• Clinical Research •

Clinical features and prognosis of carcinoma ex pleomorphic adenoma of the lacrimal gland: a comprehensive case series and literature review

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Received: 2024-03-09 Accepted: 2025-06-06

Abstract

● **AIM:** To examine carcinoma ex pleomorphic adenoma (CXPA) and its development to provide information for its clinical assessment and prognosis.

● **METHODS:** The clinical data of 26 patients with pathologically diagnosed CXPA were included for analysis. The patients' medical histories and data (*e.g.*, gender, age, eye laterality, clinical manifestations, pathologic and immunohistochemical indices, treatments, and prognosis) were recorded.

● **RESULTS:** The average age of the 26 patients was 59.6±15.7y. There was no significant difference in the gender distribution. The incidence of CXPA bone destruction was approximately 57.7%, and the incidence of optic nerve involvement and extraocular muscle involvement was approximately 15.4% and 19.2%, respectively. The most common pathological type was adenocarcinoma (34.6%), followed by ductal carcinoma (26.9%). Five patients had recurrence or metastasis (19.2%). The 5-year recurrence-free survival rate was 59.0%. There were no significant differences in survival rates among patients with different pathologic types and stages (P>0.05). Bone destruction, nerve invasion, and peripheral tissue invasion did not significantly affect survival rate (P>0.05). Surgery combined with ^{125}I radiation therapy leads to a better survival prognosis (P<0.05).

● **CONCLUSION:** CXPA has a variety of pathologic classifications, with characteristics of bone destruction and peripheral tissue invasion. Surgery combined with ^{125}I endoradiotherapy is a preferable treatment option. However, long-term follow-up and close observation for recurrence or metastasis should be performed.

● **KEYWORDS:** carcinoma ex pleomorphic adenoma; lacrimal gland; ^{125}I radiation therapy

DOI:10.18240/ijo.2025.09.05

Citation: Yang RZ, Ma MS, Liu R, Ren TT, Li J, Wang N, Xu LY, Guo QH, Ma JM. Clinical features and prognosis of carcinoma ex pleomorphic adenoma of the lacrimal gland: a comprehensive case series and literature review. *Int J Ophthalmol* 2025;18(9):1650-1657

INTRODUCTION

Pleomorphic adenoma (PA), also known as a benign mixed tumor, is the most common tumor of the lacrimal gland, accounting for approximately 50% of lacrimal gland epithelial tumors[1]. Carcinoma ex pleomorphic adenoma (CXPA) tends to appear approximately 10y after the occurrence of PA, with an incidence of malignancy of less than 10% and an increased risk of occurrence with age[2].

The incidence of CXPA accounts for 15.4% of epithelial tumors of the lacrimal gland and 33% of malignant epithelial tumors of the lacrimal gland[3]. Unilateral occurrence is generally more common in clinical practice. The clinical features of CXPA consist mainly of proptosis of the eye and mass[4]. Imaging scans show the diseased lacrimal gland as a round or irregular nodule with poorly defined borders, surrounding tissue infiltration, and bone destruction near the tumor[5]. The prognosis is poor, as the disease is markedly aggressive and tends to recur locally or metastasize distantly. Studies show that tumor-related deaths occur in approximately two-thirds of patients[6]. Pathologic examination is the most important diagnostic method, often aided by immunohistochemical examination. Because of the low incidence of CXPA, this paper reports on the analysis of only 26 cases, comprising 11 cases diagnosed in our hospital and 15 cases reported in the

literature. It summarizes their clinical presentation, treatment, pathologic and immunohistochemical features, and prognosis to provide information for subsequent studies.

PARTICIPANTS AND METHODS

Ethical Approval This article does not include the patients' names, portrait and other private information. All the subjects were fully informed the purpose of this study, and obtain informed consent. This study was approved by the Medical Ethics Committee of Beijing Tongren Hospital.

Participants The clinical data were collected from patients admitted to our hospital, between January 2016 and November 2022, who were diagnosed with CXPA by histopathology.

