

## Treatment of Meningioma in a Patient with Congenital Immunodeficiency Disorder

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### ABSTRACT

We treated a patient with meningioma suffering from a congenital immunodeficiency syndrome. The patient was diagnosed with common variable immunodeficiency (CVID) in youth, and had suffered from repeated infections, especially in the respiratory tract, requiring continuous treatment with antibiotics. Imaging revealed a tumor located in the left frontal region with a broad attachment suggesting meningioma in the convexity dura mater. Gammaglobulin was infused intravenously preceding the operation and serum gammaglobulin was controlled at over 400 mg/dl and then a Simpson grade 1 operation was performed. The patient did not show any complications in infectious susceptibility, and there was no recurrence of the tumor in the 5 years following the operation. The surgical risk for CVID patients in the neurosurgical field is still not clear, but we could maintain the condition of the patient by controlling the serum gammaglobulin level in the perioperative period.

**Key words:** Meningioma, Treatment, Common variable immunodeficiency

Common variable immunodeficiency (CVID) is a subclass of immunodeficiency disorder involving congenital antibody deficiency and occurs with an incidence of 1:50,000 to 1:200,00<sup>1)</sup>. The advancement of medical treatment, especially intravenous immunoglobulin therapy, has allowed patients with CVID to be more completely managed, resulting in improving survival. However, the mortality rate over a 25-year period is estimated at 24% because of lymphoma, chronic pulmonary disease, and other complications<sup>5)</sup>. In patients with CVID, several kinds of surgical intervention have been successfully added to their management<sup>5)</sup>, although the guidelines for surgical indication do not provide estimates of survival for these patients. Meningioma is the most common brain tumor; however, when and how an incidental meningioma should be treated is controversial. Following reviews of incidental meningiomas, it has been proposed that the observation of their course without surgical intervention is appropriate in most cases, while it is also acknowledged

that the particular situation and condition of each patient requires individual decisions<sup>19,25)</sup>. We report our experience of a patient with meningioma associated with CVID, and investigated the indications and treatment for such patients from the literature.

### CASE REPORT

A forty-five-year-old female was admitted to our hospital with an intracranial tumor. Her first symptom was headache but other neurological examination was normal. Brain CT at another hospital revealed a large tumor, 3.0-3.5 cm in diameter, with some calcification, in her left frontal region. She had been medicated for CVID in our hospital since 24 years of age and had a history of repeated respiratory tract infections. She had not yet been given intravenous immunoglobulin therapy, but had received continuous antibiotic therapy for her refractory respiratory infection. She also had complications of bronchiectasis

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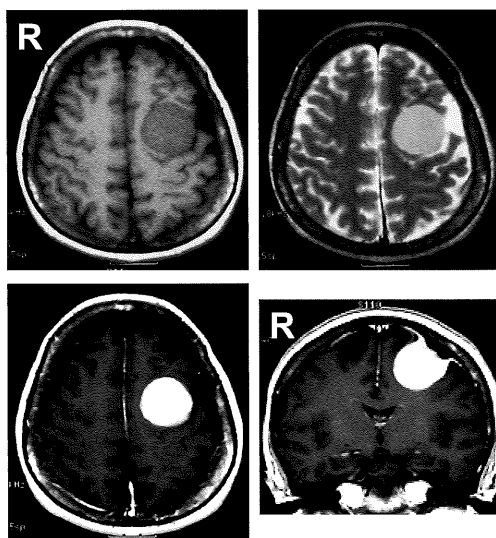
owing to the refractory infection of her respiratory organs.

