

Case Report

Severe headache in a patient with meningioma showing extensive dural tail correlates with IgG4-positive plasma cells and eosinophils: A case report and review of literature

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Abstract

Background: Meningiomas originate from meningotheial cells of the arachnoid membrane. Few cases of meningioma with infiltration of inflammatory cells, such as lymphocytes and plasma cells, have been reported, and the mechanisms underlying meningioma-induced inflammatory reactions have not been fully elucidated.

Case Description: In this study, we report an extremely rare case of meningioma with infiltration of both IgG4-positive plasma cells and eosinophils showing extensive dural tail and reactive inflammation of the surrounding arachnoid tissue. The main clinical manifestation was a severe headache, which was improved by surgical excision of the tumor.

Conclusion: Only 8 cases of meningioma with IgG4-positive plasma cells have been reported, and only one case exhibited eosinophil infiltration. IgG4-related inflammatory response might mediate inflammation in surrounding tissue, resulting in thickening of the dura adjacent to a meningioma and severe headache. The mechanisms underlying inflammation by meningiomas require further investigation.

Key Words: Eosinophil, hypertrophic pachymeningitis, IgG4, meningioma

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INTRODUCTION

Meningiomas originate from meningotheial cells of the arachnoid membrane.^[21] Meningiomas are classified into 15 subtypes according to recent World Health Organization criteria (2016). However, meningiomas with infiltration of inflammatory cells such as lymphocytes and plasma cells are rare. Lymphoplasmacyte-rich meningioma (LPM) is a relatively rare subtype with fibrosis and infiltration of both plasma cells and lymphocytes. Meningiomas with IgG4-positive plasma cell or eosinophil infiltration are extremely rare, as only 8 such cases of LPM have been reported.^[2,15,22] The mechanisms underlying inflammatory reactions

associated with meningioma have not been fully elucidated.

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Sixty percent of the patients with meningiomas show dural thickening around the tumor, which manifests as the “dural tail sign.”^[26] Hypertrophic pachymeningitis (HP) is related to IgG4-related disease,^[1] which typically shows extensive linear dural thickening and sometimes forms pseudotumors.^[17,18,28,31] Therefore, HP with pseudotumor and meningioma are sometimes confused.^[9,10,19]

This report describes an extremely rare case of a patient with severe headache caused by meningioma with extensive dural tail. Histopathological analysis of the excised tumor revealed IgG4-positive plasma cells and inflammatory eosinophil infiltration. We also review the relevant published literature on tumors including meningiomas with inflammatory cell infiltration.

CASE REPORT

Onset and course

A 49-year-old female presented with a 7 year history of severe headache. She was diagnosed with cluster headache at another hospital and began steroid therapy one-half year prior to presentation at our institution. Physical examination at the time of initial presentation revealed only severe headache without any neurological deficits. Laboratory examinations showed a C-reactive protein level of 0.07 mg/dl, white blood cell count of 6800/ μ l, erythrocyte sedimentation rate of 12 mm/hr, rheumatoid factor \leq 5 IU/ml, ds DNA \leq 1.2 IU/ml, PR3-ANCA \leq 1.0 IU/ml and MPO-ANCA \leq 1.0 IU/ml, SS-A \leq 1.0 U/ml, SS-B \leq 1.0 U/ml, and anti-cyclic citrullinated peptide antibody \leq 0.5 U/ml. Serum IgG4 was within the normal range (10 mg/dl).

Preoperative radiographical findings

Head computed tomography showed a round lesion, 2.5 cm in diameter, originating primarily from the right frontal dura mater. The lesion showed isodensity without apparent calcification and hyperostosis [Figure 1a]. Intravenous administration of contrast media resulted in strong enhancement of the tumor and revealed an apparent feeding artery [Figure 1b and c]. On head magnetic resonance imaging (MRI), the lesion appeared as a mass without peritumoral edema. The lesion appeared with low signal intensity on T1-weighted imaging (T1WI), high signal intensity on T2WI, and fluid attenuated IR (FLAIR). Contrast-enhanced MRI revealed a homogeneously enhanced extra-axial mass lesion and enhanced extensive dural thickening around the tumor [Figure 1d and e]. From these radiologic findings, a preoperative diagnosis of meningioma with extensive dural tail was made, and surgical treatment of the lesion was planned.

