Superficial Siderosis of the Central Nervous System Caused by Hemorrhagic Intraventricular Craniopharyngioma: Case Report and Literature Review

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Abstract

Superficial siderosis is a rare condition caused by hemosiderin deposits in the central nervous system (CNS) due to prolonged or recurrent low-grade bleeding into the cerebrospinal fluid (CSF). CNS tumor could be one of the sources of bleeding, both pre- and postoperatively. We report an extremely rare case of superficial siderosis associated with purely third ventricle craniopharyngioma, and review previously reported cases of superficial siderosis associated with CNS tumor. A 69-year-old man presented with headache, unsteady gait, blurred vision, and progressive hearing loss. Brain magnetic resonance (MR) imaging with gadolinium revealed a well enhanced, intraventricular mass in the anterior part of the third ventricle. T2*-weighted gradient echo (GE) MR imaging revealed a hypointense rim around the brain particularly marked within the depth of the sulci. Superficial siderosis was diagnosed based on these findings. The tumor was diffusely hypointense on T2*-weighted GE imaging, indicating intratumoral hemorrhage. The lateral ventricles were dilated, suggesting hydrocephalus. [18F]fluorodeoxyglucose positron emission tomography revealed increased uptake in the tumor. The whole brain surface appeared dark ocher at surgery. Histological examination showed the hemorrhagic tumor was papillary craniopharyngioma. His hearing loss progressed after removal of the tumor. T2*-weighted GE MR imaging demonstrated not only superficial siderosis but also diffuse intratumoral hemorrhage in the tumor. Superficial siderosis and its related symptoms, including hearing loss, should be considered in patients with hemorrhagic tumor related to the CSF space. Purely third ventricle craniopharyngioma rarely has hemorrhagic character, which could cause superficial siderosis and progressive hearing loss.

Key words: superficial siderosis, craniopharyngioma, [18F]fluorodeoxyglucose positron emission tomography, T2*-weighted gradient echo magnetic resonance imaging

Introduction

Superficial siderosis is a rare condition caused by hemosiderin deposits in the central nervous system (CNS), and is often characterized by the triad of symptoms, sensorineural hearing loss (95%), cerebellar ataxia (88%), and pyramidal signs (76%).1–4 Less frequent findings include dementia, headache, tremor, anosmia, bladder disturbance, nystagmus, and ocular motility deficits.1,2,4,5 Hemosiderin deposition in the subpial layers of the brain and spinal cord results from prolonged or recurrent low-grade bleeding into the cerebrospinal fluid (CSF) caused by various pathologies, including tumors, meningocoele and pseudomeningocoele, vascular malformations, trauma, subarachnoid hemorrhage, intracranial or spinal surgery, and brachial plexus or nerve root injury.1,6–8 The most common CNS tumor is spinal ependymoma, which includes myxopapillary ependymoma as a source of hemorrhage in superficial siderosis.3,4,6–8 Various other spinal,1,5,16–23 and intracranial tumor pathologies have been reported as causes of superficial siderosis, both pre-1,24–30 and postoperatively (Table 1).3,6,7,18,12–38 Here, we report an extremely rare case of superficial siderosis associated with purely third ventricle craniopharyngioma, and review previously reported cases of superficial siderosis associated with CNS tumors.
A 69-year-old healthy man presented with headache, unsteady gait, and blurred vision. He had hearing loss, but no difficulties in daily life. His symptoms progressed over 6 months. He was unwilling to leave his house, and whole body muscular power had declined. Brain computed tomography (CT) revealed a hyperdense lesion in the anterior part of the third ventricle, and dilation of the lateral ventricles (Fig. 1A). Magnetic resonance (MR) imaging was performed with a 1.5T system using sequences, including T2*-weighted gradient echo (GE) MR imaging, as previously reported. Brain MR imaging revealed an intraventricular mass (1.8 × 2.3 × 2.4 cm) in the anterior part of the third ventricle, appearing as isointense with the gray matter on T1-weighted imaging (Fig. 1B), hypointense on T2-weighted imaging (Fig. 1C), and with good enhancement on T1-weighted imaging after administration of gadolinium (Fig. 1D). Coronal T2*-weighted GE MR imaging revealed a hypointense rim around the brain particularly marked within the depth of the sulci (Fig. 2A, B). The hypointense rim extended to the surface of brainstem (Fig. 2C). The intraventricular tumor appeared as diffuse hemorrhagic hypointensity (Fig. 2A, B). The lateral ventricles were dilated indicating hydrocephalus. T2-weighted fast spin echo imaging also partially demonstrated the linear hypointense rim around the brain (Fig. 1C), indicating hemosiderin deposition. Superficial siderosis was diagnosed based on these findings. Spinal T2-weighted MR imaging revealed superficial siderosis over a large part of the spine (Fig. 1E).

