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Original Article

Pathology Section

Clinicopathology of Middle Ear Tumours: A Retrospective Study from a Tertiary Care Hospital, Hyderabad, India

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ABSTRACT

Introduction: Middle ear tumours are rare neoplasms that have non specific clinical presentation, otoscopic and imaging features and pose a diagnostic challenge. Most common neoplasm of middle ear are paraganglioma, schwannoma, haemangioma and middle ear adenoma.

Aim: To analyse the relative incidence, clinical presentation and histopathological spectrum of neoplasms in the middle ear at a tertiary care hospital, Hyderabad, Telangana, India.

Materials and Methods: This retrospective study was conducted in Department of Pathology at Government ENT Hospital (tertiary referral ENT Hospital), Hyderabad, Telangana, India, from July 2014 to June 2019. Total 26 cases of middle ear tumours both incisional or excisional biopsies of middle ear lesions from all age group of either gender with complete clinical details were included in the study. Clinical and histopathological data were analysed after processing the sections with Haematoxylin and Eosin (H&E) stains examined microscopically. Statistical analysis was done using Statistical Package for Social Science (SPSS) version 20.0 and mean, standard deviation and percentages were calculated.

Results: In the present study, maximum patients 11 (42.3%) were in age group of 41 to 50 years with female preponderance 18 (69.2%). Mean age of the patients were 42.92±12.53 years. Out of a total of 26 cases, 20 cases were benign neoplasms and six cases were malignant. Most common side of presentation was right side. Most of the benign tumours occurred in the 5th decade and malignant tumours were common in the 6th decade. Paragangliomas/Glomustympanicum tumours were most common benign tumours followed by schwannoma, haemangioma and middle ear adenoma. Whereas among malignant tumour, squamous cell carcinoma was common.

Conclusion: Middle ear tumours are relatively uncommon lesions presenting as mass in the ear, discharge, hearing loss, tinnitus and chronic suppurative otitis media. Benign tumours are more common than malignant tumours in the middle ear. Paraganglioma was the most common benign tumour encountered, followed by schwannomas, middle ear adenomas and haemangiomas. Middle ear tumours are rare and histologic analysis is essential for definitive diagnosis and treatment.

Keywords: Haemangioma, Polyp, Schwannoma, Squamous cell carcinoma

INTRODUCTION

Middle ear neoplasms are rare with an incidence of 1 per 20,000. Benign tumours are more common than malignant tumours. The most common primary tumours are paragangliomas (glomustympanicum tumours) which occurs more frequently in females in the fourth decade and constitute 0.2% of head and neck lesions [1]. Primary tumours from the middle ear space extend intracranial or into other portions of the temporal bone or skull base. Benign tumours of adjacent structures can invade the middle ear space; these tumours include vestibular and facial nerve schwannomas, temporal meningioma's, and parotid gland tumours. The most common middle ear malignancy is squamous cell carcinoma, which is rare in the middle ear with an incidence of 0.03% accounting for 1.5% of head and neck malignancies [2-4]. The most common symptom is mass in the ear followed by discharge, pain, pulsatile tinnitus and conductive deafness [3].

Middle ear tumours are rare and affect the quality of life due to hearing loss, pain, discharge and tinnitus. Histologic analysis is required for definitive diagnosis and adequate treatment due to non specific clinical, otoscopic and radiologic findings. The tumours of the middle ear resemble common otolaryngologic diseases, leading to delay in diagnosis or misdiagnosis [5].

In India and worldwide there are very limited studies on middle ear tumours which are mostly case reports or related to imaging studies [4-7]. So studies like the present study may help the clinician to know about rare diseases which may be helpful in early treatment and careful follow-up to prevent recurrence.

Hence, the present study was conducted to analyse the relative incidence, clinical presentation and spectrum of neoplasms in the middle ear at a tertiary referral ENT Hospital.

