Clinical Case Report

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A rare case of angiosarcoma with skull masses and erythropenia and thrombocytopenia

A case report and review of literature

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Abstract

Rationale: Primary splenic angiosarcoma (PSA) is a rare, fatal neoplasm originating from sinusoidal vascular endothelial cells, and usually metastasizes and almost always has a poor prognosis. Surgical excision is the main treatment of this highly malignant disease.

Patient concerns: We reported a special case of a 68-year-old female who had a 6-month history of scalp masses.

Diagnosis: The patient was found to have 2 skull masses on computed tomography (CT). Laboratory findings revealed erythropenia and thrombocytopenia. Enhanced abdomen magnetic resonance imaging (MRI) showed multiple masses in liver and spleen. The pathological result of the skull masses was revealed to be metastatic angiosarcoma.

Interventions: The patient underwent surgical excision of skull masses, and no subsequent radiotherapy or chemotherapy was done.

Outcomes: The patient died due to dyscrasia at August 12, 2015, with a survival of nearly 1 month.

Lessons: We highlight the importance for clinicians to be aware of this rare neoplasm, and to consider it in the differential diagnosis when encountering a skull mass. Early confirmation and treatment may improve the prognosis.

Abbreviations: CT = computed tomography, Hb = hemoglobin, MRI = magnetic resonance imaging, PSA = primary splenic angiosarcoma, RBC = red blood cell.

Keywords: erythropenia, metastasis, pathological manifestation, primary splenic angiosarcoma, skull mass, thrombocytopenia

1. Introduction

Soft tissue sarcoma is a class of uncommon malignant tumors, accounting for <1% of all cancers. Angiosarcoma is a malignant vascular tumor which accounts for about 2% in the whole soft tissue sarcomas. It may arise at any region of body, while 60% of which happens in cutis or superficial soft tissue. It appears to be very aggressive and inclined to recrudesce locally and migrate to other body regions although given active treatments.[1] Due to multifocality and subtle pervasion, total excision is scarcely possible, it has poor prognosis and the 5-year survival rate is 10% to 35% according to literature.[2]

PSA is a rare, highly malignant tumor originating from splenic vascular endothelial cells and mesenchymal cells underlining the splenic sinusoids.[3] Only 200 cases have been reported up to date. It has high rate of regional and distant metastasis and local recurrence and is therefore often fatal. PSA should be taken into consideration for any patient suffering from unexplained anemia and splenomegaly.

We presented the case of a 68-year-old female with a 6-month history of skull masses. PSA involving skull and accompanied with erythropenia and thrombocytopenia was diagnosed, and with multiple metastasis to liver and lungs. She died due to multiple organs failure nearly 1 month after operation.

2. Ethical review

This case report was approved by the clinical ethics committee of the Second Affiliated Hospital of Zhejiang University School of Medicine and the Fourth Affiliated Hospital of Zhejiang University School of Medicine.

3. Case report

A 68-year-old female was admitted to the Department of Neurosurgery of the Fourth Affiliated Hospital of Zhejiang

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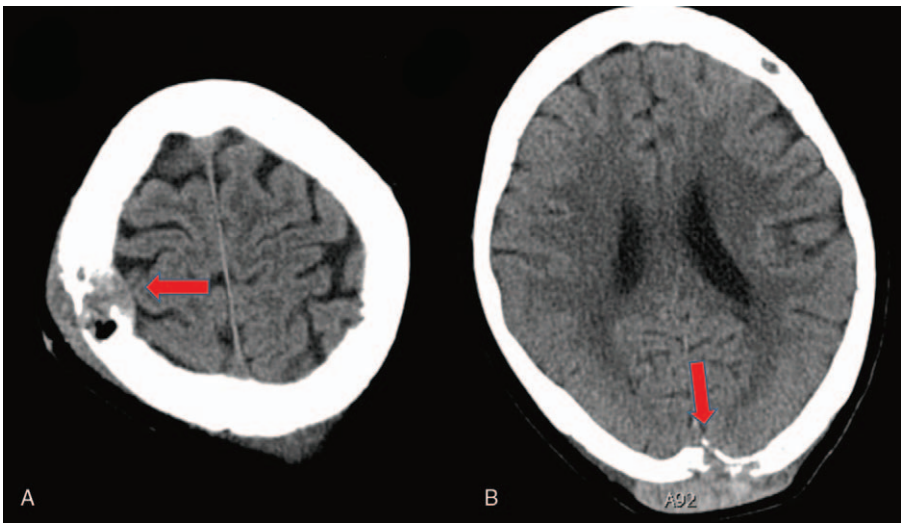

