• Clinical Research •

Clinicopathological features of cranial-nasal-orbital communicating lesions and diagnostic indicators for differentiating benign and malignant neoplasms

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Received: 2024-12-16 Accepted: 2025-03-11

Abstract

• **AIM:** To investigate the clinicopathological features of cranial-nasal-orbital communicating lesions and identify key diagnostic indicators for differentiating benign and malignant neoplasms.

• **METHODS:** The retrospective cohort study analyzed 74 histologically confirmed cases stratified by anatomical involvement at the Wuhan Union Hospital between January 2010 and December 2020: Group A (orbital-nasal group, *n*=29), Group B (orbital-cranial group, *n*=27), and Group C (cranial-nasal-orbital group, *n*=18). Clinicopathological profiles including symptom presentation, histopathology, and invasion patterns were systematically evaluated.

• **RESULTS:** The cohort comprised 49 (66.2%) benign and 25 (33.8%) malignant lesions. Compared with benign lesions, malignant lesions had a shorter onset time (12mo *vs* 2.5mo, *P*=0.004) and resulted in poorer vision (0.6 *vs* 1.53, *P*=0.025). Headache was reported in 28.6% of patients with benign lesions, but none in those with malignant lesions (*P*=0.002). Conjunctival congestion and edema were observed in 32.7% of patients with benign lesions and 60% of patients with malignant lesions (*P*=0.028). The ethmoid sinus was the most frequently invaded site (35 cases). Malignant lesions showed greater invasion in the nasal cavity (28.0% *vs* 0, *P*=0.000) and anterior cranial fossa (40.0% *vs* 8.2%, *P*=0.003) than benign lesions. The orbital-cranial group was more likely to invade through osseous foramina compared with the orbital-nasal group (*P*=0.002). Neurogenic tumors predominated benign cases (34.7%), whereas blood derived (28%) and glandular tumors (28%) were most prevalent in malignant subgroups. The proportion of malignant tumors in multi-disciplinary combined surgery was higher than that of benign lesions (61.5% *vs* 38.5%).

• **CONCLUSION:** Malignant cranial-nasal-orbital communicating lesions exhibit distinct clinicopathological signatures characterized by rapid progression, aggressive anterior fossa and nasal region, and severe visual morbidity.

• **KEYWORDS:** pathology; cranial-nasal-orbital region; lesion; benign; malignant

DOI:10.18240/ijo.2025.07.20

Citation: Xie M, Chen J, You YY, Su ZX, Zhu XY, Wang XH, Li PC, Jiang FG. Clinicopathological features of cranial-nasal-orbital communicating lesions and diagnostic indicators for differentiating benign and malignant neoplasms. *Int J Ophthalmol* 2025;18(7):1357-1368

INTRODUCTION

The orbit and its surrounding structures are intricate. The orbit is separated from the paranasal sinuses by a thin bony septum, and numerous foramina at the posterior of the orbit connect to surrounding structures[1-3]. Tumors invading through these foramina or causing bone destruction may result in cranial-nasal-orbital communicating lesions[4].

Cranial-nasal-orbital communicating lesions pose unique clinical challenges compared to isolated orbital diseases. Their cross-compartmental spread leads to a complex array of symptoms: ophthalmic manifestations (exophthalmos, diplopia, vision loss) often coexist with nasal symptoms (obstruction, epistaxis) and neurological consequences[5-6]. The

intricate anatomy, combined with the diverse histopathology, makes complete resection particularly challenging. Current understanding remains constrained by epidemiological scarcity, with most evidence derived from isolated case reports or small cohorts. The anatomical distribution of tumor involvement demonstrates significant histological correlations with underlying pathological characteristics. According to the literature[7], approximately 66% of brain tumors that invade the orbit originate from the sphenoid ridge, while orbital-nasal communicating lesions are predominantly epithelial tumors, with the maxillary sinus, ethmoid sinus, and nasal cavity being the most common sites of occurrence. Such histological correlation has significant therapeutic implications, aiding physicians in selecting surgical approaches and determining adjuvant treatment regimens.

This study analyzed the clinical, radiological, and pathological characteristics of cranial-nasal-orbital communicating lesions from a single institution and compared benign and malignant lesions, providing clinicians with a more comprehensive basis for diagnosis.

PARTICIPANTS AND METHODS

Ethical Approval The study received ethical approval from the Ethics Committee of Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology (No. [2023]-0112) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. For minors (under 18 years), consent was provided by their parents or legal guardians.

Inclusion and Exclusion Criteria This retrospective cohort study analyzed 74 patients with cranial-nasal-orbital communicating lesions treated at Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology between January 2010 and December 2020. The clinical data included sex, age, duration, best corrected visual acuity (BCVA, logMAR), intraocular pressure (IOP, mm Hg), symptoms and signs, treatment measures, and postoperative complications.

All patients met the following criteria: 1) patients diagnosed with cranial-nasal-orbital communicating lesions including non-neoplastic lesions; 2) patients with complete medical records and data available for analysis; 3) patients who had undergone diagnostic imaging to confirm the lesion; 4) patients who had undergone surgical treatment for the lesion. 5) patients with no serious liver, kidney, lung, heart or other organ dysfunction. The exclusion criteria were as follows: 1) patients with non-cranial-nasal-orbital communicating lesions including infectious lesions, such as abscesses; 2) patients with incomplete medical records or missing data; 3) patients who had underlying medical conditions that could confound the results (*e.g.*, other brain tumors, neurological disorders); 4) patients with a serious respiratory disease, heart disease, kidney disease or blood system disease.