Neurological examination was normal. Blood examination showed an extremely low level of serum immunoglobulins (IgG: 54, IgA: 10, IgM: 10 mg/dl) on admission. MRI strongly suggested a convexity meningioma in her left frontal region, 3.5 cm in maximum diameter, with a clear margin and slight calcification (Fig. 1). The tumor had a wide attachment to the convexity dura mater, and strongly compressed the superior and middle frontal gyrus. Conventional angiography was not performed to avoid the risk of infection and because 3D-CT angiography revealed that this tumor was not highly vascular and did not show an obvious feeding artery, nor did it encase large vessels (Fig. 2). A conventional but small frontal craniotomy was designed to minimize the incision and craniotomy, but to expose the tumor sufficiently. The superior location of the tumor was thought to facilitate this.

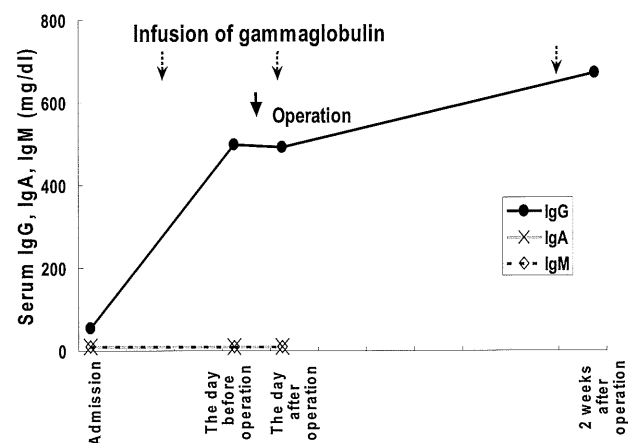
Prior to the operation, serum gammaglobulin was raised to the serum level, 400-500 mg/dl by the intravenous infusion of gammaglobulin

according to the direction of a hematologist. The operation was performed in a clean operating room to reduce the risk of infection. The part of dura mater attached to the tumor was removed, and the deficit was repaired by a pericranial flap. The tumor was totally resected (Simpson grade 1) and third-generation broad-spectrum cefem antibiotics were administered to the patient after surgery. Histopathology revealed that this tumor was a fibrous meningioma and the Mib-1 index was less than 1%.

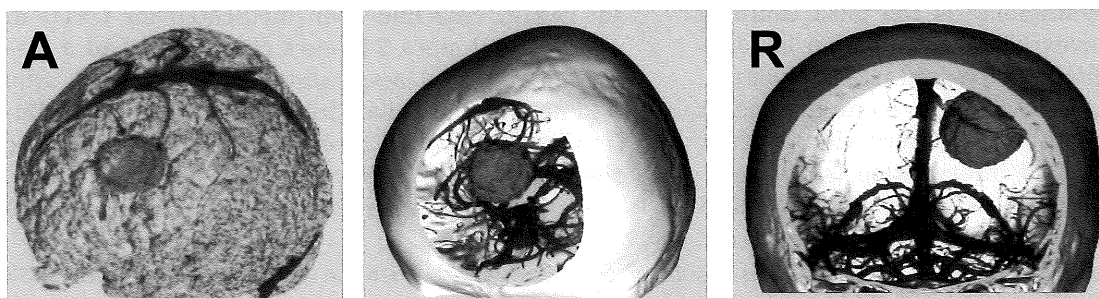
The immediate postoperative course was uneventful and suggested no features of infection. Serum gammaglobulin was maintained at over 400 mg/dl until at least 4-weeks after the operation, taking into account the half-life of the infused gammaglobulin. After this period, serum gammaglobulin was allowed to gradually decrease to its preoperative value with careful observation of the patient's condition (Fig. 3). Follow-up brain examination demonstrated no tumor recurrence and no latent infection in the operative field for six years following the operation.



**Fig. 1.** Preoperative MRI: Solid tumor uniformly enhanced in the left frontal region. The tumor had a clear margin and attachment to the convex dura mater.



**Fig. 3.** Levels of serum immunoglobulin during the perioperative period. Serum IgG was maintained at 400-500 mg/dl from the day of operation until four weeks after operation.



