



## Neurosurgery

## CARCINOMA THYROID WITH AXIAL SKELETAL METASTASES: CASE SERIES OF 12 PATIENTS

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**ABSTRACT**

**Introduction:** Role of surgery in axial skeletal metastases from carcinoma thyroid is unclear. In this study, we assess the role of surgery and adjuvant therapy such as radioiodine therapy in overall survival of these patients.

**Methods:** Twelve patients with biopsy proven spinal and cranial metastases from carcinoma thyroid were evaluated with respect to duration and mode of clinical presentation, physical examination, plain X-ray & MRI, operative and pathologic findings, adjunctive therapy such as 131I treatment and outcome.

**Results:** Five patients had metachronous and seven had synchronous metastases from carcinoma thyroid. There were 8 patients of spinal metastases, 2 patients of skull metastases and 2 patients with both skull and spinal metastases. Surgical treatment of metastatic foci was done which ranged from subtotal to total excision of the lesion. 131I therapy was administered following RAI (Radioactive iodine) assay for control of primary disease. There was no recurrence of skull site metastases in two patients in followup. One patient of skull metastases lost to follow up. All of the patients with vertebral metastases had improvement in sensorimotor deficit and pain following surgery followed by 131I therapy. One patient with follicular carcinoma thyroid who presented with spine and skull metastases expired following 5 years of surgery for skull metastases and cause of death could not be ascertained.

**Conclusions:** Satisfactory result can be anticipated in cases of carcinoma thyroid with metastases, if aggressive surgical approach for primary tumor is taken along with adequate management of metastases. Most of the metastatic foci are highly vascular and excision followed by radioiodine therapy result reasonably good outcome.

**KEYWORDS :** Axial skeletal metastasis, carcinoma thyroid, craniospinal metastasis

**Introduction**

Thyroid cancer is one of the commonest endocrinological malignancy. It is unique because of its relatively good long term survival. Disseminated disease connotes a dismal prognosis in most of the cancers in contrast to patients with metastatic carcinoma thyroid which carry a relatively good long term prognosis [4,18]. Bone metastases from carcinoma thyroid is second to lung metastases with incidence ranging from 1 to 40% [17,21]. There are limited studies which specifically address axial skeletal metastases from carcinoma thyroid and the role of surgery in this setting remains unclear [26]. In this study, we have evaluated twelve patients of carcinoma thyroid with metastases to skull and spine to see role of surgery and adjuvant therapy and its impact on overall outcome.

**Patients and Methods**

A retrospective study was conducted on twelve patients of biopsy proven spinal and cranial metastatic thyroid carcinoma treated in the department of neurosurgery at Sanjay Gandhi Institute of Medical Sciences (SGPGIMS) from 2002 to 2008. Present analysis included patients who underwent total thyroidectomy for carcinoma thyroid elsewhere and referred to our centre with craniospinal metastases after a varying interval. The primary histopathology of these patients were reevaluated at the Department of pathology at our institute. One patient with incomplete primary tumor control was excluded from the analysis. Clinical analysis was performed based on computer based medical records, case summary and radiographic images. These patients were evaluated with respect to age, sex, symptoms, duration from the primary thyroid malignancy in patients with metachronous metastases, mode of clinical presentation, physical examination and investigations including plain X-ray & MRI, operative findings, histopathology and adjunctive therapy such as radioiodine ablation. Follow up data on recurrence and survival was obtained from record maintained by senior author on his personal laptop computer and also by phone calls to patients. Statistical analysis could not be performed because of small sample size.

**Results****1. Patient characteristics**

Study included 12 patients which consisted of 8 males and 5 females. Age of patients ranged from 20 to 55 years (Average: 40.58 years) (Table 1).

**2. Mode of presentation**

Seven patients presented with synchronous craniospinal metastases

and five patients had metachronous distant recurrence following thyroidectomy for primary tumor after a varying interval (Range: 6 months to 11 years; Average 3.7 years). There were 8 patients of spinal metastases, 2 patient of skull metastases and 2 patient with both skull and spinal metastases. Skull metastases presented in the form of skull swelling and spinal metastases as backache and/ or sensorimotor deficits. Multiple discontinuous spinal metastases were present in two patients.