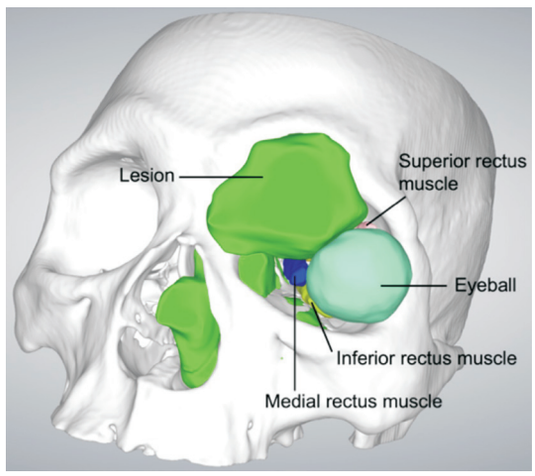

Figure 1 Three-dimensional imaging of lesion in relation to the skull, eyeball, and extraocular muscles.

Imaging Data Orbital magnetic resonance imaging (MRI) and computed tomography (CT) were evaluated to determine various parameters, including lesion size and invasion sites.

Classification Cases were categorized into three groups based on the extent of lesion invasion: Group A, Group B, and Group C. Group A included lesions involving the orbit and paranasal sinuses or nasal cavity. Group B comprised lesions extending into the orbit and cranial cavity. Group C involved simultaneous invasion of the orbit, nasal cavity/paranasal sinuses, and cranial cavity. The paranasal sinuses included the ethmoid, frontal, maxillary, and sphenoid sinuses. And the cranial cavity encompassed the frontal lobe, anterior cranial fossa base, sphenoid ala, temporal lobe, middle cranial fossa base, cavernous sinus, greater wing of the sphenoid bone, and the intracranial segment of the nerve canal. Figure 1 showed a three-dimensional (3D) imaging of communicating lesion in relation to the skull, eyeball, and extraocular muscles.

Pathological Data The study cohort comprised 72 surgical cases with available intraoperative specimens. All specimens underwent standard histological processing including 10% formaldehyde fixation, paraffin embedding, and hematoxylin-eosin staining. Diagnostic confirmation was achieved through independent review by two senior pathologists using WHO classification criteria[8]. Additionally, pathological sections from two patients who had surgery at another hospital were transferred to our institution for review. The diagnoses were consistent with those from the previous hospital and were included in the pathological data analysis.

Statistical Analysis SPSS Statistics version 17.0 (IBM Corp., Armonk, NY, USA) was used for analysis, and statistical significance was set at $P<0.05$. In descriptive data analysis, non-normally distributed data were shown as median and interquartile range (IR), and normally distributed variables

were shown as mean and standard deviation. *T*-tests and Chi-square tests were conducted to analyze the differences between groups. When the sample size was insufficient, Fisher's exact test was conducted.

RESULTS

Demographic Data The study included 47 males and 27 females, with an average age of 45.77±21.33y (range, 2-85y). Symptom duration varied from 3d to 20y. The median duration of primary symptoms was 12 (56)mo for benign lesions and 2.5 (5.3)mo for malignant lesions, with a statistically significant difference (P=0.004). The BCVA was 0.6 (1.42) for benign lesions and 1.53 (2.47) for malignant lesions, also showing a statistically significant difference (P=0.025). No statistically significant differences were found between benign and malignant lesions in terms of medical history, IOP, or average maximum lesion diameter.

The main symptoms included eyelid swelling, exophthalmos, vision loss, tearing, eye pain, headache, diplopia, abnormal facial sensation, and nasal symptoms. The main signs included ptosis, conjunctival congestion and edema, corneal edema, optic disk edema, ocular motility disorders, and eyeball dislocation. Notably, 14 (28.6%) patients with benign lesions reported headache, while none with malignant lesions did, with a statistically significant difference (P=0.002). Conjunctival congestion and edema were observed in 16 (32.7%) patients with benign lesions and 15 (60%) patients with malignant lesions, also showing a statistically significant difference (P=0.028). Further detailed demographic and clinical information was provided in Table 1.

Imaging Examinations

Involved sites The specific sites involved were statistically analyzed, revealing that the ethmoid sinus was the most frequently involved site in all cases (n=35). We analyzed the differences between benign and malignant lesions in terms of their invasion of various sites. Statistically significant differences were found in the proportions of nasal cavity invasion (P=0.000) and anterior cranial fossa invasion (P=0.003) between the benign and malignant groups. As shown in Table 2, malignant lesions were more likely to invade the nasal cavity (28%) and anterior cranial fossa (40%) than benign lesions.

Invasion modes The Fisher's exact test revealed significant differences among Groups A, B, and C (P=0.029). Post hoc analysis demonstrated that the osseous foramina invasion rates differed significantly across groups (P=0.004), with pairwise comparisons showing a marked difference between Groups A and B (P=0.002). No significant intergroup differences were observed in other invasion patterns (P>0.05; Table 3).

Pathological Classification Among the 74 patients, 49 (66.2%) had benign lesions and 25 (33.8%) had malignant tumors. Blood derived and glandular tumors were the most common (28% respectively) among malignant lesions, whereas neurogenic tumors were the most common (34.7%) among benign lesions. The majority of benign tumors in Group A were non-neoplastic lesions (37.5%), while the majority of tumors in Groups B and C were neurogenic (66.7% and 57.1%, respectively). Among malignant tumors, Group C had the highest prevalence of glandular-derived tumors (36.4%), whereas Groups A and B had the highest prevalence of blood-derived tumors (60% and 33.3%, respectively). Tables 4, 5 contained more specific information.

Treatment Measures and Surgical Complications The treatment modalities were as follows: 49 patients (66.2%) underwent ophthalmic surgery, six (8.1%) received ear, nose, and throat (ENT) surgery, five (6.8%) underwent neurosurgery, and thirteen (17.6%) received combined surgery involving multiple specialties. In ophthalmology, ENT, and neurosurgery, benign lesions accounted for the highest proportions, specifically 71.4%, 83.3%, and 80%, respectively, with neurogenic tumors being the most common, comprising 22.4%, 33.3%, and 60%, respectively. In multidisciplinary surgeries, malignant lesions had the highest proportion (61.5%), with blood-derived tumors being the most prevalent (23.1%). Additionally, nasal endoscopy-assisted resection was used in 10 cases (13.5%) of the surgeries performed, with benign tumors accounting for 70% of these cases. Further detailed information about the treatment of benign and malignant lesions was provided in Table 6.