MATERIALS AND METHODS

This retrospective study was conducted in Department of Pathology at Government ENT Hospital (tertiary referral ENT Hospital), Hyderabad, Telangana, India, from July 2014 to June 2019 and was analysed from June 2019 to December 2019. Study was approved by Institutional Ethics Committee (IEC No-136). Total 560 biopsy specimens from the ear were received. After following the inclusion and exclusion criteria, only 26 biopsy specimens of middle ear tumors were studied.

Inclusion criteria: Biopsies of middle ear tumours submitted to the Department of Pathology within the study period, for which all data were present, were included in the study.

Exclusion criteria: Inadequate tissue, biopsies of external ear, inflammations of middle ear, cholesteatomas and congenital lesions were excluded from the study.

Data Collection

All data were collected from the record book of the hospital. The relevant patient data such as age, gender, presenting complaints were collected. All the specimens were subjected to routine processing and paraffin embedding. The sections were stained with Haematoxylin and Eosin (H&E) and examined under a light microscope. Immunohistochemistry (IHC) was done for the

confirmation of the diagnosis wherever necessary. After thorough data collection; age, gender, type of tumour, histopathological diagnosis, incidence, clinical presentation and spectrum of neoplasms in the middle ear were analysed.

STATISTICAL ANALYSIS

The descriptive data were entered in Microsoft Excel and were analysed using Statistical Package for Social Science (SPSS) version 20.0 and mean, standard deviation and percentages were calculated.

RESULTS

In the present study, age ranged from 19 to 68 years with a mean age of 42.92±12.53 years. Majority of benign tumours 11 (42.3%) cases were seen in 5th decade (41-50 years), while malignant tumours four cases (15.4%) were more common in the 6th decade [Table/Fig-1]. The Male:Female ratio of benign tumors was 1:3.33 (males were five and females were 15) were as that of malignant tumors was 1:1 (males and females were three each) [Table/Fig-2].

Tumours	Age group (years)						Total
	11-20	21-30	31-40	41-50	51-60	61-70	
Benign tumours							
Paraganglioma	1	0	1	9	2	0	13 (50%)
Schwannoma	0	1	1	1	0	0	3 (11.53%)
Haemangioma	0	3	0	0	0	0	3 (11.53%)
Middle ear adenoma	0	0	0	0	1	0	1 (3.84%)
Malignant tumours							
Squamous cell carcinoma	0	0	0	1	4	1	6 (23.07%)
Total	1 (3.84%)	4 (15.38%)	2 (7.69%)	11 (42.30%)	7 (26.92%)	1 (3.84%)	26 (100%)

[Table/Fig-1]: Age wise distribution of cases (N=26).

Name of tumour	Male (n, %)	Female (n, %)
Benign tumour		
Paraganglioma	0	13 (72%)
Schwannoma	1 (12.5%)	2 (11.5%)
Haemangioma	3 (37.5%)	0
Middle ear adenoma	1 (12.5%)	0
Malignant tumour		
Squamous cell carcinoma	3 (37.5%)	3 (16.6%)
Total	8 (30.8%)	18 (69.2%)

[Table/Fig-2]: Gender wise distribution of cases (N=26).

The right ear was affected in a majority of the cases, 20 cases (76.9%) and left ear in six cases (23.1%). Out of the 26 middle ear neoplasms, benign tumours comprised of 20 cases (76.9%) and malignant tumours six cases (23.1%). Most common presentation of tumours was mass in middle ear seen in 25 (96.15%) cases followed by Chronic Suppurative Otitis Media (CSOM) in 8 (30.76%) cases, ear discharge and tinnitus 4 (15.38%) cases in each, loss of hearing in 2 (7.69%) cases and facial palsy in 1 (3.84%) case.

