Spontaneous acute epidural hematoma developed due to skull metastasis of hepatocelluar carcinoma: A case report and review of the literature

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Abstract. Acute epidural hematoma (AEDH) is one of the most common pathological types of head trauma, and may develop without an accidental event, although this is uncommon. The present study reports the case of a 41-year-old male patient that developed spontaneous AEDH due to skull metastasis of hepatocellular carcinoma (HCC). The man was admitted to Chonnam National University Hwasun Hospital and Medical School due to drowsiness and right-sided hemiparesis. A computed tomography scan of the head revealed the presence of a large AEDH and a lytic bone lesion in the left posterior fossa and parieto-occipital region, which exhibited heterogeneous enhancement. The perioperative findings revealed a large amount of mixed-stage epidural hematoma and a soft hemorrhagic mass that exhibited lytic change on the occipital bone. No evidence of head trauma, such as skull fracture or scalp contusion, was detected. The pathological diagnosis was hematoma with metastatic HCC. The current study reports the rare case of a patient with a metastatic tumor located in the skull that resulted in the development of spontaneous AEDH. Once a sudden and unpredicted neurological deficit occurs in a patient with HCC that is also diagnosed with skull metastasis, the possibility of spontaneous AEDH developing from the metastasis should be considered.

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Abbreviations: AEDH, acute epidural hematoma; CT, computed tomography; HCC, hepatocellular carcinoma

Key words: acute epidural hematoma, hepatocellular carcinoma, skull metastasis, spontaneous

Introduction

Acute epidural hematoma (AEDH) mostly occurs following head trauma, and may result in skull fracture and tearing of the middle meningeal artery or venous systems. Spontaneous AEDH is extremely rare, and may be caused by infections of the adjoining sinus or air cell structures, dural vascular anomalies, tumors or coagulopathies (1).

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide, with a high incidence in Southeast Asia and sub-Saharan Africa, where hepatitis B and C are prevalent (2). HCC commonly metastasizes to the lung, regional lymph nodes, peritoneum and adrenal glands (3). Although osseous metastasis, including metastasis to the vertebral body, sternum, ribs and long bones, is not uncommon and demonstrates an incidence between 2 and 16% in HCC, metastasis to the cranium is rare, with an incidence of 0.4-1.6% (4-6). Brain metastasis of HCC is also rare, with a similar incidence of 0.65% recently reported (7).

The development of spontaneous AEDH from metastatic HCC of the skull is extremely rare, and only 6 cases have been previously reported in the literature (3-6,8,9). The present study reports the case of a patient with spontaneous AEDH that developed from a skull metastasis of HCC, and the clinical presentation and pathogenesis are discussed with a review of the literature. Written informed consent was obtained from the patient's family.

Case report

In April 2008, a 41-year-old male was admitted to Chonnam National University Hwasun Hospital and Medical School (Hwasun, Jeollanam, South Korea) for the sudden onset of a headache, associated with vomiting and followed by drowsiness lasting several hours. On admission, no scalp wound or palpable mass was detected. The patient demonstrated right-sided motor weakness and a Glasgow Coma Scale (GCS) score (10) of 12/15 (eye opening, 3; verbal, 3; motor, 6), with reactive pupils. Pathological reflex was not noted. Based on these findings, a diagnosis of intracranial hemorrhage was promptly proposed. The patient had been diagnosed with HCC

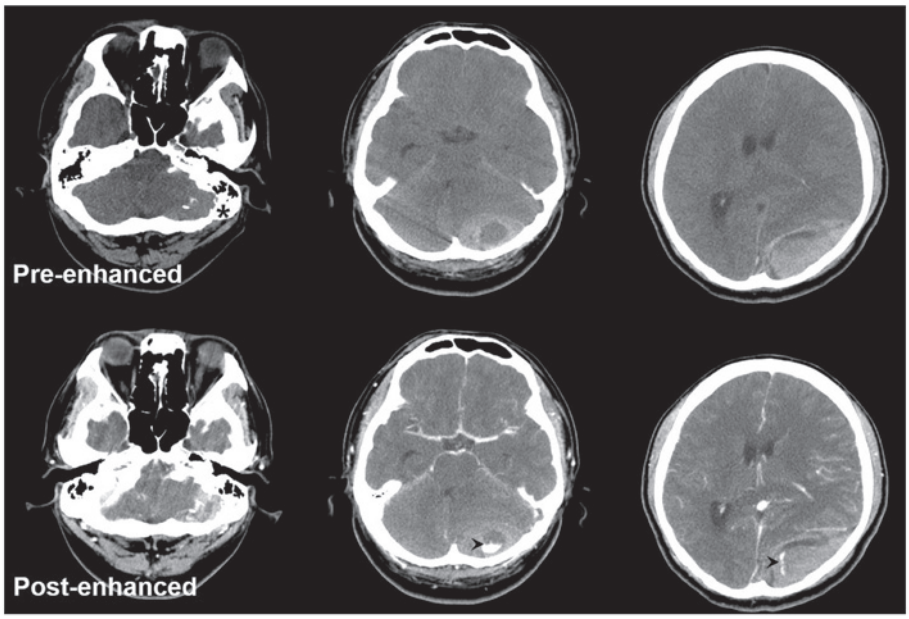

Figure 1. Preoperative computed tomography scan demonstrating a huge and mixed-density epidural hematoma on the left parieto-occipital region, with a severe mass effect. Note the osteolytic change on the occipital and petrous bone (asterisk) and the enhanced portion (arrow head) in the hematoma.