Among the 74 patients who underwent surgical treatment, 28 developed postoperative complications (Table 7). Ocular complications occurred in 18 patients, including vision loss in six, ptosis in five, ocular motility disorders in five, and tearfulness in two. Cerebral complications were noted in six cases, with cerebrospinal fluid leakage in three, facial numbness in two, and intracranial hematoma in one. Nasal complications were identified in five cases, comprising rhinorrhea in four and oral-nasal fistula in one. Systemic complications were present in five cases, including three cases of infection and two of abnormal body temperature. The Fisher's exact test revealed that there was no significant difference in complication rates among groups A, B, and C (P=0.841).

Follow-up A total of 74 patients were followed up on an outpatient basis for a mean follow-up period of 2.85y (ranging from 9mo to 4y). Patients with malignant tumors received radiotherapy and chemotherapy as adjuvant treatments. Among the benign tumors, three cases of meningioma recurred, all of which were treated with gamma knife radiation therapy. Four patients with malignant tumors died, two of whom had undergone subtotal resection. Patients with osteosarcoma and adenoid cystic carcinoma died of intracranial and systemic

Table 1 Clinical features of benign and malignant lesions

Parameters	Benign, *n*=49	Malignant, *n*=25	Total, *n*=74	*P*
Male, *n* (%)	32 (65.3)	15 (60.0)	47 (63.5)	0.654
Age, y	43.96±21.26	49.32±21.46	45.77±21.33	0.310
Symptom duration, mo	12 (56)	2.5 (5.3)	6 (58)	0.004
Anamnesis, *n* (%)				
Craniofacial trauma	8 (16.3)	2 (8.0)	10 (13.5)	0.479
Craniofacial surgery	20 (40.8)	7 (28.0)	27 (36.5)	0.279
BCVA (logMAR)	0.60 (1.42)	1.53 (2.47)	0.7 (1.65)	0.025
IOP, mm Hg	16.45±3.75	17.02±4.28	16.64±3.95	0.560
Maximum diameter (cm)	4.19±2.11	4.00±1.33	4.13±1.88	0.687
Symptoms, *n* (%)				
Eyelid swelling	9 (18.4)	9 (36)	18 (24.3)	0.151
Exophthalmos	23 (46.9)	9 (36)	32 (43.2)	0.460
External masses	6 (12.2)	4 (16)	10 (13.5)	0.725
Vision loss	17 (34.7)	5 (20)	22 (29.7)	0.283
Tearing	8 (16.3)	3 (12)	11 (14.9)	0.740
Eye pain	15 (30.6)	10 (40)	25 (33.8)	0.446
Headache	14 (28.6)	0	14 (18.9)	0.002
Diplopia	5 (10.2)	3 (12)	8 (10.8)	0.549
Abnormal facial sensation	1 (2)	1 (4)	2 (2.7)	0.565
Nasal symptoms	3 (6.1)	3 (12)	6 (8.1)	0.400
Signs, *n* (%)				
Ptosis	16 (32.7)	9 (36)	25 (33.8)	0.799
Conjunctival congestion and edema	16 (32.7)	15 (60)	31 (41.9)	0.028
Corneal edema	5 (10.2)	6 (24)	11 (14.9)	0.167
Optic disk edema	6 (12.2)	1 (4)	7 (9.5)	0.412
Ocular motility disorders	21 (42.9)	11 (44)	32 (43.2)	0.560
Eyeball dislocation	19 (38.8)	7 (28)	26 (35.1)	0.444

BCVA: Best corrected visual acuity; IOP: Intraocular pressure.

Table 2 The invasion sites of benign and malignant lesions

Parameters	Benign, *n*=49	Malignant, *n*=25	Total, *n*=74	*P*
Ethmoid sinus	24 (49%)	11 (44%)	35 (47.3%)	0.685
Frontal sinus	16 (32.7%)	5 (20%)	21 (28.4%)	0.253
Maxillary sinus	12 (24.5%)	7 (28%)	19 (25.7%)	0.744
Sphenoid sinus	5 (10.2%)	0	5 (6.8%)	0.160
Nasal cavity	0	7 (28%)	7 (9.5%)	0.000
Anterior cranial fossa	4 (8.2%)	10 (40%)	14 (18.9%)	0.003
Middle cranial fossa	16 (32.7%)	6 (24%)	22 (29.7%)	0.441

Table 3 Analysis of different orbital communication occupying invasion modes

Parameters	Group A, *n*=29	Group B, *n*=27	Group C, *n*=18	*P*
Osseous foramina	1 (3.4%)	10 (37%)	3 (16.7%)	0.004
Bone destruction	15 (51.7%)	8 (29.6%)	9 (50%)	0.209
Bony defect	1 (3.4%)	2 (7.4%)	2 (11.1%)	0.626
Direct invasion	12 (41.4%)	7 (25.9%)	4 (22.2%)	0.350

Group A: Orbital-nasal group; Group B: Orbital-cranial group; Group C: Cranial-nasal-orbital group.

multiple metastases within 3y after surgery. Consequently, the 3-year survival rate for patients with malignant tumors was 84% (21/25), and the overall 3-year survival rate was 94.6% (70/74).

Representative Cases A typical case of a malignant tumor with orbito-cranial communication: a 62-year-old woman presented with a 3-month history of right eye redness and inability to open the eye, without significant medical history. Examination revealed right eyelid swelling with complete ptosis, mixed conjunctival congestion, and scleral tenderness (+).

