MALIGNANT ANGIOENDOTHELIOMA OF THE SKIN
— A Report of Three Cases Showing Lung Metastasis and Pneumothorax —

KEIJIRO KITAMURA and NOBUYA TAMURA

Department of Dermatology, School of Medicine, Keio University, Tokyo, Japan

(Received for publication December 28, 1978)

ABSTRACT

Three cases of malignant angioendothelioma of the Wilson Jones type were reported. Patients were all aged and died of spontaneous pneumothorax and bronchopneumonia associated with metastasis of the tumor to the lung.

Pneumothorax in older patients with malignant angioendothelioma is often overlooked. Therefore, the possible association of pneumothorax must be taken into consideration, when the patient with malignant angioendothelioma has respiratory complaints, such as slight dyspnea and coughing.

It is also suggested that malignant angioendothelioma of the skin tends to invade the surrounding normal skin or to develop from a multicentric germ and metastasize to the surface of the lung.

A relatively rare, and anaplastic vascular tumor was identified as malignant angioendothelioma (MAE), by Wilson Jones in 1964, which occurs over the upper part of the face and scalp of older individuals.

This tumor reveals definite clinical and histopathological features suggesting it as a distinctive entity.

In this paper we would like to present three cases of malignant angioendothelioma (Wilson Jones) of the scalp, face, and the inguino-abdominal skin, each died of pneumothorax and bronchopneumonia due to metastasis of the tumor to the lung.

REPORT OF CASES

Case 1.

A 77-year-old Japanese man was referred to our clinic in March 1970, be-
cause of small recurrent nodules on his head. Three years previously he had noticed some small non-tender nodules with an erythematous halo on the right side of his frontal area, which gradually spread onto his scalp. About one year later, a right preauricular lymph node enlargement was discovered. These skin lesions and lymph nodes were excited in October 1968.

The tumor, however, recurred on the scalp in August 1969, and gradually increased in size. He was treated with radiation therapy (Dermopan, total dose 11200R) from March to August in 1970, and was admitted to our hospital.

The lesion was removed completely in September 1970, but the similar nodules appeared again in 1971. These lesions slowly spread onto the entire part of the right side of the scalp, cheek and submandibular region despite three separate operations and radiotherapy (Linac, total dose 5000R).

In spite of repeated excisions, the tumor recurred shortly afterward and cervical lymph nodes on the right side enlarged and some eroded nodules developed over the scalp, right external auditory canal and cheek area.

On dermatological examinations, the lesions were found to consist of reddish-brown colored nodules with verrucous crust and surrounded by a diffuse purplish area (Fig. 1). Under these scales and crusts, erosions and an edematous atrophic skin with telangiectasis were revealed (Fig. 2). Bleeding from the site of the erosive lesions was often observed.

There were some soft purplish-red cystic tumors observed, mixed with these lesions. Otherwise, physical examinations were not remarkable and his past
history showed nothing particular.

**Laboratory Findings:**

Laboratory studies on admission to our hospital revealed as follows: hemoglobin: 11.2 g/dl; red blood cell count: \(414 \times 10^4/\text{cu mm}\); white blood cell count: \(8800/\text{cu mm}\) with a normal differential; platelet count: \(25.8 \times 10^4/\text{cu mm}\); erythrocyte sedimentation rate: 55 mm/hr; total serum protein: 5.4 gm/dl; serum albumin: 2.8 gm/dl; blood urea nitrogen: 39.2 mg/dl; serum creatinine: 1.9 mg/dl; serum uric acid: 4.9 mg/dl; fasting blood sugar: 82 mg/dl.

The following tests were within normal limits: serum GOT, GPT, LDH, CPK, alkaline phosphatase, bilirubin, cholesterol, Na, Cl, K, Ca, P and protein electrophoresis. STS was negative. The tuberculin skin test was positive. ECG showed incomplete right bundle branch block. Urine and stool examinations revealed no significant changes. Chest X-ray was also unremarkable on his first admission to our hospital.

**Clinical Course:**

In spite of the operations and radiation therapy, the lesions gradually spread to the right side of neck, the right cheek bone and the submandibular region. Enlargement of right auricular and cervical lymph nodes were also progressive.

