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Case Report

A case of meningeal myxoid solitary fibrous tumor/hemangiopericytoma with unique *NAB2-STAT6* fusion gene and symptomatic intratumoral hemorrhage

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ABSTRACT

We experienced a case of meningeal solitary fibrous tumor (SFT)/hemangiopericytoma (HPC) with symptomatic intratumoral hemorrhage in a 67-year-old Japanese woman. Her chief complaints were sudden onset of motor aphasia and right hemiparesis. Brain computed tomography showed the hemorrhagic mass adjacent to the superior sagittal sinus. The mass was resected and pathological examination of the specimen revealed a tumor that is rich in vessels and accompanied with intratumoral hemorrhage. Short spindle tumor cells were proliferating with myxoid stroma. Tumor cells appeared to be arranged around the vessels and sometimes attached to the vessel wall directly. Although hyalinization of the vessel wall was observed, neither patternless pattern nor staghorn vessels were seen. Immunohistochemistry revealed that the tumor cells were positive for both CD34 and nuclear STAT6. Moreover, gene analyses revealed unique *NAB2-STAT6* fusion. Immunohistochemical findings and fusion-gene analyses enabled us to make the definite diagnosis of meningeal myxoid SFT/HPC. The present case showed the three unique features such as clinically symptomatic intratumoral hemorrhage at the onset, rare variant of myxoid SFT/HPC, and unique *NAB2-STAT6* fusion.

1. Introduction

Solitary fibrous tumor/hemangiopericytoma (SFT/HPC) is a mesenchymal tumor which is composed of spindle or round cells and has collagenous stroma and/or staghorn vessels. Recently, there was a great progress in pathological understanding of SFT/HPC. By whole-exome and transcriptome sequencing, three groups have identified *NAB2-STAT6* fusion gene in the vast majority of soft tissue SFTs [1–3]. In addition, Schweizer et al. showed that almost all meningeal SFT/HPC also had the *NAB2-STAT6* fusion, suggesting that meningeal HPC and SFT might be included in the same entity and meningeal HPC might be a malignant form of meningeal SFT [4]. They also revealed by immunohistochemistry (IHC) that SFT/HPC had nuclear localization of STAT6 protein as a result of the fusion gene. Thereafter, Doyle et al. and Yoshida et al. reported that nuclear STAT6 was a highly sensitive and specific immunohistochemical marker for SFT to distinguish SFT from histological mimics using various kinds of mesenchymal tumor samples [5,6]. These findings indicate close relationship between SFT and HPC and between SFT/HPC and *NAB2-STAT6* fusion gene/nuclear localization of STAT6 protein.

Here we report a case of a brain tumor found by the acute onset of intratumoral (intracranial) hemorrhage. Although pathological features were unusual for SFT/HPC, immunohistochemical and fusion gene analyses confirmed that the tumor was SFT/HPC. Thus, we consider that this is a case of meningeal SFT/HPC with the following three unique characteristics. The first is symptomatic intratumoral hemorrhage at the onset, the next is myxoid morphology for the most part, and the last is unique *NAB2-STAT6* fusion pattern.

2. Case report

A 67-year-old woman complaining of acute onset of motor aphasia and left hemiparesis went to Department of Neurosurgery, Yuaikai Hospital. She had been taking medicine for hypertension and diabetes

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mellitus. Brain CT showed a hemorrhagic mass adjacent to the superior sagittal sinus and falx (Fig. 1A & B). Three days after the onset, surgery was performed. The mass seemed to invade the superior sagittal sinus. Complete resection of the mass with the invaded tissue was performed (Fig. 1C & D). Intraoperative pathological diagnosis revealed that the mass was a mesenchymal tumor without any specific findings for pathological diagnosis. SFT/HPC was suspected but not definite. We performed immunohistochemical and genetic analyses using the surgically resected material.

3. Materials and methods

Resected tissues were fixed in 10% buffered formalin and embedded in paraffin. Three-micrometer-thick sections were cut and stained with hematoxylin and eosin. IHC for CD31 (DAKO, Glostrup, Denmark, 1:300), CD34 (Immunotech, Monrovia, CA, 1:10) and STAT6 (sc-621; Santa Cruz Biotechnology, Santa Cruz, CA, 1:1000) was performed using Bond Polymer Refine Detection (Leica, Wetzlar, Germany). For the detection of STAT6, pretreatment was performed in Bond Epitope Retrieval Solution 1 (Leica, pH 6.0) for 20 min. Authentic SFTs were used as positive controls. For detection of *NAB2-STAT6*, total RNA was extracted from formalin fixed paraffin-embedded (FFPE) tissue and reverse transcription-polymerase chain reaction (RT-PCR) was performed as described [7]. PCR primers were designed according to the previous reports [8]. As a control of RNA quality, amplification of GAPDH cDNA (110 bp) was done. Direct sequencing of PCR products was carried out with ABI BigDye terminator ver.3.1 (Applied Biosystems, Foster City, CA) and ABI Prism 3100-Avant Genetic analyzer (Applied Biosystems).

