Diffuse alveolar hemorrhage due to metastatic angiosarcoma of the lung: A case report

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Abstract. Angiosarcoma is a rare, heterogeneous malignant tumor that derives from endothelial cells, and it has aggressive characteristics with a marked tendency for distant metastasis. Diffuse alveolar hemorrhage (DAH) is a catastrophic clinical syndrome, however, it is rare as the presentation of pulmonary angiosarcoma. To increase awareness with regard to angiosarcoma and DAH, the current study presents a case of angiosarcoma that originated from the subcutaneous soft tissue of the mastoid process, but was subject to a delayed diagnosis and rapid invasion into the brain and lung. The metastatic angiosarcoma of the lung presented with DAH as the initial manifestation. The pathological examination of a biopsy of the subcutaneous mass and pulmonary lesions confirmed the diagnosis of angiosarcoma. The patient succumbed to respiratory failure at 1 month post-diagnosis.

Introduction

Angiosarcoma is a rare malignant tumor with an extremely poor prognosis, and metastasis occurs in ~50% cases, always ending with mortality within a year (1). Although it has been detected in all regions of the body, lung involvement is the most common site of metastasis (2,3). Diffuse alveolar hemorrhage (DAH) is a clinicopathological syndrome that results from a variety of conditions and is considered as a life-threatening event, however, it is rare as the presentation of pulmonary angiosarcoma (4). The current study presents a case of angiosarcoma that originated from the subcutaneous soft tissue of the mastoid process, but was subject to a delayed diagnosis and rapid invasion into the brain and lung. The metastatic angiosarcoma of the lung presented with DAH as the initial manifestation. The pathological examination of a biopsy of the subcutaneous mass and pulmonary lesions confirmed the diagnosis of angiosarcoma.

Written informed consent for the present report was obtained from the patient's family.

Case report

In March 2012, a 66-year-old man was referred to the Inpatient Respiratory Department of the First Affiliated Hospital, School of Medicine, Zhejiang University, with coughing and hemoptysis that had persisted for 20 days. The patient also complained of dyspnea on exertion and a mild headache. In February 2012, the patient had been diagnosed with a pulmonary infection and had been treated with antibiotics and hemostatic agents in a local clinic for 1 week, but the symptoms were unimproved. No fever, night sweats or weight loss were noted. The patient was a heavy smoker who had smoked 2 packs of cigarettes daily for 40 years. In addition, a head trauma had been suffered 2 years previously and a protuberance in the left mastoid process had been diagnosed as a hematoma. The protuberance had been slowly growing for 1 year. The patient had no history of chronic lymphedema, no known environmental exposure, including radiation, thorium dioxide, vinyl chloride and arsenic exposure, and no exposure to tuberculosis.

A physical examination revealed moist rales in the lung bases, and a large (almost 4x3-cm), hard lump with fixation in the subcutaneous soft tissue below the left mastoid process was noticed. The neurological examination was negative. Upon hemocytological examination, mild anemia was detected, with a hemoglobin level of 9.5 g/dl (normal range, 11.3-15.1 g/dl). Other blood tests, including liver and kidney function, antinuclear antibodies, thyroid hormone, immunoglobulin and complement, tumor markers, bleeding and clotting time, were all within the normal ranges. Anti-glomerular basement membrane and antineutrophil cytoplasmic antibodies, and a galactomannan test for *Aspergillus* were negative. No tubercle bacillus or fungi were found in the sputum. Electrocardiogram and abdominal ultrasonography results were normal. The patient also underwent chest and brain computed tomography (CT). Multiple low-density nodules surrounded by a wide range of ground-glass-like effusion were identified in the bilateral lungs