Inclusion criteria were CXPA diagnosed by histopathology and patients diagnosed with CXPA associated with a complete medical history and no other lacrimal gland or systemic malignancies. Exclusion criteria were 1) other malignant tumors of the lacrimal gland, 2) cases with incomplete medical history data, 3) metastatic tumors with a history of other systemic malignancies. According to the inclusion and exclusion criteria, we included 26 patients with clearly diagnosed CXPA by pathologic testing. Of these, the data of 15 patients reported in the literature met the inclusion criteria.

Collection of Clinical Data We collected patients' gender, age, eye laterality, clinical presentation, imaging presentation, tumor-nodule-metastasis (TNM) stage, pathologic presentation, immunohistochemistry-related indices (Ki-67), treatment modality, follow-up time, and prognosis. Furthermore, we recorded bone invasion, nerve invasion, other tissue invasions, or metastasis shown by imaging, intraoperative evaluation, or histopathologic examination. We judged the recurrence or metastasis cases through imaging or pathologic examination.

Statistical Analysis SPSS 26.0 software (IBM, Armonk, NY, USA) was used to process the data. The Kolmogorov-Smirnov test was used to test the normality of the data. Measures conforming to a normal distribution were expressed as means±standard deviations, and measures conforming to a nonnormal distribution were expressed as medians (P25–P75). A Kaplan-Meier survival curve was used for survival analysis. A P value <0.05 was considered statistically significant.

RESULTS

General Clinical Characteristics We collected 15 clinical case reports of CXPA diagnosed by pathologic examination through computer searches of PubMed, Web of Science, Chinese National Knowledge Infrastructure, VIP (https://www.cqvip.com/), and WanFang Data databases, with a search period from database creation to November 2022 (Table 1). A total of 26 patients' clinical data were collected for analysis, comprising eight cases (30.8%) in the right eye and 18 cases (69.2%) in the left eye. Twelve cases (46.2%) were male and 14 (53.85%) were female. The patients' mean age was 59.6±15.7y. The main clinical manifestations were protrusion of the eye in 12 cases (46.2%), intraorbital mass (reported by magnetic resonance, without discomfort or appearance changes) in 6 cases (23.1%), eyelid swelling in five cases (19.2%), ocular pain in 4 cases (15.4%), ptosis in 2 cases (7.7%), blurred vision in 4 cases (15.4%), motility restriction in 2 case (7.7%), vertigo in one case (3.8%), sensory deficit in one case (3.8%), and one case of ipsilateral hearing loss (3.8%).

A total of 15 patients (57.7%) had bone lesions involved, among which 13 patients had orbital walls involved only. There were 8 cases of single-wall involvement, 3 cases of two-wall involvement, and 2 cases of three-wall involvement. When single orbital wall involvement occurred, the most common site was the outer orbital wall (62.5%). In all the orbital wall lesions, there were 10 cases in the outer orbital wall, 8 cases in the superior orbital wall, and 2 cases in the internal orbital wall. Among the other bone lesions, the zygomatic bone was involved in 2 cases (7.7%), and the superior temporal orbital rim, maxilla, frontotemporal bone, pterygium, skull base and cavernous sinus were involved in 1 case (3.8%) each (Table 1). In one case, the location of orbital bone destruction was not specified. The nerves were involved in five patients, accounting for 19.2%. The magnetic resonance results showed that four cases involved the optic nerve and one involved the trigeminal nerve-nerveophthalmic nerve (V1, which brought sensory deficit in the V1 and V2 region of the trigeminal nerve). Five patients had lesions involving the extraocular muscles (19.2%), including the external and superior rectus muscles. Five patients had lesions involving the adipose fibrous tissue (19.2%). None of the patients had regional lymph node involvement or distant metastasis at initial presentation (Table 2).

Pathologic Features Among the 26 CXPA cases, we found malignant components were adenocarcinoma in nine cases (34.6%), ductal carcinoma in seven cases (26.9%), myoepithelial carcinoma in three cases (11.5%), mucoepidermoid carcinoma in three cases (11.5%), epithelial-myoepithelial carcinoma in three cases (11.5%), and squamous cell carcinoma in one case (3.8%).