Figure 1. (A, B) Unenhanced head CT revealed diffuse skull destruction, decreased bone density, especially at right parietal and posterior area, soft tissue mass, and intruded skull.

University School of Medicine on July 6, 2015 with a 6-month history of scalp masses. Her physical examination result showed that 2 masses without ulcers or redness were noted in the right parietal area measuring 3.0 × 4.0 cm and posterior area measuring 4.0 × 5.0 cm, respectively. Tenderness was found but no palpable superficial lymph nodes. She also looked pale with black stool, and had insomnia and anorexia. No neurological symptom and signs were found. Her past medical history included erythropenia, thrombocytopenia, and pulmonary infection diagnosed in the Department of Hematology of the First Affiliated Hospital of Zhejiang University School of Medicine. She received therapies of anti-infection, immunoglobulin injection, blood component transfusion, and then her condition had improved. The social, family and past surgical histories were noncontributory.

Laboratory findings at initial presentation revealed red blood cell (RBC) count was $1.41 \times 10^{12}\,L^{-1}$ (reference range, $3.8–5.1 \times 10^{12}\,L^{-1}$), hemoglobin (Hb) was 56 g/L (reference range, 115–150 g/L), and platelet count was $14 \times 10^{9}\,L^{-1}$ (reference range, $125–350 \times 10^{9}\,L^{-1}$). Tumor markers did not show any abnormity. A mild left-sided pleural effusion was shown in chest x-ray. According to case history, the patient had poor appetite and sleep and black stool since the illness had begun. Unenhanced CT scan of the head revealed diffused skull destruction, decreased bone density, especially at right parietal and posterior area, soft tissue mass, and intruded skull. The impression was possibly metastatic tumor (Fig. 1). Unenhanced chest CT revealed multiple dots, nodules, and slightly high-density lesions. Configuration of nodules differed, the boundary was not clear. No swelling lymph node was found, while the pleural was thickened (Fig. 2). MRI of the abdomen showed intrahepatic diffused nodules of diverse size, margin-clear lesions with low signal in T1WI, high signal in T2WI, and the signal was uneven. The spleen enlarged, and the similar signal could be found in the spleen. No swelling lymph node was noted (Fig. 3). Otherwise, multiple nodules with low signal in T1WI and high signal in T2WI were found in vertebral bodies and accessories, and ribs, remarkably enhanced. Possible diagnosis was metastatic tumor.

Surgical excision of the bigger lesion on the skull was performed on July 9, 2015 with local anesthesia. We made an arch scalp incision about 8-cm long above the tumor, and then

