www.jkns.or.kr http://dx.doi.org/10.3340/jkns.2014.55.5.300
Print ISSN 2005-3711 On-line ISSN 1598-7876
J Korean Neurosurg Soc 55 (5) : 300-302, 2014

Case Report

IgG4-Related Intracranial Hypertrophic Pachymeningitis : A Case Report and Review of the Literature

Satoru Takeuchi, M.D., Hideo Osada, M.D., Soichiro Seno, M.D., Hiroshi Nawashiro, M.D.
Department of Neurosurgery, National Defense Medical College, Saitama, Japan

Hypertrophic pachymeningitis is an uncommon disorder that causes a localized or diffuse thickening of the dura mater. Recently, the possibility that IgG4-related sclerosing disease may underlie some cases of intracranial hypertrophic pachymeningitis has been suggested. We herein report the tenth case of IgG4-related intracranial hypertrophic pachymeningitis and review the previous literature. A 45-year-old male presented with left-sided focal seizures with generalization. Magnetic resonance imaging (MRI) revealed a diffuse thickening and enhancement of the right convexity dura matter and falx with focal nodularity. The surgically resected specimens exhibited the proliferation of fibroblast-like spindle cells and an infiltration of mononuclear cells, including predominantly plasma cells. The ratio of IgG4-positive plasma cells to the overall IgG-positive cells was 45% in the area containing the highest infiltration of plasma cells. On the basis of the above findings, IgG4-related sclerosing disease arising from the dura mater was suspected. IgG4-related sclerosing disease should be added to the pachymeningitis spectrum.

Key Words : Pachymeningitis · IgG4-related disease · MRI · Immunohistochemistry.

INTRODUCTION

IgG4-related disease is a recently defined disorder characterized by an inflammatory reaction rich in IgG4-positive plasma cells associated with sclerosis[4]. This disease includes autoimmune pancreatitis, Mikulicz disease, pseudotumor of the lung, tubulointestinal nephritis, and Riedel thyroiditis[4]. Central nervous system involvement is extremely rare, and the most commonly reported location is the pituitary gland[4].

Hypertrophic pachymeningitis is an uncommon disorder that causes a localized or diffuse thickening of the dura mater[10]. Rare cases of dural spinal involvement by IgG4-related sclerosing disease have also been reported[1,2], and recently, the possibility that IgG4-related sclerosing disease may underlie some cases of intracranial hypertrophic pachymeningitis has also been suggested. However, only 9 cases of intracranial hypertrophic pachymeningitis related to IgG4 infiltration have been reported in the literature[3,5-9,11]. We herein report an additional case of IgG4-related intracranial hypertrophic pachymeningitis proved by both local infiltration of plasma cells and IgG4/IgG ratio in surgical specimen.

CASE REPORT

A 45-year-old, previously healthy male presented with focal seizure of left extremities with generalization. On admission, his neurological examination was normal. MRI revealed irregular dural thickening and a marked enhancement of the right parieto-occipital dura and falx (Fig. 1). Whole-body 2-[^{18}F]-fluoro-2-deoxy-D-glucose positron emission tomography scanning demonstrated no abnormal hyperuptake, in the whole body, including the brain and dura. The preoperative differential diagnoses included meningioma en plaque, lymphoma, tuberculosis, sarcoidosis, collagen vascular disorders, lymphoma, meningeal carcinomatosis diseases and IgG4-related disease. Surgical resection was performed via craniotomy. The mass in the convexity dural region was resected, while the mass adjacent to the superior sagittal sinus and falx was not removed. In the surgically resected specimens, a solid yellow to white-colored lesion measuring 35×33×6 mm was found in the dura mater (Fig. 2A). Histologically, the solid lesion consisted of a proliferation of fibroblast-like spindle cells and an infiltration of mononuclear cells, including predominantly plasma cells, with abundant collagenous