MR angiography and three-dimensional CT angiography indicated an unruptured anterior communicating artery aneurysm. Cerebral angiography revealed an unruptured 3-mm diameter anterior communicating artery aneurysm, with no tumor stain (data not shown). [18F]fluorodeoxyglucose positron emission tomography was performed using the previously reported method, and revealed extremely high uptake in the lesion compared with previously reported cases of craniopharyngioma (Fig. 1F). The standardized uptake value was extremely high at 15.3. Urine volume was 1,200 ml/day, and specific gravity of the urine was 1.019. Baseline measurements of pituitary hormones were all within normal limits. Tumor markers were all negative. He scored 24 points (mild dementia) on the mini mental state examination. Visual acuity and field tests revealed no problems. The isolated anterior third ventricular lesion was suspected to be craniopharyngioma with hemorrhagic character.

Surgery was performed through the basal anterior hemispheric route with a bicoronal craniotomy, and the translamina terminalis approach. The whole brain surface appeared

### Table 1  Reported cases of superficial siderosis due to central nervous system tumors

<table>
<thead>
<tr>
<th></th>
<th>Brain tumors</th>
<th>Spinal tumors</th>
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</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>44.5 ± 13.6</td>
</tr>
<tr>
<td></td>
<td>Range</td>
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</tr>
<tr>
<td>Sex (male:female)</td>
<td>5:4</td>
<td>14:5</td>
</tr>
<tr>
<td>Tumors</td>
<td>Ependymoma: 3</td>
<td>Astrocytic tumors: 10</td>
</tr>
<tr>
<td></td>
<td>Pilocytic astrocytoma: 1</td>
<td>Medulloblastoma: 3</td>
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<tr>
<td></td>
<td>Germ cell tumor: 1</td>
<td>Ependymoma: 2</td>
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<tr>
<td></td>
<td>Papillary glioneuronal tumor: 1</td>
<td>Pituitary adenoma: 1</td>
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<tr>
<td></td>
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<td>Craniopharyngioma: 1</td>
</tr>
<tr>
<td></td>
<td>Melanocytoma: 1</td>
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<tr>
<td></td>
<td>Craniopharyngioma: 1</td>
<td>Hemangioblastoma: 1</td>
</tr>
<tr>
<td>Locations</td>
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<tr>
<td></td>
<td>Suprasellar: 3</td>
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</tr>
<tr>
<td></td>
<td>Frontal lobe: 1</td>
<td>Thoracic: 2</td>
</tr>
<tr>
<td></td>
<td>Basal ganglia: 1</td>
<td>Cervical: 1</td>
</tr>
<tr>
<td>Duration after surgery (years)</td>
<td>–</td>
<td>22.3 ± 12.0 (7–44)**</td>
</tr>
</tbody>
</table>

*Symptoms developed 4 years after the surgical resection of meningioma. **Values are mean ± SD (range).