**3. Investigations**

Patients were evaluated by plain X ray followed by contrast enhanced MRI of the involved region. Tc-99m Bone scan was done as part of metastatic workup in all patients. Bone scan revealed metastases in neck of femur, sternum and rib cage in one patient each. In three patients of histopathologically documented metastatic thyroid carcinoma, occult thyroid malignancy was detected on further investigation by radioiodine assay (RAI) by 131I. Following total thyroidectomy and metastatectomy, patients were followed up for recurrence with clinical examination, chest X ray, RAI- 131I uptake scan and thyroglobulin assay at routine intervals.

**Table 1: Summary of 12 patients with axial skeletal metastasis from carcinoma thyroid**

Follow up	Deteriorated in follow up at 5 months as she defaulted on RI, improved following RI	1 year, Hypoaesthesia improved	Still to come for FU	Defaulted on RI Th. At 2 yr FU: Backache, skull swelling
Condition on discharge	Improved	Radicular pain relieved, Hypoaesthesia persisting	spasticity reduced, paraplegia persists	Spasticity improved partially
Histopathology	PTC	FTC	FTC	FTC
Treatment	1) Transclav transman near total ex & instrumentaion 2) RI	1) S 2-3 lam and subtotal ex of tumor 2)TTD 3) RI	1) Lam and subtotal ex of tumor 2)RI	1) D10-11 laminectomy and subtotal ex of tumor 2)TTD 3) RI

Radiology	MRI: Extradural soft tissue mass present, destruction of C7,D1,2,part of D3, with compression of thecal sac	MRI LS SPINE: Expansile mass in the S 2-3 sacral seg more on right side, obliterating canal and foramina,	MRI SPINE: a large soft tissue mass at D6-7 level more on right side compressing the cord	MRI SPINE: Partial destruction of D10-11 vertebral body with paraspinial soft tissue mass
Examination	Spastic paraparesis Power in LL: Gd 2	power: 5/5 except: ankle and toes: PF: 4+/5, Sensory loss in S1-4, SLR restricted	Spastic paraplegia, sensory deficit below D8	Power in lower limbs: Gd 3
Clinical presentation	Opt case of PTC( TTD) 3yrs back PC:Spastic paraparesis for 1 month	Radiating pain on the post aspect of thigh and calf 6mts, Numbness in post aspect of sole, rt calf, thigh and perigenital region for 5mts	Opt case of FTC(TTD) 1 year back PC: Rapid onset spastic paraplegia	Progressive spastic paraparesis for 3 months
Sex	F	M	M	F
Age	33	40	51	55
Patient	M	DKS	SPY	SD
SL NO	9	10	11	12

Follow up	5 Years, No rec, Power LL: 4+/5	power in LL: 4+/5(at 4 year FU) Expired at 5 years FU	Lost FU	1 mth: improved, 2mth: Deteriorated, Improved foll RI
Condition on discharge	power 3/5 in b/l LL	Paraparsis persists	Right hemiplegia, tracheostomised	Spasticity improved, Power both LL: 4-4+/5
Histopathology	FTC	FTC	FTC	FTC
Treatment	1)D 2-3 lam & total excision 2) TTD 3) RI	1) Excision of extradural Calvarial mass. 2) RTH for D10 mets 3)RI	1)TTD & subtotal excision of intracranial mets 2) Evacuation of EDH 3)RTH for sacral mets 4)RI	1)Transcalv transman total excision 2)TTD 3) RI
Radiology	MRI SPINE: 5X3 cm lesion involving the posterior elements of D 2 and D3 vertebra extending to right paraspinal region	MRI HEAD: Lesion in midparietal region involving calvarium, SSS thrombosed MRI SPINE: Destruction of D 10 vertebra	Xray skull: Lytic defect of 5 cm length in skull on left side post to coronal suture, MRI SPINE: Ca thyroid mets in sacrum, MRI HEAD: Intracranial extension of skull metastases, sup sag sinus engulfed	MRI : Collapsed D1 vertebra with ant and post cord compression

