Orbital Metastasis as a Presenting Feature of Papillary Thyroid Carcinoma: Case Report and Literature Review

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ABSTRACT

A 61-year-old woman presented with a 2-month history of non-painful left eye proptosis. Imaging studies showed a superotemporal mass in the left orbit with intracranial extension. Surgical excision of the orbitocranial mass was performed and histopathologic examination revealed metastatic papillary thyroid carcinoma. She subsequently underwent total thyroidectomy. Orbital metastasis from thyroid carcinoma is rare and can be the initial manifestation of occult disease in 63% of cases.

Keywords: orbital metastasis, thyroid cancer, thyroid carcinoma, papillary thyroid carcinoma

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Paper presentation – World Society of Ophthalmic Plastic Reconstructive and Aesthetic Surgery 2023, May 5-7, 2023, Dubai, United Arab Emirates.

eISSN 2094-9278 (Online)
Published: December 12, 2025
https://doi.org/10.47895/amp.vi0.11989
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INTRODUCTION

Orbital metastases occur infrequently and constitute 1–13% of all orbital neoplasms.[1-14] It is estimated to occur in 2–5% of patients with systemic malignancies.[1-14] Breast carcinoma is the most common malignancy to metastasize to the orbit.[1-14] Other common primary tumor sites include prostate, lung, and skin (melanoma).[5-9,12,13] Thyroid carcinoma rarely affects the orbit and accounts for 1–8.1% of orbital metastases.[8,10,11,13,15-46]

We report a case of metastatic thyroid carcinoma which initially presented as an orbital mass with intracranial extension in an adult female. This is the second documented case of metastatic thyroid carcinoma to the orbit in the Philippines. In addition, we present an updated literature review on the clinical presentation and treatment outcomes of patients with this disease.

CASE PRESENTATION

A 61-year-old Filipino female presented with proptosis of the left eye which was first noticed two months prior. She denied blurring of vision, diplopia, tearing, and pain. Past medical history was significant for hypertension and diabetes

mellitus type II. She was a non-smoker. Family history was negative for malignancies.

On evaluation, her corrected visual acuity was 20/20 in the right eye and 20/40 in the left eye. There was a 2 mm proptosis and conjunctival hyperemia in the left eye (Figures 1A and B). There was no lagophthalmos. Pupils were equal with no afferent pupillary defect. Extraocular motility was full in both eyes. Ishihara color vision and Amsler grid tests were normal in both eyes. An NO1NC1 cataract was present in the right eye and NO2NC2 cataract was noted in the left. The intraocular pressure in the right eye was 10 mmHg and 20 mmHg in the left eye. Fundus examination was unremarkable in both eyes.

The hemogram, thyroid function test (TSH, FT4, FT3), serum creatinine, eGFR, ALT, and HBA1c were within normal limits. Her blood uric acid was elevated. The chest X-ray was unremarkable.

Orbital contrast-enhanced computed tomography (CT) scan revealed a heterogeneously enhancing mass centered in the left spheno-orbital region measuring 3.9 cm × 4.0 cm × 3.1 cm (Figures 2A and B). Anteriorly, it extends intraorbitally causing inferomedial displacement and compression of the left optic nerve, superior rectus muscle, and lateral rectus muscle, as well as protrusion of the left globe. Posteriorly, it is intimately related to the adjacent left temporal lobe and M2 segment of the left middle cerebral artery, with no definite intervening fat plane in between. Associated bony lytic changes of the greater and lesser wings of the left sphenoid bone are observed. These findings are compatible with a primary or metastatic malignant process.

The patient was referred to Neurosurgery and repeat imaging was done. On cranial magnetic resonance imaging (MRI), the left spheno-orbital mass shows avid enhancement on post-contrast images. The mass measured 3.7 cm × 2.8 cm × 4.8 cm. Extension into the left intraorbital compartment and left temporal lobe as well as lytic destruction of the left sphenoid bone are again demonstrated (Figure 2C).

The patient underwent wide excision of the left orbitocranial mass via frontotemporal craniotomy with intraoperative frozen section examination. Microscopic examination of the tumor disclosed fibrohyalinized tissues containing metastatic neoplasm composed of atypical cells arranged in follicular and solid patterns (Figures 3A and B). These favored a diagnosis of papillary thyroid carcinoma, follicular subtype.

Palpation of the neck revealed a slightly enlarged right lobe of the thyroid gland. No cervical lymphadenopathy was noted. Thyroid ultrasound showed an enlarged right thyroid lobe and normal-sized left thyroid lobe with inhomogeneous echo pattern, complex thyroid nodule with calcifications in the right lobe, and solid thyroid nodules bilaterally (Figures 4A and B). The cervical and submandibular lymph nodes were unremarkable.

The patient subsequently underwent total thyroidectomy eight days after the orbitocranial surgery. The enlarged right thyroid measured 6.5 cm × 4.3 cm × 3.0 cm, and the left lobe measured 3.8 cm × 1.8 cm × 1.3 cm. Serial cut sections of the right thyroid lobe showed a 4.0 cm × 3.0 cm × 3.2 cm fairly circumscribed nodule with cream white to tan, firm to gritty surface, and ill-defined margins. Histopathologic examination disclosed papillary thyroid carcinoma, follicular subtype with solid features, dense fibrosis and dense calcifications in the right lobe (Figures 5A and B). There was also a colloid adenomatous goiter in the left lobe. The pathologic stage was T2N0M1, Stage IVB.[47]

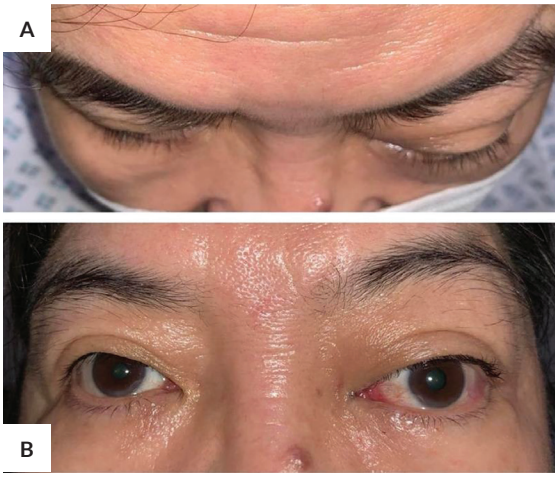

Figure 1. **(A)** Bird's eye view shows proptosis of the left eye. **(B)** External eye examination shows hyperemia of the bulbar conjunctiva of the left eye.

