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http://dx.doi.org/10.1016/j.jocn.2016.03.002

Atraumatic multifocal intracerebral hemorrhage

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ARTICLE INFO

Article history:
Received 10 March 2016
Accepted 11 March 2016

Keywords:
Atraumatic
Intracranial hemorrhage
Multiple spontaneous intracerebral hemorrhage

ABSTRACT

This article describes a patient with atraumatic multifocal intracerebral, subarachnoid, and bilateral frontal convexity acute subdural hematomas. The patient is a 46-year-old Caucasian man who presented with a spontaneous severe progressive headache. Following a description of the case, this article reviews the reported incidence, proposed etiology, and current management strategies for multifocal spontaneous intracerebral hemorrhage.

1. Introduction

In the United States and Europe, intracranial hemorrhage (ICH) accounts for 8–14% of all strokes [1]. Common etiologies of focal ICH include hypertension, coagulopathy, vasculopathy, vascular lesions, and tumors [2]. Spontaneous intracerebral hemorrhage within multiple arterial distributions is a rare phenomenon [3,4] and is a distinct entity from focal intracerebral hemorrhage. The pathophysiology for multiple spontaneous intracerebral hemorrhages (MSICH) has not been elucidated [2]. However, multiple contributing factors have been described in the literature including hypertension, multiple microbleeding, cerebral angiopathy, vasculitis, deep cerebral vein thrombosis, intravenous tissue plasminogen activator (tPA) administration, oral anticoagulant therapy, hemorrhagic cerebral infarcts, and neoplasm [2,3,5,6].

The multifocal nature of MSICH makes management more challenging and correlates this entity with an increased mortality [4,7]. There is no consensus on the best method of managing these lesions. Both medical and surgical management strategies can be considered for these patients. This article describes a case report of MSICH and concludes with a review of the incidence, etiology, and management options reported in the current literature.

2. Case report

The patient is a 46-year-old Caucasian man with a past medical history of hypertension, seizures, and alcohol use disorder who presented with a sudden onset severe headache that progressively worsened over 1–2 days. The headache was associated with neck stiffness, nausea, and vomiting. Vital signs on admission were a blood pressure (BP) of 172/84 mmHg (normal: 120/80–140/90 mmHg), heart rate of 118 beats/minute (normal: 60–100 beats/minute), and temperature of 36.7°C (normal 36.1–37.2°C).

Head CT scan at admission demonstrated acute subarachnoid hemorrhage, multifocal intraparenchymal hematomas in the left frontal and bilateral temporal lobes, and a left frontoparietal convexity acute subdural hematoma causing 8 mm of midline shift (Fig. 1). These imaging findings prompted a diagnostic cerebral angiogram, which failed to demonstrate an aneurysm, arteriovenous malformation, or evidence of vasculitis. However, it showed progressive narrowing of the left subclinoid internal carotid artery extending into the A1 and M1 segments, likely from the mass effect and vasogenic edema related to the intracerebral hemorrhages.

Laboratory results were significant for an elevated white blood cell count (15.4 k/mm^3, normal: 4.5–11 k/mm^3), slightly elevated erythrocyte sedimentation rate (20 mm/hr, normal: 0–29 mm/hr) and C-reactive protein (5.1 mg/dL, normal: <3.0 mg/dL), hyponatremia (126 mmol/L, normal: 135–145 mmol/L), and hyperglycemia (168 mg/dL, normal: <100 mg/dL). Notably, the patient had an unremarkable coagulation panel, blood cultures, antineutrophil cytoplastic antibody (ANCA), and vasculitic panel including antinuclear antibodies (ANA), anti-dsDNA antibody, ant i-Sjögren's-syndrome-related antigen A antibody (SS-A), and anti-Sjögren's-syndrome-related antigen B antibody (SS-B).

No immediate intervention was deemed necessary. The patient had a 21-day hospital course complicated by post-hemorrhage encephalopathy associated with episodes of aggression and altered mental status. Despite these episodes, he demonstrated steady improvement, such that at the time of discharge, he only suffered from minimal residual difficulty with short-term memory, judgment, and impulsivity. The patient's uncontrolled

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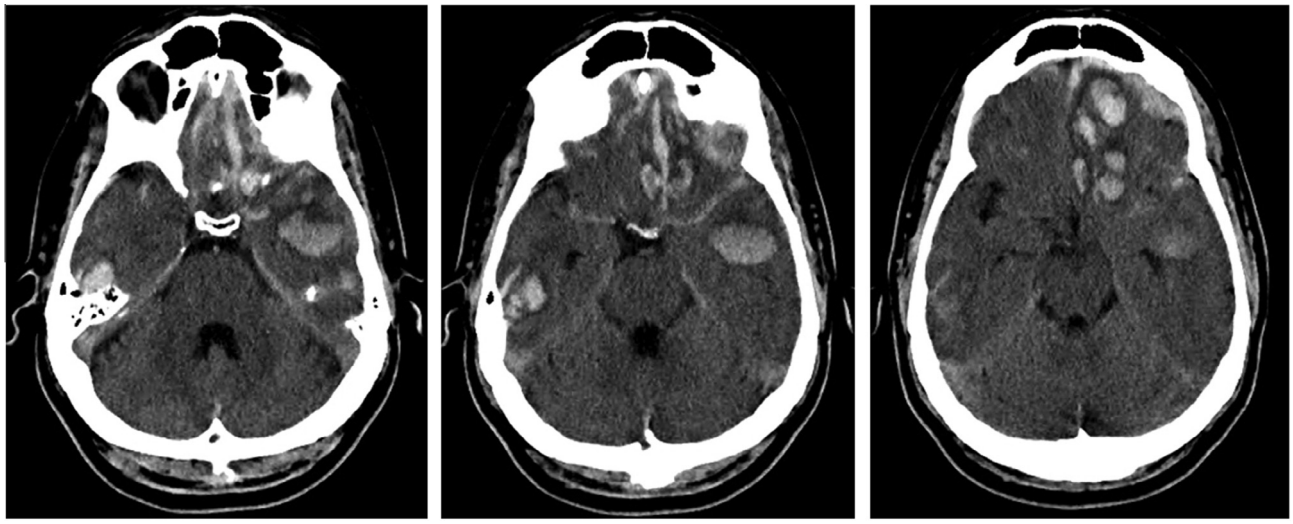