The tumor cells of CXPA have similar pathological characteristics, that is, variable size and morphology, with deep-stained nuclei and abnormal mitosis. Also, various types of CXPA have certain differences. The tumor cells of adenocarcinoma showed pleomorphic nuclei with prominent nucleoli and rich eosinophilic cytoplasm. Ductal carcinoma of the lacrimal gland infiltrates into the tumor envelope in the form of small foci. Microscopically, mucoepidermoid carcinoma of lacrimal gland consists of three main cell types in different proportions: mucinous cells, intermediate cells

Table 1 Demographics, histology, treatment, and tumor recurrence for 26 patients with CXPA

Patient number	Gender	Presenting age (y)	Histological type of malignant component	Bone destruction	Nerve invasion	Surrounding tissue invasion	Tumor size (cm)	AJCC class	Treatment	Recurrence	Ki-67	Follow-up (mo)
1	M	52	Ductal carcinoma	Superior/outer orbital wall	Optic nerve	Levator palpebrae superioris	3.5	T2cN0M0	TR+^{125}I	No	10%	58
2	M	69	Adenocarcinoma	Superior orbital wall	No	No	3.3	T2cN0M0	TR+^{125}I	Relapsing	10%	24 (deceased)
3	F	56	Ductal carcinoma	Superior/outer/medial orbital wall	No	No	2.2	T2cN0M0	TR+^{125}I	No	30%	21
4	M	52	Intraductal (*in situ*) carcinoma	Superior/outer/medial orbital wall	No	No	2.8	T2cN0M0	TR+^{125}I	No	10%	27
5	M	62	Adenocarcinoma	No	No	No	2.0	T1aN0M0	TR+^{125}I	No	10%	45
6	F	53	Ductal carcinoma	No	No	No	3.0	T2aN0M0	TR+^{125}I	No		54
7	M	68	Adenocarcinoma	No	No	No	3.0	T2aN0M0	TR+^{125}I	Metastatic		36
8	F	55	Ductal carcinoma	No	Optic nerve	Adipose tissue	3.5	T2aN0M0	TR+^{125}I	Metastatic	90%	36 (deceased)
9	F	58	Myoepithelial carcinoma	Superior/outer orbital wall	No	No	3.0	T2cN0M0	TR+^{125}I	No	10%	36
10	M	28	Myoepithelial carcinoma	Superior orbital wall/ supratemporal orbital margin	No	Supranasal points	2.0	T4aN0M0	TR+^{125}I	No	<1%	62
11	F	46	Mucoepidermoid carcinoma	No	No	No	3.0	T2aN0M0	TR+^{125}I	No		26
12[7]	M	37	Adenocarcinoma	No	No	No	3.0	T2aN0M0	TR+RT	No		24
13[8]	F	84	Epithelial-myoepithelial Carcinoma	Cheekbone/maxill/frontal bone/ temproal bone/outer orbital wall	Optic nerve	Musculi oculi	9.0	T4cN0M0	TR+RT+CT	No	50%	12 (deceased)
14[9]	M	62	Ductal carcinoma	Outer orbital wall/ suprazygomatic space/basis cranii	No	Adipose tissue	3.8	T4cN0M0	TR+RT+CT (cisplatin)	No	22%	23 (deceased)
15[10]	F	50	Adenocarcinoma	Outer orbital wall/cavernous sinus	No	Temporalis	-	T1N0M0	TR	Metastatic		17 (deceased)
16[11]	M	78	Intraductal (*in situ*) carcinoma	No	No	No	1.6	T1aN0M0	TR	No	>90%	9
17[12]	M	50	Squamous cell carcinoma	greater wings of the sphenoid bone	Trigeminal nerves (ophthalmic [V1])	Superior rectus/lateral rectus/temporalis muscle	6.4	T4cN0M0	RT+CT (cisplatin and 5-fluorouracil)	No	-	5
18[13]	F	62	Mucoepidermoid carcinoma	No	No	Superior rectus/lateral rectus	2.5	T2aN0M0	TR	Relapsing		30
19[14]	M	92	Epithelial-myoepithelial carcinoma	No	No	No	3.2	T4bN0M0	TR+RT	No	30%	3
20[15]	F	68	Myoepithelial carcinoma	Outer orbital wall	Optic nerve	Adipose tissue	4.0	T2cN0M0	TR	No		36
21[16]	M	64	Adenocarcinoma	Outer orbital wall	No	No	3.8	T2cN0M0	TR+RT+CT	No	5%-10%	9
22[17]	F	61	Epithelial-myoepithelial carcinoma	No	No	Adipose tissue	-	-	TR+RT	No		36
23[18]	F	54	Adenocarcinoma	Superior orbital wall	No	No	1.8	T1aN0M0	TR+CT	No		36
24[19]	F	84	Adenocarcinoma	Superior/outer orbital wall	No	No	5.1	T3cN0M0	TR+CT	No		2 (deceased)
25[20]	F	76	Mucoepidermoid carcinoma	No	No	No	3.0	T2aN0M0	TR+RT	No		5
26[21]	F	29	Poorly differentiated adenocarcinoma	Orbital bone	No	No	-	-	TR+RT+CT (ACNU+cisplatin)	No		4 (deceased)

