

# A Case of Synchronous Occurrence of Intracranial Germinoma and Systemic Sarcoidosis

Yuri HYAKUTAKE,<sup>1</sup> Ichiyo SHIBAHARA,<sup>1</sup> Madoka INUKAI,<sup>1</sup> Hiroyuki KOIZUMI,<sup>1</sup>  
Takuichiro HIDE,<sup>1</sup> Nobuhito MOROTA,<sup>1</sup> Tsutomu YOSHIDA,<sup>2</sup> Jiichiro SASAKI,<sup>3</sup>  
and Toshihiro KUMABE<sup>1</sup>

<sup>1</sup>*Department of Neurosurgery, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan*

<sup>2</sup>*Department of Pathology, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan*

<sup>3</sup>*Research and Development Center for New Medical Frontiers, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan*

## Abstract

Although the synchronous occurrence of testicular seminoma and systemic sarcoidosis has been reported, that of intracranial germinoma and systemic sarcoidosis is unknown. A 26-year-old man presented with symptoms of panhypopituitarism and consciousness disturbance. Imaging demonstrated a large nodule in the upper right lung field and swelling of multiple bilateral pulmonary and mediastinal lymph nodes in addition to the bifocal pineal and suprasellar tumors with obstructive hydrocephalus. The pathological diagnosis of the intracranial bifocal tumors was pure germinoma, whereas that of the mediastinal lymph nodes was epithelioid granuloma. Three courses of chemotherapy using carboplatin and etoposide were administered, followed by whole ventricle irradiation. The intracranial tumors completely disappeared, but the lung nodule and mediastinal lymph nodes progressed. Whole-body fluorine-18-fluorodeoxyglucose positron emission tomography demonstrated accumulation in the mediastinal lymphadenopathy, lung masses, and multiple lymph nodes of the whole body. Transbronchial lung biopsy revealed epithelioid granuloma with multinucleated giant cells. In conjunction with the high blood concentration of angiotensin-converting enzyme and soluble interleukin-2 receptor, these findings established a diagnosis of sarcoidosis. This is the first report of synchronous occurrence of intracranial germinoma and sarcoidosis. Such coexistence is extremely rare, but we should mind that sarcoidosis can occur with intracranial germinoma.

Keywords: intracranial germinoma, sarcoidosis, synchronous occurrence

## Introduction

Although the synchronous occurrence of testicular seminoma and systemic sarcoidosis has been reported,<sup>1–4)</sup> that of intracranial germinoma and systemic sarcoidosis is unknown. We report a unique case of synchronous occurrence of intracranial germinoma and systemic sarcoidosis.

