



## A rare malignant neuroectodermal tumour in the thyroid gland

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### Abstract

Medulloepithelioma (ME) is a rare embryonal tumor predominantly located in the eye or in the central nervous system without an established treatment. We report of a case of a peripheral ME treated with surgery and local radiotherapy. Also, a literature review suggesting a role of Chemotherapy has been included.

**Keywords:** medulloepithelioma, thyroid gland, cervical medulloepithelioma

### Introduction

Medulloepithelioma is a rare primary congenital intraocular or CNS tumor that usually arises from the primitive medullary epithelium of the ciliary body. These tumors tend to be locally aggressive and can invade the adjacent intraocular structures and they rarely metastasize <sup>[1]</sup>. ME is usually located in the eye or in central nervous system (CNS); a peripheral location has been rarely reported.

We present a rare case of a medulloepithelioma arising primarily in the neck and a review of the literature of all the medulloepitheliomas that have cervical lymph node metastasis.

### Case Report

A 36-year-old well-built and nourished male presented to our outpatient department with a history of total thyroidectomy done at a private medical centre for a suspected medullary carcinoma of the thyroid gland. The previous histopathology report mentioned multiple nodules in the left lobe of the thyroid gland, the largest being 2x4 cms with extra capsular extension. On physical examination, he had multiple level 2,3, and 4 deep cervical nodes. The slide and block were reviewed at our institution and was reported as High grade poorly differentiated Malignant small cell neoplasm with medulloepithelioma-like rosettoid pattern. TTF-1 was positive, S100 patchy moderate positive; cytokeratin (AE1/AE3), CK7 and EMA negative; Synaptophysin, Chromogranin and CD56 negative; Thyroglobulin - inconclusive. MIC-2 showed nonspecific staining; Cam 5.2 negative. Hence, they concluded that it is a medulloepithelioma of the thyroid gland. Fine needle aspiration of neck nodes revealed the same pattern. Contrast enhanced CT of the Brain, neck and thorax revealed Enlarged level 2, 3 and 4 lymph nodes on left side largest measuring 2.7 x 3x6 cm in size, shows mild contrast enhancement. There was no lesion in the brain and orbit. In view of a poorly differentiated malignant neoplasm and suspicious medullary carcinoma of the thyroid, a metastatic and syndromic work up consisting of Ultrasound abdomen, Serum calcitonin, Urinary spot VMA, Blood Parathormone

and serum calcium was done which was all within the normal physiologic range.

After a Multi-Disciplinary Tumour board (MDT) discussion and obtaining appropriate consent for surgery, the patient underwent Bilateral Modified radical neck dissection. Intraoperatively, the left cervical nodes were dark tan colour with gross extracapsular extension and densely adherent to the surrounding structures for which, the Internal jugular vein and the sternocleidomastoid were sacrificed on the left side and a functional neck dissection on the right side as there was no gross extra capsular extension. The post-operative period was uneventful and was discharged on day 5.

The final Histopathology report diagnosed 8/12 nodes on the left and 6/ 14 nodes on the right with metastatic foci with an identical microscopic picture as before and similar IHC staining pattern viz, Tumour cells diffusely express TTF-1 and are immunonegative for cytokeratin (AE1/AE3), synaptophysin, chromogranin and thyroglobulin. MIC2 shows variable staining, focally in a membranous pattern.

After discussion in MDT, Beta HCG and Alfa Fetoprotein was done which were within the normal prescribed physiologic range. External beam radiation is planned for the patient with 55Gy/ 23Fr.

### Discussion

Verhoeff in 1904 gave the first detailed histological description of a medulloepithelioma. Unfortunately, he chose to call the tumor a "terato-neuroma" even though he did not describe or illustrate any histologic elements that could be considered teratomatous. That name, terato-neuroma, never became popular. The term "medulloepithelioma" was first used for this tumor by Grinker in 19311.

Medulloepithelioma is a congenital tumor arising from the primitive medullary epithelium that is destined to form the non-pigmented ciliary epithelium of the ciliary body <sup>[1]</sup>. The tumor typically occurs in children aged between 2 and 4 years, but its diagnosis is often delayed despite the onset of symptoms because of the rarity of the tumor <sup>[2]</sup>. These

tumors are characteristically unilateral and sporadic [3]. Zimmerman [3] has classified this tumor as teratoid and non-teratoid types. The non-teratoid medulloepithelioma is a pure proliferation of cells of the medullary epithelium. Teratoid medulloepithelioma is distinguished by the additional presence of heteroplastic elements, particularly cartilage, skeletal muscle and brain tissue. Based on histopathologic criteria, both types can be either benign or malignant. As described by Broughton and Zimmerman, the histopathologic criteria for malignancy of both the non-teratoid and teratoid medulloepithelioma are: (1) poorly differentiated neuroblastic cells which resemble retinoblastoma, (2) exceptional pleomorphism and/or mitoses, (3) sarcomatous areas and (4) invasion of other ocular structures with or without extraocular extension [5]. This nomenclature was adopted by the World Health Organization in 1980 and has been used since. Based on the above criteria established by Broughton and Zimmerman, our present case can be classified as a non-teratoid malignant medulloepithelioma. Further, limited and conflicting results have been reported for chromogranin, synaptophysin, glial fibrillary acid protein, S100 protein, and HMB-45. Positive immunohistochemistry for pancytokeratins and cytokeratin (CK)18, with no reactivity for CK7, CK20, and epithelial membrane antigen, has been described [4]. The differential diagnosis includes retinoblastoma and Malignant mesenchymal tumors viz., rhabdomyosarcoma and embryonal carcinoma. Two-thirds of these tumors are thought to be malignant,

distant metastases are rare. There have been reported a few cases metastasized to lymph nodes and lungs [3].