M: Male; F: Female; CXPA: Carcinoma ex pleomorphic adenoma; ^{125}I: I-125 internal radiation therapy; TR: Surgery; RT: Radiotherapy; CT: Chemotherapy; ACNU: 1-(4-amino-2-methyl-5-pyrimidinyl)-methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride; AJCC: American Joint Committee on Cancer.

Table 2 Age, gender, clinical manifestation, peripheral invasion, tumor stage, aggressiveness and prognosis of 26 patients with different pathological types

Parameters	Adenocarcinoma (*n*=9)	Ductal carcinoma (*n*=7)	Myoepithelial/epithelial-myoepithelial carcinoma (*n*=6)	Mucoepidermoid carcinoma (*n*=3)	Squamous cell carcinoma (*n*=1)
Mean age (y)	57.4±17.0	58.3 (52.0–59.0)	64.5±21.9	62.0 (46.0–69.0)	50
Gender (male)	5 (55.6%)	4 (57.1%)	2 (33.3%)	0	1 (100%)
Position (left)	7 (77.8%)	4 (57.1%)	4 (66.6%)	2 (66.7%)	1 (100%)
Clinical manifestation					
Eye protrusion	6 (66.7%)	2 (28.6%)	1 (16.7%)	2 (66.7%)	1 (100%)
Intraorbital mass	1 (11.1%)	2 (28.6%)	2 (33.3%)	1 (33.3%)	0
Swollen eyelid	1 (11.1%)	3 (42.9%)	1 (16.7%)	0	0
Ptosis of upper eyelid	0	2 (28.6%)	0	0	0
Eye pain	1 (11.1%)	1 (14.3%)	1 (16.7%)	0	1 (100%)
Blurred vision	2 (22.2%)	1 (14.3%)	1 (16.7%)	0	0
Vertigo	0	1 (14.3%)	0	0	0
Sensory deficit	0	0	0	0	1 (100%)
Ipsilateral hearing impairment	1 (11.1%)	0	0	0	0
Motility restriction	0	1 (14.3%)	0	1 (33.3%)	0
Bone destruction	6 (66.7%)	4 (57.1%)	4 (66.6%)	0	1 (100%)
Nerve violation	0	2 (28.6%)	2 (33.3%)	0	1 (100%)
Peripheral tissue invasion	1 (11.1%)	3 (42.9%)	4 (66.6%)	1 (33.3%)	1 (100%)
T staging					
T1/2	7 (77.8%)	6 (85.7%)	2 (33.3%)	3 (100%)	0
T3/4	1 (11.1%)	1 (14.3%)	3 (50.0%)	0	1 (100%)
Ki-67 index	10%	26% (10%–90%)	20% (1%–30%）	-	-
Prognosis					
Recurrence	1 (11.1%)	0	0	1 (33.3%)	0
Transferring	1 (11.1%)	2 (28.6%)	0	0	0
Death	4 (44.4%)	2 (28.6%)	1 (16.7%)	0	0

Measures conforming to a normal distribution were expressed as mean±SD, and measures conforming to a non-normal distribution were expressed as medians (P25-P75).

and epidermoid cells. Individual differences in the expression of tumor markers are large and no statistically significant conclusions can be drawn. The average expression level of Ki-67 was 22% (10%, 30%; Figure 1).