In November, 1976, he complained of slight dyspnea and coughing. Chest roentgenograms revealed the pneumothorax of the right lung (Fig. 3). There was evidence of pleural effusion bilaterally, which was found to be hemorrhagic by pleurocentesis, and a diagnosis of bilateral haemothorax was made.

However, the drainage failed to regain a full expansion of the right lung. His condition deteriorated day by day, and he died of bronchopneumonia in
Histopathological Findings:

A biopsy specimen from the scalp revealed extensive proliferation of anaplastic endothelial cells extending from the upper corium down into the subcutaneous tissues.

In the superficial portion of the growth, there were many wide capillary spaces containing erythrocytes. These were lined by a single layer of anaplastic endothelial cells with irregularly shaped and hyperchromatic nuclei, often protruding into the vascular or slit-like lumina (Fig. 4).

In the deeper part of the growth, solid proliferation of endothelial cells with poorly defined vascular spaces formed a tumor nest which extended into the corium (Fig. 5). At the first glance, it seemed like reminiscent of an undifferentiated metastatic carcinoma of the skin.

A dense network of reticulum fibers was demonstrated around the sponge-like lumina and within the tumor cell complexes with silver impregnation (Fig. 6). There was no appreciable amount of PAS-reactive mucopolysaccharide.

Autopsy Findings:

The scalp was extensively infiltrated by the tumor, and this invasive lesion spread to the right side of neck. Furthermore, the tumor penetrated through subcutaneous soft tissues to the pharynx and the larynx.

Various-sized cystic tumors were found scattered in both lungs, especially in the surface areas. Metastasis was demonstrated in the cervical and preauricular swollen lymph nodes. There was focal bronchopneumonia in bilateral lungs.

Case 2.

A 83-year-old Japanese woman visited our hospital in March 1975, because of multiple purplish tumors with ulcer on her head. She had a 6-month history of dark-reddish skin tumors which rapidly spread over the parietal region of her head. Tumors were often tender. Hemorrhage occurred occasionally from these tumors, which increased rapidly in size. Before visiting our hospital, the tumors were removed by her family doctor in December 1974. However, they relapsed and enlarged forming ulcers with a thick crust.

The lesions consisted of various irregular-shaped, crusted firm tumors and soft cystic hemangioma-like tumors with a variation in color ranging from brownish-blue to dark-red, when she first visited our hospital. There was ulcers coated with a yellowish necrotic mass scattered among these lesions on the front parietal area of head (Fig. 7, 8).
Malignant Angioendothelioma of the Skin

Fig. 4 Many wide capillary spaces which are lined by a single layer of anaplastic endothelial cells. (HE stain, × 346, Case 1)

Fig. 5 Solid proliferation of endothelial cells with poorly defined vascular spaces. (He stain, × 346, Case 1)

Fig. 6 Silver impregnation. Note a dense network of reticulum fibers around the sponge-like lumina. (× 170, Case 1)
Involved lesions showed either colorless thickening of the skin or dusky purplish-blue infiltration.

There was no enlargement of cervical lymph nodes.

**Past History:**

The patient had a history of cerebral hemorrhage in August 1973.

**Laboratory Findings:**

Laboratory findings at the time of admission to our hospital in December 1974, revealed as follows: hemoglobin: 10.2 g/dl; red blood cell count: \(336 \times 10^4/\text{cu mm}\); white blood cell count: 6,000/cu mm with a normal differential; platelet count: \(34.7 \times 10^4/\text{cu mm}\); erythrocyte sedimentation rate: 25 mm/hr; total serum protein: 5.5 gm/dl; serum albumin: 3.2 gm/dl; blood urea nitrogen: 17.9 mg/dl; fasting blood sugar: 95 mg/dl.

The following tests were within normal limits: serum GOT, GPT, LDH, CPK, alkaline phosphatase, bilirubin, cholesterol, Na, Cl, K, Ca, P and protein electrophoresis. STS was negative. The tuberculin skin test was positive. ECG revealed supraventricular premature beats. Urine and stool examinations revealed no significant changes.

Chst X-ray on her admission showed no significant changes.

