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CORRESPONDENCE

Intravascular mucinosis: a rare cause of cerebral infarction

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Cerebral infarcts are not infrequent in cancer patients. Of 3,426 cancer patients, 500 (14.6%) had evidence of cerebrovascular disorders at autopsy, 256 (7.5%) representing infarcts [4]. Among rare causes, intravascular mucinosis (IM), the extensive plugging of microvasculature by mucin, occurs in mucin-producing adenocarcinomas and is typically diagnosed postmortem with extensive hemorrhagic infarcts in border-zone distribution [2–4, 8, 9, 12].

We report IM in a 63- and a 48-year-old woman, treated for ER/PR positive lobular cancer [AJCC T1 and T2, N0], 19 and 2 years earlier, respectively. Both presented with headache and unusual imaging findings (Fig. 1), raising a broad differential diagnosis including vasculitis and posterior reversible encephalopathy. A left temporal lobe biopsy disclosed IM (Fig. 2) with rare neoplastic cells in Case 1. Both patients progressively deteriorated and expired after 28 and 26 days.

Gross and microscopic autopsy findings are illustrated in Figs. 3 and 4. Spinal cord changes, predominantly in the posterior columns, involved the lower cervical-upper thoracic (Case 1) and upper thoracic (Case 2) region. General autopsy disclosed extensive metastatic adenocarcinoma with signet ring features and abundant mucin, involving liver (both cases), lung (Case 1), vertebrae and myocardium (Case 2). A small patent foramen ovale (0.6 cm) was noted in Case 1.

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Tumor microemboli trapped in distal vascular branches at border-zones may contribute to the pathogenesis of IM [11]. In Case 1, they could have entered the arterial circulation directly from the lung metastases or paradoxically through the patent foramen ovale; and in Case 2, from bone marrow metastases in a fashion similar to fat embolism. Some authors, having found mucin admixed with embolic fat droplets (confirmed by Oil Red O stain) hypothesized that bone marrow and vascular wall necrosis due to radiation, chemotherapy or the tumor itself, could have released mucin and fat droplets into veins, maintained open by the trabecular bone architecture [2]. Similarly, we noted "clear globules" (Fig. 4a, c), but could not confirm their fat embolic nature, since frozen tissue was not available. Tumor cells, mucin and fat globules in the bloodstream could overwhelm the trapping capacity of the pulmonary capillaries and penetrate the arterial circulation [6].

Circulating cells, distributed according to organ blood flow (approximately 20% to the brain) may lodge in major end artery terminations and at the gray–white matter junction, and continue to secrete mucin. Circulating mucin may produce intermittent occlusive events and cause hemorrhagic infarcts by repeated occlusion and reperfusion [1, 5].

Spinal cord border-zones follow a vertical distribution with vulnerability in the thoracic region, as few small radicular branches supply this cord segment [10], and a horizontal distribution, present between anterior and posterior spinal artery territories [6]. In both our cases, hemorrhagic infarcts involved the lower cervical and upper thoracic posterior columns. While this follows a vertical distribution, the posterior column by itself is rarely involved in episodes of ischemia, being richly supplied by posterior radiculo-medullary arteries [7]. However, more tumor cells in the direction of blood flow

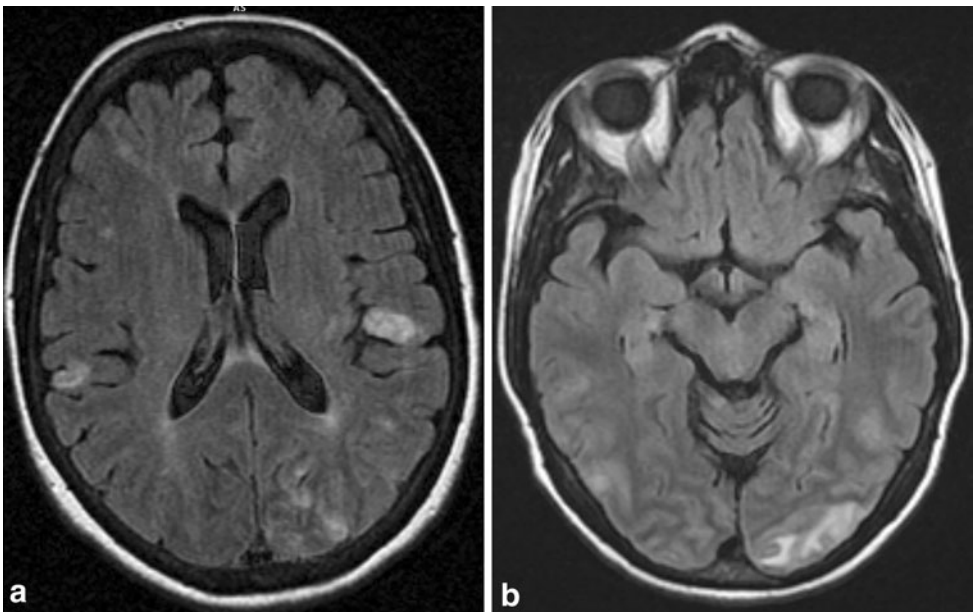

Fig. 1 MRI, focal T2 hyperintensities involving all lobes in Case 1 (**a**), most prominently left occipital lobe in Case 2 (**b**)