4. Results

The hemorrhagic brain mass was excised by operation 3 days after the onset of the symptoms. The superior sagittal sinus was also resected on suspicion of the tumor invasion. Intraoperative frozen section of the surgical material was made. Before operation, differential diagnoses included meningioma with hemorrhage, SFT/HPC with hemorrhage and metastatic carcinoma. At the time of observing the frozen section, neither metastatic carcinoma nor meningioma was suggestive. Although the pathological features were not typical, we made the possible and tentative diagnosis of meningeal SFT/HPC. Histological examination of the permanent material revealed intratumoral hemorrhage (Fig. 2A). The great majority of the tumor cells were spindle shaped and had oval nuclei with prominent myxoid stroma, partially accompanied by stromal and vascular hyalinization (Fig. 2B–D). Nuclear atypia and mitotic figures were not remarkable. Solid sheets of the tumor cells were also seen (Fig. 2E). In addition to the invasion into the superior sagittal sinus, heterogeneous cellularity, rare mitoses and no necrosis led us to the pathological diagnosis of SFT/HPC (WHO grade I or Marseille system grade IIa) [9,10]. IHC revealed that the tumor cells were positive for both membranous CD34 and nuclear STAT6, but negative for CD31 (Fig. 2F–H). Moreover, *NAB2-STAT6* fusion gene was identified by RT-PCR analysis (Fig. 3A). The fusion was in-frame and had a 7-base insertion (unknown origin) between the mid-portion of NAB2 exon 7 and STAT6 exon 16 (*7–16 fusion with 7-base insertion*). In deduced amino acid sequence, valine (V) and glutamic acid (E) in the NAB2 protein sequence were replaced by lysine (K) and threonine (T) (Fig. 3B). Thus, we confirmed the final diagnosis of meningeal myxoid SFT/HPC. Ten months after the operation, brain MRI with enhancement revealed the patency of the superior sagittal sinus, no residual tumor, and no recurrence. The patient is uneventful at approximately one year after the operation.

5. Discussion

After the recent progress in the molecular pathology of SFT/HPC [1–6], SFT and HPC are now thought to be the same category of tumors

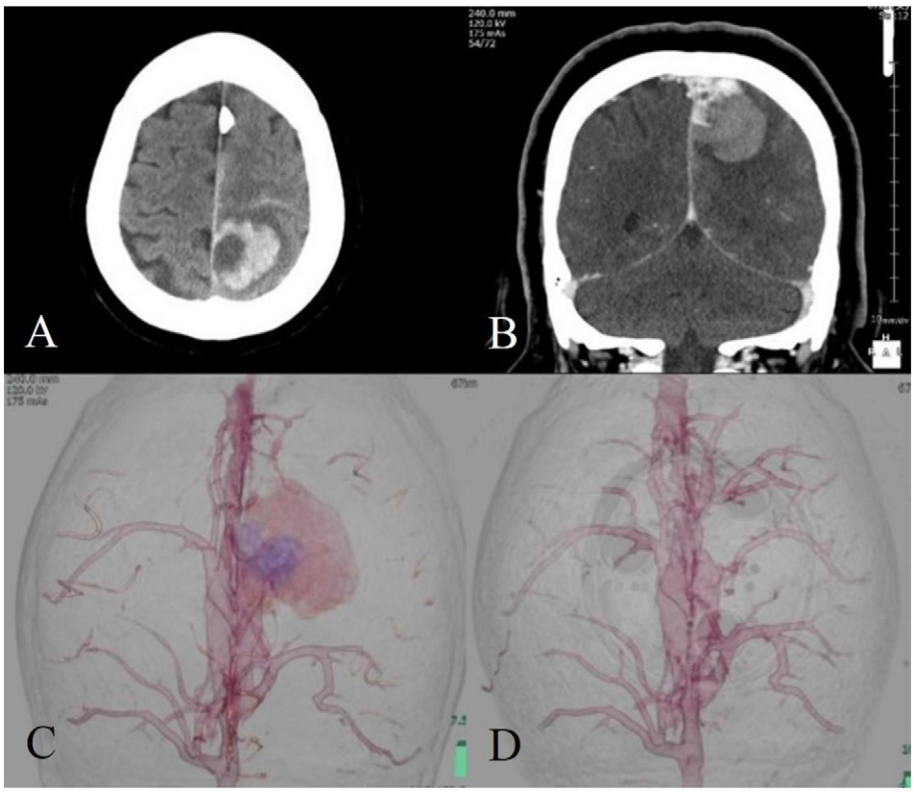

Fig. 1. Radiological findings of the patient are shown. Plain brain CT on axial section shows the hemorrhagic mass adjacent to the superior sagittal sinus (Fig. 1A). Enhanced brain CT on coronal section shows the enhancement of the superior sagittal sinus and a part of the tumor (Fig. 1B). Fig. 1C and D show the 3-dimensional CT angiography before and after the surgical resection.