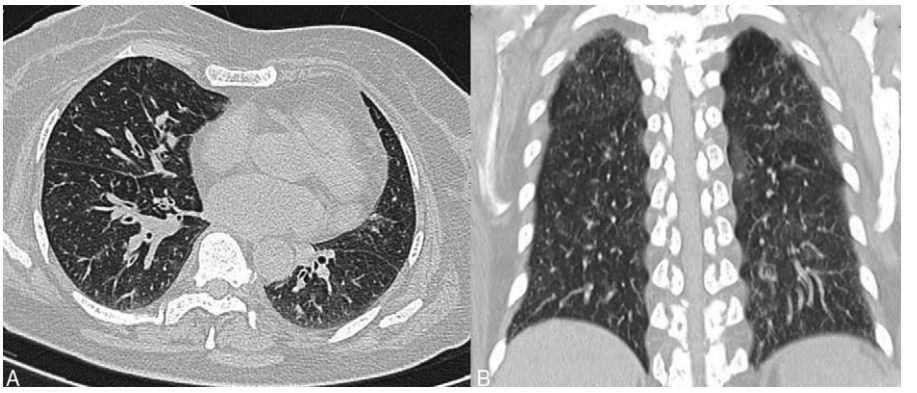

Figure 2. Unenhanced chest CT revealed multiple dots, nodules, and slightly high density lesions of diverse configuration, the boundary was not clear. No swelling lymph node, and pleural was thickened. Axial view (A) and coronal view (B).

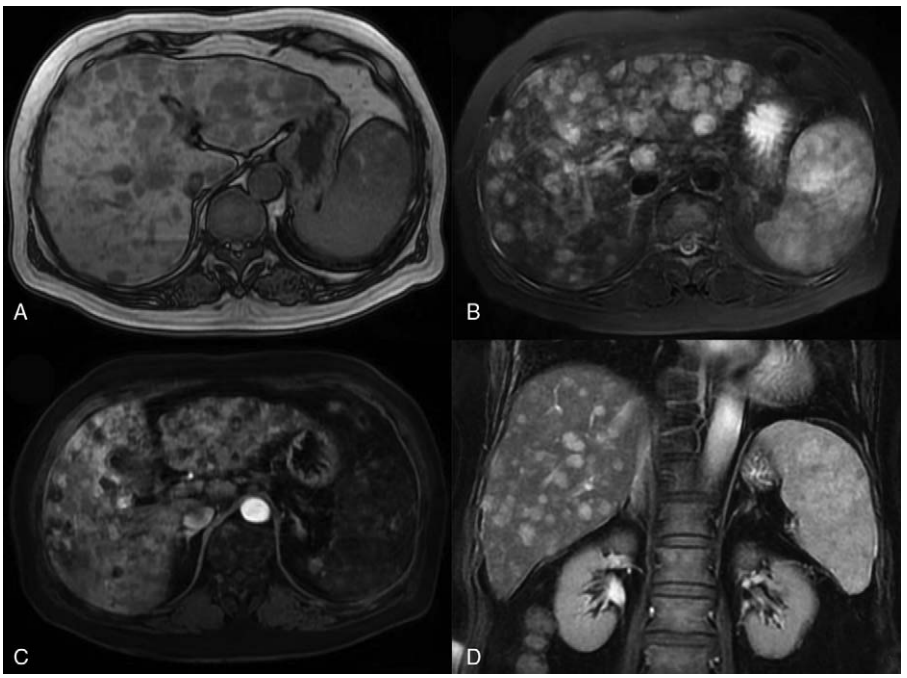

Figure 3. Abdomen MRI performed diffuse distribution of circular nodules in liver and spleen of diverse size, margin clear lesions with low signal in T1WI (A), high signal in T2WI (B), the spleen enlarged. No swelling lymph node. The signal was uneven and enhanced in axial view (C) and coronal view (D).

the tumor was exposed with gray-red appearance and the range was as broad as 5.0 × 5.0 cm. Complete resection was supposed to be achieved. The tumor was highly invasive and vascularized, while scalp, dura, and brain were unaffected. The texture of the lesion was a little hard and induced massive hemorrhage during operation. We used much medical bone wax pack on bone wound to control severe bleeding, and then close the wound.

Further pathological observation was made. In gross specimen, the tumor had complete capsule with the volume of 2 × 2 × 1 cm, and gray-red appearance with hemorrhage and necrosis. Spindle cells, atypia, nuclear fission, and necrosis could be observed microscopically (Fig. 4). Immunohistochemistry revealed ALK (−), Bcl-2(+), CD117(−), CD21(−), CD31(+), CD34(+), CD23 (−), CK(−), Vimentin(+), S-100(−), SMA(+), Ki-67(+30%), E-cadherin(−), and CD99(+), which confirmed a diagnosis of angiosarcoma (Fig. 5, only CD31 and CD34 were shown).