There were 4 cases of T1N0M0, 14 cases of T2N0M0, 1 case of T3N0M0, 5 cases of T4N0M0, and two cases (7.7%) of unidentifiable staging (Table 1).

Treatment and Prognosis Of the 26 patients, four were treated with surgery only, one was treated nonsurgically (chemotherapy combined with external radiation), and twenty-one were treated with surgery plus adjuvant modalities. Surgery combined with ^{125}I internal radiation was used in eleven cases (38.5%), and surgery combined with external radiation was used in four cases (15.4%). Surgery combined with external radiation and chemotherapy was used in four cases (15.4%), and surgery combined with chemotherapy was used in two case (7.7%). Chemotherapy regimes include cisplatin, cisplatin combined with 5-fluorouracil, and cisplatin combined with 1-(4-amino-2-methyl-5-pyrimidinyl)-methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride (ACNU). Some literatures do not mention specific chemotherapy regimens. The mean follow-up time was 26.0±17.3mo. Five patients experienced recurrence or metastasis (19.2%), comprising two cases of brain metastasis alone, two patients relapsed at the same site as the initial lesion and one patient developed brain metastasis including the spine. Patients with recurrence or metastasis were planned to undergo tumor resection combined with postoperative radiotherapy. In the case of brain and spinal metastases palliative radiotherapy for intracranial and spinal metastases was planned, but the patient declined further aggressive treatment. Seven patients died (26.9%). One died from tumor metastasis, one died from diseases associated with metastatic cancer, and five died from other diseases. Seventeen patients were alive without disease (65.4%), two were alive with disease (7.7%; Table 1).

CXPA has a poor prognosis. We analyzed the survival of 26 patients with recurrence and death as the endpoint. Pathological types of malignant components, staging, invasiveness, and treatment methods were included in the analysis. The 5-year recurrence-free survival rate was 59.0% (Figure 2). There were no significant differences in survival rates among patients with different pathologic types (P=0.725) and stages (P=0.051). The presence or absence of bone destruction (P=0.128), nerve invasion (P=0.914) and peripheral tissue invasion (P=0.446) had no significant effect on prognostic survival. Patients treated with surgery+^{125}I internal radiation therapy had a better prognosis than with other treatment modalities (P=0.038; Figure 3).

