CASE REPORT

Glioblastoma multiforme hiding behind the intracerebral hematoma

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KEYWORDS
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Summary A previously healthy man experienced a headache and confusion for 3 weeks. A cranial computerized tomography (CT) scan showed a resolving lobar intracerebral hemorrhage (ICH) in the right frontal lobe. A stereotactic aspiration of the ICH was performed to relieve the mass, and biopsy was reported to only show hematoma. However, the patient continued to have a persistent headache and unsteady gait even 2 months after surgery. A further cranial CT scan revealed a hypodense parenchymal lesion involving the whole right frontal lobe, which was shown by magnetic resonance image as a heterogeneously enhanced and poorly circumscribed lesion extending into the mesial frontal and subcortical areas. Craniotomy was done to excise the lesion, and histopathology revealed glioblastoma multiforme (GBM). The patient then underwent temozolomide-based concurrent chemoradiotherapy. This is an unusual case of GBM with intratumoral hemorrhage masquerading as hypertensive lobar ICH, causing a diagnostic pitfall for spontaneous ICH. For stereotactic aspiration for atypical spontaneous ICH, targets should include the surrounding hypodense or edematous area.

1. Introduction

Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor. Clinical manifestations and prognosis depend on tumor size and location, its range of infiltration, involvement of eloquent areas, and the range of surgical resection. Histopathologic features include necrosis, microvascular proliferation and hyper-vascularity, increased cellularity and mitoses, and microscopic intratumoral hemorrhage, among others. However, a macroscopic presentation as intracerebral hemorrhage (ICH) is rare, which is demonstrated in this case report.
2. Case report

A 72-year-old man, without a remarkable medical history, experienced headache and confusion for 3 weeks. A cranial computerized tomography (CT) scan performed in a private community hospital disclosed a resolving ICH in the right frontal subcortical area with subfalcine herniation (Fig. 1B). Stereotactic aspiration of 30 mL of liquefied blood clot was done to relieve the mass effect (Fig. 1C). The biopsy only showed hematomas.

However, the patient had persistent headache and progressively unsteady gait even 2 months after the operation. Neurologic examinations performed in our hospital demonstrated a disorientation state (Glasgow Coma Scale (GCS) E4M6V4), left hemiparesis (Medical research council (MRC) grade 4/5 of both upper and lower limbs), and a Babinski sign on the left. Other laboratory studies were normal. A follow-up cranial CT revealed a hypodense change in the whole right frontal lobe (Fig. 1D), and an MRI with gadolinium enhancement demonstrated a heterogeneously enhanced lesion with irregular margin in the right mesial frontal and subcortical areas (Fig. 1E and F). Imaging differential diagnoses included a glioma or infectious process following the previous operation; therefore, a craniotomy was performed to excise the lesion. Histopathology showed GBM (Fig. 2). The patient then underwent temozolomide (TMZ)-based concurrent chemoradiotherapy (CCRT) in accordance with Stupp’s protocol, and he has been followed up as an outpatient regularly for more than 6 months.

3. Discussion

Microscopic hemorrhage is frequently found in surgical tumor specimens of primary or metastatic malignant brain tumors with reported rates of 9%—15%, but a macroscopic intratumor hemorrhage large enough to cause clinical...
symptoms or detected by imaging study is relatively rare. A retrospective study of macroscopic intratumoral hemorrhage showed that only 2.4% of patients with brain tumors (either primary or metastatic) were found to harbor radiographically identifiable ICH associated with intratumoral bleeding. Among those reported cases of brain tumor-related ICH; GBM was the second leading cause (30% of cases) following metastatic carcinomas (36% of cases). As regards the various causes of spontaneous ICH, brain tumor accounts for only 0.8–7.4% of cases, and it follows hypertension, vascular malformation, and amyloid angiopathy.

Clinical diagnosis can become difficult when GBM has presentations similar to those of spontaneous hypertensive ICH. Several GBM cases have been reported to masquerade as traumatic ICH, intraventricular hemorrhage (IVH), or arteriovenous malformation (AVM). On CT scans, when the high-density lesions representing ICH are surrounded by disproportionately diffuse brain edema, it is essential to perform an additional imaging studies with contrast enhancement either by CT or MRI for excluding unusual causes of hemorrhage. Detecting the changes of molecular signal intensity for abnormal parenchyma by magnetic resonance spectroscopy (MRS) is an alternative to explore underlying malignancy. However, the contrast enhancement is frequently hindered by the hematoma, and patients with acute neurologic deficits and signs of mass effects are usually unable to tolerate MRI scan and MRS without appropriate sedation. In these situations, biopsies of brain tissue surrounding the hematoma would be advised.

Minimally invasive surgery for evacuation of ICH, such as stereotactic aspiration and endoscopy, has the advantage of minimizing iatrogenic brain damage, reducing glutamate content, blood-brain barrier permeability, and water content in brain tissues surrounding the hematoma; therefore, it is a popular treatment modality for ICH among neurosurgeons. Minimally invasive stereotactic puncture and thrombolysis therapy developed in 1997 have been shown to be safe, with fewer complications and a trend toward improved short-term and long-term outcomes for ICH evacuation. In this case report, although stereotactic procedures removed the hematoma without causing untoward brain injury, the diagnosis of GBM was delayed by 2 months because of missing the biopsy targets in the perifocal edematous area. Therefore, GBM confounded with ICH could be a diagnostic pitfall.

In conclusion, for ICH requiring surgical treatment either by conventional or minimally invasive methods, histopathologic investigation of edematous area surrounding the hematoma is recommended, especially in cases with disproportionately edematous parenchyma and atypical image presentations of hypertensive ICH. However, inadequate sampling is a major concern in stereotactic biopsy and needs to be redressed. Sampling targets must include all the suspicious foci revealed by image studies.

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Figure 2  (A) Tumor cells arranged in solid sheets showing high cellularity, necrosis, and microvascular proliferation (100×); (B) the tumor cells are characterized by pleomorphism, occasionally prominent nucleoli, and frequent mitotic figures (400×); (C) the tumor cells are positive for glial fibrillary acidic protein (GFAP) immunochemical stain (400×); (D) the microvascular proliferations (arrows) are outlined by CD34 immunochemical stain (100×).
References