Operation

By frontal craniotomy, the feeding artery was identified on the attached dura mater and coagulated. The tumor

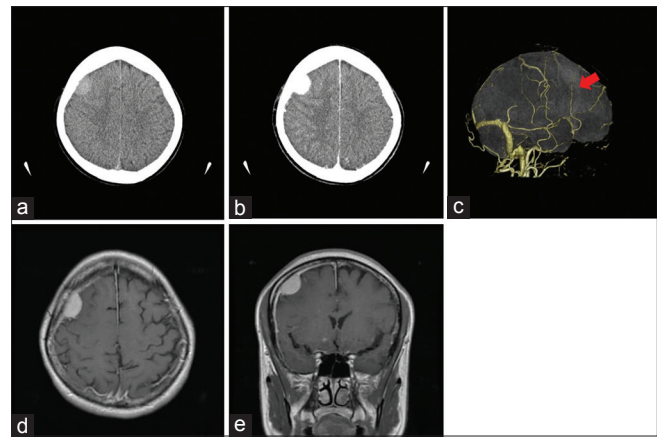


Figure 1: Preoperative radiographic images. (a) Axial head computed tomography scan shows a round lesion, 2.5 cm in diameter, originating primarily from the right frontal dura mater. (b) Enhanced axial head computed tomography shows strong enhancement. (c) Head computed tomography angiography shows an apparent feeding artery (red arrow). (d) Contrast-enhanced axial magnetic resonance imaging shows a homogeneously enhanced extra-axial mass lesion. (e) Contrast-enhanced coronal magnetic resonance imaging shows enhanced extensive dural thickening around the tumor

was soft and grayish [Figure 2a], and the attached arachnoid was yellowish [Figure 2b]. The tumor was not partially easy to exfoliate from the brain parenchyma, but total removal was achieved [Figure 2c]. However, the dural tail could not be completely eliminated because the dura mater around the tumor was extensively thickened [Figure 2c and d].

Histopathological findings

Histopathologically, the tumor was diagnosed as meningioma. In most parts of the tumor, oval-shaped arachnoid-like cells were proliferating like sheets [Figure 3a]. Intranuclear inclusions and psammoma bodies were not identified. Necrosis and mitosis were also not observed. Numerous eosinophils and IgG4-positive plasma cells were diffusely observed in the tumor with IgG and CD138 expressions [Figure 3a and d-f]. However, the lymphocyte density was less than typically observed in LPM. The adherent dura mater was strongly thickened and capillary blood vessels were dilated, both of which were typically seen in the dural tail of a meningioma [Figure 3b]. Eosinophils and IgG4-positive plasma cells were not observed in this thickened dura mater. Inflammatory signs were observed in the arachnoid, specifically a small number of eosinophils and scattered nuclear debris [Figure 3c].

Postoperative course

Total resection of the tumor mass was confirmed by postoperative MRI [Figure 2d]. After the operation, the patient’s headache dramatically improved. She was discharged from our hospital 11 days after the operation

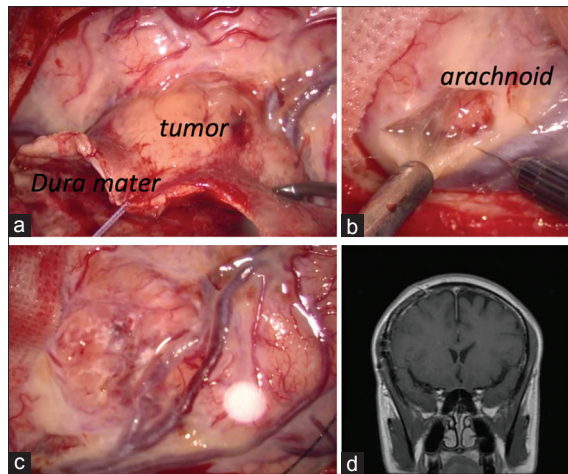


Figure 2: Operative findings. (a) The tumor was soft and grayish. Dura mater adjacent to the tumor was thickened. Capillary blood vessels on the inner layer of the dura mater were dilated. (b) Arachnoid around the tumor was yellowish. It was partially difficult to exfoliate the tumor from brain parenchyma. (c) Successful removal of the tumor was achieved by frontal craniotomy. Most of the thickened dura mater remained. (d) Contrast-enhanced coronal magnetic resonance imaging shows complete resection of the tumor. Most of the enhanced dura mater was still present

with no additional neurological sequelae. Resolution of her headache was confirmed during follow-up at 120 days after the operation.

