A rare case of anterior skull base metastasis secondary to follicular thyroid carcinoma: a systematic review and illustrative case

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Abstract

Introduction Skull base metastasis from follicular thyroid carcinoma (FTC) is uncommon, with an incidence of 2.5%. Presented here is a case of a 63-year-old female presenting with a 2-year history of progressive left eye proptosis, with a previous history of thyroid surgery for non-toxic goiter. Imaging findings were uncharacteristic of any common skull base tumor. Biopsy revealed follicular thyroid carcinoma. The authors used this case as basis and performed an analysis on available literature for FTC skull base metastasis to help guide management of future cases.

Methods Using PRISMA guidelines, a systematic search across PubMed, Google Scholar, and Cochrane Library using MeSH keywords "Skull base," "Metastasis," and "Follicular Thyroid Carcinoma," identified 18 records. After screening, 15 articles assessed for eligibility, with 8 studies meeting inclusion criteria for qualitative analysis.

Results Studies showcased a consistent age range (43 to 69 years) among patients diagnosed with FTC. Presentation varied depending on tumor location, with symptoms such as dysphagia, proptosis, epistaxis, facial dysesthesia, and visual impairment. Tumor size ranged from 3cm x 3cm x 2cm to 6.8cm x 3.9cm x 5.3cm, influencing management strategies ranging from simple biopsy to sub-temporal complete excision. Adjuvant therapies included combinations of intensity-modulated radiation therapy (IMRT) with immunotherapy, multiple courses of I-131 therapy, oral radioiodine ablation, and radiotherapy, with outcomes showing improvement in most cases. Follow-up duration varied from 12 to 60 months.

Conclusion FTC skull base metastasis remains to be an uncommon entity in neurosurgery. Its rarity creates a lack of established guidelines and treatment algorithms. A high index of suspicion as well as good history and physical examination skills are necessary to achieve an adequate diagnosis. Multi-disciplinary teams form the cornerstone of a patient-tailored approach to its management.

Key words: skull base tumor, follicular thyroid cancer, metastasis, proptosis

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Skull base metastases are rare and occur in about 4% from malignancies of breast, lungs, and prostate.[1,2] In a study of 473 cases of thyroid carcinoma, it was discovered that a mere 2.5% of these individuals exhibited metastasis to skull base, which is typically uncommon, relative to the tumor's slow growth.[3] However, this type of carcinoma still

carries a mortality rate ranging from 20% to 40%, mainly due to challenges in controlling it locally and the occurrence of distant metastasis. Tumor cells are pustulated to metastasize to the skull base via hematogenous dissemination from the primary tumor, similar to dural or calvarial metastasis.[1,4] However, some authors advocate perineural spread from the head and neck region to the skull base.[4]

Clinically, these tumors present most commonly with craniopathies and localized pain.[1,2,5,6] Skull base metastasis syndromes are classified based on their presentation and location of involvement (Table 1) and are largely based on location and their proximity to critical structures in the brain specifically cranial nerves, which mark their predominant neurologic finding.[6]

Prognosis of skull base metastasis largely relies on the nature and extent of dissemination of the primary tumor, site of metastasis, and accessibility to surgery.[1,4] This is congruent to what is currently known about metastatic disease in general. Skull base metastasis is usually a late complication of cancer; once seen, it usually portends late-stage disease.[4] In most cases, death is usually due to the progression of systemic disease.[1]

This paper aimed to review available literature and reports of cases of FTC metastasis to the skull base as to their identification, epidemiology, treatment, and follow-up to aid clinicians in the management of future cases.

The Case

Present here is a case of 63-year-old female who was referred for progressive painless proptosis of left eye (Figure 1), which was associated with generalized headache of 2 years duration. There was no history of focal deficit, decreasing sensorium, cognitive or behavioral changes, or seizure. Cranial MRI with gadolinium contrast (Figure 2) revealed a homogenous, avidly enhancing left spheno-orbital tumor measuring around 5.3cm x 5.2cm x 6.3cm with marked proptosis of the left globe and partial encasement of the left optic nerve. She was diagnosed with a meningioma and referred to the institution for neurosurgical consult. Her past medical history

Table 1. Greenberg et al.'s classification of skull base metastasis syndromes.

