



## A Diagnostic Approach to Multiple Simultaneous Intracerebral Hemorrhages

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### Abstract

Multiple simultaneous intracerebral hemorrhages are rare and varied in etiology. In the absence of known risk factors or obvious underlying disease, determining the cause may be problematic. We outline a diagnostic approach to multiple simultaneous intracerebral hemorrhages in the context of three case studies. We conclude that when there are no apparent risk factors, neuroimaging and identification of underlying diseases are central to determining the cause of multiple simultaneous intracerebral hemorrhage.

**Key Words:** MR imaging; risk factors; multiple simultaneous intracerebral hemorrhages.

(Neurocrit. Care 2006;04:267-271)

### Introduction

Non-traumatic multiple simultaneous intracerebral hemorrhages (SIHs) account for approximately 3% of all intracerebral hemorrhages (ICH) and the etiologies include uncontrolled hypertension, vasculitis, sympathomimetic drugs, primary and metastatic brain tumors, cerebral amyloid angiopathy, sinus thrombosis, coagulopathy as with blood dyscrasias as well as antithrombotic and thrombolytic medications, multiple infarctions with hemorrhagic transformation, and unexplained causes (1-4). This form of cerebral hemorrhage is rare and may pose a diagnostic dilemma. A diagnostic approach to multiple SIHs in patients with no known underlying disease or obvious risk factor is presented.

### Case Histories

#### Case 1

A 50-year-old non-insulin-dependant diabetic woman with controlled hypertension and recurrent kidney stones underwent a bilateral ureteroscopy with stone extrac-

tion and stent placement in the right ureter. The following day she had nausea and vomiting associated with a mild generalized headache. Later that day she had a seizure with left-sided jerking and eyes rolled back associated with urinary incontinence and confusion lasting several minutes.

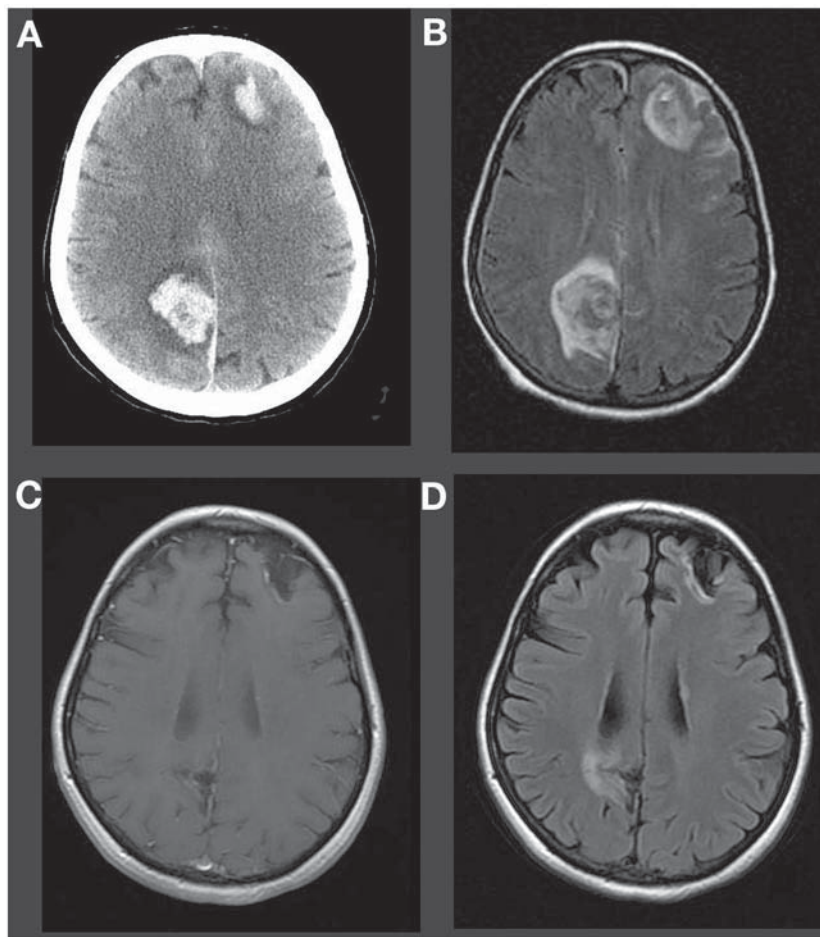
Examination showed a blood pressure of 197/93 mmHg and she was lethargic and mildly confused and manifested an extensor plantar response on the left. Complete blood count and routine blood chemistries were normal. A head computed tomography (CT) scan and magnetic resonance imaging (MRI) (Figure 1A,B) showed a 2.5-cm left frontal and 3.5-cm right parasagittal parietal lobar hemorrhage. Review of her record during her outpatient procedure showed a spike in her blood pressure to 210/110 mmHg. Other than impaired recent and remote memory her hospital course was uneventful and she was discharged on hospital day 15. Over the next 10 months her memory improved to baseline and subsequent MRI showed resolution of hemorrhages (Figure 1C,D).