**Clinical Course:**

In spite of the radiation therapy (Linac and electron beam, total 15500R)
and the topical application of antiseptic agents, the tumor invaded the face and neck. In July 1975, she complained of moderate dyspnea with a slight cough.

Pneumothorax of the left lung was evidenced by a chest X-ray (Fig. 9). The left lung was treated with continuous drainage and regained a full expansion within about 14 days.

However, she developed pneumothorax of the right lung soon (Fig. 10). Furthermore the left pneumothorax recurred. She died of bilateral pneumothorax with bronchopnemonia in August 1975.

**Histopathological Findings:**

A biopsy specimen from the scalp in April 1975, showed that the growth was characterized by extensive proliferation of highly anaplastic endothelial cells extending from the upper corium down into the subcutaneous tissues (Fig. 11). These anaplastic endothelial cells were irregular and elongated. The cytoplasm was PAS-negative, and nucleus was spindle-shaped, and hyperchromatic. Sponge-like or slit-like irregular anastomosing spaces were characteristically observed in a section of excised tumor. These spaces were lined by a single layer of the cells (Fig. 12).
Extensive proliferation of endothelial cells arranged along the collagen bundles was also observed in other parts of the specimens (Fig. 12).

**Autopsy Findings:**

The scalp, face and the right side of the neck were extensively infiltrated by the tumor.

Several small metastatic violaceous tumors were scattered over the surface of both lungs and considered to be the cause of the collapse of the lungs and bilateral pneumothorax (left lung 275 gm, right lung 260 gm).

Reddish-yellow pleural fluid was found bilaterally (left side 300 ml, right side 450 ml).

Case 3.

A 78-year-old Japanese woman, who had noticed a lesion on her right inguino-abdominal skin for 2 years, visited our hospital in April 1974.

She stated that a nodule of a purplish-red color about 2 cm in diameter was found, which gradually enlarged and increased in number. The lesion was excised by her family doctor, however, a recurrence of the tumor occurred on the skin surrounding the scar of the operation approximately one year thereafter.

Afterwards, in spite of repeated operations and radiation therapy, the tumor recurred and gradually distended, and the similar tumor was discovered on the
occipital region and the right axillary and chest area in October 1973.

On dermatological examinations, the lesions were found to consist of numerous purplish-red colored, various-sized cystic nodules which were partially eroded and crusted on the occipital region, the right inguino-abdominal skin (Fig. 13) and the axillary region.

She was in good health, but she had a history of mild diabetes of 4 to 5 years.

Laboratory Findings:

Laboratory studies on first visit to our hospital revealed as follows: hemoglobin: 12.9 g/dl; red blood cell count: $412 \times 10^4$/cu mm; white blood cell count: $12000$/cu mm with a normal differential; platelet count: $18.9 \times 10^4$/cu mm; erythrocyte sedimentation rate: 34 mm/hr; total serum protein: 6.2 gm/dl; serum albumin: 3.72 gm/dl; blood urea nitrogen: 12.1 mg/dl; serum creatinine: 0.8 mg/dl; serum uric acid: 2.2 mg/dl; fasting blood sugar: 110 mg/dl.

The following tests were within normal limits: serum GOT, GPT, LDH, CPK, alkaline phosphatase, bilirubin, cholesterol, Na, Cl, K, Ca, P and electrophoresis for serum protein.

STS was negative. ECG showed complete right bundle branch block. Urine and stool examinations showed no significant indication except for positive urine sugar.

Chest X-ray also showed nothing particular.

Clinical Course:

In spite of the operation, chemotherapy (Bleomycin, Cyclophosphamide)
and immunotherapy (BCG), the lesions were found spreading and suddenly she complained of moderate dyspnea and coughing on March 12, 1975.

Pneumothorax of the left lung was evidenced by a chest X-ray and was treated with continuous suction. However, the right lung subsequently developed pneumothorax. Her condition deteriorated day by day, and she died of bilateral pneumothorax with bronchopneumonia in May 1975.

**Histopathological Findings:**

A biopsy specimen from the abdominal lesions showed that the growth revealed almost the same findings as those found in the other two cases and she was diagnosed as malignant angioendothelioma.

