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Abstract

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SPUTUM CYTOLOGY OF A METASTATIC POSTRADIATION SARCOMA (MALIGNANT FIBROUS HISTIOCYTOMA)

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Abstract. A female patient who died of apparent postradiation sarcoma in the inguinal region after irradiating a metastatic squamous cell carcinoma of the same site was reported. For approximately 20 months, the patient had received a total of 6,600 and 9,600 Roentgen to the right para-aortic and inguinal areas, respectively. About 10 years later, she developed a sarcoma, namely a malignant fibrous histiocytoma. Sputum cytology demonstrated numerous giant cells with bizarre nuclei; subsequent chest films also presented apparent metastatic tumor shadows. The cellular characteristics and also rather low incidence of detection of nonepithelial malignant tumor by sputum cytology were briefly discussed, and ways of enhancing cytodiagnostic accuracy were proposed.

Key words : sputum cytology, postradiation sarcoma.

In man, a causal relationship between irradiation on the primary tumor and sarcoma induction can be established only in limited circumstances, the reason being in general extremely long, sometimes 10-20 years, time lapse between the two events. We have had an opportunity to follow a patient who died of apparent postradiation sarcoma in the inguinal region after irradiating a metastatic squamous cell carcinoma of the same site approximately 10 years earlier. Prior to the patient's death, sputum cytology together with chest x-ray films confirmed metastatic sarcoma. To our knowledge, the sputum cytology especially of non-epithelial malignant tumors has been little reported.

CASE PRESENTATION

This is a female patient born in March 1939. When she was seven years old, she injured the right sole in a traffic accident. Because of increasing cracks around the wound, in 1966, at the age of 27, a local biopsy was made which confirmed squamous cell carcinoma (Fig. 1). She was then hospitalized to the Department of Surgery (First Clinic), Okayama University Hospital. A right inguinal lymph node was found also metastatic from it. During the period from September 1966 to May 1968, she was admitted to the Department three times and given radiotherapy on the right para-aortic and inguinal areas, 6,600 and 9,600 Roentgen, respectively.

For about 10 years, she remained reasonably healthy. Around August 1977,

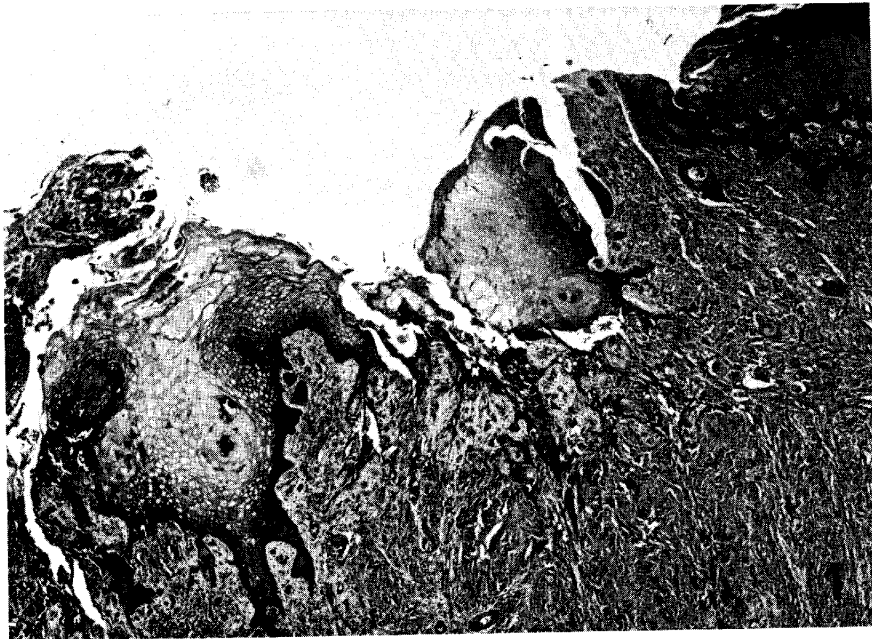


Fig. 1. Squamous cell carcinoma at the right heel showing a well differentiated, keratinizing type. HE, $\times 20$.

Fig. 2. Excised tumor at the right inguinal region by the fourth admission.

