·Clinical Research·

Space-occupying lesions of the lacrimal gland at one tertiary eye center in China: a retrospective clinical study of 95 patients

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Abstract

• AIM: To investigate the treatment status and prognosis of space-occupying lacrimal gland lesions at one tertiary eye center in China.

• METHODS: A retrospective clinical study was performed on 95 patients with space-occupying lesions of the lacrimal gland surgically treated at the Eye & ENT Hospital of Fudan University from 2003 to 2007. The reviewed clinical data included age, gender, side of the lesion, duration of signs and symptoms, histopathological diagnosis, treatment modality, recurrence (local, regional, and distant metastasis) and survival.

• RESULTS: Of the 95 cases (99 eyes), pleomorphic adenomas were the most common lesions (43 cases), followed by lymphoid disorders (14), inflammatory pseudotumors (11), carcinoma ex-pleomorphic adenomas (11), and adenoid cystic carcinomas (ACC, 6). There were 8 patients with relapsed pleomorphic adenomas. Five of these 8 cases had malignant pathological changes. All patients with ACC had metastasis and three of them died during their follow-up.

• CONCLUSION: Our study indicated that the most common lacrimal gland lesions were pleomorphic adenomas. Multiple recurrence and surgical procedures may increase the risk of tumor progression. ACC had a high incidence of tumor metastasis and a poor prognosis.

• KEYWORDS: lacrimal gland lesions; pleomorphic adenomas; adenoid cystic carcinoma; China

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INTRODUCTION

Approximately 9% of all orbital lesions are space-occupying lesions (SOLs) of the lacrimal gland. These SOLs can be divided into 4 groups: inflammatory lesions, lymphoid disorders, metastatic tumors, and primary epithelial tumors [1]. Among them, inflammatory and lymphatic lesions account for 78%, epithelial lesions for 22%, and metastatic tumors are rare [2]. According to a meta-analysis by Shields *et al* [3], 55% of lacrimal gland epithelial tumors are benign and the rest are malignant. In Western countries with a predominantly Caucasian population, the most common benign tumors of the lacrimal gland are pleomorphic adenomas (PAs), and the most common malignant tumors are adenoid cystic carcinomas (ACCs).To the best of our knowledge, the report on the SOLs of the Eastern countries is rare. In the present study, we reviewed the treatment status and prognosis of SOLs of the lacrimal gland at one tertiary eye center in China.

PATIENTS AND METHODS

The consecutive files in the Eye & ENT Hospital of Fudan University were searched for SOLs of the lacrimal gland and 95 cases were found in the period 2003-2007. Patients with dacryoadenitis (especially pseudotumor) that can be treated by corticosteroid were not included in our study. Prior to the excision of the lacrimal gland lesion, all the patients underwent a series of clinical examination including refractometry, assessment of eye motility, sonographic examination, and computed tomography, magnetic resonance imaging, or both. Depending on the size and location of the lesion, either an anterior or a lateral orbitotomy was performed. For most of nonepithelial lesions, only the lesions were resected with part of normal lacrimal gland well reserved. For epithelial lesions (generally rigid big mass) and any uncertain lesions, whole lacrimal glands comprising tumors were totally removed. The obtained specimens were then sent to the Department of Pathology, Fudan University, and the diagnosis was confirmed by pathology experts. Further treatment was based on the histopathological diagnosis. We outlined the treatment results and prognosis of SOLs of the lacrimal gland according to the obtained clinical data including age,

Table 1 Clinical characteristics of 95 patients with lacrimal gland lesions in Eye & ENT Hospital of Fudan University, 2003-2007

Type	No. of lesions	Sex M/F	Average age(years)	Laterality Right/Left/Double
Epithelial	66	31/35	44(15-79)	39/27/0
Benign				
Pleomorphic adenoma	43	18/25	44(15-79)	27/16/0
Malignant				
Carcinoma ex-pleomorphic adenoma	11	8/3	43(23-60)	7/4/0
Adenoid cystic carcinoma	6	2/4	47(29-67)	2/4/0
Adenocarcinoma	4	3/1	46(32-61)	3/1/0
Polymorphous low-grade carcinoma	2	0/2	35(25-46)	0/2/0
Nonepithelial	33	11/18	48(5-91)	15/10/4
Inflammatory				
Chronic dacryoadenitis	4	1/2	25(5-38)	0/2/1
Sarcoidosis	1	0/1	31(31)	1/0/0
Inflammatory pseudotumors	12	4/7	45(17-82)	6/4/1
Lymphoid				
BRLH	4	1/2	47(26-74)	1/1/1
Lymphoma	12	5/6	58(41-91)	7/3/1
Total	99	42/53	45(5-91)	54/37/4

