·Clinical Research·

Relationship between dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor and paranasal sinusitis

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Received: 2014-12-03 Accepted: 2015-06-08

Abstract

• AIM: To determine the clinical features of the dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor and its relationship with paranasal sinusitis.

• METHODS: A retrospective analysis of 46 patients who received surgical treatment at the Department of Ophthalmology, Beijing Tongren Hospital, Capital Medical University for the dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor from October 2010 to December 2012. Each patient underwent magnetic resonance imaging (MRI) of the orbits and the 4 paranasal sinuses. Disease status and the level of serum immunoglobulin G4 (IgG4) was measured before and 6mo after surgery.

• RESULTS: The initial clinical feature of the idiopathic dacryoadenitis type of orbital inflammatory pseudotumor was redness or swelling of the eyelids. Masses were palpated in the area of the lacrimal gland in some patients. Of the 46 patients, 16 also suffered from sinusitis (34.8%), with 14 cases of ethmoid sinusitis, 8 cases of maxillary sinusitis, 9 cases of sphenoid sinusitis, and 8 cases of frontal sinusitis. Of the 16 patients with sinusitis, 4 patients had a medical history of rhinitis (range: 10mo to 15y previously), 10 patients had occasional nasal congestion, and 2 patients had no nasal congestion. Thirteen of the 46 patients had elevated serum IgG4 levels. Nine of these 13 patients had MRI signs of sinusitis. All patients (n=46) received oral glucocorticoid treatment for approximately 3mo after surgery. No sign of recurrence was found in the orbital MRI 6mo after surgery. Of the 16 patients with sinusitis, 9 cases of elevated serum IgG4 levels improved after treatment with decreased serum IgG4 level and 7 cases of normal serum IgG4 levels remained unchanged.

• CONCLUSION: Some patients with the dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor may also suffer from paranasal sinusitis. The incidence of paranasal sinusitis was much higher in patients with IgG4–elevated dacryoadenitis subtype orbital inflammatory pseudotumor than in those with normal IgG4 levels. Dacryoadenitis subtype orbital inflammatory pseudotumor and paranasal sinusitis may both the clinical manifestations of IgG4 –related disease involved in different locations.

• KEYWORDS: orbital disease; inflammatory pseudotumor; sinusitis; immunoglobulin G4

DOI:10.18240/ijo.2016.03.21

Li J, Ge X, Ma JM. Relationship between dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor and paranasal sinusitis. *Int J Ophthalmol* 2016;9(3):444–447

INTRODUCTION

Idiopathic orbital inflammatory pseudotumor (IOIP) is a common orbital disease which severely affects human health. The incidence of IOIP is second only to thyroid-associated ophthalmopathy and lymphoproliferative disorders. IOIP accounts for 7.1% of orbital diseases [1-4]. Clinical manifestations can affect various orbital structures including the lacrimal glands, extraocular muscles, and orbital fat [5]. Since histopathologic findings in IOIP are not specific, the diagnosis of this disease is mainly based on the exclusion of other causes of the symptoms (*e.g.* cancer, infections, and other specific inflammations [5]). Further research of the etiology and pathogenesis of IOIP is needed to improve our fundamental understanding of the disease and facilitate diagnosis and treatment.

Recent studies [6-10] have suggested a possible relationship between IOIP and sinusitis. Yan *et al* [11] reported that 36 of 209 (17.2%) cases of sinusitis were accompanied by orbital inflammatory pseudotumor. IOIP can be classified into different subtypes based on the involved structures: dacryoadenitis, myositis, optic perineuritis, or diffuse inflammation subtypes. However, all the above researches didn't measure the level of serum immunoglobulin G4

Table 1 General clinical data of 16 both dacryoadenitis subtype of IOIP and sinusitis patients