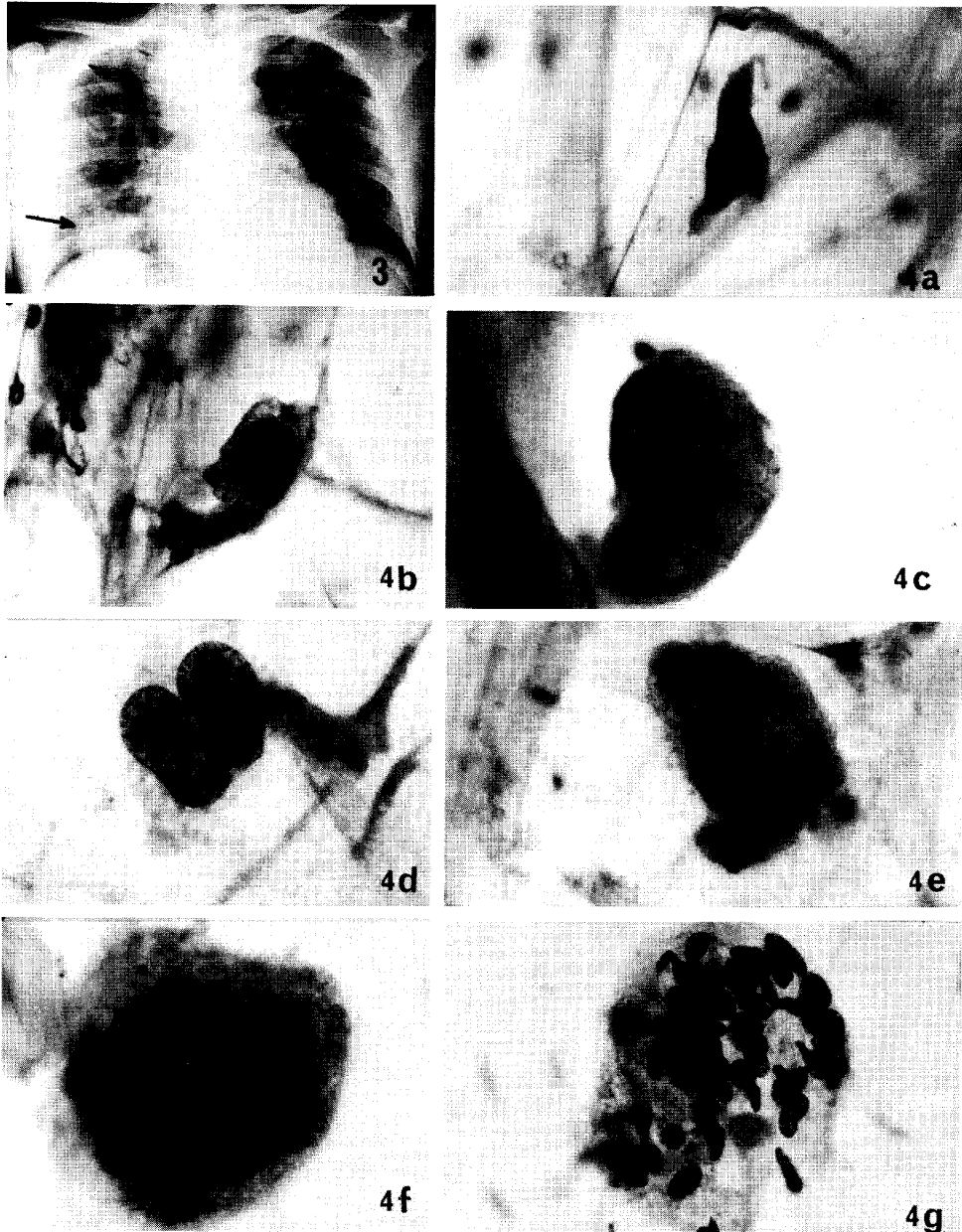