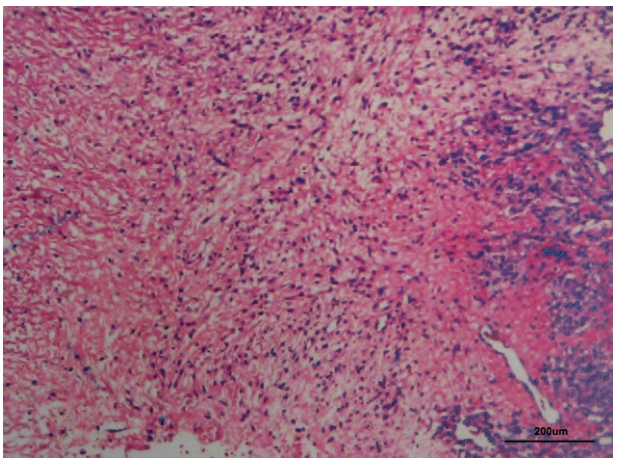

Figure 4. Microscopic image of the lesion (HE × 100), disorganized spindle cells, atypia, nuclear fission, and necrosis.

No subsequent radiotherapy or chemotherapy was done. The patient died due to dyscrasia at August 12, 2015, that is, with a survival of nearly 1 month.

4. Discussions

PSA is a rare, aggressive malignant tumor which generates from splenic sinusoidal vascular endothelial cells. First described by Langhans in 1879,[4] it is almost the most uncommon type of cancer; it is evaluated that the annual morbidity is 0.14 to 0.25 per million persons.[3] PSA has a very poor prognosis. Almost all patients die within 12 months of diagnosis regardless of treatment.[3] Very few reviews are available up to date in the literature.[5] Angiosarcoma can proliferate rapidly, its anaplastic cells incline to recrudesce locally, diffuse extensively, and have a high rate of lymph node and systemic metastases.[6] PSA has a higher incidence in male. It may occur at any time of life, and the age distribution is from 14 months to 89 years old.[7]

The pathogenesis of PSA is indeterminate. Vinyl chloride, thorium dioxide, arsenic and chemo or radiotherapy had been pointed to be risk factors. Some authors suggest PSA may come from the malignant transformation of benign splenic tumors.[8] Our case did not show any elements above as per the patient and her family.

There is no specific clinical presentation for this disease: upper abdominal pain with or without fever, weight loss, and fatigue are the main presenting symptoms.[9] The findings of splenomegaly and palpable left upper quadrant mass through physical examination are common. Owing to invasion through the capsule and significant mass effect, the splenic rupture and lethal hemorrhage has been reported in 13% to 32% of patients.[10] Laboratory abnormalities include anemia (81%), thrombocytopenia (40%), and less commonly, leukocytosis.[11] This disease is