Patient No.	Age (a)	Sex	Duration (mo)	Eye involved	Sinus included	IgG4 level (mg/dL)	Follow-up status
1	69	M	26	R	ALL	515	Improve
2	17	M	28	L	LE	160	Improve
3	0	M	36	B	BS	472	Improve
4	42	M	3	B	BE+BM+BS	136	Improve
5	48	M	60	B	LF+BE	1350	Improve
6	28	M	10	B	BF+BE+SM	1250	Improve
7	11	M	62	L	RS	740	Improve
8	43	M	37	B	ALL	1800	Improve
9	60	M	25	B	ALL	1601	Improve
10	37	F	12	R	ALL	<7.4	No obvious improve
11	42	M	12	B	BE+LM	24.2	No obvious improve
12	41	F	3	R	RE	<7.4	No obvious improve
13	22	M	2	R	BE+RS	20.7	No obvious improve
14	67	M	1	R	BF+BE	68.8	No obvious improve
15	38	F	9	R	ALL	<7.4	No obvious improve
16	58	M	38	R	LE	74.2	No obvious improve

M: Male; F: Female; L: Left; R: Right; B: Both eyes; E: Ethmoiditis; S: Sphenoiditis; M: Maxillary sinusitis; F: Frontal sinusitis.

(IgG4). Thus, this study analyzed the relationship between the dacryoadenitis subtype of IOIP and sinusitis and investigated the relationship with IgG4.

SUBJECTS AND METHODS

Subjects This study was approved by the ethics committee of Beijing Tongren Hospital, and informed consent was obtained from each patient in accordance with the Declaration of Helsinki. Forty-six patients with the dacryoadenitis subtype of IOIP that received treatment at the Department of Ophthalmology, Beijing Tongren Hospital, Capital Medical University between October 2010 and December 2012 were evaluated. All patients had their diagnosis confirmed by post-operative histopathologic exam. Benign lymphoepithelial lesions of the lacrimal gland, lymphoma, thyroid-associated ophthalmopathy, and other diseases with similar clinical manifestations as the dacryoadenitis subtype of IOIP were excluded.

Methods After histopathological confirmation of the dacryoadenitis subtype of IOIP, magnetic resonance imaging (MRI) of each patient's orbits was performed to evaluate the 4 pairs of paranasal sinuses. MRI and serum IgG4 were both performed 6mo after surgery to identify recurrence of dacryoadenitis and improvement of any paranasal sinusitis.

RESULTS

Clinical Features Sixteen of 46 patients with the dacryoadenitis subtype of IOIP had sinusitis. Among these 16 patients there were 13 males and 3 females with a median age of 42y (range: 11-69y). Seven cases involved the right eye, 2 the left eye, and 7 both eyes. The course of disease ranged from 1 to 62mo. Initial manifestations included redness or swelling of the eyelids. Soft masses were palpable in the lacrimal gland of 8 patients.

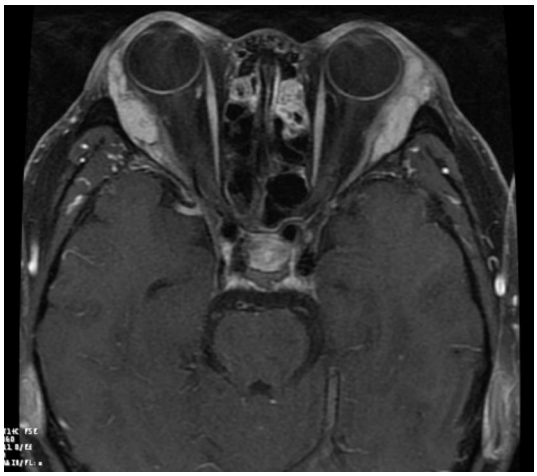

Figure 1 A IOIP patients had MRI signs of sinusitis.

Cases Combined with Sinusitis Sixteen of the 46 patients in this study had sinusitis (34.8%), with 14 cases of ethmoid sinusitis, 8 of maxillary sinusitis, 9 of sphenoid sinusitis, and 8 of frontal sinusitis. Of the 16 patients with sinusitis, 4 patients had a medical history of rhinitis (range: 10mo to 15y previously), 10 had occasional nasal congestion, and 2 had no nasal congestion. Among the patients with sinusitis, 5 patients had inflammation in 1 group of sinuses, 4 had inflammation in 2 groups of sinuses, 2 had inflammation in 3 groups of sinuses, and 5 had inflammation in 4 groups of sinuses.