SD: standard deviation.
Superficial Siderosis Caused by Craniopharyngioma

Fig. 1  A: Computed tomography scan showing a high density suprasellar lesion indicating hemorrhage, with no gross calcifications. B, C: Preoperative coronal T₁-weighted (B) and T₂-weighted (C) magnetic resonance (MR) images showing the ventricular craniopharyngioma as isointense and hypointense, respectively. D: Sagittal T₁-weighted MR image with gadolinium-diethylene-triaminepenta-acetic acid showing a well enhanced round lesion confined entirely to the third ventricle. E: Sagittal T₁-weighted MR image of the thoracolumbar spine showing a hypointense rim surrounding the spinal cord. F: Sagittal [¹⁸F]fluorodeoxyglucose (FDG) positron emission tomography scans showing marked extremely high uptake of FDG accumulation in the ventricular tumor compared with previously reported cases of craniopharyngioma.⁴²

Fig. 2  Coronal T₂* -weighted gradient echo images showing extensive hemosiderin depositions on the surfaces of cisterns, sylvian fissures, interhemispheric fissure and hemispheric sulci. Hemosiderin depositions are comparatively slight on the cerebral ventricle wall. A, B: The ventricular craniopharyngioma had a diffuse dark appearance. Hemosiderin depositions were also observed on the surfaces of the medial temporal lobe, and basal forebrain. C: Hemosiderin depositions extended over the surfaces of brainstem.

dark ocher, indicating superficial siderosis. The tumor in the third ventricle was hard to remove and hemorrhagic, but was almost totally removed except for part of the capsule, which was adherent to the floor and bilateral lower walls of the third ventricle. The anterior communicating artery aneurysm was found to be unruptured, and was clipped successfully after tumor removal. The histological diagnosis was papillary craniopharyngioma, World Health Organization grade I. Histological examination proved intratumoral hemorrhagic features with thickening and
hyalinization of the vessel walls (Fig. 3). Immunohistochemical staining was positive for CAM5.2 and negative for glial fibrillary acidic protein, S-100 protein, CK20, and epithelial membrane antigen. The MIB-1 labeling index was 3.4%. He was discharged without endocrinological problems, including diabetes insipidus. However, he had slight aggravation of hearing loss and dementia. One year after discharge, he had slight dementia, but hearing loss progressed and he required a hearing aid. MR imaging detected no tumor recurrence, and the dilation of the lateral ventricles remained stable. Although gait disturbance was present, the CSF exclusion test for the diagnosis of normal pressure hydrocephalus was negative.

Discussion

I. Superficial siderosis with CNS tumors

As in the present case, brain tumor is one of the important sources of bleeding, accounting for 15% of all reported cases of superficial siderosis.2 We reviewed a total of 45 cases of superficial siderosis associated with CNS tumors, diagnosed in vivo by MR imaging, in the English-language literature (Table 1). Many astrocytomas and medulloblastomas have been reported in cases of superficial siderosis after brain tumor surgery. The operative resection plane may become the chronic source of bleeding causing superficial siderosis. The craniotomy itself may also become the cause of superficial siderosis, regardless of the biological characteristics of the tumor.44 On the other hand, “pure tumor-related superficial siderosis” presenting before surgery was not caused by craniotomy and/or resection. Most cases of this type of superficial siderosis are caused by hemorrhagic tumor, which is located in the posterior fossa and related to the CSF space. Some hemorrhagic character was observed on CT or MR imaging in 5 of these 9 cases of pure tumor-related superficial siderosis. Two previous cases of craniopharyngioma associated with superficial siderosis have been reported,23,45 one diagnosed by postmortem examination and the other arose after a long postoperative period. In contrast, our case of craniopharyngioma was detected in vivo as pure tumor-related superficial siderosis, which excluded the involvement of surgical procedures.

II. Symptoms and superficial siderosis

Hearing loss, cerebellar ataxia, and pyramidal signs are the main clinical findings of superficial siderosis, occurring in 95%, 88%, and 76% of cases, respectively.1–4 Other common clinical findings are dementia (22%), nystagmus (19%), and anosmia because of olfactory nerve dysfunction (17%). Our review found hearing loss in 5 cases, ataxia in 5, headache in 4, and dementia in 3 of the 8 cases of pure tumor-related superficial siderosis. Our patient had slight hearing loss and slight gait disorder before surgery. Therefore, this type of symptom must be distinguished from focal brain tumor symptoms in patients with pure tumor-related superficial siderosis. In patients with brain tumor except for acoustic tumor, the hearing loss may be one of the specific symptoms of superficial siderosis.1 If unexplained hearing loss appears in patients with hemorrhagic brain tumor linked to the ventricles, superficial siderosis should be considered.