**Autopsy Findings:**

The skin covering the right inguino-abdominal region, occipital region and the right side of the chest wall and axilla was extensively infiltrated and ulcerated by the tumors.

Many small metastatic violaceous tumors were scattered over the surface of both lungs, which were thought to have caused the collapse of the lungs and bilateral pneumothorax.

The vertebra, ribs and the skull bone were also found invaded by these tumor cells.

**COMMENT**

In 1964, Wilson Jones described nine patients with skin tumors which occurred predominantly over the upper part of the face and scalp of older individuals and he proposed the new clinico-pathological entity under the title of "malignant angioendothelioma of the skin."

He reviewed the literature on this subject and found seven out of nine died and autopsy was performed in three cases revealing the internal metastasis.

He reported that the characteristic feature of these tumors was extensive infiltration into the skin before spreading to deeper structures or metastasizing to the internal organs. He stated that any treatment was not effective to prevent the progression of the disease.

The average age in nine cases was 77 years (ranging from 60 to 92 years) at the onset of the disease.

In seven patients who died of this condition, the average duration of the tumors was 20 months (ranging from 6 months to 5.5 years).

In our Case 3, the primary lesion of the tumor was initially found on the
inguino-abdominal region. However, numerous violaceous tumors were discovered on the occipital region during the course of treatment. Therefore, it is conceivable that the primary lesion at the occipital region, which was covered with hairs, was rather small at the beginning so that we had failed to find it until metastasis to the lung was demonstrated. If so, this case is also compatible with the description made by Wilson Jones. Therefore it is thought that all of our three cases could be diagnosed clinically and histopathologically as MAE of the skin.

The first clinical manifestation of our series was an erythematous indurated nodule on the head that spread to the face, neck and occasionally to other regions. Later the lesion was complicated by areas of purpura and superficial erosions. Based on our clinical observations that in spite of repeated operations, recurrences occurred near the operation scar and the lesion spread outside the eradicated part, it is suggested that perhaps when the primary lesion was found at the beginning, the invasion of tumor had already been progressing into the surrounding areas. Such area may be often looked like normal on the surface, and it is possible that the tumor might have developed multicentrically.

Internal metastasis of MAE sometimes occurred. Wilson Jones\(^1\) reported three cases who died of internal metastasis. Metastasis to the lung was found in two of the three necropsied cases. In addition, metastasis was also observed in the small intestine, liver, spleen, skull vault and orbit.

Wilson Jones attempted to re-evaluate the 42 cases of MAE and stated that it would be better to call this disease as “angiosarcoma of face and scalp,” since he experienced difficulty in identifying whether the location of histogenesis was in the vascular endothelium or the lymphatic endothelium.

In 1958 and 1959, Suurmond\(^3\) and Garrett\(^4\) reported similar cases, in which they noticed metastasis to the lung and liver.

Garrett\(^4\) showed a case with lung collapse due to metastasis to the lung.

In 1966, six cases of angiosarcoma of the scalp were reported by Reed \textit{et al.}\(^5\) These cases were extremely similar to the cases by Wilson Jones', but internal metastasis was not described in this article.

Girard \textit{et al.}\(^6\) reviewed twenty-eight cases of cutaneous angiosarcoma, in four cases of which, internal metastasis was revealed. They suggested that the organs, where metastasis occurred most frequently, were the regional lymph nodes, lungs and the heart.

Recently, Mehregan \textit{et al.}\(^7\) reported six cases of MAE. They showed two cases who died of the dissemination of cutaneous lesions and internal metastasis. They stated that the metastasis to the lungs and other organs resulted in the death of the patients within a period ranging from 3 months to 2 years.
Our three cases died of pneumothorax and bronchopneumonia which were caused by metastasis to the lung.

Similar cases were reported by many authors\textsuperscript{8-11} in Japan. The patients' complaints of slight dyspnoe and coughing suggested us the possible development of pneumothorax, which is easily demonstrated by the plane chest X-ray (Fig. 3, 9, 10).

The pneumothorax in these older patients is sometimes overlooked, therefore we must be very careful for the respiratory complaints such as slight dyspnea and coughing.

It should be recalled that the plane chest X-ray examination is very important in these cases.

REFERENCES