Subdural Hematoma Caused by Epithelioid Angiosarcoma Originating from the Skull

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Abstract Cancers metastatic to the skull or dura may cause subdural hematoma (SDH). However, the frequency is low, and the presence of underlying cancers has almost always been known in such situations. We report a case of skull angiosarcoma manifesting as SDH, posing a diagnostic challenge to physicians. A 75-year-old man visited our clinic with sensorimotor disturbance of gradual onset approximately 1 month after a minor head trauma. He was diagnosed with SDH after imaging studies, and underwent surgery to evacuate the hematoma. Because the hematoma was organized, surgery was switched from burr-hole drainage to craniotomy. The bone flap as well as the dura over the hematoma had grossly normal appearance, and only the hematoma itself was submitted for histological examination. Although postoperative recovery was uneventful, the patient experienced recurrence of the SDH 2 months after surgery. At the second surgery, the bone flap and dura were intermingled with tumor tissue, and histological examination revealed that an epithelioid angiosarcoma originating from the skull was responsible for the SDH. Timely diagnosis of angiosarcoma manifesting as SDH is difficult because of its rarity. In retrospect, however, the diagnosis might have been established earlier if the bone flap and/or the dura had been biopsied at the time of the first surgery. The present case gives us a lesson that SDH may be an unusual manifestation of malignant tumors of skull or dural origin, and histological

examination of not only hematoma capsule but also of the surrounding tissues may provide important diagnostic clues.

Keywords Angiosarcoma · Cancer · Dura mater · Epithelioid · Subdural hematoma

Introduction

Subdural hematoma (SDH) is a common disease in the elderly, and is frequently triggered by a minor trauma to the head [1]. Although cancers metastatic to the skull or dura may cause SDH in rare instances, the presence of underlying cancers has almost always been known for months to years [2–8]. We experienced a case of skull angiosarcoma manifesting as SDH, posing a diagnostic challenge to physicians because of its rarity and unusual presentation.

Case Report

This 75-year-old man with a history of colon and gastric adenocarcinoma noticed mild but gradually worsening numbness and weakness in the right leg and visited our clinic. The cancers had been detected in the early stages and had been resected totally with no signs of metastatic diseases. Approximately 1 month earlier he had sustained a minor head trauma. A brain computed tomography (CT) scan revealed an SDH over the left cerebral hemisphere (Fig. 1a), and he was diagnosed with a traumatic chronic SDH. Preoperative laboratory workups including complete blood count, blood chemistry panels, and coagulation profiles were within normal limits. Although a chest X-ray was unremarkable, a skull X-ray was not obtained. The patient was admitted for surgical treatment.

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Fig. 1 Serial computed tomography (CT) scans of the brain. **a** Initial CT showing a subdural hematoma over the left cerebral hemisphere. In retrospect, a small skull defect is present (*arrowhead*). **b** CT obtained one day after the first surgery demonstrating adequate

evacuation of the hematoma. **c** Approximately two months after the first surgery, however, the patient sustained recurrence of the hematoma with worsened skull defect (*double arrowhead*)

Fig. 2 **a, b** Hematoxylin and eosin-stained photomicrographs showing large cells with irregular shaped nuclei, rich cytoplasm and mitotic figures. Structures resembling vascular lumen were also present. Original magnification: **a** $\times 100$; **b** $\times 400$. **c, d** Immunohistochemical

studies showing tumor cells positive for CK7 (**c**) and CD31 (**d**), establishing the diagnosis of epithelioid angiosarcoma. Original magnification: **c** $\times 100$; **d** $\times 100$

Drainage of the SDH via a single burr hole was attempted under local anesthesia on the next day after admission. However, the hematoma was organized and was too hard to be evacuated through a small tube. Therefore, anesthesia was switched from local to general, and subtotal

removal of the hematoma via a craniotomy was performed (Fig. 1b). Although a mild decrease in the thickness of the bone flap over the hematoma was noted intraoperatively, colors of both the bone flap and the dura appeared normal to the surgeons, and only the organized hematoma capsule

Fig. 3 A bone scintigraphy obtained after the second surgery showing multiple metastases to the ribs (white arrows) together with a skull lesion (black arrow)

was submitted to a pathologist. The histological examination exhibited a thickened outer membrane of the hematoma and clusters of inflammatory cells, but there were no signs of malignancy. The patient made an uneventful recovery postoperatively, and was discharged 3 days after surgery. Two months after discharge, however, the patient came back to our clinic complaining of the same symptoms, and a brain CT revealed recurrence of the SDH (Fig. 1c). In addition, erosion of the left temporal bone was noted (Fig. 1c, double arrowhead). He underwent the second surgery to evacuate the recurrent SDH using the same bone flap. The bone flap as well as the dura was found to be intermingled with a granulomatous tissue which bled easily. The hematoma, the dura, and abnormal tissue were excised en block. The bone flap was discarded and the dura was replaced with Goretex®.

