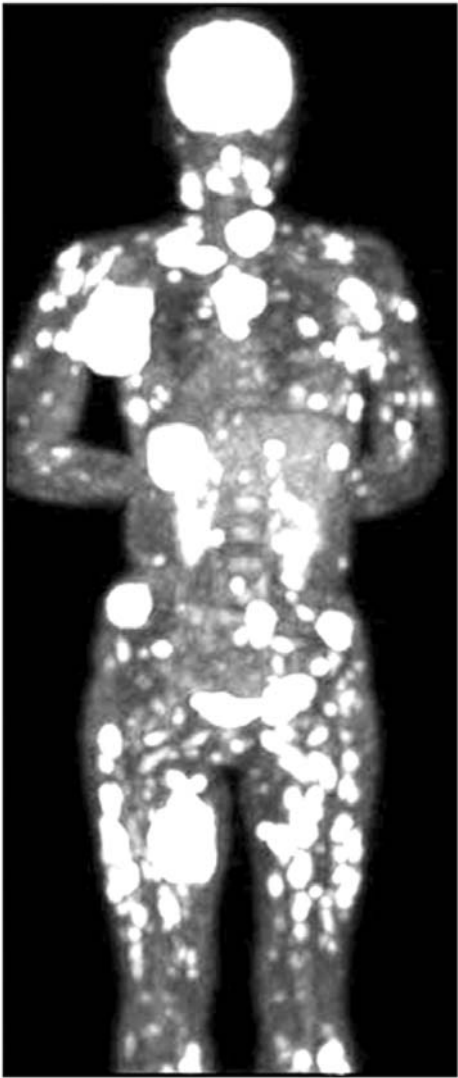


Figure 1. PET revealed numerous tumors throughout the body.

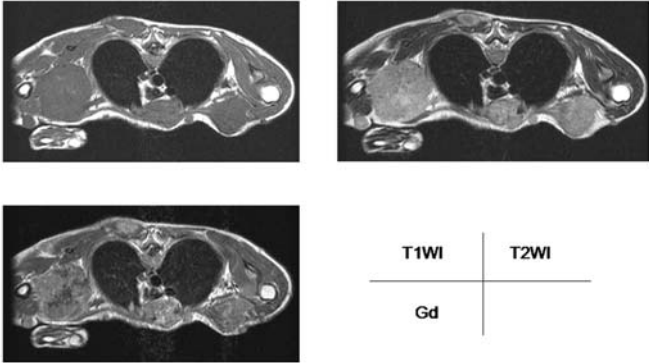


Figure 2. MRI of the bilateral axillary (left: T1WI, middle: T2WI and right: Gd-enhance).

bodies were prominent through the tumor (Fig. 3). Melanosome were absent through the tumor. Since malignant tumors with rhabdoid feature were suspected, a further immunohistochemical analysis was performed. The immuno-histochemical analysis showed the tumors to be diffusely positive for vimentin and S-100 protein; focally positive for Melan-A and epithelial membrane antigen (EMA); negative for HMB45, pan-cytokeratin, CAM5.2, CD34, λ light chain, κ light chain and desmin. In addition, the positive expression of BAF47 (SMARCB1/INI1) was also recognized (Fig. 4). These unusual aggressive tumors were diagnosed as malignant melanoma with a rhabdoid phenotype. Although we worked up the detection of primary lesion, especially of the eye and internal organs, we failed to demonstrate a primary melanoma. The patient underwent systemic chemotherapy using dacarbazin: 230 mg/m², i.v. (1 h), day 1-3 (Dacarbazin®: Kyowahakkou Co, Ltd Tokyo, Japan), nimustine hydrochloride: 60 mg/m², day 1 (Nidran®: Daiichi-Sankyo Co. Ltd Tokyo, Japan), cisplatin 25 mg/m², i.v. (4 h) day 1-3