Examination	Grade 0/5 spastic paraplegia, 50-90 % sensory loss below D 4 level	Paraparesis: Power in LL: hip 2/5 b/l, knee/ankle: 0/5 SLR restricted, Soft fluctuant swelling in the Vertex	Grade 3 colloid goitre, b/l spont limbs movements >r,	power: upper limb 5/5, Lower limb: R:4+/5, L : 2-3/5, Babinski positive, 20-30% hypoaesthesia below C8,
Clinical presentation	Lower limb weakness for one month, numbness and tingling below the level of nipples	Opt case of FTC(TTD) 3 years back swelling in midline scalp in parietal region for 1.5 yrs Spastic paraparesis: 1 mth	Neck swelling 12 yrs, Pain in right hip: 10 mts, Swelling in vertex of scalp : 8 mts	Pain in interscapular region for 5 months, Spastic paraparesis L>R for 1mth
Sex	F	M	M	M
Age	35	43	40	45
Patient	SD	KNT	DD	KKS
SL NO	5	6	7	8

Follow up	1 years, No rec	2 years, No rec	3 years, No rec, Power LL 4+/5	5 years, No rec, Power LL 4+/5
Condition on discharge	Normal, scar healthy	Normal, scar healthy	Spasticity decreased, Paraparesis improved: power 3/5	Paraplegia persists
Histopathology	PTC	FTC	FTC	FTC
Treatment	1) Frontal supraorbital approach and excision of metastatic tumor 2) RI	1) Right frontoparietal craniotomy and excision of mass 2) TTD 3) RI	1) Posterolat approach & total excision of D12 mets and L4 lam 2)TTD 3) RI	1) Subtotal ex of D 7 vertebral mets by posterolat approach & L5 lam 2)RI
Radiology	CECT : 8x9 cm enhancing soft tissue mass lesion in midline destroying bilateral frontal bones, extending into contiguous ethmoid cells and frontal sinus	CECT : 10X8.2X6.4 cm lesion, hyperdense, in right FP region, mass effect on right FP lobe with midline shift of 0.5 cm contrast enhancing,	MRI: D12 vertebral body collapse with right posterolateral compression, another lesion at L4 involving the posterior elements	MRI DL spine: Destruction of spinous process and partially of body of D 7 vertebra with extradural cord compression, L 5 posterior elements also destroyed
Examination	8x9 cm swelling in forehead just above eyebrows, firm to hard, overlying skin free	9x8 cm globular cystic swelling in right frontoparietal region, nontender, nonpulsatile	Power :Upper limb: 5/5, Spastic paraparesis power 1-2/5, 25-75% hypoaesthesia below L 1	Grade 0/5 spastic paraplegia, 80 % sensory loss below D 9 level

Clinical presentation	FU opt case of PTC(TTD) with parathyroid ad. 11 yrs back PC: Painless swelling in frontal region for 6 mth, Mild holocranial Headache for 3 months	Swelling in right frontoparietal region from 4 months, Severe headache associated with vomiting for 4 days	Mid back pain for 18 months, numbness in right lower limb for 4 months, weakness of bilateral lower limbs for one month	Opt case of FTC(TTD) six month back PC: Low backache and tingling sensation in lower limbs for 3 months, inability to move lower limbs for 15 days
Sex	F	M	M	M
Age	48	32	20	37
Patient	MD	HR	HOR	V
SL NO	1	2	3	4

**4. Surgical treatment**

**A) Treatment of primary tumors**

All patients with synchronous metastases underwent total thyroidectomy. TSH suppression therapy was administered in all patients.

**B) Treatment of metastases**

Patients with skull tumors underwent total excision of lesions except in one case where the tumor was engulfing the superior sagittal sinus in which subtotal excision could be achieved. Total excision of metastases involving the vertebral body was done in 4 patients. Of these, two patients underwent excision of vertebral body and instrumentation by transclavicular transmanubrial approach. One patient underwent excision of D 12 vertebral body metastases by posterolateral approach. Another patient underwent laminectomy as metastatic tumour was involving the posterior elements. Subtotal excision of vertebral metastases was done in 4 patients utilizing posterolateral approach in one patient and laminectomy in three patients. Two patients with discontinuous two level vertebral metastasis underwent laminectomy for the second lesion as the bulk of the mass was involving the posterior element.

**5. Pathology**

There were 2 cases of papillary thyroid carcinoma (PTC) and 10 cases of follicular thyroid carcinoma (FTC).

**6. Radiotherapy**

Two patients who had both skull and spinal metastases underwent radiotherapy for the spinal lesion for pain relief.

**7. Radioactive iodine therapy**

131I treatment was administered in patients following total thyroidectomy and metastatectomy based on RAI scan and thyroglobulin assay. One patient with both skull and vertebral metastasis underwent One patient defaulted on 131I therapy.