## Case Study

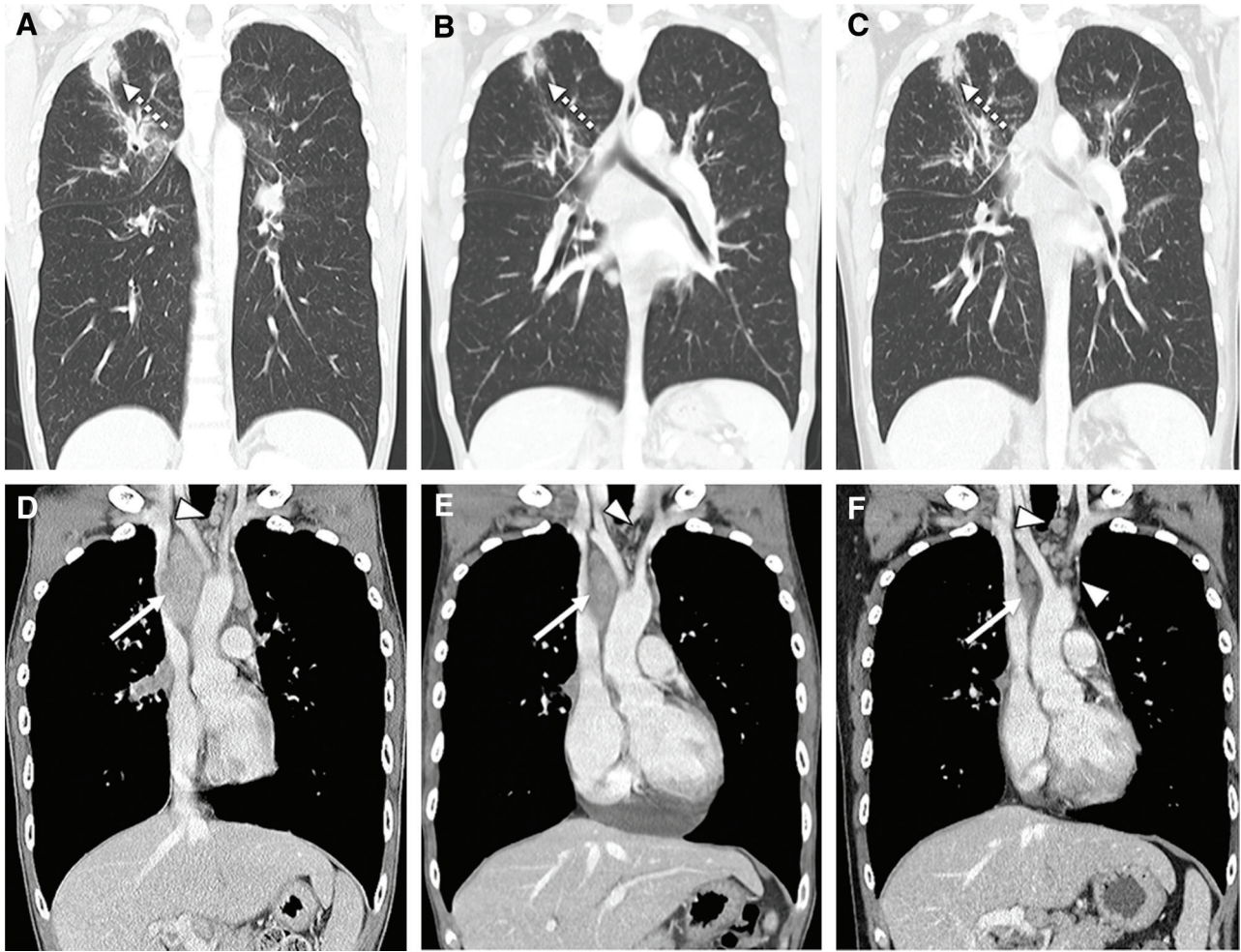
### Clinical course

A 26-year-old man presented with a 4-month history of general fatigue, walking disturbance, loss of appetite, and body weight loss. He had also suffered from polyuria, urinary incontinence, and pubic hair loss. Chest CT demonstrated a large nodule in the upper right lung field and swelling of multiple bilateral pulmonary and mediastinal lymph nodes (Fig. 1A and 1D). MRI demonstrated bifocal pineal and suprasellar tumor with obstructive hydrocephalus (Fig. 2A–C). The serum human chorionic gonadotropin (HCG), HCG- $\beta$ , and

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**Fig. 1** Coronal chest contrast-enhanced CT scans obtained before chemotherapy (A and D), 2 weeks after the start of chemotherapy (B and E), and after three courses of chemotherapy (C and F). Dotted arrows, arrows, and arrowheads indicate the nodule in the right upper lung field, mediastinal lymph node, and lymph nodes located between the recurrent laryngeal nerve and the right common carotid artery, respectively.

alpha-fetoprotein (AFP) level was 4 mIU/mL (normal, <2mIU/mL), 0.4 ng/mL (normal, <0.1 ng/mL), and 2 ng/mL (normal, <10 ng/mL), respectively. The patient underwent a biopsy of suprasellar and pineal tumors using neuro-endoscopy and endoscopic ultrasound-guided fine-needle aspiration of the mediastinal lymph nodes. The pathological diagnosis was pure germinoma of the intracranial bifocal tumor (Fig. 3A–C). In contrast, only epithelioid granuloma was found in the mediastinal lymph nodes (Fig. 3D), which were immunohistologically negative for c-KIT (Fig. 3E) and placental alkaline phosphatase (Fig. 3F).