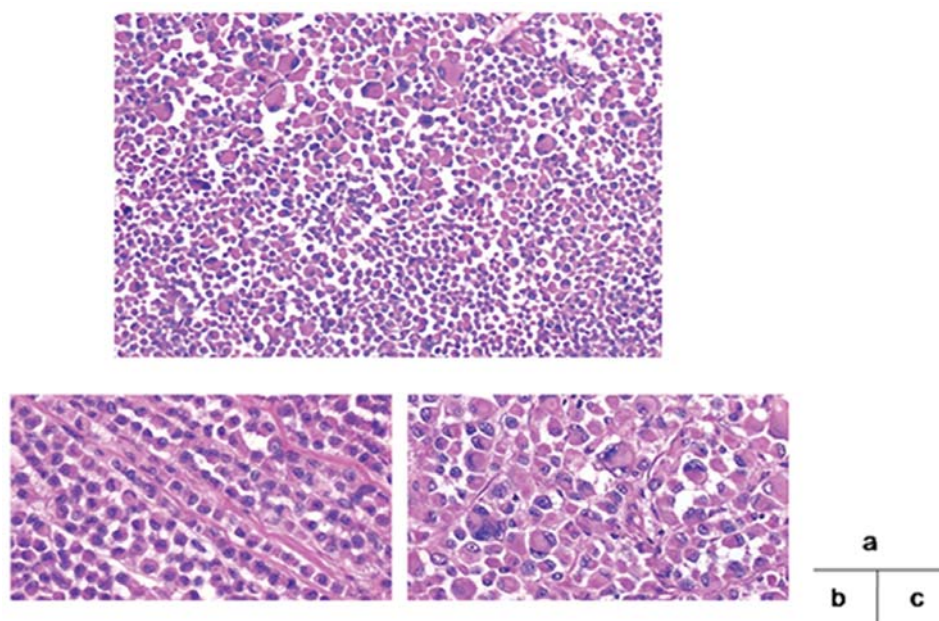


Figure 3. H&E stain (upper: x20, lower: x40): Microscopically, tumor is composed of a diffuse proliferation of rounded or polygonal cells arranged in sheets (a) and alveolar (b) pattern. Tumor cells disclose characteristic glassy eosinophilic cytoplasm, eccentric vesicular nuclei and prominent nucleoli (c).

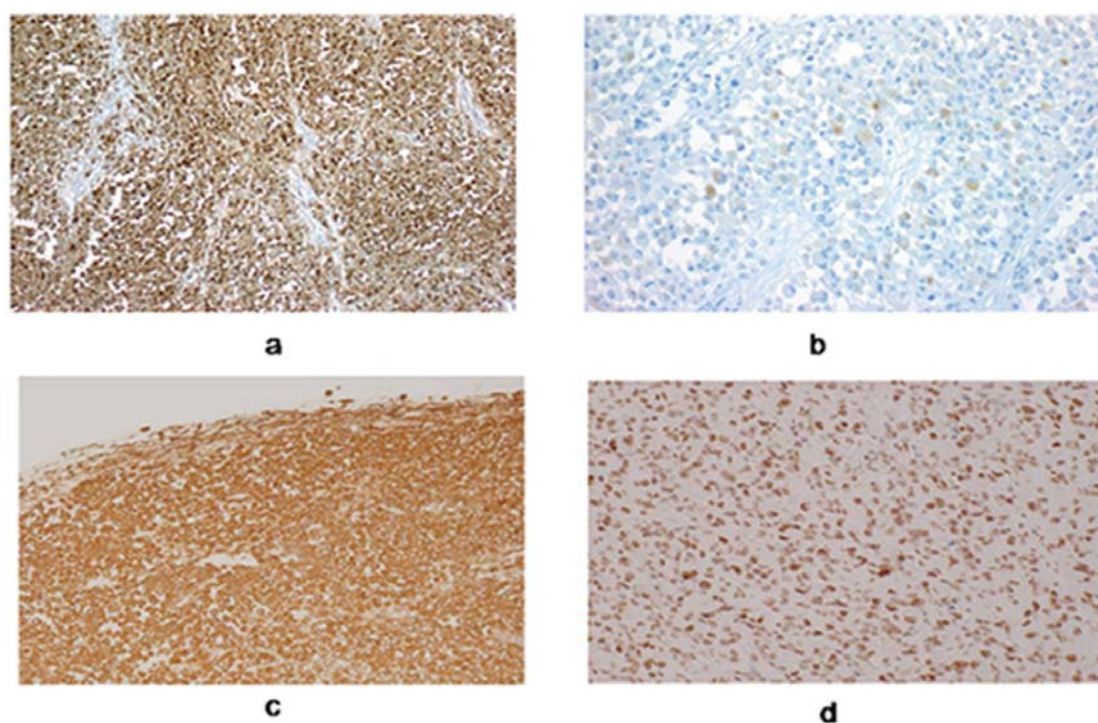


Figure 4. Immunohistochemical staining: (a) strong S100 protein expression by the neoplastic cells, (b) focally positive staining for Melan-A, (c) diffuse positive staining for vimentin and (d) diffuse BAF47 expression by the neoplastic cells.