**8. Complications**

Heavy intraoperative bleeding was the most common complication because of the highly vascular nature of the metastases. Surgery had to be interrupted in 2 patients of vertebral metastases and operative field had to be packed with ribbon gauze because of heavy bleeding (approximately three to four liters). Patients were reexplored later and rest of tumor excision was performed in second stage. Following decompression of a skull metastases engulfing the superior sagittal sinus, one patient developed extradural hematoma which had to be evacuated. Patient developed right hemiplegia in postoperative period and had to be tracheostomised for maintaining the airway. Patient lost to follow up following discharge from the hospital. One patient of D10-11 metastases defaulted on 131I therapy presented 2 year later with recurrence of backache and skull swelling. RAI assay revealed tumor recurrence at D10-11 level and skull. Patient could not be operated because of poor general condition and he was referred for 131I therapy. One patient expired at five years following treatment of metachronous metastases. This patient was an old operated case of follicular carcinoma thyroid who presented with skull and spinal metastases 3 years following primary surgery for carcinoma thyroid. He underwent excision of skull metastases and radiotherapy for

vertebral metastases and 131I therapy (Fig 1). Backache improved and power in lower limbs improved from grade 2 in the preoperative period to grade 4+ and patient was able to walk without support at follow up at 4 years. The patient didn't come for follow up at 5th year and it was conveyed by his family members on phone that the patient expired, the cause of which could not be ascertained.

**8. Follow up**

Follow up was available for 9 patients with duration ranging from one to five years (Mean follow up: 33.6 months). One patient was still to come for follow up and one patient lost to follow up.

**9. Outcome**

There was no recurrence of skull site metastases in two patients in followup period. One patient of skull metastases lost to follow up. All patients with vertebral metastases had improvement in sensorimotor deficit following surgery followed by radioiodine therapy. One patient defaulted on radioiodine therapy and had deterioration in motor power following initial improvement. One patient with follicular carcinoma thyroid expired after five years following surgery for metachronous metastases involving skull and spine and direct cause of death could not be ascertained.

**Discussion**

Thyroid carcinoma accounts for 1% of all thyroid tumors [15]. Metastases to skeletal system from thyroid carcinoma are well known constituting the second most common site of involvement after lungs [17,21].The incidence varies from 1 to 40 % depending upon factors such as duration of follow up, diagnostic parameters used (RAI uptake , histologic testing on resection or biopsy material or postmortem examination) [11,14,21,25,27].Among bone metastases, vertebral metastases range from 41 to 68% and skull metastases from 2% to 17% although multiple site bony involvement was present in most of the series [2,16,28]. Distant metastases are synchronous with the primary diagnosis in 5 to 45% of patients [3,24] but it could also be encountered 5 or 10 years after the initial treatment, thus justifying the prolonged follow up of thyroid cancer patients [1,13]. In present study, metastases occurred after a period ranging from 6 months to 11 years following initial surgery and adjuvant therapy for carcinoma thyroid. Initial presentation with distant metastases is even less common. In a study conducted by Shaha et al at Sloan-Kettering cancer center, 4% patients of differentiated thyroid cancer presented initially with distant metastases [23]. Pittas et al reported that 28% of patients had symptoms related to bone metastases as their manifestation of thyroid cancer and suggest that diagnosis of thyroid cancer should also be considered in case of skeletal metastatic disease with unknown primary. As SGPGI is a tertiary referral centre, we received patients with metastases already involving the skull and spine and hence exact incidence of these could not be assessed. In present study, cranial and spinal metastases were the presenting features in 8 patients with carcinoma thyroid. FTC has a higher propensity to have a distant metastases at presentation compared to PTC [23]. In this analysis, all ten patients who presented initially as craniospinal metastases were found to have FTC. It has also been observed that highest incidence of distant metastases in differentiated thyroid carcinoma occurs in the age group of above 45 years [23]. However in present study, the mean age group of patients with initial presentation as distant metastases is 38.18 years.

Three patients had vertebral metastases from occult thyroid carcinoma. Preoperative metastatic workup including ultrasound neck was normal and histopathological examination of metastatic tissue followed by RAI assay established the diagnosis.

