Primary cutaneous carcinosarcoma developing after chronic C-arm radiation exposure

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INTRODUCTION

Malignancy can develop after exposure to ionizing radiation. Basal cell carcinoma, squamous cell carcinoma (SCC), and sarcoma associated with ionizing radiation have been reported previously[1,2]; however, cases of ionizing radiation–induced carcinosarcoma (CS) are rare.[3] CS is a biphasic tumor with overt carcinomatous and sarcomatous features apparent with both light microscopy and immunohistochemistry.[4] Here, a case of primary cutaneous carcinosarcoma (PCCS) after chronic occupational exposure to ionizing radiation is presented.

Abbreviations used:

CS:	carcinosarcoma
IHC:	immunohistochemistry
PCCS:	primary cutaneous carcinosarcoma
SCC:	squamous cell carcinoma
SCM:	spindle cell melanoma
SMA:	smooth muscle actin
SpSCC:	spindle cell squamous cell carcinoma

CASE REPORT

A 54-year-old man presented with multiple erythematous lesions with crusts on both hands for 2 years. He had a 5-cm ulcerated and verrucous exophytic tumor on the left thumb and a 4-cm purplish tumor with an ulcerated center on the right index finger with multiple scattered verrucous and crusted plaques on both hands (Fig 1, *A* and *B*). These lesions had been growing rapidly for 3 months. As an orthopedic surgeon, he has been exposed to radiation from C-arm fluoroscopy for 20 years.

Excisional biopsy performed for the right index finger lesion found biphasic tumor with malignant epithelial and mesenchymal components. The epithelial component was an SCC consisting of atypical cells (Fig 2, *A*). The mesenchymal component comprised atypical spindle cell proliferation with a whorled pattern. Some tumor cells showed abundant eosinophilic cytoplasm and bizarre nuclei (Fig 2, *B*). Pleomorphic tumor cells and atypical mitoses were evident. These findings suggested an undifferentiated pleomorphic sarcoma. On immunohistochemistry (IHC), the epithelial component showed positivity for cytokeratin and p63 but negativity for vimentin and smooth muscle actin (SMA). The mesenchymal component showed diffuse expression of vimentin and SMA. However, cytokeratin was negative, whereas p63 was expressed in less than 5% of tumor cells in the mesenchymal part.

The patient's medical history, complete blood count, chemistry, urinalysis, and chest radiograph findings were unremarkable. Magnetic resonance imaging showed suspicion of bone involvement in the left thumb and the right index finger lesions. Ultrasound-guided aspiration of lymph nodes in both axillae were negative for malignant cells.

The patient initially refused surgical treatment and wished to try chemotherapy first. He was referred to an oncologist. One cycle of 5-fluorouracil and cisplatin combination chemotherapy was given. Because there was no significant improvement, the

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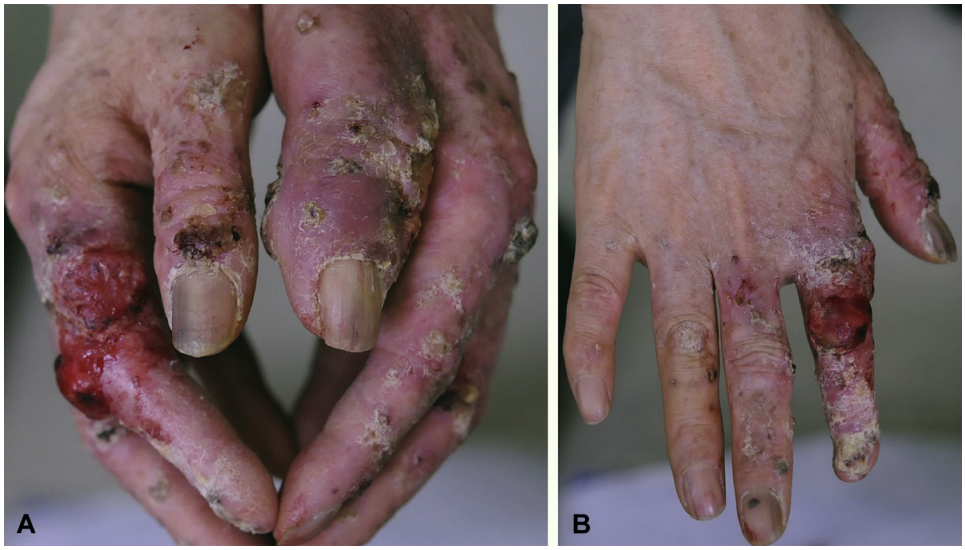

Fig 1. Carcinosarcoma. **A** and **B**, A 5-cm ulcerated and verrucous exophytic tumor on the left thumb and a 4-cm purplish tumor with ulcerated center on the right index finger were observed with multiple scattered verrucous and crusted plaques on both hands.