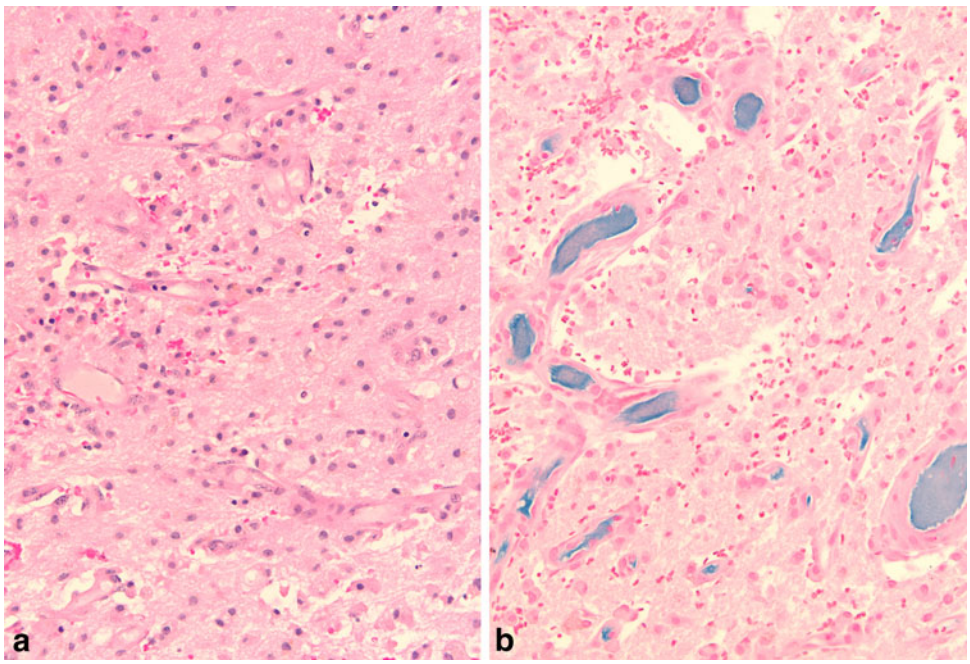

Fig. 2 Case 1: subacute, hemorrhagic infarct with intravascular mucin (**a**), Alcian blue stain (**b**)

may have lodged in the posterior spinal arteries and released mucin sufficient to occlude these smaller vessels, causing the infarcts.

Mucins play a role in activation of coagulation and platelet recruitment, causing the classic microangiopathic form of Trousseau syndrome [13]. This could explain the presence of intravascular thromboemboli/mucin-fibrin clots in the second case (Fig. 4b).

An intricate relationship between circulating tumor cells and mucin could trigger a vicious cycle leading to symptomatic IM that once established, has a poor prognosis. As our cases, most progressed to death in less than a month from onset of the symptoms [2, 3, 9, 12]. Because of its nonspecific clinical presentation and inconspicuous morphology, IM is difficult to diagnose unless one maintains a high level of suspicion in patients with history of

