Hypertrophic pachymeningitis, also well known as idiopathic hypertrophic pachymeningitis, is a rare disorder in which intracranial dura mater becomes focally or diffusely thickened, often adhering to the underlying leptomeninges. The reported imaging findings include dural thickening, dural mass, sinus thrombosis, and venous congestion with white matter changes. Cerebral parenchymal involvement is extremely rare; only 8 cases of pachymeningitis involving the cerebral parenchyma have been reported in the literature. Recently, the possibility that an IgG4-related sclerosing disease may represent a part of idiopathic hypertrophic pachymeningitis was suggested. We report a case of pachymeningitis involving cerebral parenchyma that is associated with IgG4-related sclerosing disease.

Case Report

History and Examination. This 43-year-old man, with no history of disease except diabetes mellitus and hypertension, suffered from headache and progressive motor weakness in the right upper extremity for 3 months. He was afibrile and had neither papilledema nor meningeal signs. He showed normal complete blood count, erythrocyte sedimentation rate, and serum C-reactive protein level.

Brain MR imaging demonstrated an irregularly shaped, extraaxial mass in the left frontal area compressing the prefrontal cortex (Fig. 1). A T2-weighted MR imaging study showed a hypointense focal mass, and a high-intensity area extending to the white matter corresponding to extensive edema. A T1-weighted MR imaging study obtained with added Gd showed a heterogeneously enhanced nodular mass and strong enhancement near the corpus callosum and cingulate gyrus. Cerebral angiography revealed vascular staining supplied from the left middle meningeal artery.

Operation. Our first step in preparation for the surgical treatment was embolization of the left middle meningeal artery by placement of polyvinyl alcohol particles (150–250 μm in diameter; Target Therapeutics Corp.). During surgery, the mass located at the extradural space was peeled off and the thickened dura was resected. Grossly, the mass was yellowish-white and had a hard consistency and less vascularity than a meningioma. There was no continuation between the main mass lesion and the parenchymal enhanced lesion near the corpus callosum and cingulate gyrus, and biopsy for the separate enhanced lesion was not performed.
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Pathological Findings. Histopathological examination revealed thickened fibrous tissue with marked inflammatory cell infiltration. Most of the infiltrated cells were mature lymphocytes and plasma cells, but not Langhans histiocytes or meningothelial cells (Fig. 2). There was no evidence of granuloma formation, caseous necrosis, or vasculitis. Immunohistochemical staining for IgG4 was performed using a mouse monoclonal IgG4 antibody (clone HP6025, 1:1000 dilution; Caltag Laboratory) and a rabbit polyclonal IgG antibody (dilution 1:100,000; Dako). We performed immunohistochemical staining by using a VENTANA-BenchMark XT autostainer with the XT ultraView DAB Kit (Ventana Medical Systems) according to the vendor’s protocol. The number of IgG4- and IgG-positive plasma cells was counted in 5 hpfs (microscope equipped with a 10× eyepiece and a 40× lens) containing the highest concentration of inflammation. The average numbers of IgG4- and IgG-positive plasma cells were 72.4 and 4.6, respectively. The average percentage of IgG4- and IgG-positive cells was 94% (Fig. 3).

Postoperative Course. No neurological deficits were observed following surgery. Postoperatively, laboratory evaluation was performed for autoimmune diseases and infectious diseases; however, results of all of these tests were negative. Evaluation of the pancreas, bile duct, gall bladder, thyroid, kidney, and lung showed normal findings. According to these results, we diagnosed the disease as IgG4-related hypertrophic pachymeningitis. The patient took 20 mg of oral prednisolone daily for 3 months after the surgery. Brain MR imaging studies obtained at 3 and 6 months after surgery demonstrated that the dural mass and the adjacent brain edema had completely disappeared. In addition, the isolated enhancement near the corpus callosum and cingulate gyrus had also resolved (Fig. 4). The patient has been doing very well without any significant symptoms suggestive of disease recurrence; however, long-term follow-up MR imaging was not available.

Discussion

Cranial idiopathic hypertrophic pachymeningitis is a very rare disease that causes dural thickening with unknown origins. This disease is mainly classified into 2 groups: diffuse linear and focal nodular types. The majority of cases are the diffuse linear type, which causes various symptoms due to fibrous entrapment of cranial nerves or ischemia; symptoms include 1) headache with or without increased intracranial pressure, and 2) cranial neuropathy.6,7,14,24 Immunosuppressants such as steroids, azathioprine, and methotrexate are considered the main treatment options, and are usually effective.1,10,25 The disease course is highly variable, but it usually shows a chronic relapsing and remitting course.15,24 On the con-
Fig. 2. Photomicrographs of sections stained with H & E. Low-power view showing a thickened crescent-shaped mass in the dura mater (A). High-power views showing multifocal inflammatory cell infiltration along the hyalinized vessels (B), with surrounding dense fibrosis (C). Prominent plasma cell infiltration is noted (D).