Histological examination of the resected bone flap demonstrated densely arranged tumor cells with large, irregular shaped nuclei and many mitotic figures. The tumor cells proliferated either in globular or trabecular pattern, and structures resembling vascular lumen were also present (Fig. 2a, b). Immunohistochemistry was performed, and the tumors were positive for CK7, a marker of glandular epithelium (Fig. 2c), CD31, a marker of vascular endothelium

(Fig. 2d), and vimentin [9, 10]. The MIB-1 index was 48.1 %. Based on the above histopathological findings, the patient was diagnosed with epithelioid angiosarcoma originating from the skull [9, 10]. The search for possible metastases by bone scintigraphy revealed multiple rib lesions (Fig. 3). After the second surgery, he underwent whole brain irradiation. However, he developed respiratory insufficiency due to rapidly progressing pulmonary metastases, and the irradiation had to be terminated prematurely. Systemic chemotherapy was not attempted because of his deteriorating health. He received palliative care and died 4 months after the second surgery. Autopsy was not performed.

Discussion

Cancer is an uncommon cause of SDH, with less than 100 cases reported in the literature [2–8]. Imbalances between blood coagulation and fibrinolysis and/or thrombocytopenia resulting from advanced cancer are presumed pathomechanisms of SDH in such patients [1–5]. The most frequent cancer types associated with SDH include gastric, prostate, lung, and leukemia [2–8], all of which are relatively common among geriatric population. By contrast, SDH associated with angiosarcoma is extremely rare: despite vigorous literature search, we could identify only two previous cases [11, 12]: in one case, an angiosarcoma originated from the skull [11], and in the other case, the tumor originated from the scalp [12]. In the latter, the patient had undergone multiple craniotomies for recurrent SDH before diagnosis was established [12], as seen in the present case.

Angiosarcoma is a malignant neoplasm of the vascular endothelium that develops in the bone, skin and other soft tissue [9, 10]. They are rare tumors accounting for less than 1 % of all sarcomas [9, 10]. Primary skull angiosarcomas are particularly rare with less than 20 cases reported in the literature [12–15], which primarily explains why SDH caused by angiosarcomas is so rare. There seems to be a difference between SDH caused by angiosarcomas and that caused by other common cancers in the clinical presentation. In the latter, the diagnosis of cancer has almost always been established by the time SDH develops [2–7]. By contrast, the diagnosis of angiosarcoma has been made only after surgery for SDH, and diagnostic delay is the rule rather than exception [11, 12]. Angiosarcoma has a fragile vasculature [9, 10], and tendency for the skull tumor to penetrate into the subdural space through the dura and bleed easily either spontaneously or after a minor head trauma may predispose patients to develop SDH without derangement in the coagulation/fibrinolysis cascade. Although tumor mass was unrecognizable either within the bone flap or the dura in the first surgery, it is likely that the tumor had

already infiltrated into the leptomeninges through the dura mater. Interestingly, the great majority of angiosarcoma cases overexpress vascular endothelial growth factor (VEGF) [9, 10]. Recently, high concentrations of VEGF are identified in the outer membranes of SDH [16], and development of SDH may have been promoted by overly secreted VEGF in the present case.

Timely diagnosis of skull angiosarcoma manifesting as SDH may be difficult because of its rarity. In retrospect, however, a mild bone erosion of the left temporal bone had already been present after review of the initial CT scan (Fig. 1a, arrowhead), and the diagnosis might have been established earlier if the bone flap or dura had been biopsied at the time of the first surgery. The present case gives us a lesson that SDH may be an unusual manifestation of skull sarcomas, and biopsy of not only organized hematoma capsule but also of surrounding tissue may provide diagnostic clues. Although physicians tend to focus only on the hematoma in a seemingly typical case of SDH, the importance of carefully reviewing the entire images of each patient should not be overemphasized.

Conflict of interest None of the authors have any financial relationships with other people or organizations that could inappropriately influence their work.

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