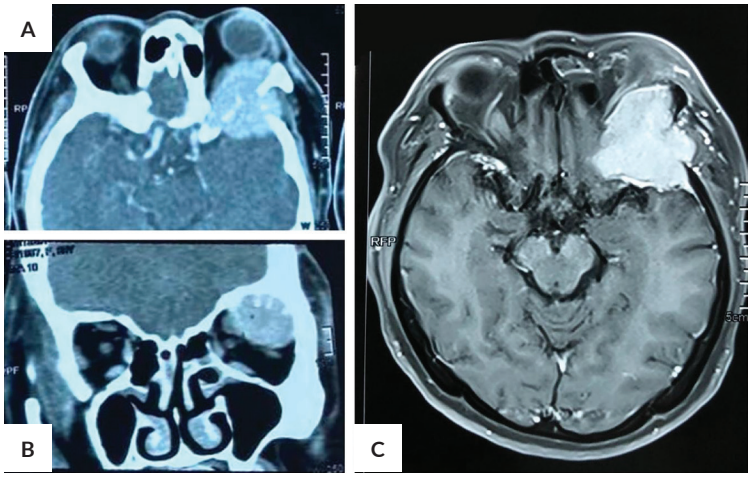

Figure 2. **(A)** Axial and **(B)** coronal CT scan views better demonstrate the mass effect on the left optic nerve, superior and lateral recti muscles, and orbit, as well as the bony lytic destruction of the sphenoid bone. **(C)** Axial MRI image shows the enhancing left spheno-orbital mass with intraorbital and intracranial extension.

At 28 days after the excision of the orbitocranial mass, the patient was stable with resolution of the left eye proptosis and conjunctival hyperemia. Bone scan, and chest and abdominal CT scan were planned to detect the presence of other sites of distant metastasis, however, the patient was lost to follow-up.

DISCUSSION

The orbit is rarely involved in metastatic thyroid carcinoma. In a study by Shields et al. comprising of 100 patients with orbital metastasis, none was found to have originated from the thyroid gland.[7] Several other studies also found no metastatic thyroid carcinoma in their cohort of patients with orbital neoplasms.[1,2,5,7,9] In a more recent paper by El-Hadad et al. consisting of 118 patients with orbital metastasis, thyroid carcinoma was the 4th most common primary tumor type accounting for 6% of the cases.[8] Thyroid carcinoma represented 1% (1 out of 93 patients), 2.17% (1 out of 46 patients), and 8% (3 out of 37 patients) of orbital metastases in Italian, Southern Chinese, and Egyptian patients, respectively.[10,11,14] In a systematic review by Palmisciano et al. comprising of 262 studies with 873 patients with biopsy-proven orbital metastases, thyroid carcinoma was the primary source in 1.5% of the cases.[3]

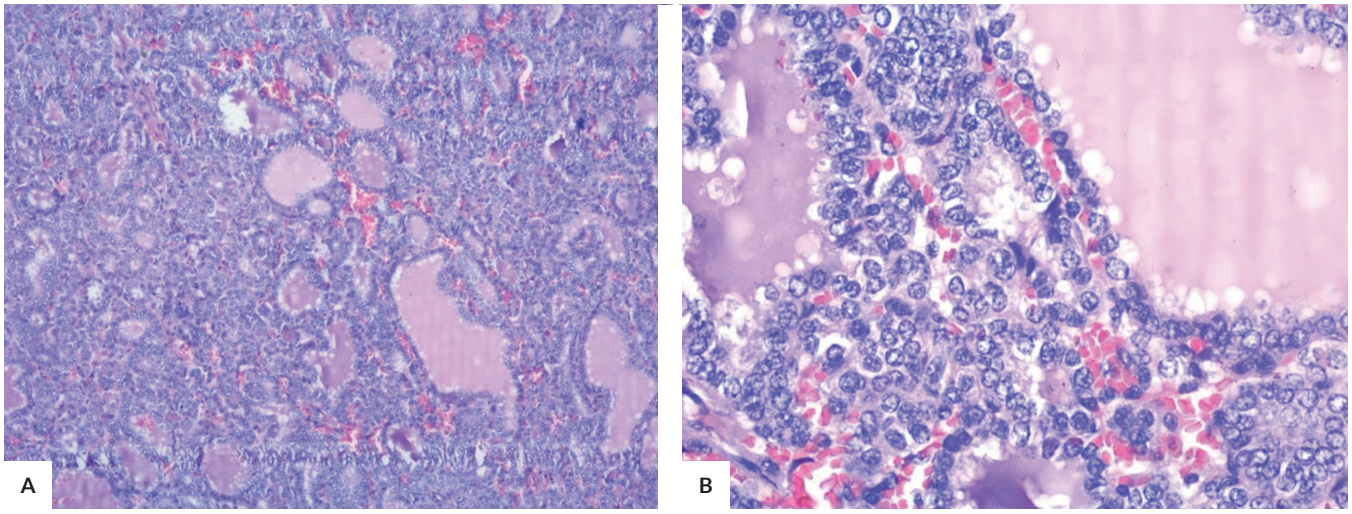

Figure 3. (A) Scanning photomicrograph of the orbital mass shows a metastatic carcinoma composed of atypical thyrocytes in follicular and solid patterns (hematoxylin-eosin, ×40). **(B)** Photomicrograph in high power magnification highlights the cytologic characteristics of the thyrocytes showing moderate nuclear enlargement and clearing, irregular nuclear contours, finely granular chromatin pattern, and variable amount of amphophilic cytoplasm (hematoxylin-eosin, ×400).