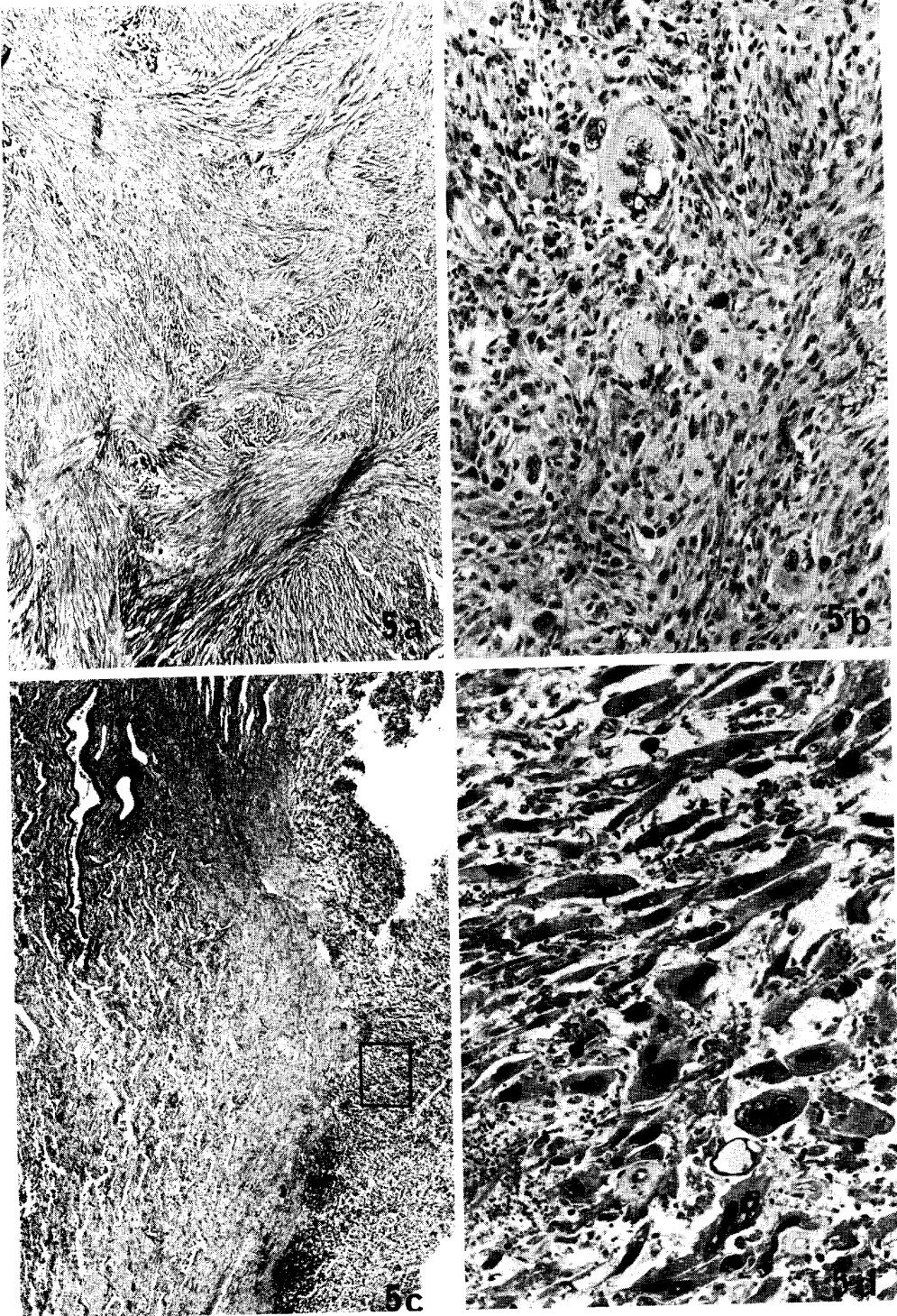


