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Case and Review

A Case of Primary Cutaneous Basal Cell Carcinosarcoma

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Keywords
Basal cell carcinoma · Carcinosarcoma · Skin · Sarcomatous basal cell carcinoma

Abstract
A 94-year-old man consulted our hospital due to a rapidly growing tumor on the left cheek. The histological diagnosis of the tumor was basal cell carcinosarcoma, which was composed of intermingled epithelial and mesenchymal components. The former was basal cell carcinoma, while the latter was spindle cell sarcoma. The tumor was completely resected with a 3-mm margin and the patient remained free of local recurrence or distinct metastasis for 2 years. We report here a case of cutaneous basal cell carcinosarcoma and a review of the literature.

Introduction

Carcinosarcoma (CS), also known as metaplastic carcinoma, biphasic neoplasm, and sarcomatous/sarcomatoid carcinoma, is a rare tumor that consists of malignant epithelial and

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mesenchymal components. CS occurs commonly in the respiratory tract, gastrointestinal tract, breast, and uterus, while cutaneous CS is rare [1]. In this study, basal cell carcinoma (BCC) was revealed to be the most frequently reported epithelial component of cutaneous CS, although squamous cell carcinoma and malignant adnexal tumors such as spiradenocarcinoma, proliferating trichilemmal cystic carcinoma, porocarcinoma, and adenocarcinoma have also been described.

Materials and Methods

A 94-year-old man presented with a 6-month history of a rapidly growing tumor on the left cheek. On physical examination, there was a pedunculated, erosive red solid tumor, 4 cm in diameter, on the left cheek (Fig. 1). Dermoscopic examination revealed several arborizing vessels. Other than his skin tumor, he suffered from an atypical mycobacterial infection, which was diagnosed based on the sputum culture and computed tomography of the chest. The tumor was completely excised with about 5-mm surgical margins. The tumor cross-section showed a whitish solid tumor with partial necrosis, which was rich in mucinous material. We studied the histopathologic findings.

Results

In the lower magnification, there was irregular basaloid cell proliferation in the dermis, which was partly connected with the epidermis (Fig. 2a). In the higher magnification, basaloid tumor cells formed nests and strands (Fig. 2b), partly showing keratinization (Fig. 2c) and comedonecrosis (Fig. 2d). Mesenchymal cells without intercellular bridges showed diffuse proliferation in the stroma (Fig. 2e), with scattered large chromatic nuclei and frequent atypical mitoses (Fig. 2f). There was chondrification in the stroma with slightly bluish amorphous mucin deposition (fig. 2g).

The immunohistochemical examination demonstrated that the epithelial components were positive for cytokeratins (AE1/AE3) (Fig. 3a), Ber-EP4 (Fig. 3b), epithelial membrane antigen, and p63, while the mesenchymal components were positive for vimentin (Fig. 3c). Both epithelial and spindle cell components overexpressed for p53 (Fig. 3d). These histological and immunohistological characteristics were consistent with those of the previously reported case of basal cell CS [2]. Both epithelial and mesenchymal components were 70–80% positive for Ki-67, which suggested that the mesenchymal cells represented a sarcomatous progression of BCC, resulting in a diagnosis of basal cell CS. The results of immunophenotyping are presented in Table 1.

Discussion

CS is a biphasic neoplasm, with malignant epithelial and mesenchymal differentiation mixed widely in one lesion. The sarcomatous components has been recognized as a meta-

plastic carcinoma of the epithelial components [2]. Metaplastic carcinoma demonstrates the proliferation of spindle cells sometimes associated with ossification and chondrification.

Metastases from distant sites, especially from the genitourinary tract and lungs, must be excluded. In the present case, computed tomography could not reveal any obvious neoplasm. We also excluded the possibility of a collision tumor because this tumor was composed of intermingled epithelial and mesenchymal components throughout.