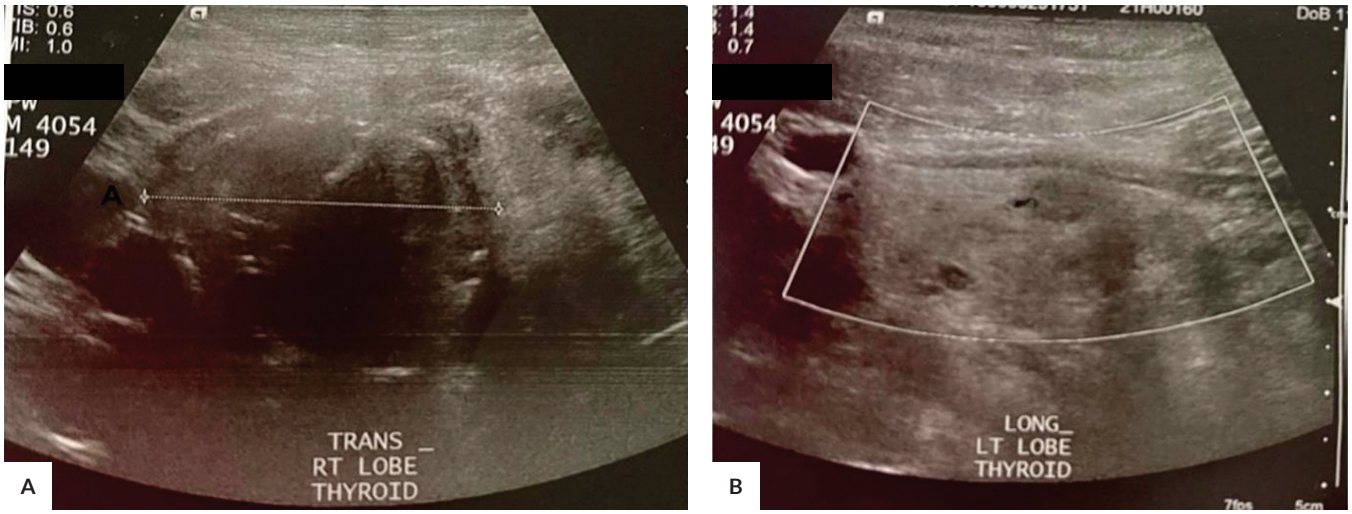

Figure 4. Sonogram of the **(A)** right and **(B)** left lobes of the thyroid gland shows inhomogeneous echo pattern with complex thyroid nodules.

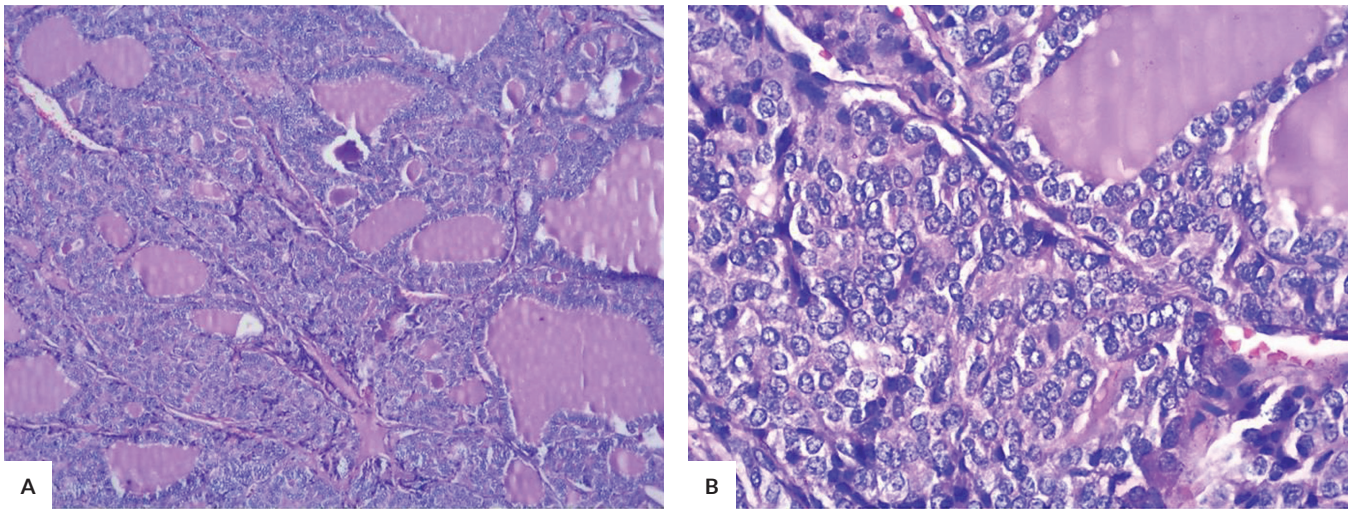

Figure 5. **(A)** Photomicrograph in low power magnification of the right thyroid lobe mass shows a malignant neoplasm composed of atypical thyrocytes predominantly arranged in solid sheets and follicular pattern (hematoxylin-eosin, ×100). **(B)** High power magnification shows the thyrocytes have large, round to ovoid, vesicular to optically clear nuclei, irregular nuclear contours, some with prominent nucleoli, and variable amount of eosinophilic cytoplasm (hematoxylin-eosin, ×400).

Pagsisihan et al. published the first case of thyroid metastasis to the orbit in the Philippines.[36] Their patient is a 49-year-old female who presented with a 2-year history of an enlarging right superior orbital mass, which was revealed to be a follicular variant of papillary thyroid microcarcinoma.[36] Similar to our case, their patient has no known primary malignancy and the orbital mass was the first sign of metastatic disease. Their patient had normal neck findings while our case had a slightly enlarged thyroid gland. Both cases presented with a superior orbital lesion with erosion of the orbital roof and intracranial extension. Their patient underwent thyroidectomy, radioactive iodine ablation (RAI), and post-RAI whole body scan which revealed additional metastatic sites in the right posterior parietal, left shoulder, and left hip areas.[36] Their patient was stable at six months after the initial RAI and was scheduled to undergo further RAI treatment.[36]

Unfortunately, our report is limited because we were unable to investigate the presence of distant metastasis and initiate RAI treatment in our patient as she was lost to follow-up despite our best efforts to contact her.