• Received : July 25, 2012 • Revised : July 14, 2013 • Accepted : May 15, 2014
• Address for reprints : Satoru Takeuchi, M.D.
Department of Neurosurgery, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359-8513, Japan
Tel : +81-4-2995-1656, Fax : +81-4-2996-5207, E-mail : s.takeuchi@room.ocn.ne.jp

tissue (Fig. 2B). For immunohistochemistry, we used monoclonal antibodies against IgG and IgG4. In the immunohistochemical study, most of the plasma cells infiltrating into the sclerosing lesion were found to be IgG-positive [IgG4-positive plasma cells/high power field (HPF), 78], and the ratio of IgG4-positive plasma cells to the overall IgG-positive cells was 45% in the area containing the highest infiltration of plasma cells (Fig. 2C, D). On the basis of the above findings, IgG4-related sclerosing disease arising from the dura mater was suspected. Thus, we evaluated a patients' serum IgG4 level and it was 51 mg/dL (normal range, 4.8–105.0 mg/dL). The patient's postoperative course was uneventful, and no radiological or clinical signs of recurrence were noted 12 months after performing a surgical resection (Fig. 3). Adjuvant steroid therapy was therefore put on hold.

DISCUSSION

IgG4-related intracranial hypertrophic pachymeningitis is extremely rare. To the best of our knowledge, only 10 cases have been reported in the literature, including the present case[3,5-9,11]. A summary of the cases is shown in Table 1. The ages of the patients ranged from 26 to 75 years (mean, 51.9 years). Seven patients were male and three were female. Headache was the most common symptom (60%). The serum IgG4 levels were evaluated in four patients, and elevated IgG4 level was observed in one patient. All patients underwent surgery. Steroid treatment was started prior to surgery in one case, and after surgery in seven cases. The outcomes were good, except for one patient who was diagnosed at autopsy.

There are no definite diagnostic criteria for IgG4-related disease. However, some researchers have recommended a cut-off level for the absolute number of IgG4-positive cells at >50/HPF, and the ratio of IgG4-positive cells/IgG-positive cells >40%[4]. The elevation of the serum IgG4 levels is not mandatory for the diagnosis, because the serum IgG4 level often correlates with the disease activity and the number of involved organs, but the levels may also be normal[4]. Our patient met the above diagnostic criteria. Additionally, our literature review suggested that serum IgG4 level

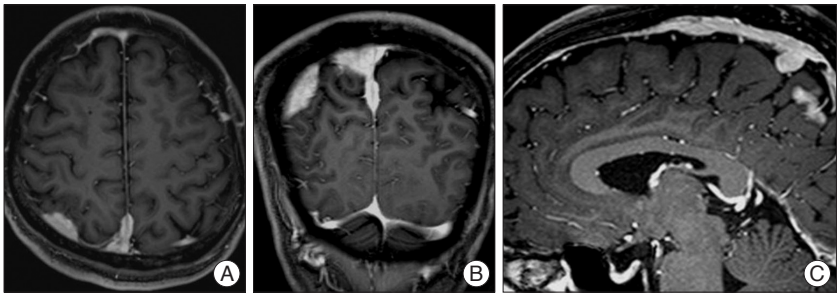

Fig. 1. Preoperative axial (A), coronal (B), and sagittal (C) gadolinium-enhanced magnetic resonance images show irregular thickening and a marked enhancement of the right parieto-occipital dura and falx.