Fig. 1. Axial CT images on admission showed acute subarachnoid hemorrhage, multifocal intraparenchymal hematomas in the left frontal and bilateral temporal lobes, and a left frontoparietal convexity acute subdural hematoma.

hypertension observed at presentation, required therapy throughout his hospital course with systolic blood pressure (SBP) ranging from 140 to 160 mmHg. His uncontrolled hypertension was thought to be the cause—or at least a major contributing factor—of his multifocal intracerebral hemorrhages.

3. Discussion

Patients with MSICH associated with different arterial distributions are rarely described. Literature describing these entities includes 13 case reports [2–6,8,9] (Table 1), one single-center prospective study [1], and one single-center retrospective study [7] (Table 2). These articles were therefore analyzed to discuss the incidence, etiology, and management of MSICH.

Several studies report the incidence of MSICH in different arterial distributions as 0.7 to 3.4% of all ICH [2,4,5,8]. MSICH may not be detected or reported as often as it truly occurs, especially if very small lesions escape detection from the current CT scan slice thickness of 4–5 mm. Death prior to hospitalization or before a CT scan is obtained may also contribute to the infrequent incidence of MSICH [1].

Multiple contributing factors have been correlated to MSICH in the literature; these include hypertension, multiple microbleeding, cerebral angiopathy, vasculitis, deep cerebral vein thrombosis, intravenous tPA administration, oral anticoagulant therapy, hemorrhagic cerebral infarcts, and neoplasm [2,3,5,6].

Hypertension has been reported as a major risk factor for MSICH in a number of case reports [2–4]. Chronic hypertension can lead to both structural and functional hemodynamic changes in the cerebral arteries [10], and untreated chronic hypertension has been linked to widespread vessel degeneration and subsequent microaneurysm formation, which can lead to the development of multiple simultaneous hemorrhages [1–3,10]. However, hypertension does not seem to be a requirement in patients with MSICH, as there have been reports of multifocal hemorrhages not associated with hypertension or any other cerebral vascular degenerative disease, which suggests the presence of an unrecognized process involving multiple small cerebral arteries [8]. Therefore, the formation of tiny pseudoaneursyms and/or true aneurysms, such as Charcot-Bouchard aneurysms, in cerebral arterioles is not limited to a patient with hypertension and seems to also be related to the normal aging process [8].

Diffuse cerebral amyloid angiopathy (CAA) in elderly patients often presents as recurrent or multifocal ICH [2]. CAA is a known risk factor for single spontaneous intracerebral hemorrhage (SICH), which is associated with lobar hematomas from amyloid protein deposition in cortical arterioles [11]. Amyloid protein rarely deposits in the basal ganglia and brainstem, which are locations commonly associated with hypertension-related single SICH [11]. Cell culture studies have shown that the amyloid proteins exert direct toxic effects on vasculature with other animal studies indicating vascular smooth muscle degeneration and capillary occlusion, which can lead to dysfunction of cerebral blood vessel regulation [12].

Hypertension and CAA are both linked to microhemorrhage formation and are most frequently associated with MSICH [1–3,6,7]. Patients with longstanding hypertension and/or CAA appear to be at greater risk for MSICH, especially when acutely affected by impaired coagulation, platelet dysfunction, or elevated BP [1]. Dysfunctional autoregulation occurs in arterioles and is caused by chronic hypertension and advanced cerebrovascular degeneration; in addition, the original hemorrhage can lead to a reflex hypertension causing increased intracranial pressure (ICP) and results in rupture of other already weakened vessels due to chronic hypertension [2]. This reflexive hypertension could explain the hypertension observed during our patient's hospital course. However, cerebral microhemorrhages have been noted in both healthy elderly patients and patients with a variety of disorders, such as ischemic cerebrovascular disease and CAA. Microhemorrhages have also been linked to smoking, lacunar infarcts, white matter disease, intracerebral hemorrhage, and a history of ischemic stroke [13].

Central nervous system (CNS) vasculitis is another potential contributing factor to the development of MSICH. Seo et al. reported two cases of MSICH with normal complete blood count and coagulation panel values but associated with an increased erythrocyte sedimentation rate (ESR) in both patients [2]. However, other case studies have reported unremarkable laboratory values, including vasculitic and coagulation panel findings [3,6]. In addition, one case report noted a normal right frontal cerebral biopsy without signs of vasculitis; however, there is a false negative rate of 25% for brain biopsies in diagnosing CNS vasculitis, likely due to the typical patchy development of vasculitis [6].

The best course of management for MSICH remains unclear due to the lack of supporting data regarding the involved causative fac-