Carboplatin and etoposide (CARE) administration with dexamethasone as an antiemetic agent was prescribed. MRI and CT obtained 2 weeks after the start of CARE therapy demonstrated apparent shrinkage of suprasellar and pineal tumors, a nodule in the upper right lung field, and the mediastinal

lymph nodes (Fig. 1B and 1E). MRI after three courses of CARE therapy and whole ventricle irradiation 23.4 Gy showed complete disappearance of the intracranial bifocal tumors (Fig. 2D–F). Chest CT demonstrated shrinkage of some mediastinal lymph nodes, but a progression of the nodule in the right upper lung and swelling of the lymph nodes located between the recurrent laryngeal nerve and the right common carotid artery (Fig. 1C and 1F).

Whole-body fluorine-18-fluorodeoxyglucose positron emission tomography (FDG-PET) demonstrated accumulation in the mediastinal lymphadenopathy, lung masses, and multiple lymph nodes of the whole body (Fig. 4). Subsequently, a transbronchial lung biopsy was performed. Histological examination of specimens from the right upper lung mass showed epithelioid granuloma with multinucleated giant cells (Fig. 3G). These findings, in conjunction with

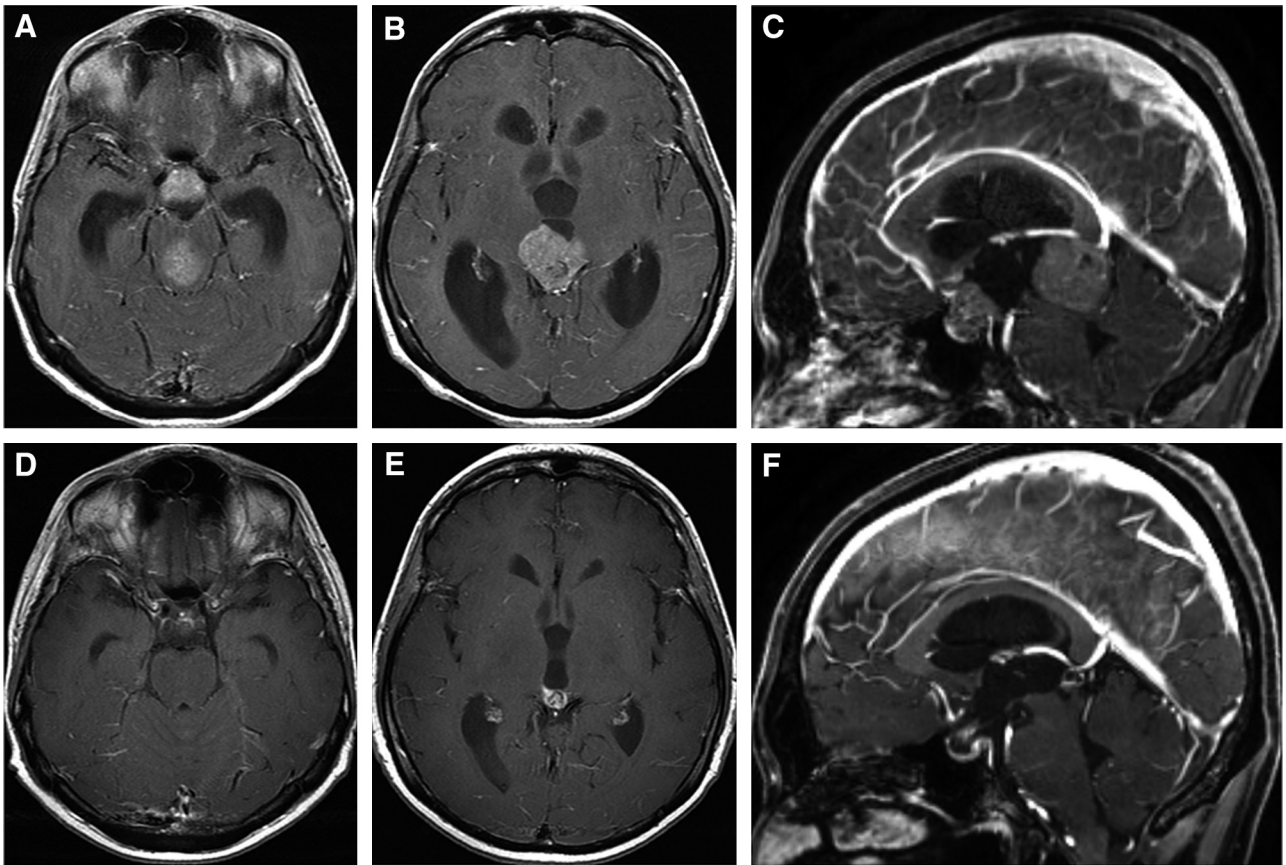


Fig. 2 Contrast-enhanced MRIs obtained before chemotherapy (A–C) and after three courses of chemotherapy and irradiation (D–F). (A, B, D, and E) Axial images, (C and F) midsagittal images.