BRLH= benign reactive lymphoid hyperplasia

Table 2 Treatment and prognosis of the 6 patients with adenoid cystic carcinoma

Patient	Gender	Age	Laterality	Staging	Treatment	Follow-up	Result
1	Male	29	Left	T3N0M0	Orbital exenteration and postoperative radiation	17 months	Metastasis/die
2	Female	41	Left	T4aN0M0	Orbital exenteration and postoperative radiation	24 months	Lung metastasis/alive
3	Male	39	Left	T1N0M0	Lateral orbitotomy, complete resection and postoperative radiation	21 months	Lung metastasis/alive
4	Female	64	Right	T4bN0M0	Lateral orbitotomy, complete resection and postoperative radiation	38 months	Metastasis/die
5	Female	44	Rigt	T2N0M0	Orbital exenteration and postoperative radiation	26 months	Lung metastasis/alive
6	Female	67	Left	T3N0M0	Orbital exenteration and postoperative radiation	54 months	Metastasis/die

gender, side of the lesion, duration of signs and symptoms, histopathological diagnosis, treatment modality, recurrence (local, regional, and distant metastasis) and survival.

RESULTS

Among the 95 cases (99 eyes), 42 (43 eyes) were male and 53 (56 eyes) were female. The age range of the patients was from 5 to 91 years with an average of 45 years. The clinical characteristics of the 95 patients are shown in Table 1.

All the 43 cases of PA patients were treated with surgical excision, and postoperative histopathology confirmed the diagnosis. There were 8 relapsed cases, 5 of which had malignant pathological changes. Four of the 5 cases had recurrence during an average follow-up of 55 months (range: 39 to 83 months), while one treated with additional orbit exenteration had no evidence of recurrence during the follow-up of 82 months.

There were 11 cases of carcinoma ex pleomorphic adenoma (CXPA). Three of them treated with orbit exenteration and postoperative radiation had no recurrence during the average follow-up of 78 months (range: 57 to 96 months). Of the 8 cases treated with lateral orbitotomy and complete resection, 5 had no recurrence during the average follow-up of 43 months (range: 23 to 54 months) and the other 3 cases patients were lost during follow-up.

All the 6 cases of ACC were classified according to the TNM definitions for carcinoma of the lacrimal gland set by the American Joint Committee on Cancer (AJCC) [4]. Treatment and prognoses of the 6 patients are shown in Table 2. Of the 4 cases with adenocarcinoma, 3 were treated with orbital exenteration and postoperative radiation, and one with lateral orbitotomy and complete resection and postoperative radiation. The mean follow-up period was 48 months. Two cases died and 2 cases had no evidence of recurrence during their follow-ups. In addition, there were 2 cases of polymorphous low-grade carcinoma, which were treated with lateral orbitotomy and complete resection and postoperative radiation. None had evidence of recurrence during the follow-up of 42 months (ranging from 39 to 45 months).

Among the nonepithelial lesions, there were 15 cases with inflammatory lesions and 14 cases of lymphoid disorders. The 15 cases included 3 chronic dacryoadenitis, 11 inflammatory pseudotumors, and one sarcoidosis. All patients were treated with corticosteroids for several weeks,

but the treatment was not effective. Then a sub-eyebrow incision with complete resection was performed. Post-surgery, no evidence of recurrence was found in the 3 cases of chronic dacryoadenitis during the average follow-up of 43 months (range: 28 to 66 months). Of the 11 inflammatory pseudotumor cases, 7 had no evidence of recurrence during an average follow-up period of 77 months (range: 61 to 84 months), 2 cases recurred after 11 and 13 months, and 2 cases were lost to follow-up. The one case with sarcoidosis was lost during follow-up.

Among the 14 cases of lymphoid disorders, there were 3 benign reactive lymphoid hyperplasia (BRLH) and 11 lymphoma. For the 3 patients with BRLH, an sub-eyebrow incision with tumor resection was performed. One had recurrence during the follow-up of 61 months and the other 2 cases had no recurrence at follow-up of 33 and 57 months.

Of the 11 cases with lymphomas, 9 were mucosa-associated lymphoid tissue (MALT) lymphoma and 2 were lymphoplasmacytic lymphoma (LPL). All the 9 patients with MALT lymphoma were treated with sub-eyebrow incision and tumor resection. Three of these cases received additional radiotherapy, 5 with additional chemotherapy, and one 91-year-old patient died of another disease after the follow-up of 26 months. These 8 MALT patients had no evidence of recurrence during follow-ups averaging 52 months (range: 30 to 81 months). The two cases with LPL were treated with tumor resection and additional radiotherapy and chemotherapy. They had no evidence of recurrence during their follow-ups at 64 and 82 months.

