Hemorrhagic Brain Metastases: A Diagnostic Dilemma and Diagnosis of Exclusion

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Introduction

Spontaneous intracerebral hemorrhage (ICH) is commonly caused by hypertension, advanced age, prior ICH, renal failure, use of anticoagulant drugs, cerebral amyloid angiopathy, and tumor. Tumor-related spontaneous ICH is relatively uncommon. The leading causes of tumor-related ICH are metastases of extracranial origin (36%), followed by glioblastoma multiforme (30%).¹ In adults, the most common source of brain metastases is lungs. Pulmonary pleomorphic carcinoma (PC) is an infrequent tumor with an incidence rate ranging from 0.1% to 0.3% of all lung tumors and has a poor prognosis because surgery, irradiation, and chemotherapy are ineffective.² Here, we report a rare case of PC lung in a 56-year-old female presenting as unknown primary as well as manifesting ICH, causing sudden unconsciousness with left-sided hemiparesis as well as multiple thrombi in anterior and middle cerebral artery. Thus, the current case highlights the importance of brain biopsy together with immunohistochemistry (IHC) for a case of unknown primary as well as rare tumor presentation.

Abstract

Pleomorphic carcinoma is a malignant and aggressive primary lung carcinoma that occurs at a rate of approximately 0.3%. This rarely encountered tumor may present a diagnostic challenge to neuroradiologists and pathologists, as it has propensity to present as hemorrhagic brain metastasis with unknown primary and result in delay in diagnosis that could impact clinical outcome. Herein, we report a unique case in its presentation in a 56-year-old female, having symptomatic brain metastasis prior to the discovery of the pulmonary lesion.

Keywords

► hemorrhagic brain metastasis
► lung carcinoma
► pleomorphic carcinoma

Case Report

A 56-year-old female admitted in neurosurgery department with complaints of vomiting and sudden unconsciousness with left-sided hemiparesis. Patient was managed with supportive treatments. During hospitalization, preliminary blood investigations were done which were normal (normal coagulation function, total leukocyte count [TLC] and platelet count). On examination, patient had Glasgow coma scale (GCS) score E1V1M4. CT scan of brain showed a heterogeneous hypodense lesion of $4.5 \times 5 \times 4.8$ cm in right parietal lobe with edema in right parieto-temporal-occipital lobe, and thalamoganglionic region causing effacement of right lateral ventricle, midline shift of 8 mm toward left side and right uncal herniation (►Fig. 1A). CT angiography of brain showed thrombi in anterior and middle cerebral artery. Urgent craniotomy was performed, and while evacuating hematoma, suspicious clotted tissue was seen and sent for pathological examination. Grossly, we received several gray-brown to gray-white soft-tissue pieces, collectively measuring $3 \times 2 \times 1$ cm. On histopathological examination, sections showed gliosis and edematous brain parenchyma

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with intraparenchymal hemorrhage. In between the hemorrhage, there were discohesive sheets of large pleomorphic cells having abundant eosinophilic cytoplasm as well as bi and multinucleate cells present. Lymphocytic infiltrate was seen in between these cells. Small foci of necrosis and atypical mitosis were also noted, favoring neoplastic pathology (►Fig. 1B, C). On performing IHC, tumor cells were positive for PanCK, CK7, TTF-1, Napsin A, EMA, and Vimentin. These tumor cells were negative for GFAP, S-100, Neu N, CD68, Synaptophysin, Chromogranin, CDX2, PAX-8, Beta-HCG, and GATA3. Ki 67 index was 20% (►Fig. 1D). On the basis of morphology and IHC, case was diagnosed as metastatic carcinoma lung’pleomorphic giant cell variant. So, after histopathological diagnosis, CT of chest and abdomen was done, which revealed a rounded heterogeneously enhancing area of parenchymal consolidation, measuring 2.7 x 2.7 x 2 cm, in left lower lobe of lung as well as a mildly prominent lymph node, measuring 12.5 x 11 mm, in the left hilum, suggesting a neoplastic etiology. In abdomen, there was a hypodense thrombus completely filling in and obliterating the lumen of left external iliac vein, extending superiorly into left common iliac vein and further into infrarenal inferior vena cava, indicating deep venous thrombosis. The patient was therefore finally diagnosed as PC of the lung with a single brain hemorrhagic metastasis and multiple thrombi. The patient was subsequently referred to the oncology department, where six cycles of chemotherapy (carboplatin day 1 and gemcitabine 800 mg/m2 on days 1 and 8, repeated every 3 weeks). She showed a good clinical outcome with chemotherapy.

**Discussion**

Lung cancer can be classified into two types: small-cell lung carcinoma and nonsmall-cell lung carcinoma (NSCLC). Pulmonary PC is defined as a poorly differentiated NSCLC containing at least 10% sarcomatoid components of spindle or giant cells, or a carcinoma consisting solely of sarcomatoid components.3 The male to female ratio of pleomorphic carcinoma varies from 3:1 to 6:1, with the median age of presentation being 59 years.4 However, the patient in the current report was a 56-year-old female. Sixty percent of these tumors are present as a peripheral mass without endobronchial involvement, making it difficult, in some cases, to achieve a diagnosis with bronchoscopic examination or endobronchial biopsy. Approximately 50%


6 Shoji F, Maruyama R, Okamoto T, et al. Long-term survival with early hematogenous spread may allow ICH to be discovered prior to the detection of lung cancer. A neuroradiologist and pathologist should be aware of the metastatic presentation of this uncommon lung cancer. Further study of detailed factors affecting tumor bleeding requires more cases and animal model simulation.

Conflict of Interest
None declared.

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