Table 4 Histopathology of benign communicative occupying lesions

Histopathology	Total, *n*=49	Group A, *n*=24	Group B, *n*=18	Group C, *n*=7
Neurogenic	17 (34.7%)	1 (4.2%)	12 (66.7%)	4 (57.1%)
Meningoma	9 (18.4%)	1 (4.2%)	4 (22.2%)	4 (57%)
Schwannoma	4 (8.2%)	0	4 (22.2%)	0
Neurofibroma	4 (8.2%)	0	4 (22.2%)	0
Epithelial	10 (20.4%)	8 (33.3%)	0	2 (28.6%)
Mucous cyst	4 (8.2%)	4 (16.7%)	0	0
Dermoid cyst	2 (4.1%)	1 (4.2%)	0	1 (14.3%)
Benign cyst	2 (4.1%)	2 (8.3%)	0	0
Epithelial cyst	1 (2%)	0	0	1 (14.3%)
Inverted papilloma	1 (2%)	1 (4.2%)	0	0
Vascular	5 (10.2%)	3 (12.5)	1 (5.6%)	1 (14.3%)
Vascular tumors	4 (8.2%)	3 (12.5%)	1 (5.6%)	0
Hemangiopericytoma	1 (2%)	0	0	1 (14.3%)
Osteogenetic				
Osteoma	1 (2%)	1 (4.2%)	0	0
Muscle derived				
Myocutaneous cell tumor	1 (2%)	1 (4.2%)	0	0
Lacrimal gland derived				
Pleomorphic adenoma	1 (2%)	1 (4.2%)	0	0
Germ cell derived				
Teratoma	1 (2%)	0	1 (5.6%)	0
Non-neoplastic lesions	13 (26.5%)	9 (37.5%)	4 (22.2%)	0
Inflammatory pseudotumor	8 (16.3%)	5 (20.8%)	3 (16.7%)	0
Cell proliferation	3 (6.1%)	2 (8.3%)	1 (5.6%)	0
Haematoma	2 (4.1%)	2 (8.3%)	0	0

Group A: Orbital-nasal group; Group B: Orbital-cranial group; Group C: Cranial-nasal-orbital group.

Table 5 Histopathology of malignant communicative occupying lesions

Histopathology	Total, *n*=25	Group A, *n*=5	Group B, *n*=9	Group C, *n*=11
Blood derived	7 (28%)	3 (60%)	3 (33.3%)	1 (9.1%)
Lymphoma	4 (16%)	2 (40%)	2 (22.2%)	0
Plasmacytoma	1 (4%)	0	0	1 (9.1%)
Myeloid sarcoma	1 (4%)	0	1 (11.1%)	0
Leukemia	1 (4%)	1 (20%)	0	0
Glandular derived	7 (28%)	1 (20%)	2 (22.2%)	4 (36.4%)
Adenoid cystic carcinoma	3 (12%)	0	1 (11.1%)	2 (18.2%)
Sebaceous carcinoma	2 (8%)	1 (20%)	1 (11.1%)	0
Adenocarcinoma	2 (8%)	0	0	2 (18.2%)
Epithelial	3 (12%)	1 (20%)	1 (11.1%)	1 (9.1%)
Squamous cell carcinoma	2 (8%)	1 (20%)	0	1 (9.1%)
Tricholemmal carcinoma	1 (4%)	0	1 (11.1%)	0
Mesenchymal tissue derived				
Spindle cell sarcoma	3 (12%)	0	1 (11.1%)	2 (18.2%)
Metastatic				
Metastatic carcinoma	2 (8%)	0	1 (11.1%)	1 (9.1%)
Osteogenetic				
Osteosarcoma	1 (4%)	0	0	1 (9.1%)
Retinal derived				
Retinoblastoma	1 (4%)	0	0	1 (9.1%)
Undifferentiated				
Undifferentiated carcinoma	1 (4%)	0	1 (11.1%)	0

Group A: Orbital-nasal group; Group B: Orbital-cranial group; Group C: Cranial-nasal-orbital group.

Table 6 Treatment between benign and malignant lesions

Parameters	Ophthalmic surgery, *n*=49	ENT surgery, *n*=6	Neurosurgery surgery, *n*=5	Combined surgery, *n*=13	Nasal endoscopy-assisted, *n*=10
Benign	35 (71.4%)	5 (83.3%)	4 (80%)	5 (38.5%)	7 (70%)
Neurogenic	11 (22.4%)	2 (33.3%)	3 (60%)	1 (7.7%)	4 (40%)
Vascular	2 (4.1%)	1 (16.7%)	0	2 (15.4%)	1 (10%)
Muscle derived	1 (2%)	0	0	0	0
Epithelial	10 (20.4%)	0	0	0	0
Osteogenetic	0	0	0	1 (7.7%)	0
Lacrimal gland derived	1 (2%)	0	0	0	0
Germ cell derived	1 (2%)	0	0	0	0
Non-neoplastic lesions	9 (18.4%)	2 (33.3%)	1 (20%)	1 (7.7%)	2 (20%)
Malignant	14 (28.6%)	1 (16.7%)	1 (20%)	8 (61.5%)	3 (30%)
Glandular derived	4 (8.2%)	0	1 (20%)	2 (15.4%)	0
Undifferentiated	1 (2%)	0	0	0	0
Mesenchymal tissue derived	2 (4.1%)	1 (16.7%)	0	0	1 (10%)
Osteogenetic	1 (2%)	0	0	0	0
Blood derived	4 (8.2%)	0	0	3 (23.1%)	2 (20%)
Retinal derived	0	0	0	0	0
Epithelial	1 (2%)	0	0	2 (15.4%)	0
Metastatic	1 (2%)	0	0	1 (7.7%)	0

ENT: Ear, nose, and throat.