Although the pathogenesis of CS is unknown, there are two hypotheses, i.e., the monoclonal and the multiclonal hypotheses [3]. The monoclonal hypothesis proposes that undifferentiated totipotent neoplastic cells undergo multiple pathways of terminal differentiation into histologically recognizable mesenchymal and epithelial components. In support of the monoclonal hypothesis, the same genetic abnormalities (allelic loss of chromosome 9p, loss of heterozygosity on chromosome 17p, and microsatellite instability on chromosome 4p) were shared by the two different components of CS in a case of CS in urinary bladder. Harms et al. [4] reported that basal cell CSs are genetically similar to conventional BCC but display additional changes such as homozygous loss of *CDKN2A*. In addition, Inoue et al. [5] reported that uterine CS represents an example of cancer associated with epithelial-mesenchymal transition, and that Sox and β-catenin signal transductions play key roles in the regulation of epithelial-mesenchymal transition/cancer stem cell properties.

In contrast, the multiclonal theory hypothesizes that epithelial and mesenchymal components arise independently from two or more undifferentiated progenitor cells, and regards CS as a true collision neoplasm.

Following a review of the literature, the 5-year disease-free survival rate of patients with CS associated with epidermal-derived tumors (squamous cell and basal cell) is 70% which is better than that of 25% in patients with CS associated with adnexal (eccrine, apocrine, or follicular) differentiation [6]. The kind and ratio of sarcomatous components do not influence the prognosis of CS [6, 7].

We reviewed 94 cases of primary cutaneous CS, including the present case, reported between 1972 and 2016. The comparison of the recurrence or metastatic rate among CSs derived from BCC and CSs from other skin tumors, such as squamous cell carcinoma and adnexal neoplasms, demonstrated 4.3% in basal cell CS and 38% in other skin tumors (Table 2). The recurrence or metastatic rate of CS may depend on the histological characteristics of epithelial components but not on those of mesenchymal components. In addition, since it is reported that the metastatic rate of BCC larger than 3 cm in diameter is 2% [2], the prognosis is not necessarily worse than that of large BCC.

Finally, although the relatively small number of cases of basal cell CS limits the conclusions regarding prognostic factors, complete resection is a sufficient treatment for most cases.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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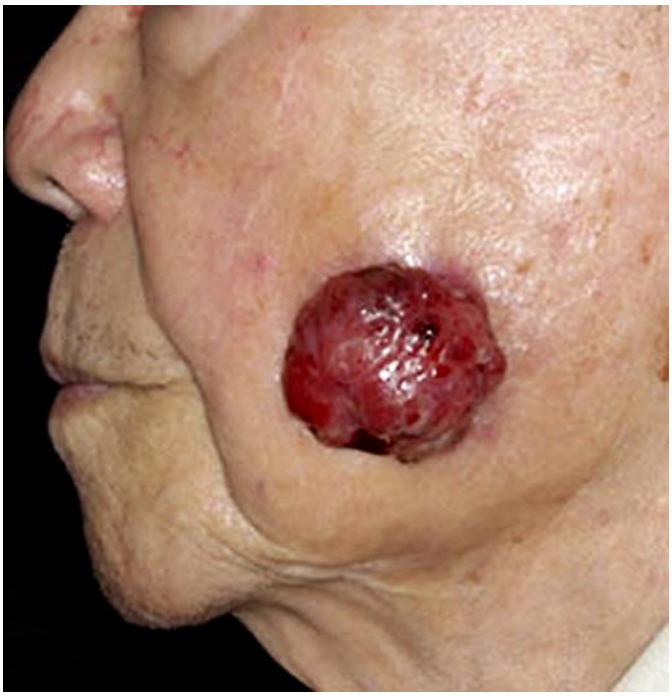

Fig. 1. Clinical appearance. A 4-cm rapidly growing exophytic pedunculated erosive tumor is evident on the left cheek.