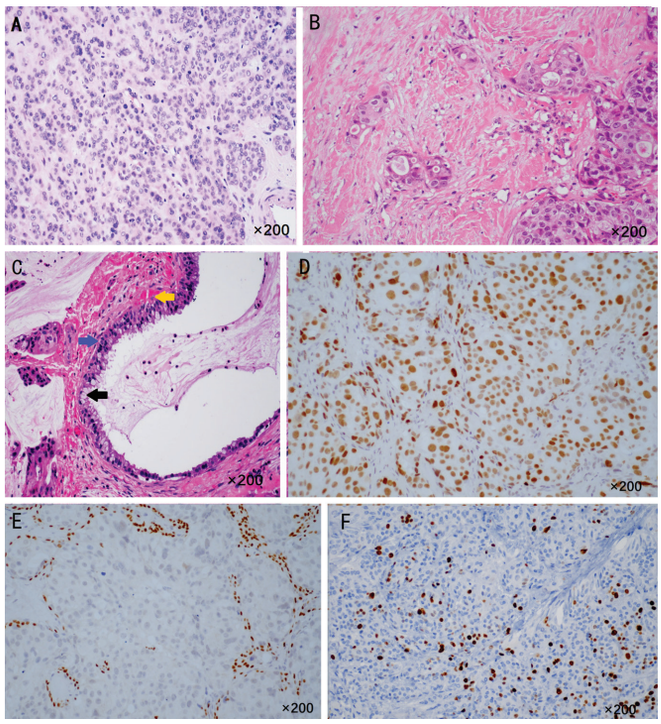

Figure 1 Pathological manifestations of carcinoma ex pleomorphic adenoma of the lacrimal gland A: HE staining (×200). Adenocarcinoma of the lacrimal gland. The tumor cells showed pleomorphic nuclei with prominent nucleoli and rich eosinophilic cytoplasm. B: HE staining (×200). Ductal carcinoma of lacrimal gland infiltrates into tumor capsule in small focus. C: HE staining (×200). Mucoepidermoid carcinoma of lacrimal gland consists of columnar, transparent and eosinophilic mucinous cells (black arrow), intermediate cells (blue arrow) and epidermoid cells (yellow arrow). D: IHC staining shows positive expression of P53 in intraductal carcinoma of lacrimal gland. E: IHC staining shows positive expression of P63 in nuclei of lacrimal gland intraductal carcinoma cells. F: IHC staining shows positive expression of Ki-67 in intraductal carcinoma of lacrimal gland. HE: Hematoxylin-eosin; IHC: Immunohistochemical.

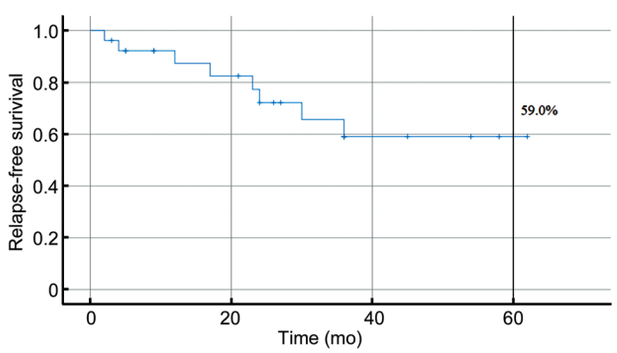

Figure 2 Overall survival analysis of carcinoma ex pleomorphic adenoma of the lacrimal gland Five-year survival rate without recurrence or death was 60.6%.

DISCUSSION

Orbital tumors primarily originate from blood vessels, muscles, cartilage, nerve tissue, lacrimal glands, and lymphatic structures. Approximately 5%–25% of intraorbital masses originate in the lacrimal gland[9]. The presentation and diagnosis of CXPA were earlier (5mo) compared to PA (12mo) and other lacrimal gland tumors[22]. CXPAs can be detected at the initial diagnosis of primary PA or can develop secondary to years of treatment after PA diagnosis. CXPA is the most commonly transformed malignant disease of PA[23]. Studies have shown malignant transformation rates of 5.9% for primary PA and 20.0% for recurrent PA[24]. However, no clinical evidence has been found to suggest that recurrence in the setting of PA favors malignant transformation, and a long latency period seems to be a potential key factor in the malignant transformation of recurrent PA. Since both myoepithelial and ductal cells of the lacrimal gland can undergo malignant transformation, the pathologic types of CXPAs are diverse. The most common malignant component is adenocarcinoma; the other malignant components are mucoepidermoid carcinoma, myoepithelial carcinoma, adenoid cystic carcinoma, and epithelial-myoepithelial carcinoma[25]. Nuclear pleomorphism, atypical mitotic features, hemorrhage, and necrosis characterize the malignant component. It has been shown that the positive expression of EGFL7, CD34, and Ki-67 in CXPA is significantly higher than that in PA and normal tissues and that this can be used as an immunohistochemical indicator to aid in diagnosis[26]. The positive expression of C-myc and Ki-67 is lower in PA, whereas CXPA had the higher positive expression of these two biomarkers. Thus, these biomarkers could provide valuable clues for the differential diagnosis of CXPA and PA[25].

The mechanism of CXPA is not fully understood. A research showed that CXPA showed TP53 and CIC mutations and an amplification of ERBB2[27]. The rearrangement of PLAG1 (PA gene 1) and HMGA2 and the expression of the corresponding proteins are common and specific findings in lacrimal PA and CXPA[28]. PLAG1 is frequently activated in PA and is mostly associated with myoepithelial differentiation; its loss of expression could be considered a marker of CXPA carcinogenesis[29]. Andreasen *et al*[30] found that the interleukin-6/Janus kinase/signal transducer and activator of transcription 3 (IL-6/JAK/STAT3) pathway is overexpressed in PA. This overexpression is more pronounced in CXPA, which may point to the importance of the IL-6/JAK/STAT3 pathway for the development and malignant transformation of PAs. De Lima-Souza *et al*[31] analyzed the metabolic profile of CXPA in the lacrimal gland and found that Fatty acid synthase and lipophilic proteins are overexpressed in CXPA, which may reflect a metabolic shift toward adipogenesis in cancer cells. Mariano *et al*[32] found gains in chromosomes 3 and 8 and genomic amplification at 8p and 12q in CXPA transformed from recurrent PA, mainly including high mobility group AT-hook 2 (HMGA2), mouse double minute 2 homolog (MDM2),