**Fig. 2.** Preoperative 3D-CT: CT angiography did not reveal hyper-vascularity, or a feeding artery.

## DISCUSSION

CVID was reported to lead to a higher mortality rate compared with the general population in a survey<sup>5,6</sup>. However, it is possible for CVID patients to have a full-time job and also achieve pregnancy under its treatment<sup>23</sup>. Of supervening tumors in congenital immunodeficiency patients, lymphoma is well known<sup>5,6</sup>. As for other kinds of brain complications, primary leiomyosarcoma and cases of infectious disease like encephalomyelitis and cerebral toxoplasmosis have been reported in CVID patients<sup>9,11,18</sup>, but benign brain tumors are not commonly associated with CVID.

A previous report about CIVD revealed that 2 of 16 patients with splenectomy had perioperative complications and another 2 patients suffered from sepsis more than 1 year after operation<sup>5</sup>. Cases of organ transplantation were reported in liver, lung, and lung-heart<sup>5,8,10</sup>. A case with bilateral lung transplantation was lost through surgical complications, but the others showed good courses after operation without incidence of severe infection. These cases revealed that surgical procedure could be beneficial to CIVD patients. Adequate serum IgG concentration for congenital immunodeficiency patients is not certain in the case of brain surgery, therefore serum IgG was kept at 400-500 mg/dl during and after the operation. Infections occurred in 2.6% of patients who underwent neurosurgical operations after the exclusion of all known factors that influence sepsis<sup>20</sup>. A recent report indicated that the incidence of infection after neurosurgical procedure was less than 1%<sup>16</sup>. These reports indicated that infectious complications in brain surgery were not higher than in splenectomy<sup>2</sup>. The issue was how long serum IgG should be kept at above concentration because this patient was not receiving intravenous immunoglobulin treatment. A shunt operation is one of the high-risk operations that cause infection because a foreign body is placed in patients<sup>20</sup>, and 84% of infection occurred in the acute period<sup>3</sup>. Needless to say, careful observation was necessary to detect delayed infection, but replacement of serum IgG until the subacute period after the operation seemed reasonable in this case.

Previous studies of incidental meningioma recommended the observation of its course as a first step<sup>19,25</sup>. The tumor in the present patient showed slight calcification that was considered to indicate the slow growth of the meningioma<sup>19,21</sup>. On the other hand, high intensity on T2-WI of MRI and tumor location at the non-skull base indicated tumor progression<sup>12,22</sup>. In the case of asymptomatic meningioma, our usual recommendation is simply course observation, but surgical risk in elderly patients with meningioma is higher than that in younger patients<sup>14</sup>. Observation of

the tumor course included the possibility that an infection in her respiratory tract would contraindicate surgical invasion if necessary, especially when she became advanced in age. Radiosurgery was also highlighted. Gamma Knife radiosurgery provides 5- and 10-year actuarial tumor control rates of 93% for benign meningioma<sup>15</sup>. Pollock et al reported that gamma knife radiosurgery provides equivalent tumor control to Simpson grade 1 resection for patients with small to medium sized meningioma<sup>22</sup>. However, meningiomas of the convexity, parasagittal region, or falx cerebri have a higher incidence of peritumorous imaging changes, which were related to neurological symptoms in 40% of the patients after gamma knife surgery, than those of the skull base<sup>4</sup>. Gamma knife surgery would also control relatively large meningiomas, while the complication rate became higher<sup>4,13</sup>. In CVID patients, malignant transformation after radiosurgery must be considered because they have a higher risk for cancer<sup>7,17</sup>.

In this case, we selected surgical resection after considering the above, with the background that the tumor control ratio after Simpson grade 1 resection for benign meningioma of the convexity dura mater was 94% / 9 years around that period in our institute<sup>24</sup>. The surgical risk for CVID patients with an intracranial benign tumor in the neurosurgical field is not clear; however, maintaining the serum immunoglobulin level in the perioperative period could stabilize their condition.

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