Our comprehensive literature review shows a total of 32 relevant papers describing 34 patients with orbital metastasis from thyroid carcinoma between 1985 and 2023.[15-46] The clinical profile of the previously reported cases, as well as the current patient, are summarized in the Appendix. Combining the current patient with the previously published cases, there are a total of 35 patients who presented with orbital mass from metastatic thyroid carcinoma; 26 were females (74%) and nine were males (26%).[15-46] The median age at diagnosis was 59 years (mean, 57 years; range, 16–75 years).[15-46]

The most common histologic type of thyroid carcinoma metastasizing to the orbit was papillary (16 patients, 10 of which had follicular variant), followed by follicular (10 patients), medullary (three patients), anaplastic/undifferentiated (two patients), poorly differentiated (two patients), and Hurthlë cell (one patient).[16-30,32-46] The histotype was unknown in one patient.[15]

Most patients with orbital metastatic lesions have a known primary tumor site at the time of diagnosis.[3,7,8] Thyroid carcinoma behaves differently; 22 out of the 35 patients (63%) presented with an orbital mass before a diagnosis of metastatic disease was established.[16,17,19,21-23,25-27,29-32,34-37,39,42,43] For the 10 patients (29%) with a history of thyroid carcinoma, orbital metastasis was detected at a median time of 23 months (mean, 47 months; range, 1–120 months) after the primary tumor diagnosis.[18,20,28,32,33,38,41,44-46] In three patients (9%), the interval from diagnosis of thyroid carcinoma to detection of orbital metastasis was not mentioned.[15,24,40] A study of orbital metastasis in Italian patients reported that the mean time from diagnosis of thyroid carcinoma to the appearance of orbital lesion was 41 months (range, 26 – 70 months).[10]

Among the 22 patients who initially presented with an orbital mass, seven patients had a neck mass discovered on physical examination, three patients had normal neck findings, three patients had a long-standing neck mass, three patients had undergone thyroid surgery for a benign condition, and one had a history of hypothyroidism.[16,17,19,22,26,27,29,30,34-36,39,42,43] Since a majority of these patients have findings suggestive of thyroid disease, a thorough history-taking and physical examination should be performed in a patient with suspected orbital metastasis. If possible, a careful review of histologic slides should be done for a seemingly benign thyroid lesion because it may harbor areas of carcinoma.[16]

Metastatic orbital tumors commonly present with relative afferent pupillary defect, diplopia, impaired eye movement, palpable mass, and orbital pain.[3] We found that proptosis (49%) is the most common presenting symptom of metastatic thyroid carcinoma, followed by blurred vision (43%), diplopia (26%), palpable mass (20%), periorbital swelling (14%), eye pain (11%), tearing (9%), headache (9%), limited eye movement (6%), temporal swelling (6%), ptosis (3%), orbital discomfort (3%), orbital pain (3%), periorbital discomfort (3%), eye redness (3%), ecchymosis (3%), periorbital erythema (3%), periorbital pain (3%), corneal opacity (3%), inferior globe displacement (3%), neuralgic pain (3%), and poorly fitting prosthesis (3%).[15-23,25-40,42-46] The duration of symptoms varied from 0.1 to 48 months, with a median of eight months (mean, 13 months).[16,17,19,21,26,27,29-37,43,44,46] The most common sign is proptosis (60%), followed by reduced visual acuity (34%), restricted ocular motility (29%), palpable mass (29%), inferior globe displacement (23%), periorbital edema (14%), conjunctival hyperemia (14%), pupillary abnormalities (11%), lagophthalmos (9%), resistance to retropulsion (9%), ptosis (6%), chemosis (3%), optic atrophy (6%), exposure keratopathy (6%), strabismus (3%), increased intraocular pressure (3%), choroidal and retinal folds (3%), serous detachment of the macula (3%), blurred disc margins (3%), periorbital erythema (3%), and V1 and V2 dysesthesia (3%).[15-23,26-31,33-37,39,42-46]

Most cases are unilateral (34 patients, 97%); 19 involved the right orbit (54%), while 15 involved the left side (43%).[15-32,34-46] One case had bilateral orbital involvement (3%).[33]

CT scan was the most common imaging modality performed (29 patients, 83%), either as a standalone procedure (24 patients, 69%)or in combination with MRI (5 patients, 14%).[15-19,21-37,41,43-45] MRI was the only imaging procedure done in six patients (17%).[20,38-40,42,46]

A systematic review on metastatic lesions from various primary sites found that these tumors have a predilection for the superolateral orbit.[3] In metastatic thyroid carcinoma, the superolateral orbit was also the most common location involved (29%), followed by the superior (26%), medial (17%), lateral (11%), inferior (6%), apex (6%), superomedial (3%), and inferomedial (3%).[15-46] In a large single center study on orbital metastasis, a majority of the lesions presented with sole involvement of soft tissue.[8] In contrast, 66% of metastatic orbital tumors from thyroid carcinoma involved both soft tissue and bony orbit, 29% involved only the soft tissue, and 6% involved only the bony orbit.[15-46] Extraocular muscle mass or enlargement was present in 26% of the cases.[18-20,28,31,32,35,38,45] Lacrimal gland involvement was present in 6% of cases.[17,27] While most metastatic lesions are confined to the orbit and do not cause osteolysis, 66% of patients with metastatic thyroid carcinoma presented with bony erosion and extension to contiguous structures, while 3% had an osteoblastic lesion in the orbit.[3,8,15-17,21-23,25-27,29,30,33,34,36,37,39,40,42,43,46]

In general, most orbital metastatic tumors show no evidence of additional sites of distant metastasis at the time of diagnosis.[8] On the other hand, many patients with orbital metastasis from thyroid carcinoma presented with disseminated disease, with 22 of the 35 patients (63%) having synchronous or metachronous metastasis in other distant sites.[15,17,19,21,22,24,25,27,28,30,31,33,34,36-38,41,43-46] In nine patients (26%) with thyroid carcinoma, the orbit was the only site of distant metastasis.[16,20,23,26,32,35,39,40,43] Data was incomplete in four patients (11%).[18,29,42] The most common locations of distant metastasis in thyroid carcinoma are the lungs and bones, which are also the top two most frequent sites of concurrent metastasis in patients with orbital lesions.[19,21,22,24,25,27,30,31,33,34,36,37,41,43,45,46] Among the 22 patients who had other sites of distant metastasis, the bone was the most frequently involved site (13 patients, 59%), followed by the lungs (seven patients, 32%), brain (five patients, 23%), liver (two patients, 9%), skin (two patients, 9%), sinuses (one patient, 5%), and choroid (one patient, 5%).[15,17,19,21,22,24,25,27,28,30,31,33,34,36-38,41,43-46]

Orbital metastasis from thyroid carcinoma was confirmed by open biopsy in 31 patients (89%); while in four patients (11%), the diagnosis was made solely by a history of thyroid carcinoma and imaging studies.[15-46] A surgical biopsy is necessary to confirm the diagnosis in patients with orbital metastasis from an occult primary tumor, multiple primary malignancies, and solitary orbital tumor with no evidence of other sites of metastasis.[8,13] In addition, open biopsy facilitates tissue analysis for novel treatment modalities (targeted therapy).[8,13]

