American Journal of Otolaryngology and Head and Neck Surgery

Case Report
Published: 25 Apr, 2020

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 [1]. 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 medulloepithelioma that have cervical lymph node metastasis.

Case Presentation

A 36 years 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 2 cm × 4 cm 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 cm × 3 cm × 6 cm in size, shows mild contrast enhancement (Figure 1). 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 color 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 *via*, 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 (Figure 2).

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Received Date: *07 Apr 2020*
Accepted Date: *21 Apr 2020*
Published Date: *25 Apr 2020*

Citation:
George NA, Patil S, Suresh S, George C. A Rare Malignant Neuroectodermal Tumour in the Thyroid Gland. Am J Otolaryngol Head Neck Surg. 2020; 3(3): 1090.

Table 1: The various studies which report of peripheral and metastatic medulloepithelioma.

S. No	Study group	No. of cases	Primary	Metastatic site	Treatment	Outcome
1	Nakamura et al. [9]	1	Pelvis	No	Surgery	84 months
2	Figarella-Branger et al. [10]	1	Pelvis	Lung	Surgery+CT	Expired
3	Kleinman et al. [11]	4	Ovary	Nill	Surgery ± RT ± CT	Early stage- NED and Advanced stage- Expired
4	Donner et al. [12]	1	Pelvis	No	CT	36 months
5	Eken et al. [5]	1	Orbit	Cervical neck lymph nodes	Surgery+RT+CT	12 months
6	Meel et al. [13]	2	Orbit	Parotid, neck	Surgery+ RT+CT	Expired- 1, alive 1
7	Qureshi S [6]	1	Orbit	Parotid, Neck	Surgery+CT+RT	Alive
8	Viswanathan et al. [7]	3	Orbit	Parotid, Neck	Surgery+RT ± CT	Not mentioned

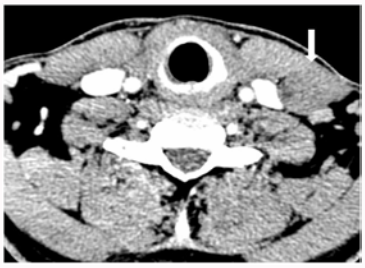

Figure 1: Axial view of the CECT neck showing a 2 cm × 2 cm node in the left level 3 with infiltration into the sternocleidomastoid (Arrow).

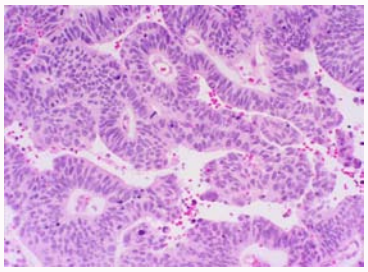

Figure 2: A typical small round to oval cells with scanty to moderate cytoplasm and small angulated nuclei with granular chromatin some showing tiny nucleoli predominantly in tubular, papillary and glandular pattern. There are closely packed rosette formation also. Foci of necrosis and brisk mitosis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

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

Discussion

Verhoeff in 1904 gave the first detailed histological description of a medulloepithelioma [1]. 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 1931.

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 [1]. The tumor typically occurs in children aged between 2 years and 4 years, but its diagnosis is often delayed despite the onset of symptoms because of the rarity of the tumor [2]. These tumors are characteristically unilateral and sporadic [3].

Zimmerman has classified this tumor as teratoid and non-teratoid types [3]. 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 [3]: (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 extra ocular extension. 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-teratoma 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 Qureshi [6] and Vishwanathan et al. [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, represent 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. 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 tumor 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 medulloepithelioma 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.

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