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**Fig. 1.** (A) CT scan and (B) MR fluid attenuated inversion recovery (FLAIR) sequence show left frontal and right parasagittal ICH. (C) MR T1-weighted enhanced and (D) FLAIR image show no evidence of enhancement and resolution of hemorrhage.

## Case 2

A 55-year-old man developed sudden frontal headache while driving, followed by a single car motor vehicle accident caused by neglect of his left side. The following day he had a grand-mal seizure and was taken to the hospital. Past history is significant for grand-mal seizures following resection of a right temporal-lobe meningioma 2.5 years prior. He also was exposed to asbestos as a teenager, and smoked one-half pack of cigarettes per day until 5 years ago. His mother died of lung carcinoma.

Examination showed a left homonymous hemianopia but was otherwise normal. A bone scan was negative and CT of chest, abdomen, and pelvis was significant for scattered nodules in the lung parenchyma that were non-diagnostic. Complete blood count and routine blood chemistries were normal. Head CT and MRI (Figure 2) showed a 1.5-cm left frontal and 4-cm right parietal lobar hemorrhage with enhancement of the left frontal lesion. Biopsy of the wall of the right parietal hematoma suggested malignancy on histological study that was definitive for malignant melanoma on immunohistochemical study.

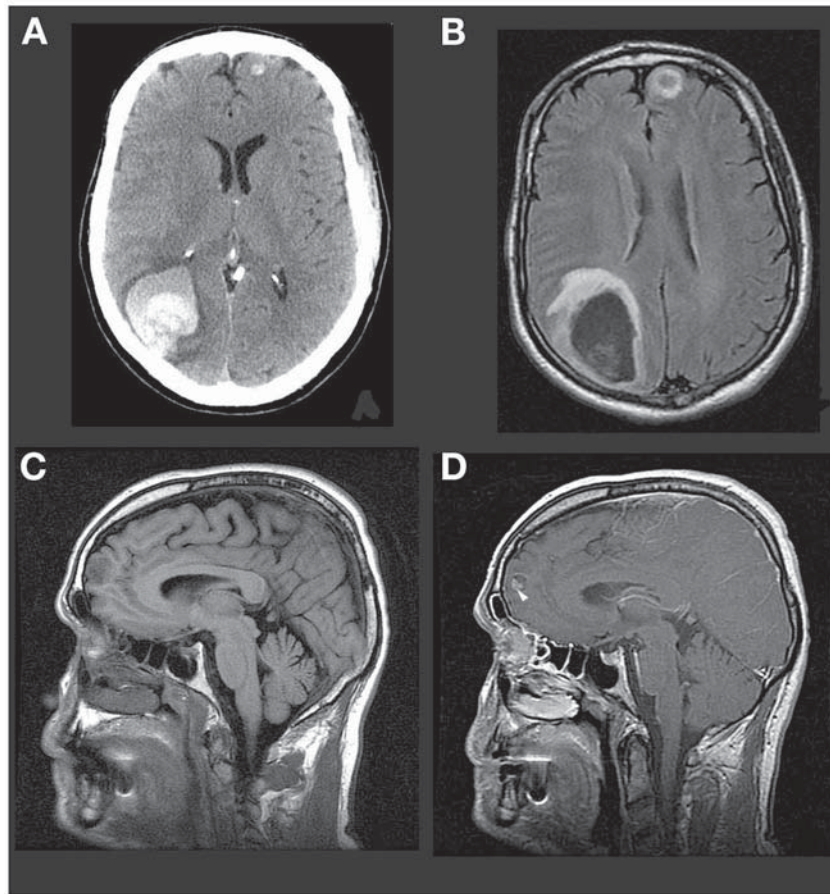
## Case 3

A 46-year-old man with transfusion-dependent myeloproliferative syndrome, treated with recombinant human erythro-