Patients with orbital metastasis from thyroid carcinoma were followed for a median of eight months (mean, 11 months; range, 0.16–72 months).[17-19,21,22,25,29,30,32,34-39,41-45] On the last follow up, 17 patients (49%) were in remission, six (17%) had disease progression, three (9%) were alive (disease status unknown), and three (9%) died of metastatic disease complications.[17-19,21,22,25-32,34-46] The outcome was unknown in six patients (17%).[15,16,20,23,24,33] Survival analysis was done for the 23 patients (66%) with adequate data on follow up and treatment outcome.[17-19,21,22,25,29,30,32,34-39,41-45] The median survival of patients for all histologic types is 22 months [95% confidence interval (CI): 7.7–36.3 months] (Figure 6A). Because the only patient with Hurthlë cell type died, and on the contrary, no patient with papillary, medullary, undifferentiated, and poorly differentiated types died, calculation of median survival and comparison of the six histologic types of thyroid carcinoma was not performed. For the follicular type, the median survival is 22 months (95% CI: 6–38 months) (Figure 6B).[17,18,21,22,29,32,37,41]

In a study of 118 patients with orbital metastasis from various primary sites, the median overall survival time for all patients was 17 months after diagnosis.[8] Orbital metastasis from thyroid carcinoma (seven patients) had the worst overall survival (8.18 months) among the different primary cancer types.[8] According to the American Cancer Society, the 5-year

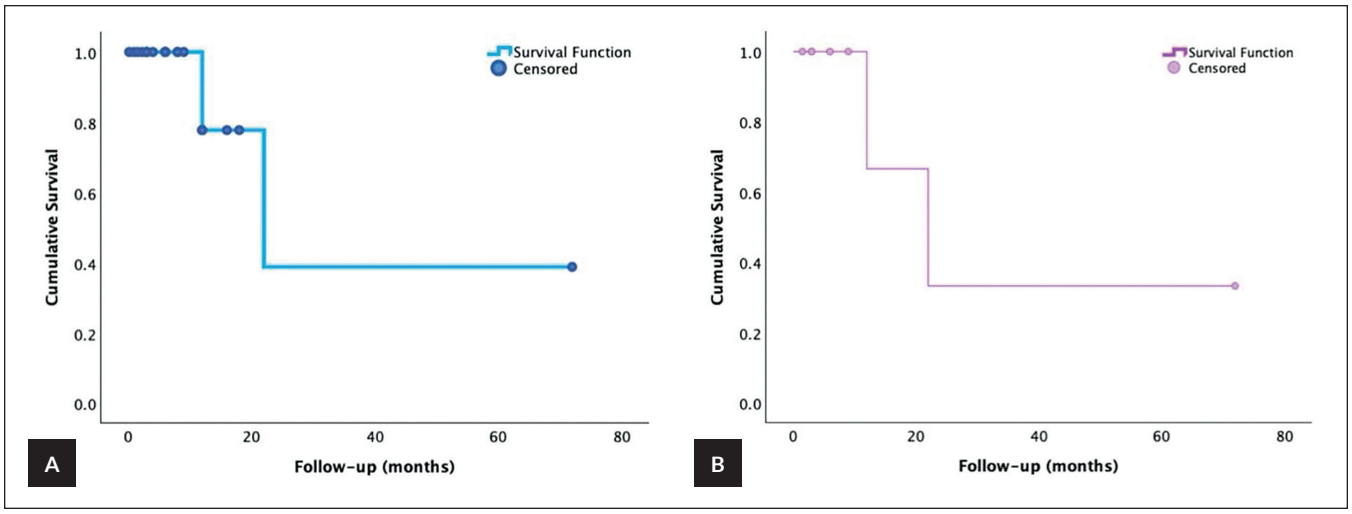

Figure 6. Survival analysis using Kaplan-Meier curve of orbital metastasis from **(A)** all histologic types of thyroid carcinoma and **(B)** follicular thyroid carcinoma.

survival rates for the different histologic types of the thyroid carcinoma with widespread disease are as follows: 74% for papillary, 67% for follicular, 43% for medullary, and 4% for anaplastic.[48]

The management of orbital metastasis from thyroid carcinoma requires a multidisciplinary approach. Thyroid carcinoma is typically managed by total thyroidectomy followed by RAI with ^{131}I and suppressive treatment with L-thyroxine.[25,27,31] Total thyroidectomy was performed in 25 patients (71%), right thyroid lobectomy and isthmusectomy in one patient (3%), and near-total thyroidectomy in one patient (3%).[15-17,19-32,34-36,38,40,41,44-46] RAI was performed in 19 patients (54%).[16,19,21-23,25,26,29-33,36,40,41,43,46] Radiotherapy is used for tumors unresponsive to RAI and as a palliative treatment for inoperable or residual disease.[8,31,37] This can also be used in solitary orbital metastatic lesions to facilitate chemoreduction while protecting vital structures such as the globe, extra-ocular muscles, and optic nerve.[3,36] Orbital irradiation was performed in 10 out of the 35 patients (29%); five underwent external beam radiotherapy, one underwent Gamma knife radiosurgery, while the exact method of radiotherapy was not mentioned in four patients.[19,26,27,29,30,34,35,38,39,45] Chemotherapy is seldom used in advanced thyroid carcinoma, except in anaplastic thyroid carcinoma where it is used together with radiotherapy as a palliative treatment.[48] Palliative chemotherapy was initiated in two patients (6%) with papillary thyroid carcinoma and in one patient (3%) with poorly differentiated carcinoma.[27,43,46] Targeted therapy is used in advanced RAI-resistant differentiated thyroid carcinoma and medullary thyroid carcinoma in the setting of rapidly enlarging tumors not amenable or unresponsive to a different localized treatment, symptomatic disease, or tumors in a threatening location.[49] The use of lenvatinib and cabozantinib has been shown to stabilize disease in a patient with RAI-resistant papillary thyroid carcinoma with orbital, lung, and skeletal metastases.[45] Targeted therapy can also be employed in anaplastic thyroid carcinoma as a neoadjuvant treatment for inoperable stage IVB tumors or as long-term management for stage IVC disease.[49]