Site	Symptoms	Signs
Orbit (7%)	Supraorbital headache Diplopia	Proptosis Ophthalmoplegia ± Facial numbness (V1) ± Decreased vision ± Periorbital swelling
Parasellar (16%)	Frontal headache Diplopia	Ophthalmoplegia Facial numbness (V1) Periorbital swelling
Gasserian ganglion (35%)	Facial numbness Parasthesias Atypical facial pain	Facial numbness (V2, V3) Abducens palsy (anterior ridge) Facial palsy (posterior ridge)
Jugular Foramen (21%)	Occipital pain Hoarseness Dysphagia	Cranial palsies IX, X, XI
Occipital Condyle (21%)	Occipital pain Dysarthria	Cranial nerve XII palsy

revealed a previous history of thyroid surgery for a non-toxic multi-nodular goiter; however, no official histopathologic report was presented by the patient. On physical examination, gross tumor was visible and palpable over the left fronto-temporal area, the rest of the physical examination was unremarkable. Her neurologic examination revealed a patient with alert intact mental status examination, with no light perception on the left eye, no appreciable motor function on the left eye and marked lagophthalmos. The patient displayed no other sensorimotor deficit. A repeat cranial CT scan with contrast (Figure 3) was taken, showing increase in tumor dimensions, as well as lysis of the surrounding bony structures, including the sphenoid wing, temporal bone, orbital roof and floor, as well as the ethmoids medially.

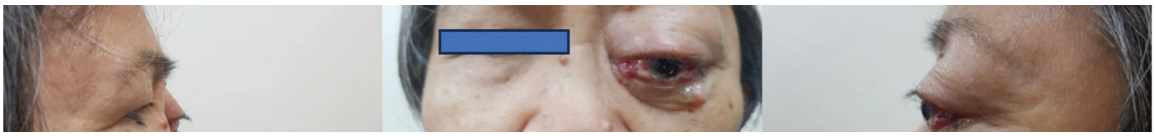

Figure 1. Gross photo of patient with marked proptosis of left eye.

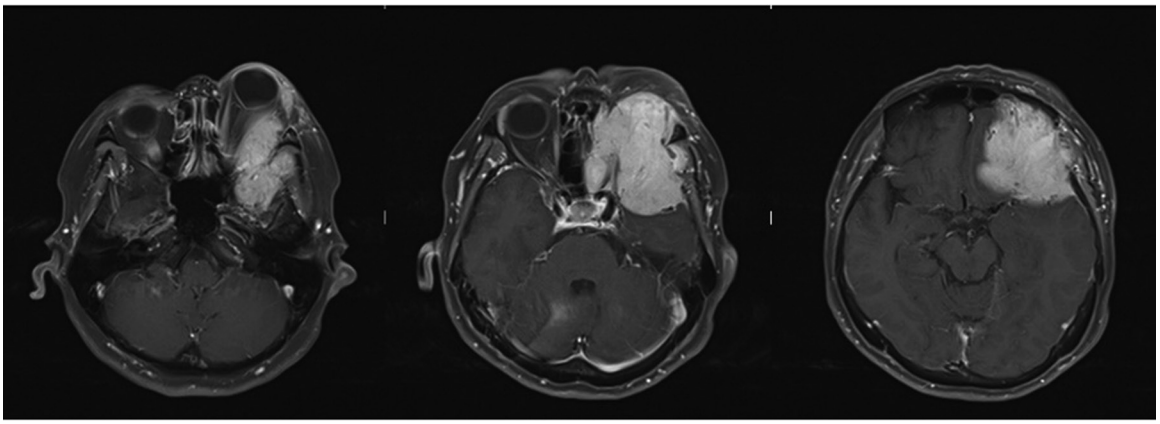

Figure 2. Cranial MRI with Contrast showing the left spheno-orbital tumor.

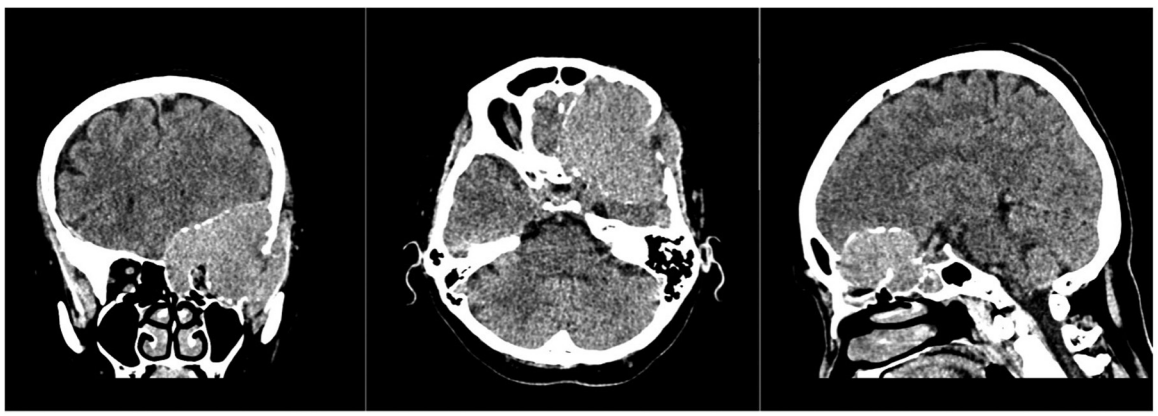

Figure 3. Lytic bony erosions seen in the cranial CT scan.