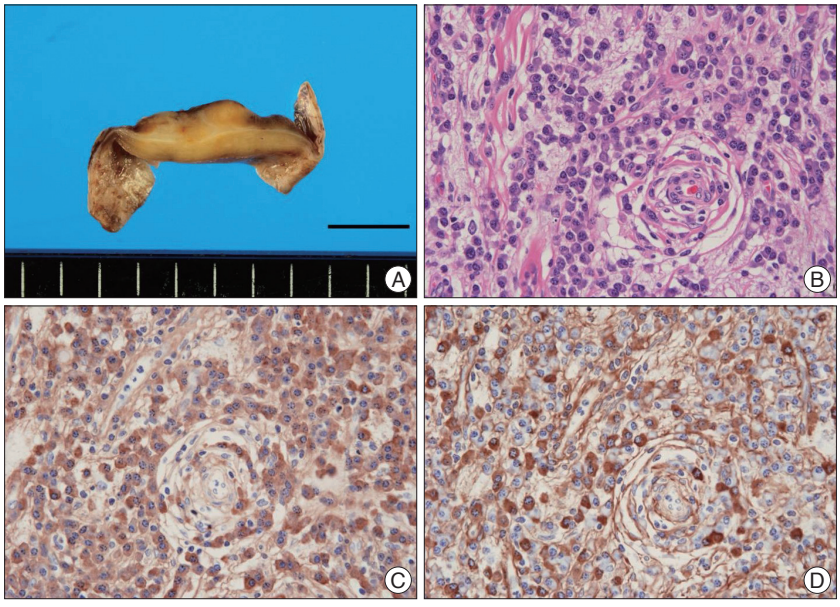

Fig. 2. Pathological findings. A : A macroscopic observation shows a solid yellow to white-colored lesion in the dura mater. B : The photomicrograph shows the solid lesion consisting of the proliferation of fibroblast-like spindle cells and an infiltration of mononuclear cells, including predominantly plasma cells, with abundant collagenous tissue (H&E; original magnification, ×400). C and D : IgG (C) and IgG4 (D) staining reveal that most of the plasma cells infiltrating into the sclerosing lesion are IgG-positive (IgG4-positive plasma cells/high power field, 78), and that the ratio of IgG4-positive plasma cells to the overall IgG-positive cells is 45% in the area containing the highest infiltration of plasma cells (original magnification, ×400).

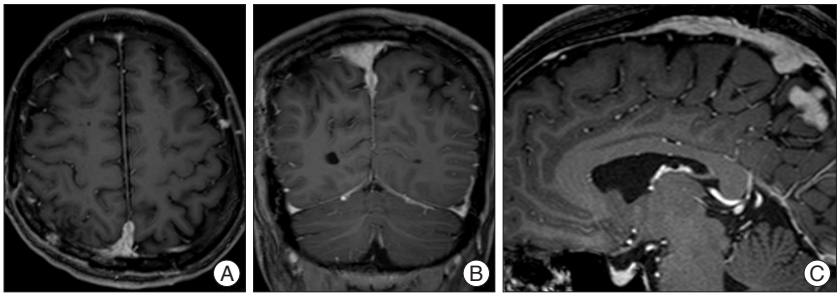

Fig. 3. The twelve-month postoperative axial (A), coronal (B), and sagittal (C) gadolinium-enhanced magnetic resonance images show the disappearance of the mass in the convexity dural region. The mass adjacent to the superior sagittal sinus and falx is left in place.

Table 1. Summary of reported patients of IgG4-related hyprtrophic cranial pachymeningitis

Author	Age (y) Gender	Symptoms	Location	Serum IgG4	Surgery	IgG4+/HPF	IgG4+/IgG+	Steroid†	Outcome	Follow-up
Lui et al.[8]	45M	Weakness	Frontal region	NA	Near total resection	41	NA	No	Good	NA
	26F	Headache, eye symptoms, ear pain	Fronto-temporal region	NA	Biopsy	36	NA	Yes	Good	7 months
Riku et al.[11]	75M	Appetite loss, wobbliness, decreased consciousness	Falx, tentorium	NA	Biopsy	NA	NA	Yes	Death	40 days
Kosakai et al.[6]	54F	Eye symptoms, facial sensory disturbance, deafness, headache, fever	Orbital dura, the parasellar area, middle skull base	251 mg/dL	Yes*	NA	>50%	Yes	Good	1 month
Lindstrom et al.[7]	60F	Bilateral optic neuropathy		NA	Yes*	41.6	24%	Yes	Good	17 months
	53M	Headache	Posterior fossa	NA	Yes*	26.8	NA	Yes	Good	115 months
Kim et al.[5]	43M	Headache, weakness	Frontal region	NA	Subtotal resection	72.4	NA	Yes	Good	6 months
Norikane et al.[9]	53M	Headache, ophthalmoplegia	Fronto-temporo-parietal region	97 mg/dL	Biopsy	NA	NA	Yes	Good	NA
Della Torre et al.[3]	65M	Headache, dysarthria	Posterior fossa	152 mg/dL	Biopsy	NA	40–70%	Yes	Good	10 months
Present case	45M	Seizure	Parieto-occipital region, falx	51 mg/dL	Partial resection	58	45%	No	Good	12 months