Surgical resection of distant metastasis facilitates disease control, reduces the symptoms associated with compressive effects of the tumor, and enhances RAI uptake in other sites of metastasis.[31] In addition, it was found to provide symptom and survival benefit compared to biopsy alone in patients with metastatic orbital lesions.[3] Partial or complete tumor resection was performed in 18 of the 35 patients (51%) with orbital metastasis from thyroid carcinoma and provided improvement in orbital signs and symptoms in 10 patients (29%).[16-18,20,22,26,28,31,33,35,37,41-45] Two of the 18 patients underwent orbital exenteration.[31,44] Palmisciano et al. found that orbital exenteration had no survival benefit compared to patients undergoing orbital-preserving complete metastatic tumor resection.[3] Their findings support the idea that survival is more dependent on systemic disease control than on local treatment of orbital metastasis.[3] However, orbital exenteration may be considered as a treatment option to provide relief of severe intractable pain and/or diplopia in patients with already poor vision, as was found in two patients with orbital metastasis from thyroid carcinoma.[31,44]

CONCLUSION

In summary, orbital metastasis from thyroid carcinoma is rare, but can present as the initial manifestation of systemic disease in more than half of cases. Orbital metastasis from thyroid malignancy is frequently a sign of widespread disease with most patients presenting with concomitant distant metastasis at the time of diagnosis. We found that the median survival time in this disease is higher than previously reported.

Ethics Statement and Informed Consent

This report was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki of 1964, as revised in 2024. Written informed consent was obtained from the patient for the publication of the case report and accompanying images.

Acknowledgments

The authors would like to thank Nilo Vincent DG. Florcruz II, MD, Alexander Nino L. Gungab, MD, and Xandro Alexi A. Nieto, LPT, MoS, MEd for their technical assistance in the preparation of this manuscript.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

None.

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Orbital Metastasis from Papillary Thyroid Carcinoma

APPENDIX

Table 1. Clinical Features of Patients with Orbital Metastasis from Thyroid Carcinoma

Author(s) (year)	Histologic Type	Age (years)	Sex	Laterality	Symptoms*	Duration of Symptoms	Examination Findings*	Interval from Diagnosis of Thyroid Carcinoma to Detection of Orbital Metastasis	Orbital Imaging Findings	Other Sites of Distant Metastasis	Management of Orbital Metastasis	Follow-up Duration	Outcome
Betharia et al. (1985)[15]	NA	16	F	Right	Diplopia, proptosis, and blurred vision	NA	Reduced visual acuity (LP with accurate projection), axial proptosis, nonreducible eye, restricted ocular movements; hard, nontender mass along the upper and lower temporal parts of the orbit; lagophthalmos; mid-dilated pupil and sluggishly reactive to light; and optic atrophy	NA	X-ray: enlargement of the right orbit with destruction of the sphenoidal wings and the lateral orbital margins; extensive new bone formation in the right orbit CT scan: mass in the right orbit with intracranial extension	Extradural mass in the right middle cranial fossa	Palliative	NA	NA
Hornblass et al. (1987)[16]	Papillary	35	F	Right	Swelling along the temple, tearing, and proptosis	3 years	Proptosis, fullness in the superior orbit, inferior globe displacement, and hard mass along the orbital rim with marked excavation of the lateral orbital wall	Initial presentation	CT: large destructive mass involving the superolateral margin of the right orbit and extending to the outer cranial surface of the skull in the right temporal fossa	None	Tumor excision and RAI	NA	NA
Bernstein-Lipschitz et al. (1990)[17]	Follicular	56	F	Right	Diplopia, ptosis, and discomfort in the orbit	1 month	Proptosis, resistance to retropulsion, downward and nasal displacement of the eye, firm mass in the region of the lacrimal gland, increased IOP, choroidal and retinal folds in the macular region; conjunctival redness, chemosis, decreased BCVA from 6/9 to 6/24, and serous detachment of the macula due to choroidal leakage over the next few weeks	Initial presentation	X-ray: small, decalcified mass on the vortex with destruction of the right orbital roof CT: lacrimal fossa mass with bone destruction in the orbital roof and intracranial extradural extension	Ethmoid and maxillary sinuses	Tumor resection	1.5 months	Recurrence of orbital mass which was subsequently debulked
Friedman et al. (1990)[18]	Follicular	72	M	Right	Pain, redness, and proptosis of the eye; visual loss after 3 months	Several months	Proptosis and resistance to retropulsion of the eye, and dilated, tortuous conjunctival vessels over the insertion of the medial rectus muscle; NLP and APD after 3 months	6 months	CT: large, fusiform soft tissue mass involving the right medial rectus muscle	NA	Tumor excision	1 year	Died of complications from metastatic disease
Vanderpump and Tunbridge (1992)[19]	Hurthlë cell	61	M	Right	Double vision and painful swelling in the eye	3 months	Bilateral periorbital edema, reduced visual acuity, and blurring of the optic disc	Initial presentation	CT: large well-defined mass involving the right medial rectus muscle	Left tibia and right humerus	Orbital decompression, RAI, and EBRT	1 year	Died
Margo and Levy (1993)[20]	Medullary	67	M	Right	Proptosis and double vision in upgaze	Several weeks	Segmental conjunctival vascular injection localized to the inferior bulbar surface, proptosis, and limitation of the right inferior rectus muscle (positive forced duction)	9 years	MRI: irregular mass contiguous with the right inferior rectus muscle	None	Tumor resection	NA	NA
Daumerie et al. (2000)[21]	Follicular	59	F	Left	Upper eyelid swelling, proptosis, and blurred vision	6 months	Maximal visual acuity of 20/40, limitation of the abduction of the left eye with limitation in left upper gaze, proptosis, and ptosis and edema of the upper eyelid	Initial presentation	CT: 4-cm solid mass in the superotemporal aspect of the left orbit, with destruction of the greater wing of the sphenoid bone and intracranial extension	Mediastinum and iliac bones	RAI	3 months	Improvement in visual acuity and regression of proptosis at 2 months after RAI; regression of orbital mass at 3 months after RAI
Basu et al. (2001)[22]	Follicular	54	F	Left	Proptosis, epiphora, and blurred vision	NA	Proptosis	Initial presentation	CT: well-defined, heterogeneously enhancing lobulated soft tissue mass measuring 4.7 × 2.7 × 2.8 cm with destruction of the lateral wall of the left orbit and extension to the middle cranial fossa	Right shoulder joint	Tumor resection and RAI	6 months	Resolution of proptosis and epiphora
Boughattas et al. (2004)[23]	Follicular	51	F	Right	Right temporal mass, proptosis, ocular pain, visual disturbance, and ecchymosis	NA	Proptosis	Initial presentation	CT: 6-cm hyperdense solid mass with destruction of the right temporal bone, and superior and lateral orbital walls, and endocranial extension	None	RAI	NA	NA
Boughattas et al. (2005)[24]	Papillary	25	F	Right	NA	NA	NA	NA	CT and MRI: well-circumscribed mass on the right supraorbital ridge	Lung	NA	NA	NA
Mansberg et al. (2006)[25]	Papillary (follicular variant)	70	F	Left	Visual disturbance	NA	NA	Initial presentation	CT: destructive mass on the left sphenoid triangle with intracranial extension	Superficial right posterior pelvic region	RAI	3 months	Progression of orbital disease
Shyla et al. (2007)[26]	Papillary (follicular variant)	70	F	Left	Loss of vision	4 months	Absent visual acuity, restricted medial eye movement on left, and absent direct light reflex on left eye and indirect light reflex on right side	Initial presentation	CT: extensive soft tissue mass in the medial aspect of the left orbit with extension to the ethmoids, sphenoid sinus, and nasal cavity	None	Tumor excision, RT, and RAI	NA	No remnant thyroid tissue on follow up CT scan and Radio Iodine scan