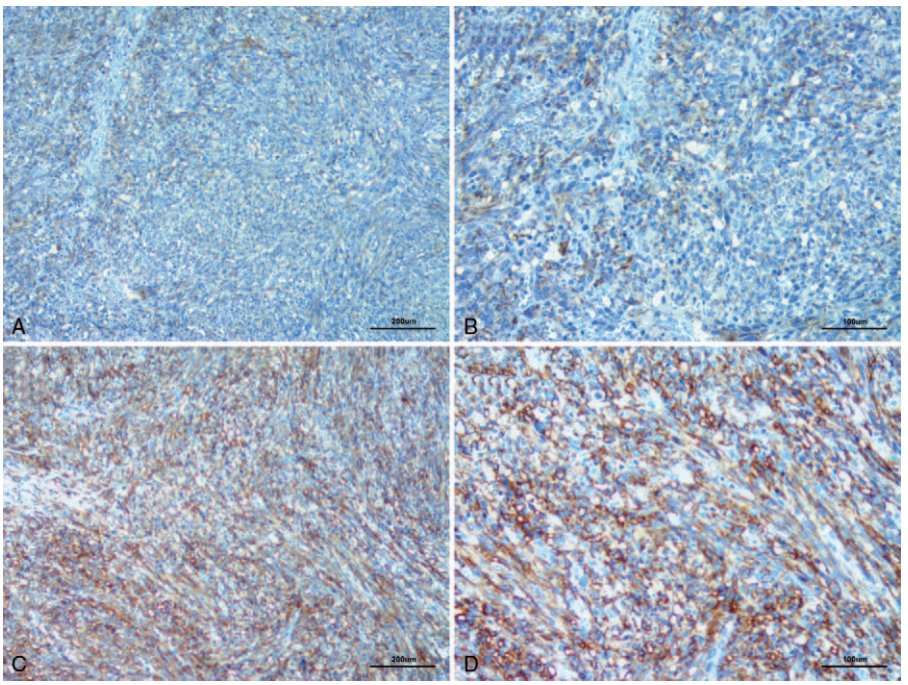

Figure 5. Immunohistochemistry revealed CD31(+) and CD34(+), which confirmed a diagnosis of angiosarcoma. (A) CD31(+) ×100, (B) CD31(+) ×200, (C) CD34 (+) ×100, (D) CD34(+) ×200.

most often fatal, for the vast majority of patients will be dead within 1 year of diagnosis. In our case, the patient's chief complaint was a 6-month scalp masses without upper abdominal pain or palpable mass or other symptoms, although she had splenomegaly found by abdominal MRI, anemia and thrombocytopenia determined by lab test.

Bicytopenia is common in many blood diseases and non-blood diseases. Bicytopenia is defined as any of the 2 findings: Hb <100 g/L, total leucocyte count $<4\times10^9$ L^{-1}, and platelet count $<100\times10^9$ L^{-1}.[12] Our case displayed decrease of Hb and thrombocytopenia. Bicytopenia can be an independent disease or secondary to other diseases, which always represents the early stage of pancytopenia. It can be sorted to deficiency of hematopoietic substance, excessive consumption, bone marrow suppression, autoimmune diseases, and idiopathic bicytopenia.[13] Three most common causes of bicytopenia are megaloblastic anemia, acute myeloid leukemia, and chronic liver disease. The main concurrent symptoms include fever, generalized weakness, fatigue, and symptoms of primary diseases.[14] Bicytopenia can also be induced by marrow infiltration of malignant tumors. Sami Cifci et al reported rectal carcinoma could cause bicytopenia which is due to bone marrow infiltrations.[15] In our case, the patient displayed erythropenia and thrombocytopenia, possibly due to metastasis of PSA to spleen, thus causing the splenomegaly and hypersplenism, which was a rare reason of bicytopenia. Besides, certain drugs, chemotherapy, radiotherapy, and severe infection can also induce bicytopenia. The diagnosis should be based on systemic information and the underlying primary diseases should be taken into consideration. Bone marrow examination is the gold standard for diagnosis and differential diagnosis for the reason of bicytopenia. Pathological examination of suspicious lesions may also contribute to make an accurate conclusion, taking our case as an example.

The imaging characteristics of splenic angiosarcoma vary with imaging modalities. Type B ultrasound, CT, and MRI can all indicate sufficient proofs of splenomegaly or masses in liver, spleen, lung lymph node, or other parts of the body, such as skull in our patient. Ultrasound shows a complex mass of miscellaneous echo. Necrosis, hemorrhage or cystis degeneration are often revealed in the tumor.[5] On CT scans, the most common finding is an ill-defined heterogeneously enhanced splenic mass with areas of necrosis. CT scan can also demonstrate the metastatic lesions in liver, lungs, bones, and lymph glands.[6] Diffused bone destruction, decreased bone density, and soft tissue mass formation can be seen in patients with bone metastasis just as what happened in our patient. MRI shows low signal in T1WI, high signal in T2WI, and inhomogeneous signal masses; contrast enhancement shows heterogeneous enhancement within the tumor which is the reflection of solid tumor with areas of necrosis.[5] Additionally, other tumors must be diagnosed differentially, such as lymphoma, metastatic disease, and other rare sarcomas.[6]