*There were no descriptions about whether these patients underwent biopsies or resections, †Steroid treatment was started prior to surgery in this case, and after surgery in seven cases. F : female, HPF : high power field, M : male, NA : not available

may be normal in most patients with IgG4-related intracranial hypertrophic pachymeningitis.

Steroid treatment has been recommended for intracranial hypertrophic pachymeningitis as well as IgG4-related disease. However, conservative observation can also be applied in some patients. As a result, we therefore put adjuvant steroid therapy on hold for our patient. Some authors have suggested that a biopsy, followed by steroid treatment, may be safe and valid[7,8]. However, due to their rarity, there is no unified treatment protocol for such cases. To date, it remains unclear whether biopsy or partial/subtotal resection is better, and whether steroid treatment is necessary. In our patient, easily resectable lesion was removed, whereas we consider that biopsy might be sufficient to obtain definitive diagnosis. Further investigations are required to determine the optimal treatment strategy.

CONCLUSION

We presented a case of IgG4-related intracranial hypertrophic pachymeningitis. We suggest that IgG4-related disease should be added to the pachymeningitis spectrum, even when serum IgG4 level is normal.

References

1. Chan SK, Cheuk W, Chan KT, Chan JK : IgG4-related sclerosing pachymeningitis : a previously unrecognized form of central nervous system involvement in IgG4-related sclerosing disease. **Am J Surg Pathol 33** : 1249-1252, 2009
2. Choi SH, Lee SH, Khang SK, Jeon SR : IgG4-related sclerosing pachymeningitis causing spinal cord compression. **Neurology 75** : 1388-1390, 2010
3. Della Torre E, Bozzolo EP, Passerini G, Doglioni C, Sabbadini MG : IgG4-related pachymeningitis : evidence of intrathecal IgG4 on cerebrospinal fluid analysis. **Ann Intern Med 156** : 401-403, 2012
4. Divatia M, Kim SA, Ro JY : IgG4-related sclerosing disease, an emerging entity : a review of a multi-system disease. **Yonsei Med J 53** : 15-34, 2012
5. Kim EH, Kim SH, Cho JM, Ahn JY, Chang JH : Imunoglobulin G4-related hypertrophic pachymeningitis involving cerebral parenchyma. **J Neurosurg 115** : 1242-1247, 2011
6. Kosakai A, Ito D, Yamada S, Ideta S, Ota Y, Suzuki N : A case of definite IgG4-related pachymeningitis. **Neurology 75** : 1390-1392, 2010
7. Lindstrom KM, Cousar JB, Lopes MB : IgG4-related meningeal disease: clinico-pathological features and proposal for diagnostic criteria. **Acta Neuropathol 120** : 765-776, 2010
8. Lui PC, Fan YS, Wong SS, Chan AN, Wong G, Chau TK, et al. : Inflammatory pseudotumors of the central nervous system. **Hum Pathol 40** : 1611-1617, 2009
9. Norikane T, Yamamoto Y, Okada M, Maeda Y, Aga F, Kawai N, et al. : Hypertrophic cranial pachymeningitis with IgG4-positive plasma cells detected by C-11 methionine PET. **Clin Nucl Med 37** : 108-109, 2012
10. Park IS, Kim H, Chung EY, Cho KW : Idiopathic hypertrophic cranial pachymeningitis misdiagnosed as acute subtentorial hematoma. **J Korean Neurosurg Soc 48** : 181-184, 2010
11. Riku S, Hashizume Y, Yoshida M, Riku Y : [Is hypertrophic pachymeningitis a dural lesion of IgG4-related systemic disease?]. **Rinsho Shinkeigaku 49** : 594-596, 2009