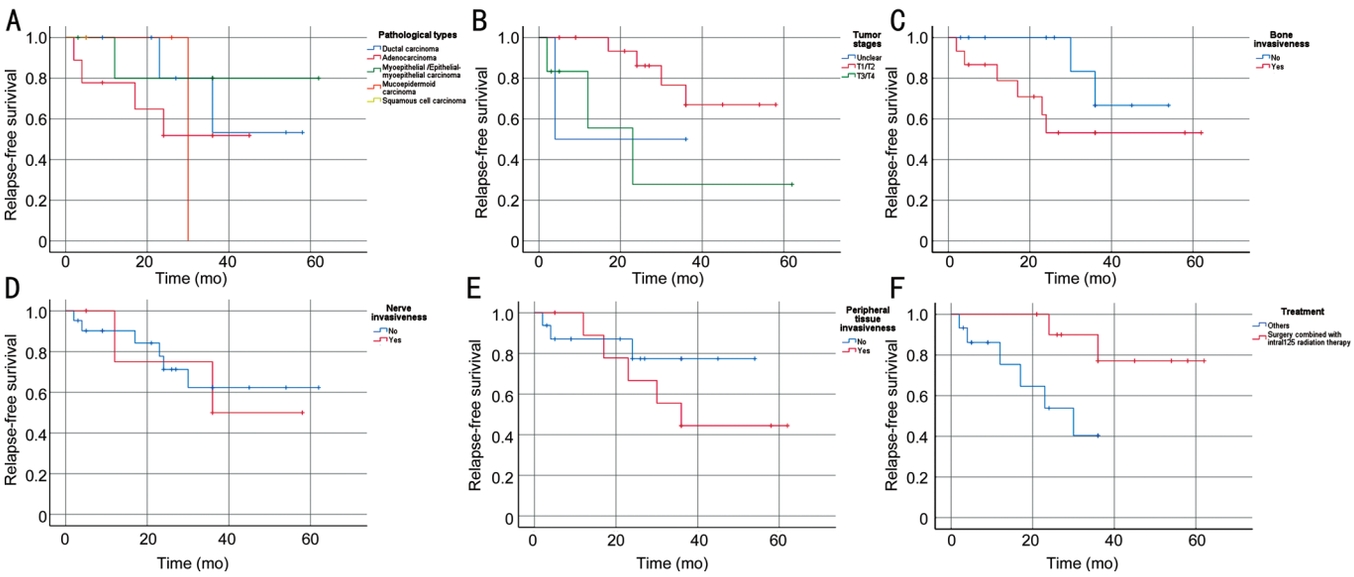

Figure 3 Survival analysis of carcinoma ex pleomorphic adenoma of the lacrimal gland A: Survival analysis of different pathological types (*P*=0.725); B: Survival analysis of different tumor stages (*P*=0.051); C: Survival analysis of different bone invasiveness (*P*=0.128); D: Survival analysis of different nerve invasiveness (*P*=0.914); E: Survival analysis of different peripheral tissue invasiveness (*P*=0.446); F: Survival analysis of different treatment modalities (*P*=0.038).

wingless-type MMTV integration site family inhibitory factor 1 (WIF1), Wolf-Hirschhorn syndrome candidate 1-like 1 (WHSC1L1), and cyclin-dependent kinase 4 (CDK4); these may be important contributors to malignant transformation.