(Randa®: Nippon Kayaku Co. Ltd, Tokyo, Japan), but no reduction of the tumors was observed. Since the tumor mass of the left axillary region increased in size, and caused severe neuralgia, radiation therapy was performed at a dose of 36 Gy/9 fractions.

Two months after the excision biopsy, the patient died of an intracranial hemorrhage from a metastatic brain tumor. Permission to perform an autopsy was rejected by the family.

Discussion

The microscopic findings of the present case showed a proliferation of rounded or polygonal cells with vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm, arranged in sheets or alveolar patterns, accompanied with necrosis. Rhabdoid cells with cytoplasmic inclusion bodies were prominent throughout the tumor. The term 'rhabdoid' is

generally used when the microscopic findings resemble rhabdomyoblasts, although muscle markers are absent. Rhabdoid features are defined by characteristics such as morphological findings, sheets or solid trabeculae of neoplastic cells with large, vesicular, round to bean-shaped nuclei, prominent centrally located nucleoli, and abundant eccentric cytoplasm. Mitotic figures were frequently seen, and tumor necrosis was common. Initially, malignant rhabdoid tumors (MRT) were categorized among pediatric renal neoplasms as a rhabdomyosarcomatous variant of Wilms tumor in a pediatric renal neoplasm, but it was later re-categorized into a malignant rhabdoid tumor (MRT) as a separate entity (8,9). Thereafter, numerous cases of MRT arising from extra-renal sites including the liver (10,11), brain (10,11), skin (11) and soft tissue (10-13) have been reported. Subsequent studies revealed the rhabdoid cells have also been seen in other tumors, such as some carcinomas (14,15), sarcomas (16-18), in the central nervous system (19) and malignant melanoma (6,7). The rhabdoid features are thought to represent a common dedifferentiated end point for a variety of neoplasms. Therefore 'rhabdoid features' may be a term which represents phenotypes of malignant neoplasms (20-22). The histological findings of the present case showed the characteristic features of rhabdoid cells.

Although various histological differential diagnoses were cited for the present case that showed 'rhabdoid features', most of them were excluded on the basis of the clinical history, tumor location, clinical behavior, and a broad panel of immunohistochemical stains. First, epithelioid sarcoma, which usually affects the distal extremities, may have rhabdoid cells. However, in the present case, the number of rhabdoid cells was small and they were focally recognized. Epithelioid sarcoma is commonly diffusely positive for the CK (17). Additionally, it is not usually as aggressive as the present case. Second, rhabdomyosarcoma with extensive rhabdomyoblastic differentiation may look morphologically similar to the present case, but usually shows diffusely positive staining for myogenic makers (18).

Finally, extra-renal-MRT (EMRT), which has overlapping features with malignant melanoma with a rhabdoid phenotype (6,7) could be cited. Certainly, the immunohistochemical characteristics overlapped with EMRT in the present case including the diffusely positive S-100 protein and vimentin marker, and the negative staining for desmin, CD34, cytokeratin and LCA marker. Recently, subsequent studies have consistently found deletions or mutations of the INI1 gene (also known as hSNF5/SMARCB1/BAF47) in the vast majority of MRT and EMRT, although overall up to 20% of rhabdoid tumors of all sites show no evidence of INI1 gene alterations (23,24). Therefore, a negative immunohistochemical reaction for a monoclonal anti-SMARCB1/hSNF/INI1 antibody (BAF47) has been proposed to diagnose rhabdoid tumors (6,11,14). The present case, however, showed positive BAF47 staining. In addition, the majority of the cases of EMRT were infants or children (12).

In the present case, the immunohistochemical findings were positive for vimentin, S-100 protein, melan-A, and EMA, but negative for HMB45, cytokeratin (CAM5.2, AE1/AE3), CD34 and desmin. In addition, the positive expression of BAF47 (SMARCB1/INI1) was also recognized. These immunoprofiles

were similar to that of previous studies of malignant melanoma with a rhabdoid phenotype (3-7), namely, positive for S-100 protein, vimentin and EMA. However, Laskin *et al* reported that malignant melanoma with a rhabdoid phenotype was negative for S-100 protein, unlike with the present case (5). One explanation is that this discrepancy might be attributed the differences of the specificities of the antibodies used. Furthermore, this variability in immunohistochemical features is frequent among the rhabdoid features which represent a common dedifferentiated end point for a variety of neoplasms (3-7,15-17). Further molecular and cytogenetic studies of the differentiation and the dedifferentiation of the neoplasm are warranted.

All these findings lead to the conclusion that this quite unique aggressive soft tissue tumor should be diagnosed as a malignant melanoma with a rhabdoid phenotype.

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