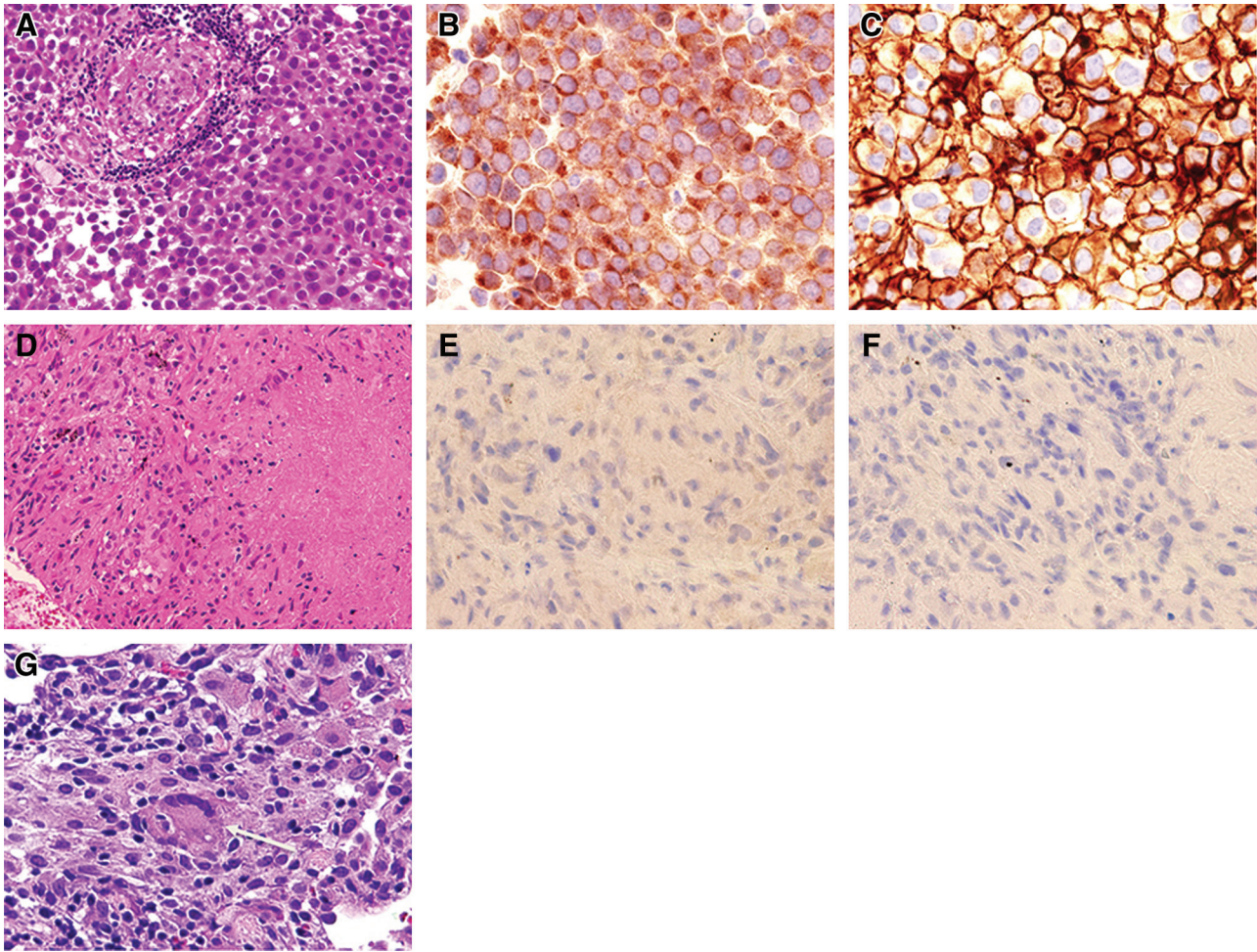
the high blood concentration of angiotensin-converting enzyme (ACE, 32.4 U/L) and soluble interleukin-2 receptor (sIL-2R, 962 U/mL), established diagnosis of the body lymphadenopathies as sarcoidosis.