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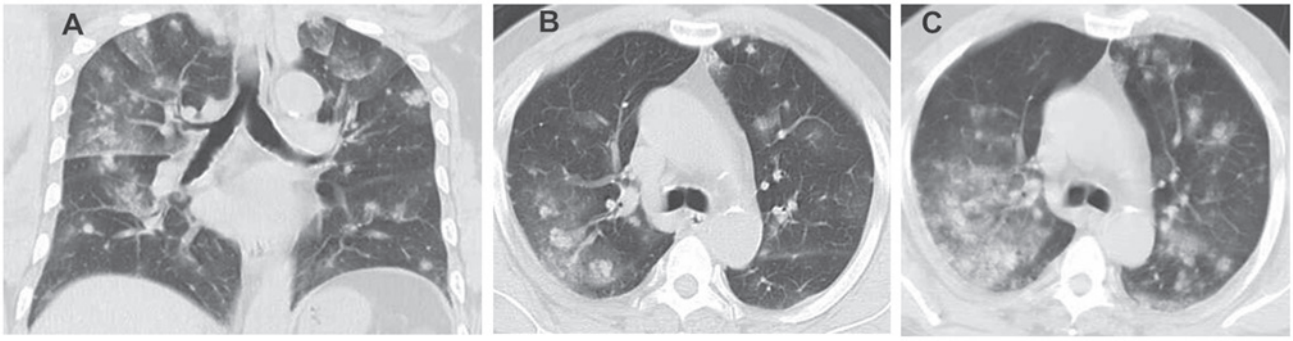

Figure 1. Chest CT. (A) Posteroanterior CT showing spotted or patchy shadows with obscure margins in the bilateral lung field, and no mediastinal lymph node enlargement. (B) Axial CT showing multiple low density nodules surrounded by a wide range of ground-glass-like effusions in the bilateral lung field. (C) Axial CT rechecked after 2 weeks showing more nodules with ground-glass-like shadows in extensive lung fields, indicating the rapid aggrevation of the lesions compared with (A) and (B). CT, computed tomography.

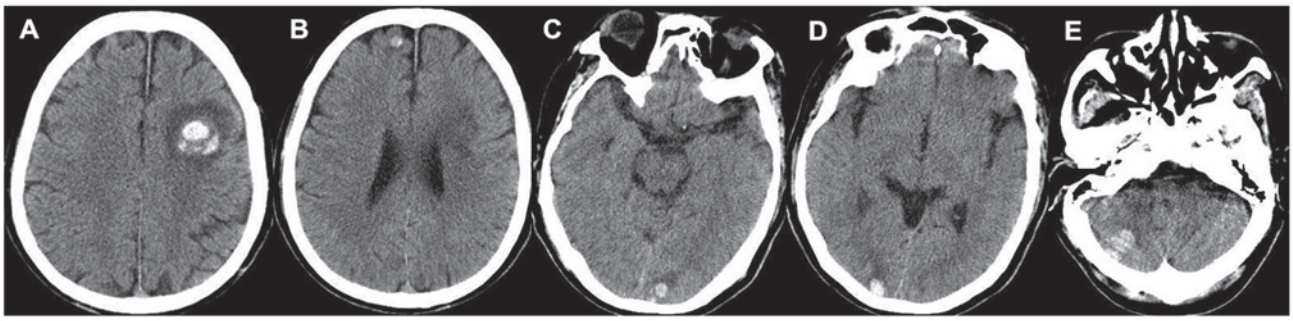

Figure 2. Brain CT. Axial CT showing multifocal intracranial lesions with hyperdensity masses and perilesional edema in (A) the left parietal lobe, (B) the right frontal lobe, (C and D) the bilateral occipital lobes and (E) the right cerebellum.

(Fig. 1A and B). Multifocal invasion and cystic lesions with perilesional edema were detected in the brain (Fig. 2); however, the brain CT was negative 1 year previously, in January 2011. Single photon emission CT of the bone was negative.

Based on the symptoms and imaging findings, a possible diagnosis of intracranial and pulmonary metastasis was suspected. To form a definitive diagnosis and determine nature of the primary lesion, a lung biopsy was performed using CT-guided percutaneous fine-needle aspiration. A biopsy of the subcutaneous soft tissue below the left mastoid process was also performed by ultrasound-guided puncture. Histological examination of both biopsy samples revealed atypical round or spindle-shaped cells arranged with a fascicular pattern, and consisting of focal luminal differentiation, necrosis and hemosiderin pigmentation. Immunohistochemical staining revealed that the tumor cells were positive for vascular antigens, including cluster of differentiation (CD) 31 and CD34, while being negative for cytokeratin and thyroid transcription factor-1. The definitive diagnosis was confirmed as a primary epithelioid angiosarcoma of the subcutaneous soft tissue, with pulmonary and intracranial metastases.