accompanied by jaundice and abdominal pain at the Samsung Medical Center (Seoul, South Korea) 1 year prior (May 2007), based on the results of abdominal magnetic resonance imaging and serological findings. Over the year following diagnosis with HCC, the patient received four sessions of transarterial chemoembolization for the treatment of HCC at the Samsung Medical Center. The patient was then transferred to Chonnam National University Hwasun Hospital and Medical School for radiotherapy of multiple bone metastases, involving multiple ribs and the pelvic bone, as detected by a positron emission tomography-computed tomography (CT) scan performed in February 2008. In April 2008, the platelet counts were below normal limits ($73x10^3/mm^3$; normal range, $130\text{-}450x10^3/mm^3$), but blood coagulation profiles, including prothrombin (13.5 sec; normal range, 11.0-14.9 sec) and activated partial thromboplastine (30.2 sec; normal range, 26.5-41.0 sec) times, were within normal limits.

A head CT scan revealed a large AEDH located in the left parieto-occipital area and posterior fossa, and a midline shifting. The CT scan also revealed a heterogeneously enhanced mass that was associated with a lytic cranial lesion in the left occipital bone (Fig. 1). A left-sided parieto-occipital craniotomy and evacuation of AEDH was performed. No evidence of head trauma, including skull fractures or scalp contusion, was detected. A mixed-stage (acute and subacute) hematoma was located in the epidural space, with no gross invasion of the dura. Additionally, a soft mass demonstrating osteolytic change on the occipital bone was found. The soft mass demonstrated continuity with the hematoma in the parieto-occipital region and growth to the muscle close to the foramen magnum. The large epidural hematoma was completely removed.

Histopathological examination of the lesion revealed a highly cellular epithelial tumor intermingled with fresh blood clots (Fig. 2A-B). The tumor cells contained abundant eosinophilic cytoplasm and were arranged in a compact trabecular pattern (Fig. 2C). Immunohistochemical analysis using the monoclonal mouse anti-human Hep Par 1 antibody (clone OCH1E5; cat. no. M7158; 1:100; Dako, Glostrup, Denmark) revealed marked cytoplasmic expression of Hep Par 1 (Fig. 2D). The histopathological diagnosis was metastatic hepatocellular carcinoma. Postoperatively, the patient experienced a sudden deterioration of mental status due to the obstructive hydrocephalus, which was resolved using extraventricular ventricular drainage. The patient gradually recovered to normal status 2 months subsequent to the surgery. However, the patient succumbed to hepatic failure due to HCC progression 4 months subsequent to the surgery.

Discussion

Metastatic intracranial tumors, including intraaxial and extraxial lesions, are the most common type of brain tumor, with an incidence of ≥40% (11). Common primary neoplasms of metastatic intracranial tumors are lung cancer, breast cancer, melanoma and colorectal cancer (12). Intracranial hemorrhage from brain tumors is not common, and accounts for 0.9-11% of all spontaneous intracranial hemorrhages. The majority of these intracranial hemorrhages occur in an intratumoral or intracerebral location, and therefore, occurrence in an epidural location is exceptional (13).

The development of spontaneous AEDH has been previously reported to have developed from several malignant lesions involving the skull, including lung cancer, ovarian cancer, esophageal cancer, Ewing's sarcoma and Langerhans cell histocytosis lesions (11,14-17). Spontaneous AEDH of skull metastases from HCC is a rare condition, and only 6 cases have been previously reported in the literature (Table I) (3-6,8,9). Based on the review of the cases, the majority of AEDH patients experience a severe headache followed by neurological deficits, including the deterioration of consciousness or hemiparesis (3,4,6,8,9). Osteolytic

Table I. Previously published cases of spontaneous acute epidural hematoma from skull metastasis of hepatocellular carcinoma.