Eken *et al.* [5], reported a case of orbital ME with to the submandibular cervical neck nodes which was treated with surgery followed by radiation and chemotherapy and is on regular follow up after 1 year

Vishwanathan S *et al.*, [6] and Qureshi S [7] have also reported few cases of orbital Medulloepithelioma with metastasis to the intra parotid and cervical neck nodes, all of which were treated with Surgery + RT +/- Platinum and alkylating agents-based Chemotherapy. However, their survival was not mentioned.

De Pasquale *et al.*, [8] reported a case of peripheral ME which occurred in the kidney and was treated with surgery and adjuvant chemotherapy and had a relapse. A protein profile of the relapse revealed a PDGFR receptor and hence Sorafenib, a TK inhibitor was administered and had a good result. However, this was just a single case report and further multi centric trials are required to substantiate.

Similar to classical ME which occurs in the CNS or orbit, surgery in Peripheral ME, with or without systemic chemotherapy and/or local radiotherapy, represents a therapeutic option. Complete surgery seems to be associated with better outcome [9, 13].

The prognosis is poor in cases with extraocular extension as evident from many series. The benefits of local radiotherapy and chemotherapy have not been established; however, they are recommended in cases with local recurrence or distant metastasis [1, 5, 13].

## Review of literature

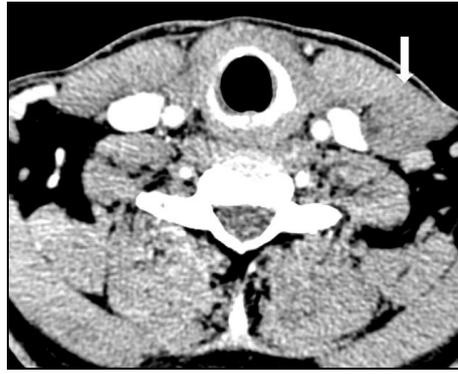
**Table 1:** showing the various studies which report of peripheral and metastatic medulloepithelioma.

| S. No | Study group   | No. of cases | Primary | Metastatic site           | Treatment             | outcome                                       |
|-------|---|--------------|---------|---------------------------|-----------------------|---|
| 1     | Nakamura <i>et al.</i> <sup>10</sup> (1982)           | 1            | Pelvis  | No                        | Surgery               | 84 months                                     |
| 2     | Figarella-Branger <i>et al.</i> , <sup>9</sup> (1992) | 1            | Pelvis  | Lung                      | Surgery + CT          | Expired                                       |
| 3     | Kleinman <i>et al.</i> , <sup>11</sup> (1993)         | 4            | Ovary   | Nil                       | Surgery +/- RT +/- CT | Early stage – NED<br>Advanced stage - Expired |
| 4     | Donner <i>et al.</i> <sup>12</sup> (2003)             | 1            | Pelvis  | No                        | CT                    | 36 months                                     |
| 5     | Eken <i>et al.</i> , <sup>5</sup> (2006)              | 1            | Orbit   | Cervical neck lymph nodes | Surgery + RT + CT     | 12 months                                     |
| 6     | Meel <i>et al.</i> , <sup>13</sup> (2010)             | 2            | Orbit   | Parotid, neck             | Surgery + RT + CT     | Expired – 1, alive 1                          |
| 7     | Qureshi S <sup>7</sup> (2010)                         | 1            | Orbit   | Parotid, Neck             | Surgery + CT + RT     | Alive   |
| 8     | Viswanathan S <i>et al.</i> , <sup>6</sup> (2008)     | 3            | Orbit   | Parotid, Neck             | Surgery + RT +/- CT   | Not mentioned                                 |

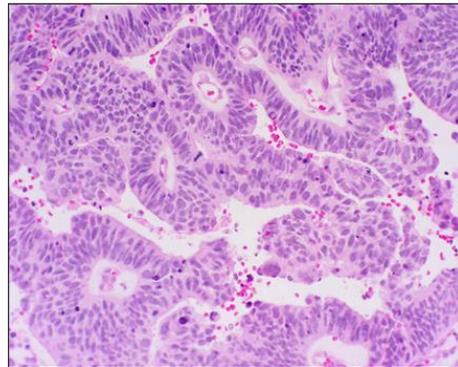
A google scholar and Pubmed central search for a medulloepithelioma in the thyroid gland did not reveal any reports. Hence this can be considered as the first case report of medulloepithelioma in the thyroid gland. Also, metastasis of this tumour is a very rare event and only a few case reports of metastasis to the cervical neck nodes have been reported. As the embryological origin of the parafollicular C cells of the thyroid is neuroectoderm, this could have been the origin of the tumour in the thyroid gland.

## Conclusion

This is the first case report of medulloepithelioma in the thyroid gland. Also, Cervical neck metastasis is a very rare event. Our current understanding and literature review shows that metastatic and peripheral medulloepitheliomas have a poor prognosis and there is no optimal treatment protocol. Hence there is a lot of scope for research and molecular analysis of this disease



**Fig 1:** Axial view of the CECT neck showing a 2x2 cm node in the left level 3 with infiltration into the sternocleidomastoid (Arrow).



**Fig 2:** atypical small round to oval cells with scanty to moderate cytoplasm and small angulated nuclei with granular chromatin some showing tiny nucleoli predominantly in tubular, papillary and glandular pattern. There are closely packed rosette formation also. Foci of necrosis and brisk mitosis noted. Adjacent thyroid show lymphocytic thyroiditis

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