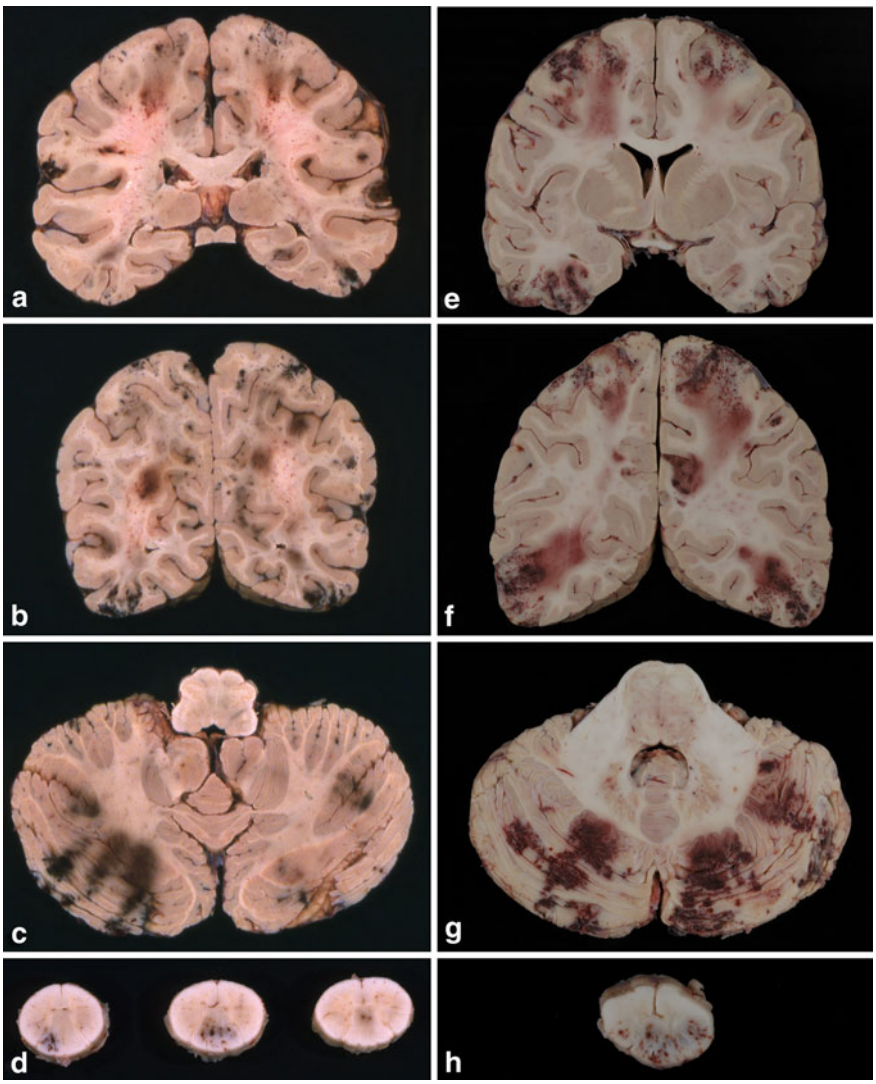

Fig. 3 Case 1 (*left*) and Case 2 (*right*), autopsy: hemorrhagic infarcts involving cerebral, cerebellar, and spinal cord (largely posterior columns) gray and white matter, with a border-zone distribution

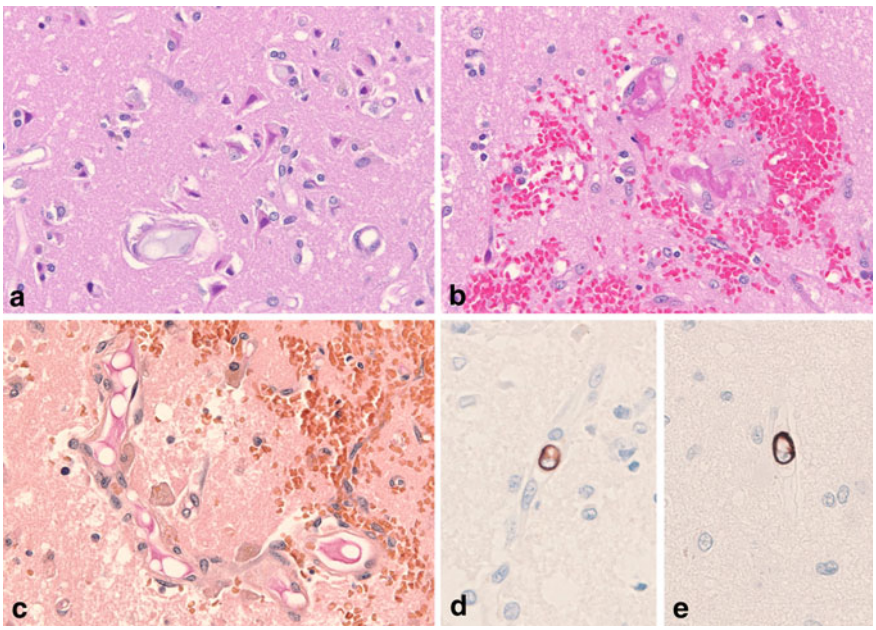

Fig. 4 Case 2—acute infarct with intravascular mucin in cortical microvessels (**a**), microscopic thromboemboli (**b**); mucicarmine stain highlights mucin and clear globules (**c**); CAM5.2 highlights tumor cells (**d**, **e**)

mucin-producing adenocarcinoma presenting with neurologic symptoms.

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