poietin while awaiting a donor for a bone marrow transplant, presented with severe headache to a local emergency room. Examination, including a complete blood count, blood chemistries, and head CT were normal. Two days later he developed right-sided weakness and lethargy and repeat head CT and MRI were again negative. On subsequent review of the MRI, there was a suggestion of widening of the superior sagittal sinus on T1-weighted sagittal image but no increase in signal intensity. Four days later he developed new right-sided weakness, lethargy, and slurred speech. A lumbar puncture showed a xanthochromic CSF with 2685 red cells. Seizures followed by coma developed later that day. The next day a repeat CT scan (Figure 3) showed a 3-cm left parietal and 2-cm right frontal lobar hemorrhage. In view of a poor prognosis, his family elected to withhold further therapeutic measures and the patient expired. Autopsy showed hemorrhagic infarction of the frontal and temporal lobes secondary to thrombosis of the sagittal and left transverse sinus and superficial cortical veins (Figure 3).

## Discussion

Much of the literature on multiple SIHs is case reports of patients with known underlying disease or case series of single causes as hypertension (5) and metastasis (6,7), with little



**Fig. 2.** (A) CT scan and (B) MR FLAIR sequence show left frontal and right parietal ICH. MR T1-weighted (C) non-enhanced and (D) enhanced image show area of enhancement (arrowhead).

discussion on diagnostic evaluation. Most cases of multiple SIHs are associated with apparent risk factors or known underlying disease; however, when no cause is obvious, neuroimaging and risk-factor identification is the mainstay in defining the underlying etiology. Awareness of medical conditions, particularly hypertension, trauma, drug usage (prescribed and otherwise), patient's age, prior history of ICH or deep-vein thrombosis as well as cancer risk factors such as smoking history, or known malignancy can help classify patients (Table 1).

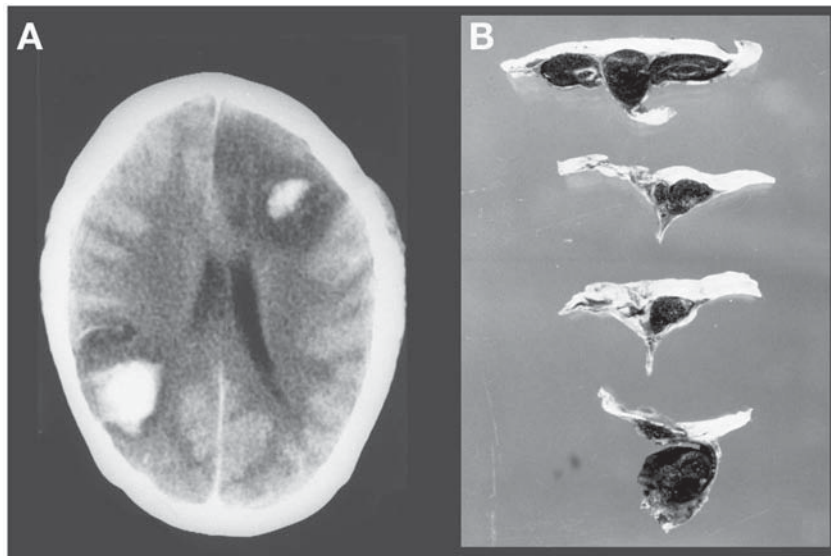
Because of the inherent limitations of case reports and patient selection bias in large case series (5–7) the incidence of specific causes of this condition remains uncertain. Nevertheless, excluding trauma, uncontrolled hypertension or a hypertensive event most likely accounts for the majority of cases with multiple SIHs (5). Even in the setting of controlled hypertension, transient critical blood pressure elevations as in case 1 can be missed unless carefully sought.

In the absence of vascular/coagulopathy risk factors, malignancy caused by metastatic disease is the most likely etiology, regardless of malignancy risk factors, as a primary neoplasm is frequently unknown when multiple SIH is caused by metastasis (6). In this circumstance a malignancy survey is undertaken for bronchogenic carcinoma, renal cell carcinoma, choriocarcinoma, or malignant melanoma, the neoplasms most commonly associated with multiple SIHs. Evaluation for the underlying causes is

listed in Table 2. In patients older than age 60 with no risk factors cerebral amyloid angiopathy may be as likely as malignancy (8). Gradient echo sequence on MRI can be beneficial in detecting prior silent hemorrhage suggestive of underlying amyloid angiopathy as well as direct clot visualization as an area of hypointensity in cerebral venous thrombosis (11).