Table 7 Complications of communicative occupying lesions *n* (%, benign+malignant)

Parameters	Total, *n*=74	Group A, *n*=29	Group B, *n*=27	Group C, *n*=18	*P*
Ocular complications					
Vision loss	6 (8.1%, 2+4)	2 (6.9%, 1+1)	1 (3.7%, 0+1)	3 (16.7%, 1+2)	0.321
Ptosis	5 (6.8%, 3+2)	1 (3.4%, 0+1)	2 (7.4%, 1+1)	2 (11.1%, 2+0)	0.626
Ocular motility disorders	5 (6.8%, 2+3)	2 (6.9%, 1+1)	2 (7.4%, 0+2)	1 (5.6%, 1+0)	0.999
Tearfulness	2 (2.7%, 0+2)	0	2 (7.4%, 0+2)	0	0.187
Cerebral complications					
Cerebrospinal fluid leakage	3 (4.1%, 1+2)	0	1 (3.7%, 0+1)	2 (11.1%, 1+1)	0.178
Facial numbness	2 (2.7%, 1+1)	0	1 (3.7%, 0+1)	1 (5.6%, 1+0)	0.517
Intracranial hematoma	1 (1.4%, 0+1)	0	0	1 (5.6%, 0+1)	0.243
Nasal complications					
Rhinorrhea	4 (5.4%, 3+1)	2 (6.9%, 1+1)	0	2 (11.1%, 2+0)	0.225
Oral nasal fistula	1 (1.4%, 0+1)	1 (3.4%, 0+1)	0	0	0.999
Systemic complications					
Infection	3 (4.1%, 1+2)	0	1 (3.7%, 0+1)	2 (11.1%, 1+1)	0.178
Abnormal body temperature	2 (2.7%, 1+1)	1 (3.4%, 1+0)	0	1 (5.6%, 0+1)	0.710

Extraocular movements were limited in all directions except medial rotation of the right eye. Proptosis measured 10 mm in the right eye and 9 mm in the left eye, with an interorbital distance of 87 mm. MRI (Figure 2A-2F) showed an irregular soft tissue mass in and adjacent to the right orbit, extending from the inferior posterior region to the temporal fossa *via* an enlarged inferior orbital fissure and possibly along the superior orbital fissure. The mass was hyperintense on T1-weighted images (T1WI; Figure 2A-2C) and hypointense on T2-weighted images (T2WI; Figure 2D-2F). CT scan of the orbit (Figure 2G-2I) revealed a heterogeneous density mass in the posterior inferior part of the right orbit, with partial erosion of the outer orbital wall and extension into the temporal fossa. Based on the location, a surgical approach was made *via* a skin incision at the lower palpebral margin of the right eye. The intraoperative lesion was white and tough. Prophylactic antibiotics were administered preoperatively, and postoperative management included anti-inflammatory agents, dehydrating treatments, hormones, and mannitol. Histopathological examination (Figure 2J, 2K) confirmed extranodal marginal zone lymphoma. Follow-up within two years showed no tumor recurrence.

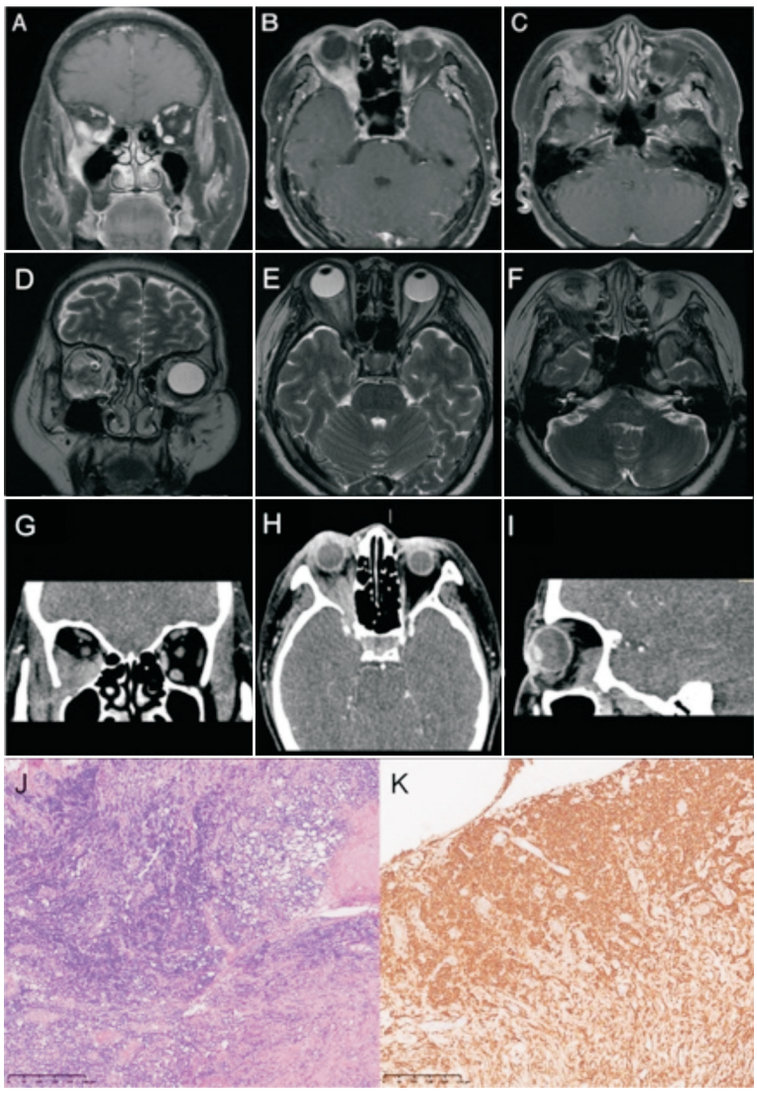

Figure 2 A typical case of a malignant tumor with orbito-cranial communication A: T1-weighted coronal MRI; B, C: T1-weighted axial MRI; D: T2-weighted coronal MRI; E, F: T2-weighted axial MRI; G: Coronal CT scan; H: Axial CT scan; I: Sagittal CT scan; J: HE staining ×100; K: IHC staining of CD20 ×100. Scale bar: 250 μm. Pathological examination reveals that the tumor is composed of morphologically heterogeneous small B cells. MRI: Magnetic resonance imaging; CT: Computed tomography; HE: Hematoxylin and eosin; IHC: Immunohistochemistry.