DISCUSSION

Infiltration of inflammatory cells has been known to occasionally occur in neoplasia. Twenty-three cases of neoplasia with intratumoral infiltration of IgG4-positive plasma cells and eosinophils have been previously reported [Table 1].^[3,4,6,11-13,25,32] This infiltration needs to be distinguished from IgG4-related systemic disorders. Strehl *et al.* demonstrated that the ubiquitous occurrence of high numbers of IgG4-positive plasma cells has been identified in diverse chronic inflammatory conditions.^[23]

Infiltration of inflammatory cells in meningioma is extremely rare. Lal *et al.* summarized 16 cases of meningioma with infiltration of inflammatory cells.^[15] In the report, 15 cases showed the marked infiltration of CD68+/CD163+ macrophages, and the authors suggested “inflammation-rich meningioma” as a new entity of meningioma. IgG4-positive plasma cells were observed in only 6 cases and eosinophils in only one case. In all cases, inflammatory cells were observed in the focal perivascular area. In contrast, our case showed diffusely infiltrated IgG4-positive plasma cells and numerous eosinophils in the tumor. Our review of the literature has identified two more cases of meningioma with IgG4-positive plasma cells [Table 2].^[2,15,22]

Tumor formation promoted by IgG4-mediated chronic inflammation should be considered in the present case.

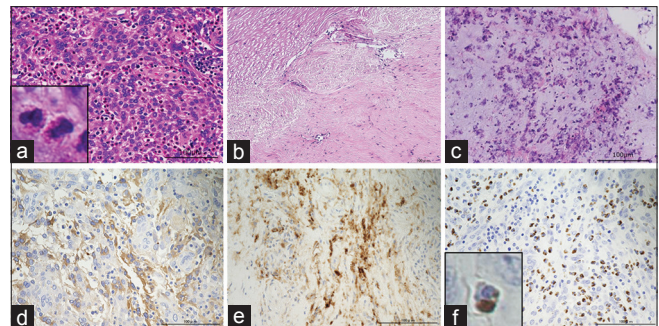


Figure 3: Histopathological findings. (a-c) Hematoxylin-eosin staining, (d-f) immunohistochemical analysis of IgG, CD138, and IgG4. (a) In most parts of the tumor, oval-shaped arachnoid-like cells were proliferating like sheets. Numerous eosinophils were diffusely observed in the tumor. Square area demarcates eosinophils at higher magnification ($\times 20$, magnification bar: 100 μm). (b) Dura mater was strongly thickened and capillary blood vessels were dilated. Eosinophils were not observed in the dura mater. Degenerated collagenous fibers were observed ($\times 20$, magnification bar: 100 μm). (c) An inflammatory reaction was observed in the arachnoid attached to the tumor as evidenced by a small number of eosinophils and nuclear debris ($\times 20$, magnification bar: 100 μm). (d) Diffuse IgG-positive cell infiltration was observed in the tumor ($\times 20$, magnification bar: 100 μm). (e) CD138 (also known as syndecan-1, SDC1) is a highly specific marker for terminally differentiated normal plasma cells. Diffuse CD138-positive cells infiltration was also observed in the tumor ($\times 20$, magnification bar: 100 μm). (f) Most of the CD138-positive plasma cells also expressed IgG4. Diffuse IgG4-positive plasma cell infiltration was observed in the tumor. The ratio of IgG/IgG4 was 70%. Square area demarcates IgG4-positive plasma cells at high magnification ($\times 20$, magnification bar: 100 μm)

Previous reports demonstrated that pancreatic cancer was mediated by IgG4-related autoimmune pancreatitis.^[8,11] However, meningiomas originating from inflammatory reaction have never been reported.

HP shows extensive thickened dura mater and sometimes forms pseudotumors mimicking meningioma.^[10,19] HP is often mediated by IgG4-related autoimmune reaction.^[1,5] However, it is accompanied by abundant collagen fibers, inflammatory cells (lymphocytes and plasma cells), giant cells, and necrosis, which were inconsistent with histopathological findings in the present case.

The histopathology of this tumor and dura mater is consistent with meningioma. The tumor was mainly formed by oval-shaped arachnoid-like cells, and dilated vessels were identified in the dura mater. As suggested in a previous report,^[20] these findings are indicative of a subtype of dural tail. IgG4-positive plasma cells and numerous eosinophils were not observed in the thickened dura mater of the current case. After the operation, the patient’s headache was dramatically improved, which suggested that the tumor itself was the origin of the inflammation and ensuing pain. In our study, we considered the possibility that meningioma may elicit an IgG4-related autoimmune reaction, leading to reactive hypertrophic dura mater and severe headache in our study.