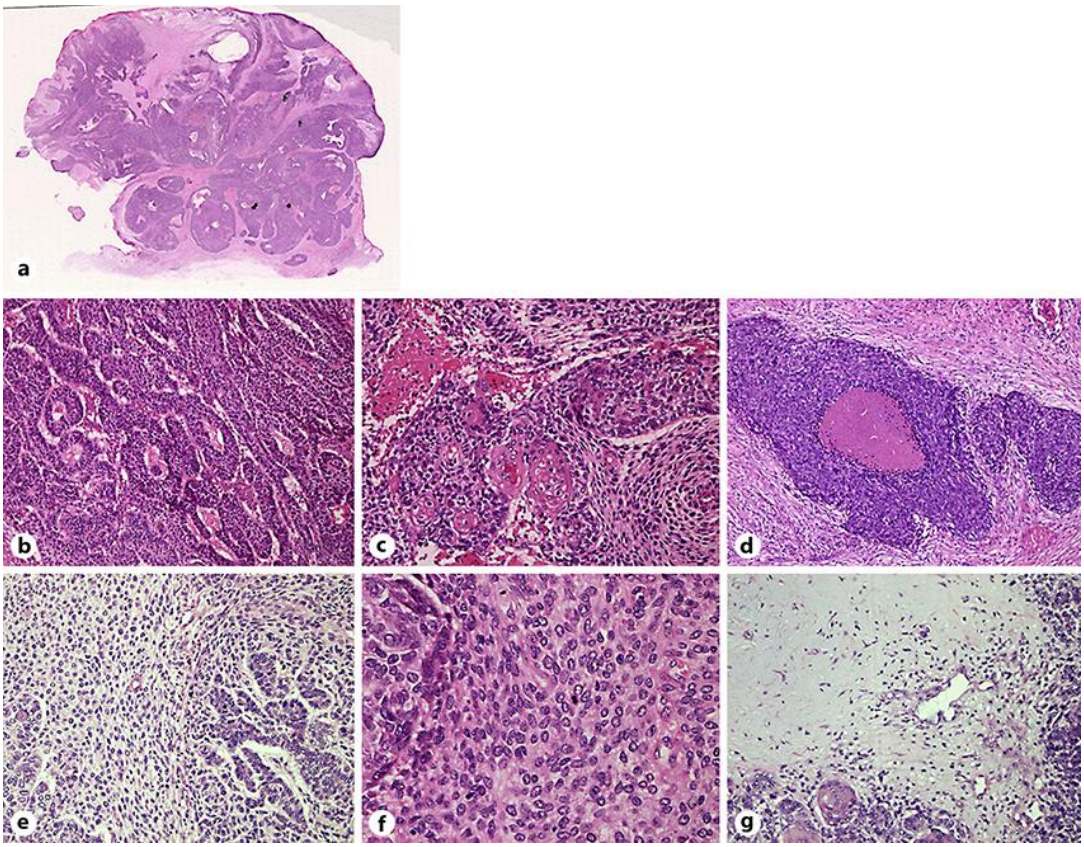

Fig. 2. Histopathologic examination reveals basaloid cell proliferation from epidermis to entire dermis (**a**), basaloid tumor cells forming nests and fords (**b**), keratinization (**c**), central necrosis (comedonecrosis) (**d**), atypical spindle cells without intercellular bridges showing diffuse proliferation in the stroma (**e**), scattered large nuclei and frequent atypical mitoses (**f**), and chondrification in the stroma with slight basophilic/bluish amorphous mucin deposition (**g**). **a** Hematoxylin and eosin. **b–g** Magnification, ×200.