A typical case of a benign tumor with cranial-nasal-orbital communication: a 47-year-old woman presented with a 2-year history of redness and swelling of the right eye, accompanied by protrusion for 2mo. She had a history of palpitations and a head injury 18y prior. Examination revealed visual acuity of LogMAR 0.0 and IOP of 17 mm Hg in both eyes. The right eyelid was red and swollen, with a soft, indistinct mass protruding from the upper outer quadrant of the conjunctiva. Limited upward and outward gaze was observed in the right eye. Proptosis measured 20 mm in the right eye and 14 mm in the left eye, with an interorbital distance of 98 mm. MRI (Figure 3A-3F) showed localized thickening and expansion of the right lateral and superior orbital walls, involving parts of the frontal bone, temporal bone, greater and lesser wings of the sphenoid bone, and the posterior wall of the ethmoid sinus. The affected bones were hypointense on T1WI (Figure 3A-3C) and hyperintense on T2WI (Figure 3D-3F), with increased periosteal reaction and unclear borders. Soft tissue thickening was noted in the extraconal space, eyelids, temporal muscle, and diffuse thickening of the dura mater in the right frontal-temporal region. CT scan of the orbit (Figure 3G-3I) revealed extensive thickening and expansion of the right lateral and superior orbital walls, frontal bone, greater and lesser wings of the sphenoid bone, temporal bone, and bilateral posterior ethmoidal sinus walls. The affected bones had uneven density, rough cortical surfaces, and significant periosteal reaction with layered and radial needle-like projections. The patient underwent combined surgery by the ophthalmology and neurosurgery departments. The ophthalmic approach was an incision in the middle and lateral third of the right eye's double eyelid, and the neurosurgical approach was a craniotomy of the right frontal and temporal arcs. Prophylactic antibiotics were used preoperatively, and postoperative management included anti-inflammatory and dehydrating treatments,

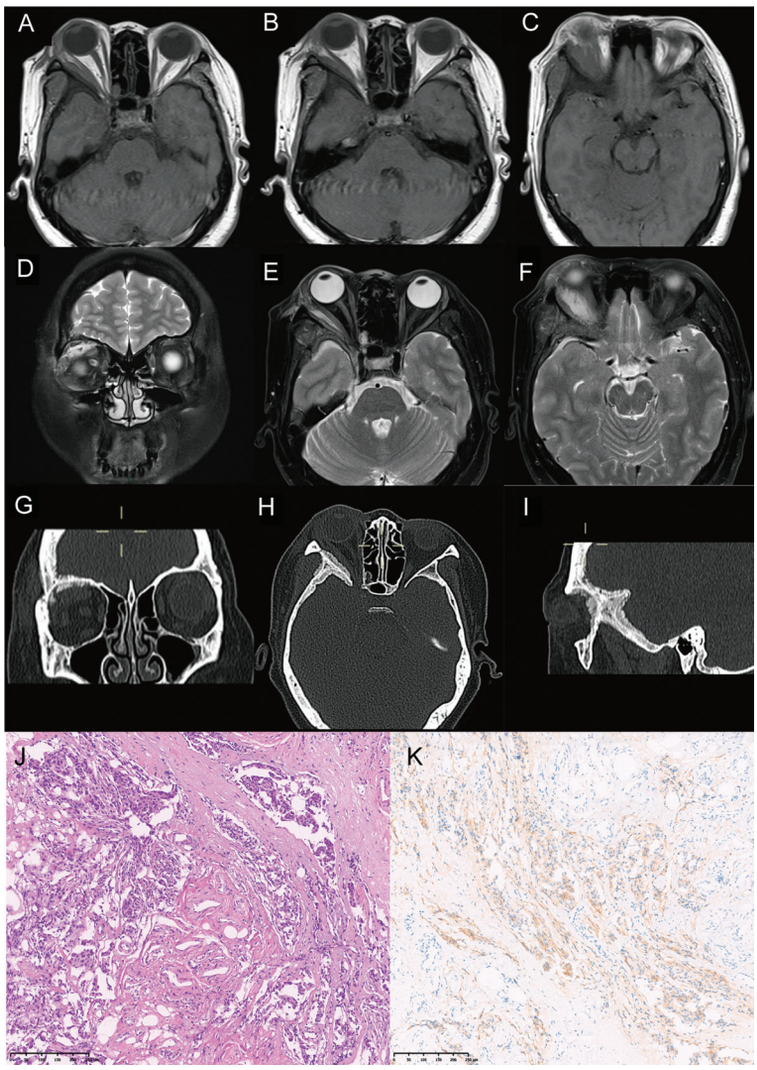

Figure 3 A typical case of a benign tumor with cranial-nasal-orbital communication A-C: T1-weighted axial MRI; D: T2-weighted coronal MRI; E, F: T2-weighted axial MRI; G: Coronal CT scan; H: Axial CT scan; I: Sagittal CT scan; J: HE staining ×100; K: IHC staining of EMA ×100. Scale bar: 250 μm. Pathological examination reveals that the tumor is composed of sheets of meningothelial cells with small nucleoli. EMA: Epithelial membrane antigen; MRI: Magnetic resonance imaging; CT: Computed tomography; HE: Hematoxylin and eosin; IHC: Immunohistochemistry.

hormones, and mannitol. Histopathological examination (Figure 3J, 3K) confirmed a fibroblastic meningioma (WHO grade I). Postoperative follow-up within three years showed no complications such as cerebrospinal fluid leakage, and no tumor recurrence was observed.

DISCUSSION

Clinical Features Cranial-nasal-orbital communicating lesions involve complex pathology that affects the eyes, nose, and brain, with main symptoms including protrusion of the eyeball, nasal congestion, and dizziness[5,9-10]. Proptosis or vision loss often serves as the initial clinical manifestation. Other symptoms, such as nasal congestion or dizziness, are typically unrecognized until a comprehensive patient history is collected post-admission[11]. In some cases, patients may present with multiple symptoms, highlighting the need for clinicians to consider the possibility of orbital-cranial or orbital-nasal involvement in patients with multi-site symptoms, as this may indicate more extensive tumor invasion.