Given the marked progression of tumor size in a span of a few weeks, a malignant, aggressive tumor was suspected as opposed to the initial impression of a meningioma based on the MRI. Systemic metastatic work-up was done revealing unremarkable findings. She was then scheduled for core needle biopsy of the fronto-temporal tumor under local anesthesia. Microscopic specimen showed cuboidal cells in follicular arrangement invading surrounding soft tissues and eroded eosinophilic bone fragments with osteoclast-like giant cells, with hyperchromatic and round nuclei, which eventually turned out to be a Metastatic Follicular Thyroid Carcinoma (Figure 4). As of this writing, the patient is undergoing completion of metastatic work-up, as well as chemo- and radiotherapy to address the metastatic tumor.

Methods

After obtaining consent from the patient and securing a certificate of exemption from the Ethics Review Committee, the authors reported a case of a 63-year-old female who presented with proptosis and headache, diagnosed for left anterior skull base metastasis secondary to follicular thyroid carcinoma and did a systematic review which adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2015 (PRISMA). MeSH keywords "Skull base", "Metastasis", "Follicular Thyroid Carcinoma" were used for the systematic search across multiple databases: PubMed, Google Scholar and Cochrane Library.

The following inclusion criteria were used: (1) Case of skull base metastasis secondary to follicular thyroid carcinoma, (2) Case Reports, Case Series and Cohort Studies. Metastasis from other histopathology, editorial and non-English articles were excluded. Data collected included demographics, pathological characteristics, surgical approaches and clinical outcomes and follow-up.

A total of 18 records were identified through a database search. Of these, 17 were screened and 16 were retrieved thereafter, but only 15 articles were assessed for eligibility. Seven articles were excluded because they did not meet the inclusion criteria. Eight studies were included in the final qualitative analysis.

Results

Demographics

All the studies included were case reports and case series with the mean age of patients ranging from 43 to 69 years, showing a minimal variability in age distribution (Table 2). These studies focused on patients diagnosed with follicular thyroid carcinoma. Surgical interventions for the primary malignancy varied among the studies, including total thyroidectomy, subtotal thyroidectomy, and in some cases, no surgical intervention was mentioned. This indicates a range in the extent of surgical management used for follicular thyroid carcinoma patients with metastasis.

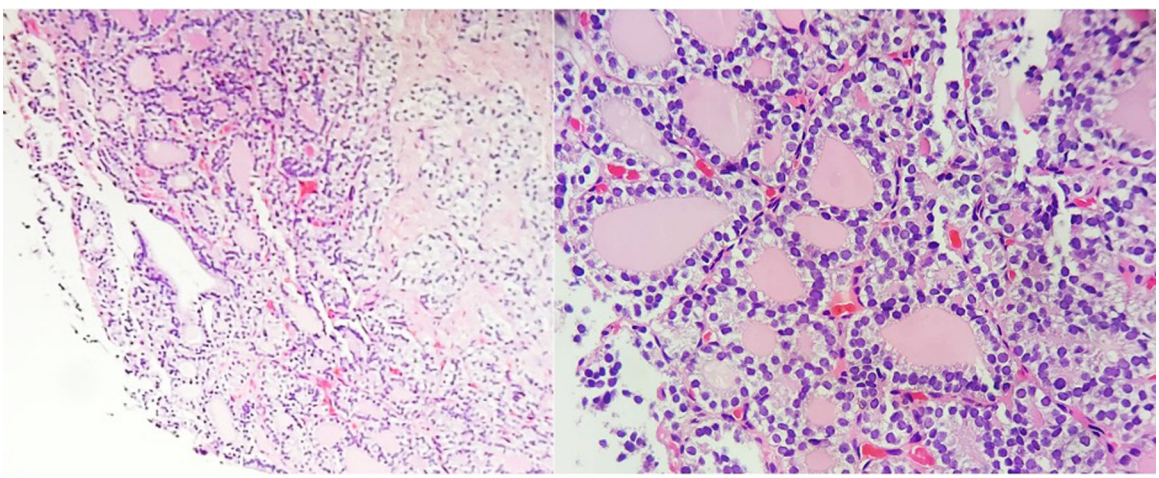

Figure 4. Microscopic findings showing follicular arrangement.