Fig. 3. Photomicrographs of sections prepared with immunohistochemical staining, demonstrating predominant IgG4-positive plasma cells in the inflammatory cell–infiltrated area (B–D) compared with IgG-positive cells (A). The absolute number of IgG4-positive plasma cells and the ratio of IgG4+/IgG-positive plasma cells are sufficient for the diagnosis of IgG4-related sclerosing disease.
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trary, a nodular type is not common and resembles a neoplasm, which could lead to surgical removal.

Basically, the diagnosis of idiopathic hypertrophic pachymeningitis is usually made by excluding other possibilities. There is no doubt that meningeal biopsy is the most confirmatory diagnostic study, but the diagnosis can be made clinically based on laboratory and radiological evaluation and the effectiveness of corticosteroid or immunosuppressive therapy in a patient with a diffuse linear lesion. However, in a patient with a focal nodular type that mimics a meningioma, pathological confirmation is strongly recommended.

Even though inflammation is usually localized on the dura mater, it sometimes involves nearby cerebral parenchyma as well. In a diffuse type of idiopathic hypertrophic pachymeningitis, Matsushita et al. performed biopsies in lesions with high signal intensity on T2-weighted images in the white matter as well as thickened dura mater. The biopsies revealed microglial proliferation and lymphocytic perivascular infiltration. Thus, some authors named this condition “pachymeningoencephalitis” and suggested that inflammatory cells can infiltrate the brain parenchyma after invading the subarachnoid and Virchow-Robin spaces. Since 1993, there have been 8 cases of cranial idiopathic hypertrophic pachymeningitis in which intraaxial inflammatory involvement was found (Table 1).

In our case, this mass-forming lesion was located on the cerebral convexity, mimicking a meningioma. However, the presence of brain parenchymal involvement was very unusual. The histopathological findings were consistent with hypertrophic pachymeningitis. It is interesting that preoperative MR imaging showed strong enhancement at the lower periphery of adjacent brain parenchyma. After 3 months of steroid medication, follow-up MR images showed that the remaining enhanced lesion near the corpus callosum and cingulate gyrus had completely resolved and become a defect with encephalomalacic change. Although pathological confirmation of parenchymal involvement was not available in our case, findings such as the presence of a lesion separated from the main mass, its enhancement on MR imaging, and especially good response to steroid medications are suggestive of parenchymal involvement of hypertrophic pachymeningitis.

Immunoglobulin G4–related sclerosing pancreatitis, which was thought to be a distinct subtype of autoimmune pancreatitis, was first described by Hamano et al. Because IgG4-related sclerosing pancreatitis is frequently found to be associated with extrapancreatic lesions, this condition is called “IgG4-related sclerosing disease.”

Pathologically, this disease is characterized by extensive infiltration of IgG4-positive plasma cells in various organs. It predominantly occurs in middle-aged and elderly men, and shows good response to glucocorticoid medication. Clinically, IgG4-related sclerosing disease often presents as a mass-like lesion that can be confused with malignancy. Central nervous system involvement in this disease is very rare. It has been reported that IgG4-related sclerosing disease commonly involves the pituitary gland.

Recently, there has been an increasing number of reports focusing on the relationship of hypertrophic pachymeningitis and IgG4-related sclerosing disease. The reports suggested that idiopathic hypertrophic pachymeningitis might be part of a disease spectrum, although not all such cases can be categorized as IgG4-related sclerosing disease. In the diagnosis of autoimmune pancreatitis, biopsy followed by immunohistochemical staining is not always mandatory because the diagnosis can be made when its radiological finding is typical and serum IgG4 is elevated. Response to steroid therapy and other organ involvement help the diagnosis as well. Thus, meticulous evaluation including serum IgG4 levels, other autoantibodies, and imaging studies for other organ involvement are recommended. Although our case did not involve multiple organs, the average percentage of IgG4- and IgG-positive cells was 94%, which seemed sufficient to diagnose this CNS lesion as IgG4-related sclerosing disease. The patient’s sex, age, and good response to corticosteroids also favored an IgG4-related condition.

Fig. 4. Six-month postoperative brain MR imaging studies obtained with Gd contrast material. Axial T2-weighted image (A) showing complete resolution of cerebral edema. Coronal (B) and sagittal (C) T1-weighted images showing no remaining contrast-enhanced mass. The preoperatively observed enhancement near the corpus callosum and cingulate gyrus also disappeared, and was left as a defect (arrowheads).
A nodular type of hypertrophic pachymeningitis that mimics a meningioma and has an isolated parenchymal lesion is rare, and differential diagnosis of such a condition is very challenging. However, because the treatment strategy of hypertrophic pachymeningitis is usually different from the treatment for neoplastic disease, the preoperative presumption of this rare condition is very important. Its association with IgG4-related sclerosing disease should be clarified with careful radiological, serological, and immunohistochemical evaluations.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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