In our study, malignant lesions tended to present more abruptly and cause more severe visual impairment compared to benign lesions. The rapid onset of symptoms is due to the invasive nature of these lesions, which can disrupt critical anatomical structures in the cranial, nasal, and orbital regions, leading to significant clinical manifestations. Given their rapid progression and significant impact on vision and overall quality of life, early diagnosis and Treatment are crucial.

The prevalence of headache symptoms demonstrated significant disparity between patients with benign and malignant lesions (28.6% and 0, respectively). The difference may be attributed to distinct tumor biological behaviors. Benign lesions usually grow slowly and mainly compress the surrounding tissues, which may stimulate the dura mater or pull the blood vessels, stimulating the pain nerve endings and leading to headache. Conversely, malignant lesions

demonstrate aggressive biological behavior characterized by rapid proliferation and tissue infiltration, which may lead to structural damage of nociceptive nerve fibers, potentially resulting in diminished or absent pain perception[12].

The incidence of conjunctival edema and congestion was higher in malignant lesions than in benign lesions (60% and 32.7%, respectively). This may be related to the compression of surrounding structures and inflammatory responses caused by the lesion, or due to chronic mechanical forces induced by the lesion leading to long-term changes in ocular structures[13]. Malignant tumors, due to their rapid growth and high invasiveness, may more readily cause acute changes in ocular structures[14].

Medical History According to our research, some patients with these communicative lesions previously underwent craniofacial surgery or experienced trauma, which might indicate a link between tumor invasion and these particular medical histories. A communication channel between the orbit and the cranial cavity may be established by craniofacial trauma or surgery, which could promote the growth of malignancies. Numerous case reports and epidemiological studies previously established the relationship between traumatic brain damage and the development of brain tumors[15-17]. But there is still no proof that the two are causally related. As they may be more susceptible to orbital-nasal and orbito-cranial communication cancers, patients with a history of craniofacial surgery or trauma should be managed with greater caution.

Pathological Characteristics The histopathological classification of cranial-nasal-orbital communicating lesions is complex, encompassing 31 types in this study. About two-thirds of the instances in our analysis were benign tumors. In line with earlier findings[18], 34.7% of these were neurogenic tumors, primarily meningiomas. Meningiomas may spread from intracranial meningiomas or be primary in the orbit. Sphenoid ridge meningiomas were the primary source of intracranial meningioma spread[19]. Twenty-eight percent of the malignant tumors were blood-derived, primarily lymphomas, which accounted for 5% to 15% of all extranodal lymphomas and were a common malignant tumor of the ocular adnexa[20]. With the improvement of medical standards, most communicating benign tumors could be detected and treated early, leading to a relatively decreased proportion of malignant tumors.

Among orbital-nasal communicating lesions, 82.8% were benign tumors and 17.2% were malignant tumors. The 58.7% benign rate reported by Wu *et al*[21] is different from this distribution, most likely as a result of different inclusion and classification methods. Benign and malignant tumors made up 66.2% and 33.8% of the orbital-cranial group, respectively, which is consistent with the proportion of benign tumors described by Mendoza-Santiesteban *et al*[22]. Malignant tumors made up 61.1% of the cranial-nasal-orbital group, whereas benign tumors made up 38.9%. The relatively high proportion of malignant tumors in cranial-nasal-orbital communicating lesions may be due to the rapid growth and strong invasiveness of malignant lesions, as well as the stimulation of cell proliferation and promotion of malignant transformation caused by chronic inflammation and inflammatory factors.

Invasion Sites Our study revealed that lesions communicating with the orbit, anterior cranial fossa, or nasal cavity were more likely to be malignant, with no statistically significant difference in invasion of other areas. Due to their great invasiveness, malignant tumors can quickly destroy bone and spread widely. Particularly susceptible to tumor invasion are the anterior cranial fossa and the middle cranial fossa[23]. The middle cranial fossa is the most susceptible location when a tumor invades the orbit since it contains the supraorbital fissure, infraorbital fissure, and optic foramen[24]. A tumor that invades the anterior cranial fossa may spread from the middle cranial fossa or paranasal sinuses, or it may erode the bone wall. As a result, a greater percentage of malignant tumors than benign lesions have the ability to penetrate and communicate with the anterior cranial fossa. This also applies to lesions that occupy orbital space and communicate with the nasal cavity[25]. In cases where tumors invaded through osseous foramina, the orbital-cranial group had a higher proportion (37%) than the orbital-nasal group (3.4%). This may be due to the orbital roof and the floor of the anterior cranial fossa were made up of thinner bone plates[2], such as the cribriform plate and the orbital roof, which are more easily eroded by tumors.

Differentiation of Benign and Malignant Tumors Before Surgery MRI is the gold standard for preoperative orbital lesion characterization[26]. By analyzing differences in morphology and signal characteristics on T1WI and T2WI, it is possible to differentiate between benign and malignant orbital neoplasms[27]. Malignant neoplastic lesions typically exhibit irregular morphology, while benign lesions tend to have more regular shapes. Malignant lesions, characterized by high cellular density, generally show low or isointense signals on T1WI and predominantly isointense or hyperintense signals on T2WI. In contrast, benign neoplastic lesions typically demonstrate isointense signals on T1WI and hyperintense signals on T2WI[28-30]. These imaging characteristics are crucial for accurate diagnosis and treatment planning in patients with orbital neoplastic lesions.

Understanding the prevalence of tumors at specific anatomical locations is essential for optimizing surgical access and determining appropriate resection margins. For instance, cavernous hemangiomas and optic nerve sheath tumors are

typically found in the intraconal space, while lymphomas and inflammatory pseudotumors are commonly located in the extraconal space. Optic nerve meningiomas and optic nerve gliomas tend to occur within the optic nerve and optic nerve sheath region. Metastatic tumors and subperiosteal hematomas are typically located in the orbital wall and subperiosteal septum, while mucous cysts and inflammatory pseudotumors can arise in the lacrimal fossa[31]. This information is invaluable for surgeons, as it enhances their ability to select appropriate surgical techniques and pathways, thereby minimizing the risk of damage to critical structures such as the optic nerve and ocular motor nerves during the procedure[28].