Pathologically, the tumor is characterized by neoplastic proliferation with a vasoformative component; the vascular interspaces are underlined by diverse extent of atypical endothelial cells, and the tumor may mimic the characteristics of malignant fibrous histiocytoma or fibrosarcoma. Immunohistochemical studies representatively show positive endothelial markers: CD31 and CD34.[3] CD31 is a marker of vascular endothelial differentiation, which suggests that tumor cells have vascular endothelial differentiation. The sensitivity and specificity of CD31 for diagnosing PSA are both higher than 90%. CD34 could indicate the origin of vascular tumor. CD34 showed positive in PSA.[16–18] Our case described the typical pathological characteristics of angiosarcoma.

Metastases occur in 69% to 100% of the cases of splenic angiosarcoma.[19] Falk et al reported the metastatic preference,

that is, 41% to the liver, 22% to bone or marrow, and 3% to lymph nodes.[9] Neuhauser et al reported the metastatic rate as 89% to the liver, 78% to lungs, 56% to lymph nodes, and 44% to bones.[3] In our case, the patient was admitted with a 6-month history of 2 scalp masses, surgical excision proved that the tumor developed from skull. Gross specimen and microscopical and immunohistochemical study suggested the diagnosis of angiosarcoma. Given that the imaging results showed intrahepatic and intrasplenic diffused nodules and enlarged spleen, we deduced the patient was suffering from PSA, which might have already metastasized to liver, spleen, skull, and even lungs, according to chest CT. No skull metastases of angiosarcoma are reported at present.

PSA is usually treated with splenectomy, although it is rarely effective due to the aggressive and metastatic nature of the disease.[3] Splenectomy before rupture has been demonstrated to increase the length of survival compared with splenectomy after rupture.[9] There is no forceful evidence to prompt a clinical effect of chemotherapy in the treatment of PSA.[3] This patient was in advanced stage of angiosarcoma with multiple metastasis of the body and did not receive early diagnosis and treatment. Although no literature suggests metastatic lesions resection could extend the life of patient, we performed a complete resection of skull mass to confirm the pathological diagnosis of angiosarcoma, No splenectomy, radiotherapy or chemotherapy was done. Our patient died at August 12, 2015 and obtained a survival of nearly 1 month.

The median survival time of PSA is around 5 months without any treatments. The only dependable ingredients to estimate prognosis are deemed to be tumor size and mitotic counts,[20] for the cases with no neoplasm metastasis. The worst prognosis is due to spontaneous or traumatic rupture of spleen, which would cause sudden death from hypovolemic shock and disseminated intravascular coagulopathy. According to the report from Mark et al pathological features or classification is not bound up with the prognosis, because the patients with well-differentiated tumors may also experience poor prognosis as the malignant ones.[21]

5. Conclusions

PSA is a rare and aggressive malignancy found primarily in adults and almost universally fatal despite treatment. Its pathogenesis remains indistinct, and its clinical and radiologic diagnosis are complex. The diagnosis should be considered in any patient with unexplained splenomegaly and anemia. Chemotherapy and radiotherapy have been proved to be unsuccessful to promote the outcome historically. Metastases can occur in most cases and to almost any tissues and organs. The best treatments are early diagnosis and positive splenectomy before rupture of spleen; metastatic lesions resection cannot extend the life of patients.

In our current case study, we showed detailed symptoms, signs and clinical imaging and lab studies, distinct intraoperative findings, and follow-up after operation in a 68-year-old patient. The present case contributes to our understanding of this rare disease.

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