III. Neuroradiological findings

In vivo diagnosis of superficial siderosis is possible based on the T2-weighted fast spin echo MR imaging. However, T2*-weighted GE imaging has higher sensitivity for hemosiderin deposition.7,12,20–22,30,39 The magnetic susceptibility effects of blood degradation products such as ferritin and hemosiderin are also more pronounced at higher field strengths. In our craniopharyngioma case, the diffuse hemorrhagic pattern of hypointensity was also observed intratumorally (Fig. 1). However, we should be cautious about interpreting T2*-weighted GE MR imaging, since the frequency of calcification is high in craniopharyngioma. In the present case, calcification was little seen on CT (Fig. 1A). The intratumoral hemorrhage in the craniopharyngioma and the superficial siderosis could be clearly demonstrated simultaneously by T2*-weighted GE MR imaging (Fig. 2A, B).

IV. Craniopharyngioma with intratumoral hemorrhage

Craniopharyngiomas with symptomatic intratumoral hemorrhage has been rarely reported, with only 11 previous cases.46,47 Spontaneous intratumoral hemorrhage in craniopharyngioma has been reported only in 4 cases, which

Fig. 3 A: Photomicrograph of the solid tumor showing mainly papillary proliferation of well-differentiated squamous epithelium around cores of fibrovascular stroma, consistent with papillary craniopharyngioma. Hematoxylin and eosin stain, original magnification ×200. B: Photomicrograph showing hemorrhage in papillary craniopharyngioma with thickening and hyalinization of the vessel walls. Hematoxylin and eosin stain, original magnification ×200.
does not include cases after partial removal of the tumor, after lumbar tap, or after trauma. However, asymptomatic intratumoral hemorrhage in craniopharyngioma may possibly be more common. The pathogenesis of intratumoral hemorrhage in craniopharyngioma is unknown. Blood vessel walls in the craniopharyngioma and connective tissue stroma may undergo degenerative changes and rupture. The presence of numerous immature blood vessels may cause hemorrhage. Small vessels, related to inflammation and degenerative changes, caused spontaneous hemorrhage in craniopharyngioma. In the present case, no particular pathological feature associated with intratumoral bleeding could be identified in the limited surgical specimen. However, the blood vessel changes due to inflammatory and degenerative changes peculiar to craniopharyngioma remain the leading candidate for the cause of intratumoral bleeding in this tumor. A similar pathogenesis of intracystic bleeding in Rathke’s cleft cyst has been suggested.

V. Prognosis after surgery

Rapid pathological recovery may be difficult once hemosiderin, which is converted from free heme, has accumulated on the brain surface. However, progression of symptoms can be stopped by removing the tumor as the cause of bleeding. In our case, hearing loss and dementia progressed even after brain tumor resection. A cause of bleeding other than the craniopharyngioma may be suspected as the cause of this deterioration. However, we could not detect any other likely abnormality by brain and spinal MR imaging. \( T^*_2 \)-weighted GE MR imaging indicated that the tumor had hemorrhagic features and was located upstream of the CSF circulation, indicating that this purely third ventricle craniopharyngioma might have caused the bleeding and superficial siderosis. Another explanation is that a small tumor remnant may have remained the source of low-grade bleeding after the operation. Intradural surgery may also be a risk factor for low level subarachnoid hemorrhage, resulting in worsening superficial siderosis. Previous case reports of superficial siderosis before surgery for brain tumor (Table 1) have not described change in symptoms after surgery except for one case, which remained asymptomatic pre- and postoperatively. Further investigations and case experience are required to clarify the prognosis of pure tumor-related superficial siderosis after removal of the tumor as the source of bleeding.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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