Orbital Metastasis from Papillary Thyroid Carcinoma

Table 1. Clinical Features of Patients with Orbital Metastasis from Thyroid Carcinoma *(continued)*

Author(s) (year)	Histologic Type	Age (years)	Sex	Laterality	Symptoms*	Duration of Symptoms	Examination Findings*	Interval from Diagnosis of Thyroid Carcinoma to Detection of Orbital Metastasis	Orbital Imaging Findings	Other Sites of Distant Metastasis	Management of Orbital Metastasis	Follow-up Duration	Outcome
Rocha Filho et al. (2008)[27]	Papillary (follicular variant)	66	F	Right	Proptosis	1 year	Proptosis, inferior dislocation of the right eye	Initial presentation	CT: expansive solid mass in the superior aspect of the right orbit in the lacrimal gland fossa with intracranial extension	Cerebral, coxofemural and dorsovertebral regions; thoracic vertebrae (T3 and T8 to T10)	RT and chemotherapy	NA	Palliative care
Seiff and Seiff (2008)[28]	Medullary	46	F	Left	Diplopia, proptosis	NA	Restricted extraocular movements in all fields of gaze, most notably in upgaze; proptosis; and exposure keratopathy	3 years	CT: enlargement of the left inferior rectus muscle	Abdominal subcutaneous area	Excisional biopsy	NA	Improvement in proptosis but vertical ductions still compromised
Anoop et al. (2010)[29]	Follicular	63	F	Right	Swelling over the right temporal region and proptosis	8 months	Proptosis and a 5 × 5 cm subcutaneous swelling in the temporal region	Initial presentation	CT: isodense, enhancing mass in the right temporal region with erosion of the temporal bone and greater and lesser wings of sphenoid and intracranial extension	NA	RAI and EBRT	3 months	Reduction of proptosis and swelling on the right temporal region
Krishnamurthy et al. (2010)[30]	Papillary (follicular variant)	55	M	Left	Upper eyelid mass, pain, and blurring of vision	1 year	Upper eyelid mass	Initial presentation	CT: large heterogeneous mass with destruction of the left orbital roof and intracranial extension	L3 vertebrae and left ilium	Palliative EBRT and RAI	1 year	Partial response of orbital mass
Repanos et al. (2011)[31]	Papillary	75	M	Right	Diplopia, proptosis and reduced visual acuity	9 months	Proptosis	Initial presentation	CT: well-defined 29 × 20 × 25 mm mass on the mid portion of the right medial rectus muscle	Lungs	Orbital exenteration and RAI	NA	No evidence of extracervical metastasis on post ^{131}I whole body scan
Okere and Tushar (2012)[32]	Follicular	63	M	Right	Double vision	1 year	NA	1 year and 11 months	CT: brightly enhancing fusiform mass in the belly of the right medial rectus muscle measuring 2.9 × 1.4 cm	None	RAI	6 years	Reduction in lesion thickness on CT scan and resolution of diplopia
Bidari-Zerehpoosh et al. (2014)[33]	Follicular	70	F	Bilateral	Proptosis and periorbital swelling	3 years	Proptosis and inferolateral displacement of both eyes	10 years	CT: bilateral destructive orbital roof masses with erosion of the roof, floor, and lateral walls, and extension to the inferior orbital fissure, infratemporal fossa, and pterygomaxillary fissure	Facial skin and lungs	Tumor resection and RAI	NA	NA
Yethadka et al. (2014)[34]	Papillary	70	F	Right	Proptosis and blurring of vision	1.5 years	Proptosis and NLP in the eye	Initial presentation	CT: mass in the superior part of the right orbit with erosion of the roof and extension to the parasellar region and anterior cranial fossa	Left femur	EBRT	1 year	Developed pain and limping of the left lower limb from metastasis to the left femur
Gupta et al. (2015)[35]	Anaplastic/ undifferentiated	52	F	Right	Orbital pain, nausea, binocular diplopia, blurring of vision, and dizziness	5 months	VA of 20/50, proptosis, esotropia, and unable to abduct right eye	Initial presentation	MRI and CT: 3.1× 1.7 × 1.9 cm enhancing mass within the right lateral rectus muscle	None	Surgical resection and Gamma knife radiosurgery	18 months	Tumor free, developed a surgical traumatic optic neuropathy
Pagsisihan et al. (2015)[36]	Papillary (follicular variant)	49	F	Right	Supraorbital mass	2 years	Supraorbital mass, inferolateral globe displacement, ptosis, minimal limitation on upward gaze	Initial presentation	CT: expansile lytic lesion in the orbital plate of the right frontal bone	Right posterior parietal, left shoulder, and left hip areas	RAI	6 months	Doing well
Shen et al. (2015)[37]	Follicular	67	M	Right	Blurred vision in the right eye and mass in the frontal region	7 months	Palpable tumor in the frontal region and VA of 0.8	Initial presentation	CT: isodense mass with osteolytic features in the right orbit and frontal sinus MRI: 2.8 × 3.4 × 3.5 cm homogeneously enhancing, well-defined mass	Thorax and mediastinum	Tumor resection	22 months	Died
Ruiz et al. (2016)[38]	Medullary	53	F	Left	Headache	NA	NA	9 years	MRI: 13.7 mm mass in the left medial rectus muscle	Liver	EBRT	4 months	Global morphological stability on MRI and a reduction in calcitonin levels
Feffer et al. (2017)[39]	Poorly differentiated insular	55	F	Left	Headache, blurred vision, and proptosis	Several weeks	Proptosis	Initial presentation	MRI: exophytic mass on the wing of the left sphenoid bone measuring 2.4 × 4.6 cm with intracranial extension	None	Excisional biopsy and RT	9 weeks	Developed pulmonary emboli, increased tumor size on MRI, referred to home hospice services due to poor prognosis
Palaniswamy and Subramanyam (2018)[40]	Papillary	58	M	Right	Swelling close to lateral aspect of the right eye	NA	NA	NA	MRI: enhancing soft tissue mass measuring 3.2 × 2 cm along the superolateral aspect of right orbit with erosion of the posterolateral wall of orbit and extension to the middle cranial fossa	None	RAI	NA	Complete resolution of right orbital soft tissue mass with no new functioning metastases elsewhere on whole body ^{131}I scan