Fig. 3. Chest film showing apparent metastatic tumor shadows (arrows).

Fig. 4. Sputum cytology. Papanicolaou, $\times 400$. 4-a. A mononuclear, short spindle-shaped cell. 4-b. A tadpole-shaped cell having round nucleus with irregular nuclear membrane. 4-c. An ovoid cell with giant mononucleus. 4-d. A binucleated cell with coarse chromatin. 4-e. A binucleated cell consisting of two indented nuclei. 4-f. A multinucleated, bizarre giant cell. 4-g. A multinucleated giant histiocyte.



at the age of 38, she noticed a swelling in the inguinal area and was hospitalized. By surgery, a tumor adhered to the Mm. pectineus and adductor longus, measured about 12×25cm, and extended further towards the retroperitoneum. Following a partial dissection of the tumor (Fig. 2) she was discharged, but admitted in the end of January 1978 for the fifth time due to the local recurrence. In the middle of March, a chest film disclosed spherical tumor shadows (Fig. 3). In spite of combined chemo-, immuno- and radiotherapies, severe cough with blood-stained sputa developed and the patient died in the middle of July 1978; approximately one year since she noticed a huge tumor in the inguinal area, and 12 years from the onset of squamous cell carcinoma and its irradiation.

As to sputum cytology, the first specimen received in the middle of March 1978 showed numerous giant cells with bizarre nuclei, and cells with round to oval nucleus which was rich in chromatin (Fig. 4a - g); Fig. 4-g indicated an apparently benign multinucleated giant histiocyte. These were rather dispersed without prominent cellular cohesion; no fibroblast-like cells with elongated cytoplasm were present. Metastasis to the lung was highly suspected. A chest film was immediately taken which showed apparently metastatic tumor shadows as described before. Following this, sputa were sent to this laboratory altogether 12 times; among these, cells ranging from normal to abnormal morphology, *i.e.*, classes I and II, were found 11 times including saliva only in six occasions, and cells with class III once. Specimens consisting of saliva only were based on lack of complete expectoration, apparently due to gradually deteriorating physical condition of the patient.

Histopathologically, the excised tumor (Fig. 2) consisted of elongated spindle-shaped cells which were interlaced forming what looked like a storiform pattern (Fig. 5a), and of giant cells with various morphology (Fig. 5b). These two features militated against a fibrosarcoma and were more characteristic of a malignant fibrous histiocytoma, *i.e.*, a tumor derived from tissue histiocytes acting as facultative fibroblasts. Metastatic nodules in the lung obtained by necropsy appeared similar to the above findings showing conspicuous pleomorphism of tumor cells, although cellular cohesion became in general loose probably because of post-mortem artefact (Figs. 5c & 5d).

DISCUSSION

Cahan *et al.* (1) originally defined sarcoma arising in irradiated bone as follows: 1) nonmalignant nature of the initial bone condition; 2) sarcoma induced corresponding to the irradiated site; 3) a latent period of longer than five years

Fig. 5. Tumor pathology. 5-a. Interlacing spindle-shaped cells showing a storiform pattern. Silver, ×20. 5-b. Numerous bizarre giant cells with various morphology. HE, ×400. 5-c. A metastatic nodule in the lung. HE, ×20. 5-d. Close-up view of the boxed area in Fig. 5c. HE, ×400.

between the time of irradiation and tumor induction; and 4) development of sarcoma proved histologically. Concerning the criterion 1, the metastatic squamous cell carcinoma in the inguinal area was histologically similar to the original squamous cell carcinoma in the sole as shown in Fig. 1. Our case does unquestionably fulfil the criteria 2, 3 and 4. There have been several reports concerning radiation-induced fibrosarcoma (2) or malignant fibrous histiocytoma (3). Light and electron microscopic findings of the present case were most characteristic of a malignant fibrous histiocytoma.

As to cytological characteristics of nonepithelial malignant tumors, Yamada *et al.* (4 - 6) mentioned the presence of 1) freely separated cells, 2) cell morphology consisting of smooth, thin nuclear membrane, fine granular chromatin, prominent round nucleolus and basophilic cytoplasm, and 3) multinucleated or mononuclear giant cells. Hajdu and Hajdu (7) emphasized the concomitant presence of 1) round or oval cells with medium mononucleus, giant mononucleus and binuclei, 2) multinucleated, bizarre giant cells, and 3) mononuclear, short spindle cells. Cellular features of the present case were consistent with these findings. Some of cells, however, had rather coarse granular chromatin that almost effaced the presence of nucleoli.

Koss (8) stated that "approximately 50 per cent of metastatic tumor to the lung may be diagnosed cytologically". He referred this observation mainly to epithelial tumors. As to nonepithelial tumors primarily of the lung, Sato (9) collected a total of 70 cases reported in Japan; out of these, only two were diagnosed as sarcoma by sputum cytology. Regarding metastatic lung tumors, Sawada *et al.* (10) found positive sputum cytology in eight of 17 cases (47%). Only one of the eight cases proved to be a metastatic rhabdomyosarcoma; the remaining seven were epithelial. These data indicated a relatively low incidence of detection of nonepithelial tumor cells by sputum cytology. In fact, our case presented with definitely positive malignant cells (class V) only in the very first specimen followed by the cells ranging from classes I to III.

In order to enhance the accuracy of cytodiagnostics, it is our impression that a combination of direct smear with either of the followings, *i.e.*, three-day pooling of spontaneous sputa according to the Saccomanno's method, transbronchial brushing, TV brushing or transthoracic needle biopsy, is imperative in the future.

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