In the vascular/coagulopathy group, hemorrhage occurs in otherwise normal brain parenchyma, whereas in the neoplastic group hemorrhage is into an existing structural abnormality, namely a neoplasm that is most commonly metastatic (6,7). Resulting neuroimaging changes suggestive of an underlying neoplasm include (1) the location of the ICH in sites that are rarely affected in hypertensive ICH; (2) edema and mass effect out of proportion to the acute hematoma; (3) any enhancement, and particularly nodules adjacent to the hemorrhage; (4) an MR pattern of heterogeneous signal changes within a mass lesion, surrounded by a hemosiderin hypointense ring and increased signal caused by edema at the periphery on T2-weighted sequences; (5) CT scan characterized by a ring of increased attenuation hemorrhage surrounding a low-density center in a non-contrast study; and (6) interval change as increased lesion size or enhancement on repeat imaging (9).

In one study enhancing lesions on CT were noted in all 20 patients with multiple SIHs from metastasis (7). Also, the use of double-dose delayed enhanced imaging both with CT and



**Fig. 3.** (A) CT scan showing right frontal and left parietal ICH. (B) Gross specimen of dura with organized thrombus within the superior sagittal sinus.

Table 1  
Etiological Classification of Multiple SIHs

I. Vascular / Coagulopathy
a. Uncontrolled hypertension
i. Primary, sympathomimetic drugs, <sup>a</sup> or procedure-related
b. Vasculitis
i. Primary or secondary (e.g., sympathomimetic drugs <sup>a</sup> )
c. Cerebral amyloid angiopathy
d. Coagulopathy
i. Antithrombotic therapy (e.g., thrombolytics, anticoagulants)
ii. Blood dyscrasias (e.g., leukemia)
e. Cerebral Sinus Thrombosis
i. Prothrombotic drugs, <sup>b</sup> hypercoagulable states, other causes
II. Neoplastic
a. Metastasis
i. Bronchogenic carcinoma
ii. Renal cell carcinoma
iii. Choriocarcinoma
iv. Malignant melanoma
v. Other
b. Primary
i. Glioblastoma
ii. Oligodendroglioma

<sup>a</sup>Cocaine, phenylpropanolamine, amphetamine, antimigranous medications. <sup>b</sup>Tamoxifen, oral contraceptives, erythropoietin.

MR increases the yield of CNS metastasis (10). When no primary or biopsiable extracranial site is determined from a non-invasive evaluation, a brain biopsy of the wall of the hematoma is recommended (9). Seizures were a common accompaniment seen in all three of our patients and in 11 of 20 patients as a result of CNS metastasis (7).

As multiple SIHs may occur in the absence of an identifiable cause (2) brain biopsy should be reserved for those patients

Table 2  
Investigations of Multiple SIHs

• Complete blood count, platelet count, sedimentation rate, urine toxicology
• Coagulation profile: PT, PTT, INR (to include hypercoagulable evaluation for sinus thrombosis)
• Echocardiogram
• MRI/MRA/MRV with gadolinium and gradient echo sequence
• Malignancy survey: chest X-ray, bone scan, CT of chest, abdomen, pelvis, and mammogram
• Cerebral angiogram
• Brain biopsy

demonstrating neuroimaging features indicative of neoplasm or when vasculitis is a consideration after a negative cerebral angiogram. The diagnosis of cerebral amyloid angiopathy may also be confirmed by brain biopsy. Brain biopsy site selection is based on eloquence of the area and likely yield of a positive biopsy. As histologic evidence of tumor may be absent or inconclusive, immunohistochemistry of the biopsy tissue is essential.

In the absence of apparent risk factors, appropriate neuroimaging and identification of underlying diseases are central to defining the etiology of multiple SIHs. In the absence of uncontrolled hypertension or other vascular/coagulopathic risk factors, metastasis to the CNS is a likely consideration and a malignancy screen is necessary. In patients over age 60, cerebral amyloid angiopathy is as likely as metastasis. Brain biopsy is recommended when neuroimaging features suggest an underlying neoplasm or vasculitis is a diagnostic consideration.

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