Metastasis Location and Presentation

Presentation of the metastases across the studies were dependent on the tumor's location. These included dysphagia, dysphonia and weak shoulder shrug associated with metastasis to the right jugular foramen, proptosis secondary to clivus and orbital extension, epistaxis and diplopia associated with sphenoid and clival extension, facial dysesthesia from the infratemporal and cavernous sinus involvement and visual impairment and galactorrhea from sellar metastasis (Table 3).

Tumor Size and Surgical Management

Dimensions of reported tumor sizes differed among the studies, ranging from approximately 3cm x 3cm x 2cm as the smallest to 6.8cm x 3.9cm x 5.3cm as the largest. Various approaches were employed in treating tumors of varying sizes and

Table 2. Demographics and tumor characteristics.

Author/ Year	Study	Population	Mean Age	Primary Malignancy	Surgical Intervention for Primary Malignancy	Location of metastasis	Clinical Presentation
Yang 2022	Case Report	1	57	Follicular Thyroid Carcinoma	Total thyroidectomy	Right jugular foramen	Dysphagia, hoarseness of voice and weak shoulder shrug
Altinay 2015	Case Report	1	69	Follicular Thyroid Carcinoma	Thyroidectomy	Skullbase (Clivus, sella, cavernous sinus, orbital)	Proptosis
Shen 2015	Case Series	3	64	Follicular Thyroid Carcinoma	Total Thyroidectomy	Right intraorbital, parietooccipital, occippital	Right frontal, parietal and occipital mass
Bhandary 2011	Case Report	1	59	Follicular Thyroid Carcinoma	None	Skullbase (Clivus, sella, sphenoid sinus)	Epistaxis and Diplopia
Matsuno 2010	Case Report	2	64.5	Follicular Thyroid Carcinoma	Thyroidectomy	Skullbase (Infratemporal fossa, cavernous sinus)	Facial dysesthesia
Coca Pelaz 2009	Case Report	1	61	Follicular Thyroid Carcinoma	Subtotal thyroidectomy	Left infratemporal fossa	Left hemifacial pain and facial dysesthesias
Yilmazlar 2004	Case Report	1	43	Follicular Thyroid Carcinoma	Subtotal thyroidectomy	Sella turcica	Visual impairment and galactorrhea
Rosahl 2000	Case Report	1	50	Follicular Thyroid Carcinoma	Subtotal thyroidectomy	Left middle cranial fossa (Clivus, dorsum sella)	Dysphagia and dysphonia

Table 3. Management and outcomes.

Author/Year	Location of metastasis	Diagnosis of Metastasis	Tumor size	Surgical intervention Metastasis	Adjuvant therapy	Outcomes	Follow-up
Yang 2022	Right jugular foramen	Cranial MRI	Not specified	Cortical mastoidectomy	IMRT + Immunotherapy (Lenvatinib + Pembrolizumab)	Not specified	No data
Altinay 2015	Skullbase (Clivus, sella, cavernous sinus, orbital)	PET/CT	6.8 x 3.9 x 5.3 cm	Punch biopsy	I-131 therapy	Improved	No data
Shen 2015	Right intraorbital, parietooccipital, occippital	Cranial CT/MRI	2.8 -6.0 x 3.4 - 8.0cm	Craniotomy, resection of tumor, cranioplasty	I-131 therapy	1 -mortality	22-30 months
Bhandary 2011	Skullbase (Clivus, sella, sphenoid sinus)	Cranial MRI	Not specified	None	Oral radioiodine ablation	Improved	No data
Matsuno 2010	Skullbase (Infratemporal fossa, cavernous sinus)	Cranial CT/MRI	Not specified	Subtotal resection	Radiotherapy (30 Gy)	Improved	No data
Coca Pelaz 2009	Left infratemporal fossa	Cranial MRI	5 x 4 x 3.5 cm	Subtemporal preauricular approach, excision of tumor, split temporalis muscle flap	Radioiodine + TSH Suppressive therapy	Improved	19 months
Yilmazlar 2004	Sella turcica	Cranial MRI	4 x 2.5 x 3.5 cm	Transsphenoidal decompression	I-131 therapy	Improved	60 months
Rosahl 2000	Left middle cranial fossa (Clivus, dorsum sella)	Cranial CT/MRI	3 x 3 x 2 cm	Suboccipital craniotomy, excision of tumor	I-131 therapy	Improved	12 months

locations, illustrating the intricate nature of treatment strategies in such instances. These approaches ranged from minimal intervention, like punch biopsy, to more extensive procedures such as sub-temporal excision with muscular flap reconstruction (Table 3).