### Discussion

The present case is the first report of synchronous occurrence of intracranial germinoma and systemic sarcoidosis. The diagnosis of sarcoidosis is based on three major criteria<sup>5,6</sup>: clinical presentation, histological findings of non-necrotizing granulomatous inflammation, and the exclusion of alternative causes of other granulomatous diseases, which were all met by the present case. Germinomas sometimes appear predominantly as a granulomatous reaction,<sup>7</sup> so we presumed that this patient had intracranial and mediastinal multiple germinomas at the initiation of therapy. Indeed, there were case reports of metachronous intracranial germinoma and mediastinal seminoma<sup>8</sup> or mediastinal growing teratoma syndrome.<sup>9</sup> However, after three courses of CARE therapy, chest CT showed progression of

lymphadenopathy and FDG-PET demonstrated accumulation of FDG into the whole-body lymph nodes. Evidence of multisystem organ involvement supports sarcoidosis, not a sarcoid-like reaction<sup>10</sup>; therefore, we could diagnose sarcoidosis in this patient.

Several epidemiological studies suggested a correlation between sarcoidosis and cancer.<sup>10–12</sup> Sarcoidosis affects immune dysregulation and chronic inflammation, which may increase the frequency of mutation and potentiate the risk of generating malignancy.<sup>10–12</sup> On the contrary, whether cancer causes sarcoidosis is not fully understood due to its rarity.<sup>10,13</sup> Among the rare, a literature review presented that the cumulative incidence of sarcoidosis after testicular cancers is approximately 100-fold higher than a general population of young white men,<sup>4,14</sup> and the interval between the initial diagnosis of testicular cancer and the following sarcoidosis was 12–288 months.<sup>13,14</sup> We should note the presence of selection bias and surveillance bias,<sup>10,12</sup> but previous findings suggested a correlation between testicular tumor and sarcoidosis. Similarly, intracranial germinoma, a counterpart of the testicular