Treatment of carcinoma thyroid with metastases requires total/near total thyroidectomy followed by radioiodine therapy, which is treatment of choice in iodine avid metastases, and which responds favourably to 131I therapy [7,16]. Total thyroidectomy facilitates the use of thyroglobulin as a marker and it is possible to give a large dose of radioactive iodine without any competition for radioactive iodine by normal thyroid gland. Performing total thyroidectomy initially will also help long term survivors to avoid massive local recurrence or spread into extrathyroidal tissue where surgery may be more difficult in the future.

Surgical resection is recommended for the bony metastases and a complete resection is associated with improved survival as compared to palliative surgery which has not been found to have an impact a

survival [16]. However Pittas et al observed that surgery conferred an early benefit but didn't have a statistically significant benefit in overall survival [14]. Radioiodine alone is not curative because the metastases are often bulky and widespread but repeated high activity radioiodine may be beneficial [12]. External beam radiotherapy offers significant palliation in unresectable painful bone lesions. For spinal epidural metastases, decompressive laminectomy was traditionally accepted treatment. However, the neurological recovery following laminectomy was not satisfactory and the reasons could be twofold. First, majority of epidural metastases arise from the vertebral body and invade the epidural space anteriorly. Second, laminectomy bears risk of destabilizing the spinal column with vertebral bodies destroyed by tumour infiltration. Various studies have shown that anterior decompression lead to neurological improvement in 55 to 97% and relief of pain in 60 to 97% of patients [8,9]. Surgical results could be improved by anterior decompression of vertebral body and stabilization instrumentation [9]. Early postoperative mobilization of the patient is another important advantage of surgical techniques which include stabilization procedures. In present analysis, the surgery was done according to the site and quantum of compression in relation to cord and nerve roots. Involved vertebral body was approached anteriorly using transclavicular transmanubrial route in two patients. In two patients, vertebral body was approached by posterolateral route. Laminectomy was done in 5 patients. Lesion was highly vascular in all of the cases. In two cases, surgery had to be interrupted and ribbon gauze packed in the operative cavity because of heavy bleeding and rest of the procedure completed in second stage. Two patients with both skull and vertebral metastases underwent excision of skull metastases and vertebral metastases were irradiated because of no compression.

<sup>131</sup>I treatment appears highly effective in younger patients with <sup>131</sup>I uptake and with small metastases. Durante et al observed that best responses (92% 10 year survival rate) were observed in patients younger than 40 years old with papillary or follicular well differentiated subtypes and a limited extent of disease [7]. These patients should be treated until the disappearance of any uptake or until a cumulative activity of 22 GBq is attained. High cumulative activities of radioiodine (>22 GBq;600mCi) are associated with a significantly increased risk of leukemia [5], secondary cancers [18] and pulmonary fibrosis [20]. All the patients in present study group underwent <sup>131</sup>I therapy. However one patient defaulted and presented with local and distant recurrence 2 years later.

Differentiated thyroid cancer usually carries a good prognosis [22]. Patients with distant metastases are known to have a markedly reduced survival rate of 50% at 5 years, decreasing to 13-33% at 10 years [6,10,13]. Pittas et al [16] reported the overall 10 year survival from the time of diagnosis of thyroid carcinoma was 35% and from diagnosis for initial bone metastases was 13%. Similar results were by Proye et al [17]. Reugeuer et al [19] that 10 year survival of 25% from all causes in patients with distant metastatic disease. However few studies have quoted a good overall long term survival (43%) in thyroid cancer with metastases [23]. In present study, follow up was available for 9 patients with duration ranging from one month to 6 years (Mean follow up: 33.6 months).

Overall outcome of patients in present study was good. There was no recurrence following excision of skull metastases in 2 patients. One patient with both skull and spinal metastases lost to follow up. There was significant improvement in sensorimotor deficit and pain in eight patients with vertebral metastases who underwent surgery followed by <sup>131</sup>I therapy. One patient defaulted on radioiodine therapy and deterioration in motor power following initial improvement. However, the survival analysis could not be performed because of short duration of follow up.

## Conclusions

Metastases rarely may occur from thyroid carcinoma even if the primary may remain occult. Prognosis of carcinoma thyroid with metastases is quite satisfactory if aggressive surgical approach for primary tumor is taken along with appropriate management of metastases. Surgery may be difficult because of highly vascular nature of metastases but if performed successfully, the role of radioiodine therapy is enhanced. Even multiple metastases if successfully excised along with adequately controlled primary disease may have a good outcome.

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