The age of onset of CXPA ranges from approximately 20 to 50y, and there is no significant difference in incidence between men and women[3]. The incidence of ductal carcinoma, nonspecific carcinoma, and myoepithelial carcinoma is high, whereas mucoepidermoid carcinoma and epithelial-myoepithelial carcinoma are less common. This result is generally consistent with previous studies. Lacrimal gland CXPA is a very rare malignant disease. Only a small number of cases have been reported previously. Its clinical manifestations are lack of specificity, and it mainly depends on pathological diagnosis to differentiate it from other malignant tumors of the lacrimal gland. Lacrimal gland tumors are histologically similar to salivary gland tumors[28]. but it is unclear whether they share similar prognostic influences. It has been shown that salivary gland CXPA with higher tumor stage, lymph node metastasis, and strong peripheral invasiveness has a worse prognosis[33]. However, few relevant prognostic factors have been evaluated for lacrimal PA/CXPA. In this study, we analyzed the clinical cases of 26 patients with CXPAs to determine the prognostic factors affecting their survival. According to our analysis, the 5-year overall survival rate without recurrence was 59.0%. There was no significant difference in the survival rate among patients with different pathologic types, tumor stages, and tumor origins. Neither bone destruction nor nerve or peripheral tissue invasion had a significant effect on survival, but this result may be influenced by the small number of cases. A recent study suggested that high microbial diversity may serve as a potential prognostic marker for lacrimal CXPA, bringing new ideas for future prognosis assessment[34].

Treatment modalities for orbital malignancies include surgical resection and, if necessary, exenteration. Adjuvant treatment modalities include radiation therapy (external radiation therapy and ^{125}I internal radiation), chemotherapy, and targeted drug therapy. We found that the treatment of lacrimal gland CXPA is generally consistent with the treatment of other orbital malignancies. Survival analyses of all 26 patients show that surgical resection plus ^{125}I therapy leads to a better survival rate than do other treatment modalities. ^{125}I internal radiation is a rapidly evolving treatment modality for the treatment of tumors. A growing number of clinical trials support the efficacy and safety of ^{125}I internal radiation therapy for almost all tumors. Its lesionwide dose level far exceeds that of external radiation and minimizes the exposure of uninvolved surrounding normal tissue[35]. The prognosis of surgery combined with ^{125}I internal radiation therapy in this study points to this regimen's advantages in treating CXPAs. Moreover, recent studies have shown Neoadjuvant intraarterial cytoreductive chemotherapy with multimodal therapies can achieve favorable outcomes with locoregional control and improve disease-specific survival in patients with locally invasive advanced-stage CXPA of the lacrimal gland[36]. The new treatment of CXPA is still being gradually explored.

This study has several limitations: first, the disease is rare and the number of clinical cases analyzed is relatively small, so the results of this study have certain limitations. Second, outcome indicators are not abundant, and case data focusing on multiple

types of immunohistochemistry are scarce. Third, some cases derived from the literature lack relevant information on tumor staging. Therefore, this study did not evaluate regional lymph node involvement and distant metastasis in these cases. Finally, because of the rarity of the disease, previous studies were almost exclusively case reports. Therefore, the study included only case reports and did not comprehensively review all study types on lacrimal gland CXPA, limiting the generalizability of the findings. We hope to analyze more cases in the future. We here report a single-center clinical study analyzing the clinical prognostic features of CXPA in the context of the current literature. The results show that CXPA has a poor prognosis and poses a risk for recurrence and metastasis. Surgical resection combined with ^{125}I intraparticle radiation may be a better treatment modality.

ACKNOWLEDGEMENTS

Authors' Contributions: Yang RZ and Ma MS conducted data analysis studies, wrote the manuscript. Liu R, Ren TT and Li J conducted data collection. Wang N and Xu LY collated the data. Guo QH prepared Figure 1. Ma JM read and criticized the manuscript. All authors critically read and edited the manuscript. All authors read and approved the final manuscript.

Foundations: Supported by National Key R&D Program of China (No.2023YFC2410203); Beijing Hospitals Authority' Ascent Plan (No.DFL20190201); Beijing Hospitals Authority Clinical Medicine Development of Special Funding Support (No.ZLRK202503); Natural Science Foundation of Beijing (No.7222025).

Conflicts of Interest: Yang RZ, None; **Ma MS,** None; **Liu R,** None; **Ren TT,** None; **Li J,** None; **Wang N,** None; **Xu LY,** None; **Guo QH,** None; **Ma JM,** None.

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