Relationship Between Serum IgG4 Levels and Idiopathic Orbital Inflammatory Pseudotumor and Sinusitis Thirteen of the 46 patients had elevated serum IgG4 levels. Nine of these 13 patients had MRI signs of sinusitis (Figure 1 and Table 1).

Follow-up Cases All patients (n=46) in this study received oral glucocorticoid treatment for approximately 3mo after

surgery. No sign of recurrence was found in all patients on the 6mo post-operative MRI. Of the 16 patients with sinusitis, 9 cases with elevated serum IgG4 levels had a decrease in these levels after treatment and 7 cases with normal serum IgG levels had no change in these levels.

DISCUSSION

IOIP is a non-specific orbital inflammation that may occur in any age group, although it is more common in the elderly. Both genders are equally affected. IOIP may occur unilaterally, in both eyes simultaneously, or sequentially in both eyes [1-4]. Correlation studies between IOIP and sinusitis have been reported as early as the 1980s. The conclusion of each study varied, but most showed a correlation between the two diseases. In 1980, Fortson *et al* [6] first reported 5 cases of IOIP invading the maxillary sinus. In 1981, Eshaghian and Anderson [7] reported 2 IOIP cases with a recent history of sinusitis. Few studies have shown no correlation between the two diseases. In our study, a total of 46 cases of the dacryoadenitis subtype of IOIP were treated, and 16 patients had sinusitis. The frequency of co-existing sinusitis in our patients was higher than in previous reports. This higher rate may be due to ineffective previous treatment at other hospitals, the severe condition, and long medical history. Previous reports have not classified the subtypes of IOIP. To improve the comparability and objectivity of our findings, we only studied the dacryoadenitis subtype of IOIP. Our results suggest that the dacryoadenitis subtype of IOIP is associated with paranasal sinusitis at a higher rate than in previous reports [6-11]. Further research will be necessary to determine the reason. Most patients we treated had no obvious symptoms of sinusitis, even though the imaging tests were compatible with sinusitis.

The spectrum of IgG4-related diseases (IgG4-RD) has been expanding since the first report of autoimmune pancreatitis by Hamano *et al* [12] in 2001. To date, the diagnostic criteria of IgG4-RDs have not been unified, but elevated IgG4 serology or the presence of numerous IgG4-positive plasma cells suggests their involvement in the pathogenesis of autoimmune diseases [13-20]. Thirteen of the 46 patients in this study had elevated serum IgG4 levels, suggesting that some dacryoadenitis subtypes of IOIP belong to the category of IgG4-RDs. A correlation between IgG4-IOIP and paranasal sinusitis has not been previously reported. Among the 13 patients with the dacryoadenitis subtype of IOIP and elevated serum IgG4, 9 had MRI findings of sinusitis and these patients had significantly higher IgG4 levels than patients with sinusitis alone, suggesting that IgG4 may play an important role in sinus and orbital disease.

Treatment of IOIP consists of symptomatic treatment, radiotherapy, and surgery. Glucocorticoids are widely recognized as the preferred treatment [1-2]. All patients in this study received oral glucocorticoids for approximately 3mo after surgery. No sign of recurrence was found in any patient on the 6mo post-operative MRI. Of the 16 patients with sinusitis, 9 improved after treatment and 7 had no significant change in symptoms. Patients that improved after treatment had high serum IgG4 levels before surgery, suggesting the presence of an IgG4-RD subtype. Thus, glucocorticoids effectively controlled orbital and sinus inflammatory lesions in patients with IgG4-RD.

In summary, this study showed a close relationship between the dacryoadenitis subtype of IOIP and sinusitis. The frequency of sinusitis in patients with the IgG4-elevated dacryoadenitis subtype of IOIP was significantly higher than that in patients with normal serum IgG4 levels. A possible explanation is the close anatomic relationship between each group of paranasal sinuses and the orbital cavity. Further research is necessary to confirm this hypothesis. Dacryoadenitis subtype of idiopathic orbital inflammatory pseudotumor and paranasal sinusitis may both the clinical manifestations of IgG4-related disease involved in different locations.

ACKNOWLEDGEMENTS

Foundation: Supported by the National Natural Science Foundation of China (No. 81371052).

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of Interest: Li J, None; **Ge X,** None; **Ma JM,** None.

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