Adjuvant and Outcomes

Adjuvant therapies included combination of approaches such as IMRT coupled with immunotherapy using Lenvatinib and Pembrolizumab, multiple courses of I-131 therapy, oral radioiodine ablation, radiotherapy with a dose of 30 Gy, and treatment involving radioiodine alongside Thyroid Stimulating Hormone (TSH) suppressive therapy. Outcomes across studies were not specified, with most of the cases reporting improvement but one case indicated mortality. Follow-up ranged from 12 months to as long as 60 months, indicating a variable range in the duration of monitoring for outcomes (Table 3).

Discussion

Although thyroid carcinoma has the potential to spread to the bones of the head and neck area, such as the skull, maxilla, and mandible; even rarer, is its spread to the skull base.[7] Papillary thyroid carcinomas (PTC) are typically more prevalent than follicular carcinomas (FTC).[8] Yet FTCs have a higher tendency to spread through hematogenously, particularly to the lungs and bones.[3,8] Majority of individuals experiencing skull base metastasis from FTC had primary thyroid lesions that were asymptomatic and only identified through extensive investigation of metastasis, tissue biopsy of the metastatic site, or both.[9] In a case series, the cohort revealed 6 of 12 patients who underwent previous thyroid surgeries for goiter, only 1 of these 6 was diagnosed with thyroid carcinoma.[2] Skull base FTC metastasis is an uncommon occurrence and may be the initial clinical presentation of FTC with silent primary tumors.[2,3,9] In one study, they found that the mean duration between initial presentation and skull base metastasis was 4 years.[2]

Many reported cases highlight the frequent misidentification of the initial skull base tumor as a chordoma or chondrosarcoma.[2,10] The presence of a significant soft tissue mass typically affects the skull base skeleton and exhibits bony destruction on imaging, along with local extension into surrounding soft tissue, all resembling characteristics observed in chordomas and chondrosarcomas.[2,11,12] The possibility of skull base metastasis from FTC must be considered in patients presenting with cranial nerve dysfunction and on radiography shows a highly lytic tumor.[2] The challenges in diagnosis prompted the creation and utilization of valuable immunocytologic markers tailored for differentiated thyroid tumors. Among these markers are Thyroid transcription factor-1 (TTF-1), the mesothelioma antibody (HBME-1), and galectin-3, all of which play crucial roles in aiding the diagnosis and classification of thyroid lesions.[13] These markers are, however, costly, and are not easily accessible to lower income countries.

Management of FTC skull base metastases was also largely individualized, with no single guideline to recommend a specific treatment plan. For primary thyroid carcinoma, the treatment algorithm suggests total thyroidectomy, with post-operative Iodine 131 therapy.[2,3,12] Iodine 131 (131I) has been known to accumulate well in the follicular elements of thyroid tissue, hence, cementing its efficacy for thyroid metastasis.[14] For the skull base tumor, varying degrees of resection, from simple debulking to maximal safe resection can be performed. Some authors, however, suggested that debulking may be dangerous in most cases at risk of severe bleeding due to its proximity/involvement of vital structures, including large arteries and cranial nerves.[2,12] Hence, internal irradiation with 131I has been suggested as another option, coupled with chronic suppression of TSH secretion through thyroid hormone supplementation.[3]

Limitation of the present study arose from the reliance on case reports as the primary data source. With only case reports available, they lacked the breadth and depth of data needed for robust analysis and generalization such that the case reports/series included lacked the power and treatment standardization necessary to accurately determine the impact of skull base metastasis from differentiated thyroid carcinoma on patient outcomes. Although typically, distant metastasis indicates a poor prognosis, suggesting that survival rates may decrease due to widespread systemic disease.

Conclusion

Due to the rarity of these lesions, an adequate description of the natural history of FTC skull base metastases has yet to be solidified to allow early identification of these malignancies. A thorough

history and physical examination, coupled with a high index of suspicion is necessary to avoid misdiagnosis and unnecessary steps in management. A multidisciplinary team is required, which includes a neurosurgeon, orbit specialists, maxillofacial surgeons, medical oncologists, rad-oncologists, and even palliative care specialists. There is currently no established consensus regarding the diagnosis, work-up, management, and prognosis for such cases of tumors, as such, management is still largely tailored to each patient and relies heavily on systemic factors including the control of primary tumor and the extent of its spread.

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