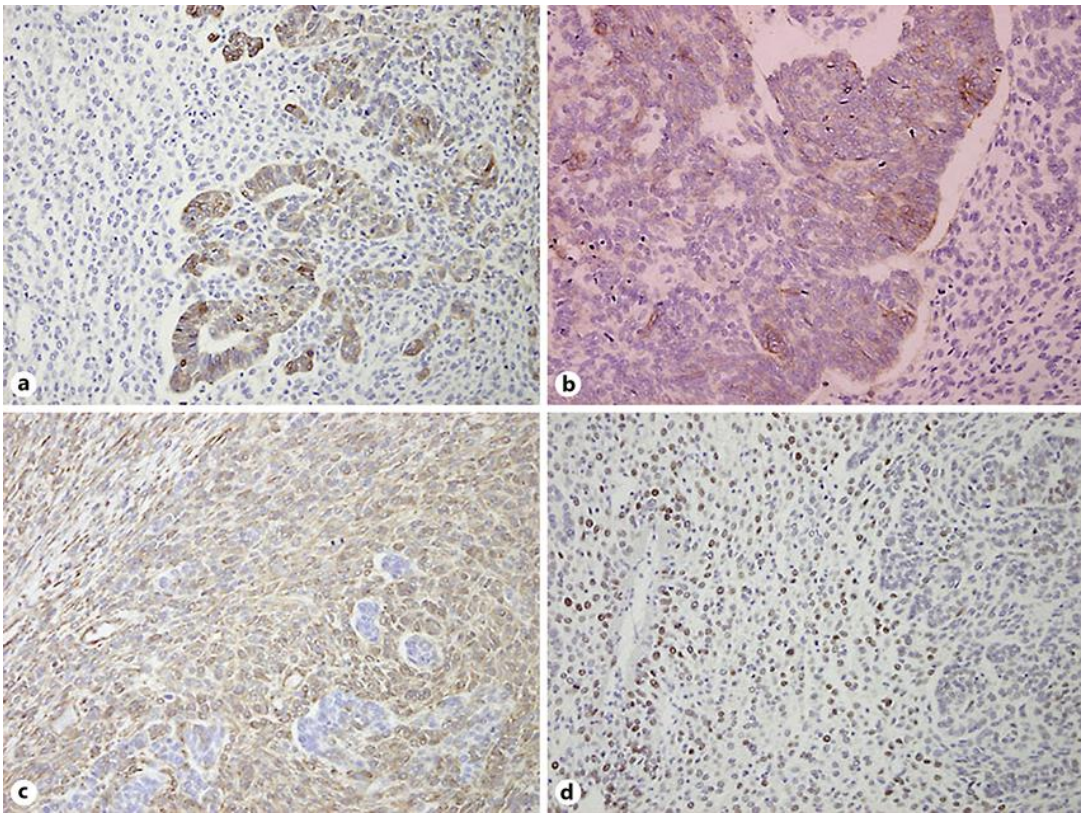

Fig. 3. Immunohistochemical examination reveals positive results for cytokeratin (AE1/AE3) (**a**) and Ber-EP4 (**b**) in epithelial cells. **c** On the other hand, positive staining for vimentin is seen in the spindle cell component. **d** Both epithelial and spindle cell components overexpress for p53. Magnification, ×200.

Table 1. Results of immunophenotyping

	Epithelial component		Mesenchymal component	
	basal cell CS	this study	basal cell CS	this study
CK	(+)	(+)	(–)	(–)
Ber-EP4	(+)	(+) focal	(–)	(–)
EMA	(+)	(+) focal	(–)	(–)
p63	(+)	(+)	(–)	(–)
Vimentin	(–)	(–)	(+)	(+)
p53	(+)	(+)	(+)	(+)
SMA	(–)	(–)	(–)	(–)
S-100	(–)	(–)	(–)	(–)
Ki-67		(+) 70–80%		(+) 70–80%

The epithelial component was positive for CK, Ber-EP4, EMA, p63, and p53. The mesenchymal component was positive for vimentin and p53. Both epithelial and mesenchymal components were 70–80% positive for Ki-67. CS, carcinosarcoma; CK, cytokeratins; EMA, epithelial membrane antigen; SMA, smooth muscle actin.

Table 2. Summary of the 94 cases of primary cutaneous CS†

Epithelial component	BCC‡	Others
Cases (male:female)	50 (3:1)	44 (1:1)
Mean age, years	76 (44~94)	68 (36~92)
Location (sun exposed:unexposed)	3:2	1:1
Size, cm	3 (0.3~15)	4 (1~15)
Clinical features	nodule, ulcer, growing	nodule, ulcer, growing
Prognosis (recurrence or metastatic rate)	4% (2/50)	38% (17/44)

Comparing CS derived from BCC and CS derived from others (squamous cell carcinoma, spiradenocarcinoma, proliferating trichilemmal cystic carcinoma, porocarcinoma and adenocarcinoma), the prognosis of basal cell CS is better than that of others. The recurrent and metastatic rate of basal cell CS is 4 %, compared to 38% for other CS. The prognosis of squamous cell CS is as poor as that of CS derived from other appendage tumors. The prognosis of basal cell CS, including our case, is the best among all forms of CS. Values in parentheses represent the lowest and highest values for that group (youngest and oldest ages, and minimum and maximum sizes). † Carcinosarcoma; ‡ basal cell carcinoma.