First author, year (ref)	Age, years	Gender	Osteolytic change on CT scan	Clinical manifestations	Coagulopathy	Postoperative outcomes
Nakagawa *et al*, 1992 (9)	52	M	No	Headache Mental deterioration	Yes	Succumbed to liver failure subsequent to 1 month
Hayashi *et al*, 2000 (3)	70	M	No	Headache Left hemiparesis Palpable mass	Yes	Succumbed to pneumonia subsequent to 2 months
McIver *et al*, 2001 (8)	50	M	Yes	Palpable mass Slurred speech Right hemiparesis	Unknown	No neurological deficits on most recent follow-up
Kanai *et al*, 2008 (4)	56	M	Yes	Palpable mass Headache Mental deterioration	No	Succumbed to liver failure subsequent to 3 weeks
Kim *et al*, 2010 (5)	53	M	Yes	Mental deterioration	Yes	Succumbed to multi-organ failure 5 days following surgery
Woo *et al*, 2010 (6)	46	M	No	Headache Mental deterioration	Yes	Persistent vegetative state
This case	41	M	Yes	Headache Vomiting Mental deterioration	No	Succumbed to liver failure subsequent to 4 months

M, male; CT, computed tomography.

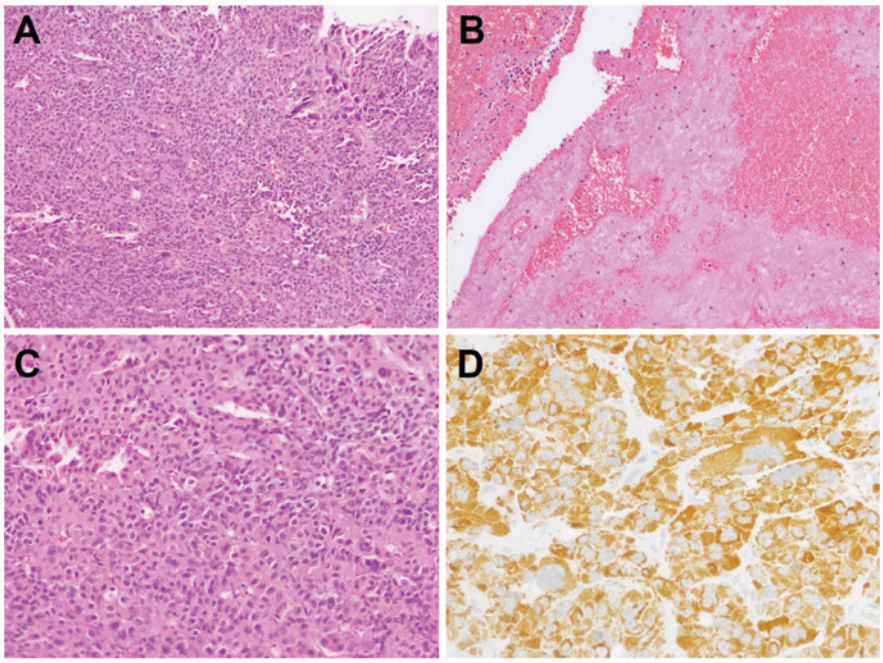

Figure 2. Histopathological features of the epidural lesion. (A) The lesion was a highly cellular lesion composed of epithelial cells (H&E stain; original magnification, x100). (B) The lesion was accompanied by organizing blood clots (H&E stain; original magnification, x100). (C) The tumor cells exhibited abundant eosinophilic cytoplasm and a trabecular growth pattern consistent with metastatic hepatocellular carcinoma (H&E stain; original magnification, x200). (D) The tumor cells were markedly positive for Hep Par 1 expression (immunohistochemistry; original magnification, x400). H&E, hematoxylin and eosin.

changes are frequently detected in the radiographic and intraoperative findings (4,5,8).

Skull metastasis of HCC is relatively rare, in contrast to the incidence of skull metastasis in lung, breast, thyroid and prostate cancers (18). Based on the review of the literature, however, ~10% (7/68) of patients with skull HCC metastasis presented with intracranial hemorrhagic events (18). An increased incidence of hemorrhagic events is also found in

the intracerebral metastasis of HCC. Recent data revealed that more than one-half of brain metastases in HCC patients exhibited intratumoral or extratumoral hemorrhagic change (7).

It is unclear why skull metastasis from HCC causes epidural hematoma more frequently than other tumors. However, several characteristics of HCC may contribute to intracranial bleeding. First, HCC contains numerous sinusoid-like vessels, and the fragility of these vessels may lead to hemorrhage and the formation of the epidural hematoma (3-6,8,9). Second, coagulopathy caused by hepatic dysfunction may increase the risk of tumor bleeding (3,5,6,9). Third, the destructive growth of metastatic HCC may lead to the breakdown of the vessel structures in the peritumoral tissue, as demonstrated in osteolytic change (5,6,8). Fourth, injury of the main feeders from the external carotid artery or the surrounding venous structures, induced by a trivial accident, may be involved (5,6,8).

In conclusion, spontaneous AEDH from skull metastasis is a rare event in HCC patients. Once a sudden and unpredicted neurological deficit occurs in a HCC patient diagnosed with skull metastasis, however, the possibility of spontaneous AEDH developing from skull metastasis should be considered.

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