DISCUSSION

In this retrospective study of 95 patients, epithelial lesions accounted for 67% of all the SOLs of the lacrimal gland, and PA was the most common type of tumor. Similarly, the Lacrimal Gland Tumor Study Group in Japan [5] also found that PA was the most common tumor of lacrimal fossa lesions. However, Shields *et al* [2] found that only 22% were epithelial lesions, and chronic non-granulomatous disorder was the most common lesion. These discrepancies may be due to the differences of patient selectivity. The patients with dacryoadenitis (especially pseudotumor) that can be treated by corticosteroid were not included in this study. Obviously, studies with larger sample populations and wider disease scope are needed in the future.

PA of the lacrimal gland should be excised completely, with its pseudocapsule and a surrounding margin of orbital tissue [6,7], because incomplete or piecemeal removal of the lesion may result in recurrence [7,8]. In this study, 5 of the 8 patients with relapsed PA had malignancies and 3 of them underwent more than 2 surgeries. This is in accordance with the report of Tang et al [9], in which 7 cases out of 8 patients with relapsed PA had more than two surgeries, and 4 of 7 cases had malignancies. All the above studies reveal that repeated recurrence or surgical procedures may lead to malignancy. As a result, the complete excision of PA during the primary surgery is critical and mandatory.

In this retrospective study, CXPA of the lacrimal gland was the most common malignant tumor. This finding is inconsistent with the report by Font *et al* [10], who found that ACC was the most common malignant epithelial tumor of the lacrimal gland. Besides, CXPA was considered as a malignant transformation of PA of the lacrimal gland [11-14]. Recently, Takahira *et al* [15] reported a case of CXPA of the lacrimal gland developing in a cyst, which ruptured during surgery. This indicates that any damage to the surface of the tumor during surgery may cause leakage of malignant cells, thus leading to malignant progression.

In the 6 patients with ACC, all the cases had metastasis during follow-up. Three (50%) of them died of this disease. This finding of our study is similar to that of Esmaeli *et al*[16], who also found that ACC had a bad prognosis. In addition, we found relatively better prognoses for patients with ≤T2 tumors at diagnosis, based on the AJCC's classification of lacrimal glands (seventh edition), which is similar to the study conducted at the University of Texas M. D. Anderson Cancer Center [17]. This group also assessed treatment outcomes by type of surgery (orbital exenteration vs. eye-sparing surgery) and clarified the role of adjuvant radiation therapy for malignant epithelial neoplasms of the lacrimal apparatus. They found that for appropriately selected patients, an eye-sparing surgery for lacrimal apparatus tumors can achieve survival outcomes similar to orbital exenteration, and adjuvant radiation therapy should be considered for all patients with malignant epithelial tumors of the lacrimal gland. However, the dismal prognosis of ACC for patients in our study challenges the presently accepted ACC treatment protocol.

In summary, we reviewed the medical treatment status and outcomes of lacrimal gland lesions at one tertiary eye center in China. Our results are similar to those reported in the Western literature. A more effective treatment protocol for malignant epithelial tumors remains remain to be explored.

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·Letter to the Editor·

Proteomic analysis in diabetic retinopathy

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Dear Sir,

I am Prof. Beuy Joob from Sanitation 1 Medical Academic Center, Bangkok, Thailand. I write to discuss the recent publication on proteomic analysis in diabetic retinopathy(DR). Liu *et al*[1] concluded that their approach by two dimensional fluorescence difference gel electrophoresis (2D-DIGE) combined with matrix-assisted laser desorption/ionization time of flight tandem mass spectrometry (MALDI-TOF MS) could be useful in proteomic study, with some limitations, for DR and further claimed that this could be the way to find the candidate biomarker on DR diagnosis. First, it is no doubt that the use techniques, which are the basic proteomics techniques, can be useful in proteomic study. However, it has to be noted that proteomics study is the study of the already expressed proteins, not the genes. Hence, the exact pathogenesis might not be completely revealed from this approach. Finding proteins from proteomics study might be the exact proteins from the focused disease, which hereby is DR, or from other confounding diseases. In this work, there is no ruling out of other possible concomitant diseases such as renal disease. The simple question is whether the detected proteins in this work are actually due to the DR or other disorders that are not clarified in this work. Also, the conclusion that this work can be a way to find candidate biomarker for DR should be discussed. With the already mentioned concerns, the detected proteins might not be good biomarkers. In addition, the next question is whether the blood biomarker is reliable and acceptable in the specific case of DR. As a gold standard, retinopathy has to be diagnosed based on the opthalmological assessment. The finding of protein which is the biochemical assessment might not be as good as anatomical eye assessment.

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