Table 1: Summary of reports documenting neoplasia with IgG4-positive plasma cells and eosinophils

Author (year)	Number of patients	Location	Histopathology	Inflammatory cells
Gill J <i>et al.</i> (2009)	1	Salivary duct	Carcinoma	Eosinophils, IgG4-positive plasma cells
Ito M <i>et al.</i> (2011)	1	Thyroid	Papillary carcinoma	Eosinophils, IgG4-positive plasma cells
Choe JY <i>et al.</i> (2013)	6	Spleen	Follicular dendritic cell sarcoma	5 cases with focal eosinophils 6 cases with IgG4-positive plasma cells
Tasaki T <i>et al.</i> (2013)	1	Salivary gland	Sclerosing mucoepidermoid carcinoma	Eosinophils, IgG4-positive plasma cells
Zhang X <i>et al.</i> (2014)	10	Pancreas	Ductal adenocarcinoma	IgG4-positive plasma cells
Inoue T <i>et al.</i> (2014)	1	Lung	Adenocarcinoma	IgG4-positive plasma cells
Dum TW <i>et al.</i> (2014)	1	Urachal	N/A	IgG4-positive plasma cells
Ikeura T <i>et al.</i> (2014)	2	Pancreas	Ductal adenocarcinoma	IgG4-positive plasma cells

N/A: Not available

Table 2: Summary of reports documenting meningioma with IgG4-positive plasma cells and eosinophils

Author, (year)	Age/sex	Symptoms	Location	EDH	Grade (sybtype)	Inflammatory cells
Lal <i>et al.</i> (2014)	22/male	Seizure	Left frontal	N/A	II (chordoid)	Eosinophils, IgG4-positive plasma cells
	54/female	Seizure	Right parietal	N/A	II (N/A)	IgG4-positive plasma cells
	50/female	N/a	Suprasellar	N/A	I (N/A)	IgG4-positive plasma cells
	32/male	Numbness	Left temporal	N/A	I (N/A)	IgG4-positive plasma cells
	46/female	Facial weakness	Left frontoparietal	N/A	II (atypical)	IgG4-positive plasma cells
	78/female	Headaches, mild ataxia and tinnitus	Left cerebellopontine angle	N/A	I (N/A)	IgG4-positive plasma cells
Cha <i>et al.</i> (2016)	55/male	Ataxia	Left tentorium cerebelli	Yes	I (LPM)	IgG4-positive plasma cells
Son <i>et al.</i> (2017)	56/female	Severe epistaxis	Odontoid process and clivus	Yes	I (LPM)	IgG4-positive plasma cells
Our case	49/female	Severe headache	Right frontal	Yes	I (meningothelial)	Eosinophils, IgG4-positive plasma cells

EDH: Extensive dural hypertrophy, LPM: Lymphoplasmacyte rich meningioma, N/A: Not available

In IgG4-related autoimmune reaction, interleukin-5/10/13 and transforming growth factor- β (TGF- β) produced by Th2 cells, regulatory T cells (Tregs), and mast cells are upregulated.^[24] Interleukin-10 promotes the class switch of IgG4 and proliferation of plasma cells, and TGF- β contributes to tissue fibrosis.^[27] IL-13 produced by Th2 cells is associated with the migration of eosinophils,^[16] and IL-5 promotes the proliferation and survival of eosinophils.^[29,30] As a result, eosinophils proliferate and produce basic proteins such as major basic protein and eosinophil cationic protein, leading to cell damage. In addition, eosinophils produce leukotriene, leading to surrounding inflammation.^[7,14] In our case, numerous eosinophils were activated by the IgG4-related immune reaction and enhanced inflammatory changes in the surrounding dura matter (producing reactive extensive dural tail) and arachnoid. Mehta *et al.* reported 2 cases in which IgG4-related inflammation expanded to the arachnoid, leading to IgG4-related leptomeningitis.^[18] The histopathological findings in those 2 cases resembled our case.

The characteristics and pathophysiology of inflammation cell-rich meningioma are currently not fully elucidated because this type of meningioma was extremely rare. It might be related to some clinical information including radiographic images and patients' symptoms. Further investigations were desirable to understand the mechanisms.

CONCLUSION

A meningioma exhibiting an extensive dural tail as well as IgG4-positive plasma cells and eosinophil infiltration has not been previously reported.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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