Orbital Metastasis from Papillary Thyroid Carcinoma

Table 1. Clinical Features of Patients with Orbital Metastasis from Thyroid Carcinoma *(continued)*

Author(s) (year)	Histologic Type	Age (years)	Sex	Laterality	Symptoms*	Duration of Symptoms	Examination Findings*	Interval from Diagnosis of Thyroid Carcinoma to Detection of Orbital Metastasis	Orbital Imaging Findings	Other Sites of Distant Metastasis	Management of Orbital Metastasis	Follow-up Duration	Outcome
Jeon GH et al. (2019)[41]	Follicular	74	F	Left	Asymptomatic	NA	NA	1 month	CT: irregular shaped bone mass in left orbital roof MRI: 2.2 cm mass on the left superior orbital wall	Right frontal lobe, right occipital bone, right humerus, thoracic spine, sternum, left 6th rib, right 8th rib, sacrum, and right femur	Tumor removal and RAI	9 months	Alive and in good overall condition
Sánchez-Sánchez et al. (2021)[42]	Papillary	56	F	Left	Proptosis, headache, neuralgic pain, epiphora, and limited eye movement	NA	Optic atrophy, proptosis, conjunctival hyperemia, lagophthalmos, limitation in abduction, and dysesthesia in V1 and V2	Initial presentation	MRI: single solid intraconal mass in the lateral border of the left orbit and apex, with invasion of the intracranial and intracanalicular segments of the optic nerve and extension to the ipsilateral cavernous sinus	NA	Tumor resection	5 days	Decrease in proptosis and lagophthalmos, and resolution of conjunctival hyperemia
Mahyuddin et al. (2022)[43]	Papillary (follicular variant)	65	F	Left	Painful mass on left upper eyelid	3 months	VA of 20/40, proptosis, downward displacement of the eye, limitation on upward gaze, palpable mass along the superior orbital rim	Initial presentation	CT: extraconal solid contrast-enhancing mass in the superior left orbit with intracranial extension	Lung, liver, vertebrae, humerus, and iliac	RAI and total tumor removal with pre-operative digital subtraction angiography embolization	8 months	Doing well
	Papillary (follicular variant)	28	F	Right	Right upper eyelid mass	4 years	VA of 20/40, right upper eyelid mass, proptosis, and inferior displacement of the eye	Initial presentation	CT: Aggressive solid mass, measuring 2.3 × 3.5 × 4.1 cm on the right frontal bone with intracranial extension	None	RAI and tumor removal	8 months	Doing well
	Papillary (follicular variant)	62	F	Left	Left upper eyelid mass, inferior globe displacement, blurring of vision, and white lesion on cornea	18 months	VA of NLP, mass on the superior orbital rim, restriction of eye movement in all gazes, proptosis, inferolateral globe displacement, lagophthalmos, and corneal opacity and neovascularization from exposure	Initial presentation	CT: irregular lobulated extraconal solid mass measuring 5.5 × 5.3 × 5.6 cm with well-defined margins with destruction of the medial-superior wall of the left orbit and intracranial extension	Lung	RAI and chemotherapy	6 months	Suffering from cancer pain
Tran et al. (2022)[44]	Anaplastic	52	F	Left	Periorbital edema, erythema, discomfort, and poorly fitting ocular prosthesis	3 months	Periorbital edema and erythema	19 months	CT: heterogeneous inferomedial mass in the left orbit	Choroid and brain	Exenteration	12 months	No evidence of orbital recurrence (on remission)
Sapuppo et al. (2022)[45]	Papillary (follicular variant)	36	M	Right	Diplopia, proptosis, and oculomotor nerve palsy	NA	Right eyelid edema and limited eye elevation	18 months	CT: 18 mm mass on the right lateral rectus muscle	Right supraclavicular paratracheal region, lungs, sternum, sacrum, right scapula, left upper acetabular roof, femoral neck and ipsilateral pubic branch, and spine	Excisional biopsy, RT, and targeted therapy	14 months	Decrease in size of orbital metastasis, improvement in ocular symptoms, and mild eyelid ptosis; disease stabilization and biochemical response
Altiner et al. (2023)[46]	Poorly differentiated	70	F	Left	Decreased vision	3 days	Relative afferent pupillary defect	5 months	MRI: well-circumscribed mass measuring 20 × 18 × 20 mm in the left orbital apex with extension to the sphenoid sinus	9th rib and lung	RAI and chemotherapy	NA	Alive
Present study (2024)	Papillary (follicular variant)	61	F	Left	Proptosis	2 months	Proptosis and conjunctival hyperemia	Initial presentation	CT: enhancing, left extraconal spheno-orbital soft tissue mass measuring 3.9 × 4.0 × 3.1 cm with associated lytic destruction of the greater wing of the sphenoid bone MRI: enhancing expansile solid bone lesion measuring 3.7 × 2.8 × 4.8 cm involving the greater wing and the lesser wing of left sphenoid bone with intracranial extension	NA	Tumor excision	28 days	Resolution of proptosis and conjunctival hyperemia

NA, data not available; M, male; F, female; RAI, radioactive iodine (^{131}I); RT, radiotherapy; APD, afferent pupillary defect; VA, visual acuity; BCVA, best corrected visual acuity; LP, light perception; NLP, no light perception; IOP, intraocular pressure; EBRT, external beam radiation therapy; CT, computed tomography; MRI, magnetic resonance imaging

**Symptoms and signs on the affected side unless stated otherwise*