Role of Molecular and Genetic Markers Molecular genetic approaches have become the gold standard for diagnosing tumors with overlapping histological and immunophenotypic features[32]. Gene fusions play a crucial role in the development of both benign and malignant tumors. For instance, the NAB2-STAT6 fusion transcript and its variants have been identified as molecular markers for solitary fibrous tumors[33]. RNA sequencing has been pivotal in tumor research[34]. Yang *et al*[35] used RNA sequencing combined with molecular biology assays to find that RBMS1 is associated with pigment granules and melanosomes and is involved in cell proliferation and apoptosis pathways. The combination of proteomics and transcriptomics has provided new insights into malignant tumor development and progression. Dunn *et al*[36] conducted the first transcriptome-proteome analysis of meningiomas, identifying several novel transcripts and proteins with potential biomarker and therapeutic implications. The detection of molecular and genetic markers offers new perspectives for future tumor research.

Surgical Approaches A detailed analysis of tumor location is essential for effective surgical intervention. Customizing the tumor resection approach based on the three-dimensional localization allows safe access to most orbital tumors, reducing complications and improving postoperative aesthetics[31]. Surgical approaches include superior (supraorbital), lateral (orbital lateral or medial), inferior (infraorbital), or anterior (transconjunctival) incisions. The transorbital approach is not only increasingly important for orbital lesions but also serves as a pathway to the anterior and middle cranial bases. The surgical treatment of orbital lesions should determine the choice of approach based on the coronal and anteroposterior characteristics of the pathology[37-38]. For example, in cases of superior lateral optic nerve lesions, the palpebral fissure incision combined with the lateral orbital incision can provide good exposure of both anterior and posterior masses. This method ensures comprehensive treatment of all posterior globe lesions while minimizing complications and enhancing aesthetics[39].

Reducing Complications Our data indicates a postoperative complication incidence rate of 37.8%, including vision loss and cerebrospinal fluid leakage, consistent with the reported incidence rate of 30%-50% for the traditional basal approach in literature[40-41]. Among them, vision loss occurred most frequently, which may be related to orbital involvement by the lesions.

Navigation-assisted biopsy techniques protect critical anatomical structures, reduce postoperative pain, swelling, and infection risk, and enhance aesthetics through minimally invasive methods[42]. Image-guided surgery is vital for tumor treatment. A method using a 3D navigation system that combines PET/CT and MRI images has been developed for minimally invasive biopsies of orbital lesions. This aids histological diagnosis, minimizes scarring, and preserves visual function[43]. Minimally invasive techniques are also an effective alternative to traditional orbital tumor resection. The endoscopic transnasal approach, particularly when combined with external techniques, reduces tissue damage between the orbit, nasal cavity, and skull. It improves visualization of the orbital apex and provides an optimal pathway for the optic nerve in medial orbital tumors[44]. Endoscopic techniques offer superior postoperative recovery and the best cosmetic results *via* a no-incision nasal approach[45].

Interdisciplinary Cooperation When imaging tests show lesion communication with the orbit, paranasal sinuses, or brain, surgical planning should be done with a preoperative multidisciplinary team approach. In this study, 17.6% of the surgeries were completed through multidisciplinary collaboration, with 61.5% of the lesions being malignant. This indicates that malignant lesions tend to have a larger invasion range and thus require more multidisciplinary collaboration to be successfully treated. The treatment of cranial-nasal-orbital communicating lesions requires multidisciplinary collaboration. The imaging department makes an initial assessment of the scope and nature of the lesion. A multidisciplinary team, including ophthalmology, otolaryngology, and neurosurgery, performs a combined surgical procedure, with the assistance of a nasal endoscope for resection[46]. Additionally, for cases suspected of malignancy, intraoperative frozen section pathology is recommended whenever possible, as it aids in rapid diagnosis, distinguishing the tumor nature during surgery, and determining the resection range[47]. Mendoza-Santiesteban *et al*[22] suggested that if the frozen biopsy confirms the tumor as malignant, the resection should be expanded to achieve as complete a removal as possible. Pathologists analyze the pathological results, and finally, a postoperative treatment plan is jointly formulated. This approach aims to facilitate the complete resection of the tumor, reduce the possibility of recurrence and potential

complications, and lower the perioperative mortality rate[7]. The management of cranial-nasal-orbital communicating lesions requires close cooperation among multidisciplinary teams to ensure that patients receive the best possible diagnosis, treatment, and management.

This study is a retrospective analysis from a single institution and may have limitations such as selection bias. Further prospective studies with larger sample sizes and multi-center involvement are needed to deeply analyze cranial-nasal-orbital communicating lesions.

In conclusion, malignant cranial-nasal-orbital communicating lesions exhibit distinct clinicopathological signatures characterized by rapid progression, aggressive anterior fossa and nasal region, and severe visual morbidity. This study emphasizes the importance of multidisciplinary surgical evaluation.

ACKNOWLEDGEMENTS

We would like to extend our sincere appreciation to the participants for their invaluable contributions to this research. We are grateful for the valuable contributions of our colleagues in the departments of Radiology, Neurosurgery, ENT and Pathology, who provided expertise and support throughout the study. We would like to thank *Editage* [http://www.editage.com] for editing and reviewing this manuscript for English language.

Authors' Contributions: Jiang FG and Wang XH designed the research. Xie M and Chen J collected and analyzed the data. Li PC drafted the manuscript. Xie M and Chen J drew the figures. You YY and Su ZX supervised the study and revised the manuscript. Zhu XY performed a statistical analysis. All authors have made significant contributions to the article and have approved the final submitted version.

Foundations: Supported by Natural Science Foundation of Hubei Province (No.2023BCB147; No.2023AFB1026).

Conflicts of Interest: Xie M, None; **Chen J,** None; **You YY,** None; **Su ZX,** None; **Zhu XY,** None; **Wang XH,** None; **Li PC,** None; **Jiang FG,** None.

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