Due to poor general fitness, the patient was not a candidate for chemotherapy and was therefore prescribed with methylprednisolone (40 mg daily for 2 weeks) and aminomethylbenzoic acid (400 mg daily for 1 week) for hemostasis, and glycerol-fructose (500 ml daily for 2 weeks) for brain edema. The patient rapidly deteriorated, with dyspnea and hemoptysis. A reexamination of the hemoglobin level showed a decrease to 4 g/dl and a repeat chest CT scan showed more nodules with ground-glass-like shadows had appeared in extensive lung fields (Fig. 1C). Based on the characteristic progress of the manifestations, the patient was diagnosed with DAH. The patient finally succumbed to respiratory failure 1 month after the definitive diagnosis.

Discussion

Angiosarcoma is a rare and aggressive malignant vascular tumor that originates from endothelial cells, accounting for only 1-2% of all soft-tissue sarcomas (2,5). The tumor can occur in any region of the body, and a wide variety of anatomical locations have been described for this malignancy (6). In the clinic, angiosarcoma tends to exhibit local recurrence and distant metastasis, and the overall prognosis is poor (5,6).

Angiosarcoma is associated with aggressive clinical behavior, and its manifestations vary depending on the anatomical location (7). Patients with angiosarcoma usually present with metastatic disease at the time of diagnosis, and the lung is the most common site of metastatic involvement, followed by the liver, cervical lymph nodes, spleen, and rarely by the heart and brain (3). The patient in the present study presented with coughing and hemoptysis as the first symptom, but rapidly deteriorated, exhibiting progressive anemia and dyspnea. On the follow-up examination chest CT scan, spotted or patchy shadows with obscure margins were observed in the peripheral sides of the bilateral lung fields, which were rapidly

aggravated over a course of 2 weeks. All the presenting symptoms of this case are included in the known characteristics of DAH. DAH is a clinicopathological syndrome describing the accumulation of intra-alveolar red blood cells originating from the alveolar capillaries, and it is recognized by the clinical constellation of symptoms consisting of hemoptysis, anemia, diffuse radiographic pulmonary infiltrates and hypoxemic respiratory failure (4). A number of diseases can cause DAH, including Wegener's granulomatosis, Goodpasture's syndrome, microscopic polyangiitis, antiphospholipid antibody syndrome, connective tissue disorders, infectious or toxic disorders, and neoplastic diseases (8). Neoplastic diseases are not generally considered in the differential diagnosis of DAH and it is rare as the manifestation of angiosarcoma (9). In the present study, the diverse etiologies were ruled out through auxiliary examinations. The chest CT scan revealed nodules surrounded by ground-glass opacity, indicating lung metastasis with peripheral hemorrhage, and the pathological examination confirmed angiosarcoma. As DAH is a catastrophic clinical syndrome causing respiratory failure, vigilance should be maintained with regard to noting the possible etiology of DAH due to metastatic angiosarcoma of the lung, and a differential diagnosis of DAH should be established.

Angiosarcoma of the scalp has a predilection for pulmonary metastasis (10), and it appears to be a naturally privileged barrier that hinders local spread and resultant seeding in the cranial cavity, thus angiosarcoma metastasizing to the brain is relatively rare (11,12). In the present study, metastases of the lung and brain occurred at the time of diagnosis. The lesions of the lung developed progressively and led to respiratory failure. However the brain metastasis was only slowly aggravated, which caused a mild headache, and was detected with multiple mass lesions on brain CT.

Although angiosarcoma has a number of unknown etiological sources, trauma, and exposure to polyvinyl chloride, thorium dioxide and radiation have been suggested in its etiology (13). The most common sites of involvement are cutaneous, and the malignancy occurs most frequently in the scalp and facial skin of elderly men (3). Angiosarcoma arising in the skin or subcutaneous soft tissues may typically appear as multinodular hemorrhagic masses, which tend to be overlooked and delay the diagnosis of angiosarcoma (14). In the present study, the patient had experienced a previous head trauma and presented with a hematoma of the left mastoid process. After a delay, the pathological analysis confirmed the diagnosis of a primary angiosarcoma. As early diagnosis is the key for a better clinical outcome in angiosarcoma, it is suggested that the site of trauma in the skin should be followed up by observing the changes to the lesion in elderly individuals, and that a biopsy is necessary to establish a definitive diagnosis.

In conclusion, the present case demonstrates that angiosarcoma has aggressive characteristics, with a marked tendency for distant metastasis, and that pulmonary metastasis may present with DAH as the initial manifestation. Pulmonary angiosarcoma should be considered as an important differential diagnosis of DAH and the requirement for a systematic approach for the early recognition of angiosarcoma should be emphasized.

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