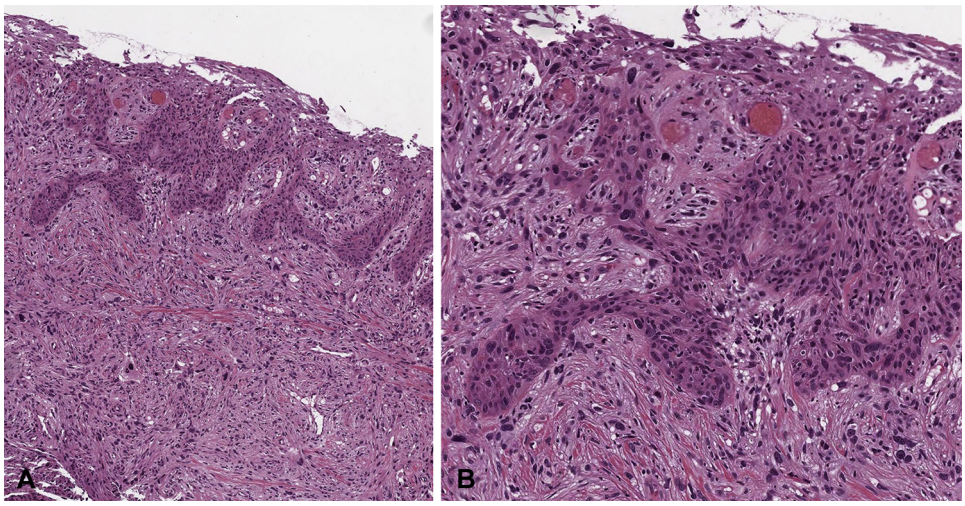

Fig 2. Biphasic tumor with malignant epithelial and mesenchymal components. **A** and **B**, The epithelial component was a squamous cell carcinoma consisting of atypical cells. The mesenchymal component showed atypical spindle cell proliferation, and some tumor cells showed abundant eosinophilic cytoplasm and bizarre nuclei. (**A** and **B**, Hematoxylin-eosin stain; original magnifications **A**, ×100; **B**, ×200.)

patient finally underwent left thumb and right index finger amputation and skin grafting.

DISCUSSION

CS is a biphasic tumor with distinct carcinomatous and sarcomatous features apparent with both light microscopy and IHC.[4] Variable terms including metaplastic carcinoma, sarcomatous carcinoma, and biphasic sarcomatoid carcinoma could be considered synonyms of CS.[4,5] Müller et al[4] proposed 3 diagnostic criteria for primary cutaneous CS: (1) a bimodal neoplasm consisting of both malignant epithelial and mesenchymal components confirmed by histological examination and IHC (2) exclusion of distant metastasis and true collision neoplasm defined as coexistence of 2 different tumors in the same specimen, and (3) a solid coherent neoplasm with exclusion of reactive stromal changes.

PCCS can have basal cell carcinoma, SCC, or adnexal carcinoma as its epithelial component.[4-6] The epithelial component has shown positivity for cytokeratin markers including CK 5/6, MNF116,

34βE12, and AE1/AE3.[4-7] In PCCS with basaloid epithelial component (basal cell carcinosarcomas), markers such as BerEP4 and Bcl-2 have also shown positivity.[6] The mesenchymal part can be composed of osteosarcoma, neurogenic sarcoma, rhabdomyosarcoma, chondrosarcoma, and malignant fibrous histiocytoma.[4-6] The mesenchymal component has been reported to be positive for vimentin, SMA, desmin, and neuron-specific enolase according to mesenchymal differentiation.[4-6] It has been reported that p53 is coexpressed by both epithelial and mesenchymal components.[6] Recently, p63 was proposed to be a useful adjunct tool for the diagnosis of PCCS.[4,6]

As differential diagnoses, spindle cell neoplasm (including spindle cell squamous cell carcinoma [SpSCC], spindle cell melanoma [SCM], and atypical fibroxanthoma) and biphasic neoplasms (including biphasic synovial sarcoma and malignant mixed tumor) should be considered. The 3 diagnostic criteria mentioned above and results of IHC are helpful for diagnosis of PCCS.

SpSCC consists of malignant spindle cells with variable components of invasive SCC. If spindle cells are not clearly segregated to epithelial or mesenchymal component with expression of cytokeratin with or without p63, they are confirmed as SpSCC rather than CS.[5] Up to 40% of SpSCC expresses vimentin. Therefore, it is difficult to use vimentin in CS for diagnostic purposes.[4] However, vimentin can provide additional information in differentiating the 2 neoplastic components of CS.[4] To distinguish between SCM and CS, S100 and SOX10 are the best markers because Melan-A and HMB-45 are mostly negative in SCM.[8] Atypical fibroxanthoma has no epithelial component. Therefore, it can be distinguished from CS by showing negativity for high-molecular-weight cytokeratin and p63. Biphasic synovial sarcoma consists of cord, nest, or gland-shaped epithelial cells and spindle cells with expression of TLE1 or EMA in both cell types.[5,9] Malignant mixed tumor shows a carcinoma component, whereas the stromal component shows benign myxoid or chondroid proliferation.[5]

C-arm fluoroscopy is a device using x-rays to obtain real-time moving images of internal structures. This method has been used for several decades in orthopedic surgery to guide fracture reduction and placement of implants. Surgeons are at high risk of radiation-induced complications because of their proximity to the exposure area.[10] Commonly recommended protective equipment include lead aprons and thyroid guards. When such equipment is properly worn, the amount of exposure to both wrists is found to be the highest among neck, chest, gonad, and wrists.[10] Lead gloves can reduce exposure dose to the hand. However, they are not widely used. In this case, the patient had used C-arm fluoroscopy for 2 decades without any special protective equipment for his hands. Such chronic radiation exposure was presumed to be a major cause of his disease.

This case report of PCCS developing after chronic C-arm radiation exposure is interesting. It highlights the importance of protection from occupational radiation exposure. Risk groups with long-term occupational radiation exposure should be aware of the possibility of skin cancer development. Exposure dose and duration should be minimized, and the use of protective equipment should be emphasized.

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