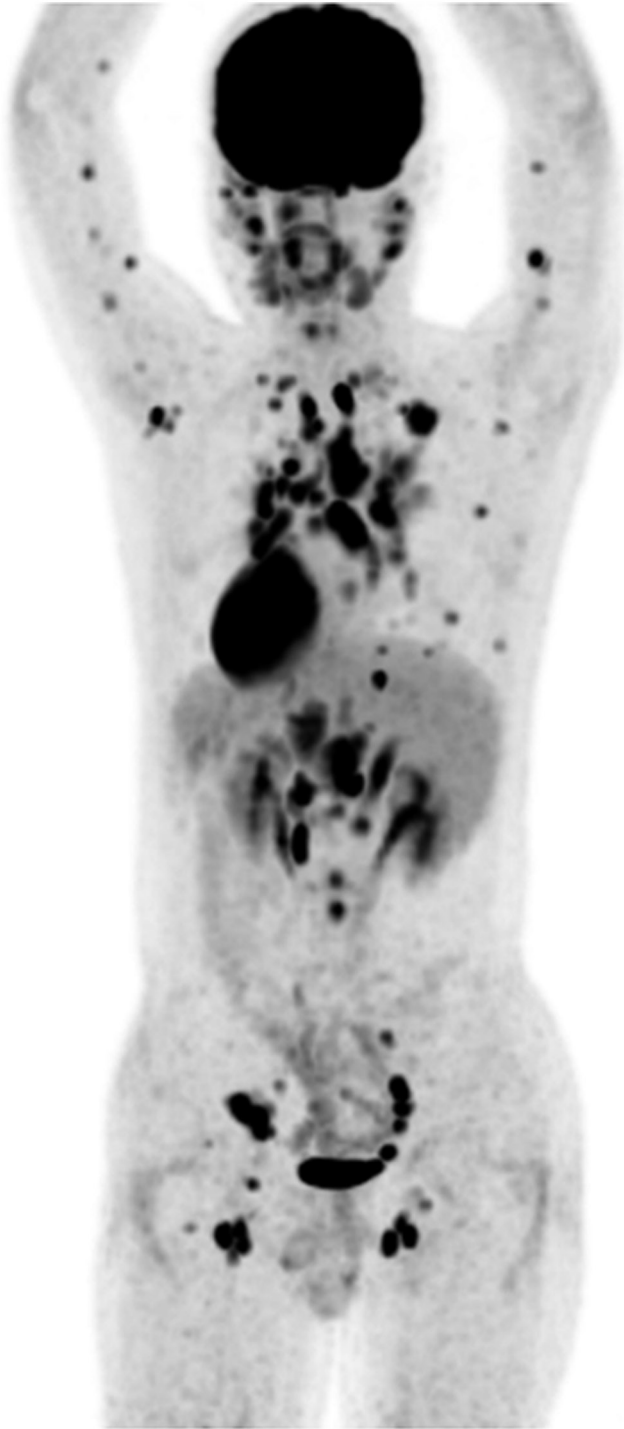


**Fig. 3** Photomicrographs of hematoxylin and eosin staining ((A, G) original magnification  $\times 200$ ; (D) original magnification  $\times 100$ ), and immunohistochemical staining (original magnification  $\times 400$ ) for c-KIT (B and E) and placental alkaline phosphatase (C and F) of the biopsied specimens from the pineal lesion (A–C), from the mediastinum lymph nodes obtained by endoscopic ultrasound-guided fine needle aspiration before chemotherapy (D–F), and from the mediastinum lymph node specimen obtained by transbronchial lung biopsy after three courses of chemotherapy (G).

tumor, and sarcoidosis can correlate. These two diseases were synchronously found in our case, and symptomatic disease duration was 4 months; therefore, we suspected that the preceding sarcoidosis might cause intracranial germinoma and not vice versa. In general, simultaneous sarcoidosis and cancer are associated with poor prognosis,<sup>15,16)</sup> but particularly sarcoidosis in testicular cancer is not related to prognosis.<sup>17)</sup> The prognostic importance of simultaneous sarcoidosis and germinoma is unknown; therefore, careful observation is mandatory.

Sarcoidosis is generally treated with steroids and immunosuppressive agents. The nodule in the upper right lung field and mediastinal lymph nodes were reduced after the first course of CARE chemotherapy, probably because the protocol included steroid

administration. These lesions could easily be misdiagnosed as germinoma. Since CT and MRI cannot clearly differentiate between germ cell tumors and sarcoidosis, tissue biopsy and blood sampling to examine the concentrations of ACE and sIL-2R were necessary to make the definitive diagnosis of sarcoidosis. Also, FDG-PET was not sufficient to diagnose germinoma,<sup>18)</sup> but helped to detect sarcoidosis.<sup>19)</sup> Some patients with mediastinal lesions coexistent with testicular germ cell tumor have been treated under misdiagnoses of sarcoidosis, resulting in inadequate interventions for true metastatic germ cell tumor, or have died due to unnecessary chemotherapy for sarcoidosis.<sup>3,20)</sup> We should be aware that sarcoidosis can occur in patients with intracranial germ cell tumors.



**Fig. 4** Whole-body fluorine-18-fluorodeoxyglucose positron emission tomography image.

### Conclusion

We reported a case of synchronous occurrence of intracranial germinoma and systemic sarcoidosis. The etiological association between intracranial

germinoma and sarcoidosis is still unclear, but neurosurgeons should be aware of such coexistence.

### Ethics Approval

The ethics committee of Kitasato University School of Medicine and the Japan Neurosurgical Society do not require ethics approval for case reports.

### Informed Consent

Written informed consent was obtained from the patient.

### Conflicts of Interest Disclosure

The authors declare that they have no conflict of interest.

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Corresponding author: Ichiyo Shibahara, MD, PhD  
Department of Neurosurgery, Kitasato University  
School of Medicine, 1-15-1 Kitasato, Minami-ku,  
Sagamihara, Kanagawa 252-0374, Japan.  
e-mail: shibahar@med.kitasato-u.ac.jp