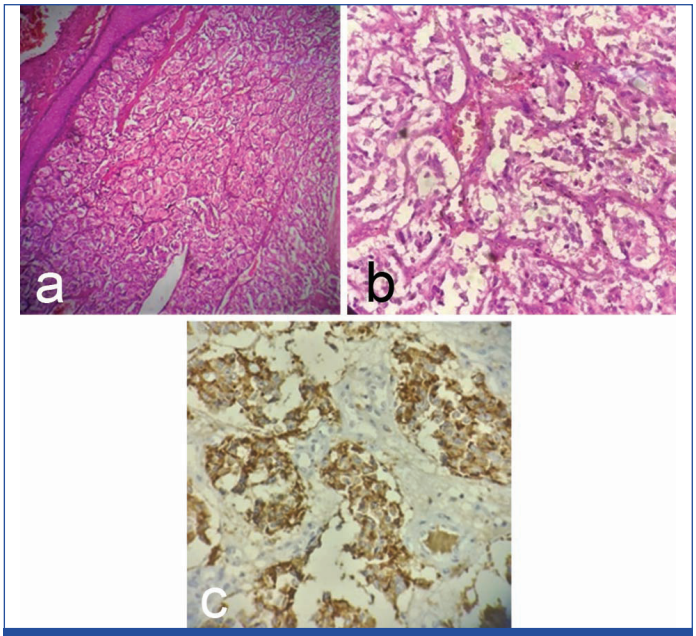
The most common presentation in paraganglionoma was pinkish pulsatile mass in 13 (100%) cases, followed by fowl smelling discharge 4 (30.76%), pulsatile tinnitus 4 (30.76%) and Chronic Suppurative Otitis Media (CSOM) and polyp 4 (30.76%). Also in schwannoma, haemangioma and squamous cell carcinoma, the most common presentation was mass in the ear [Table/Fig-3].

The most common benign tumour in present study was paraganglioma. The histopathological images of paraganglioma revealed nest and zellballen pattern of chief cells separated by vascular septa and eosinophilic granular cytoplasm. Also showed chromogranin positive for tumour cells consistent with paraganglioma [Table/Fig-4a-c]. There were three cases of haemangioma revealed capillary sized blood vessels of varying sizes lined by endothelial cells in histopathological findings [Table/Fig-5a].

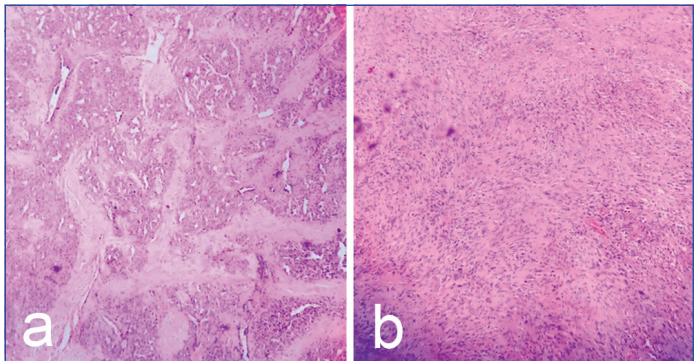
Name of the tumour	Presentation of symptoms	n, %
Paraganglioma (13)	Pinkish pulsatile mass	13 (100%)
	Foul smelling discharge	4 (30.76%)
	Pulsatile tinnitus	4 (30.76%)
	Chronic Suppurative Otitis Media (CSOM) with polyp	4 (30.76%)
	Pain in the ear	2 (15.38%)
	Conductive deafness	2 (15.38%)
Schwannoma (3)	Mass in the ear	2 (66.67%)
	Loss of hearing	1 (33.33%)
	CSOM	1 (33.33%)
	Facial nerve palsy	1 (33.33%)
Haemangioma (3)	Mass in the ear	3 (100%)
Middle ear adenoma (1)	Mass in the ear, loss of hearing	1 (100%)
Squamous cell carcinoma (6)	Mass in the ear	6 (100%)
	CSOM	3 (50%)

[Table/Fig-3]: Clinical Presentation in different tumours (N=26).

[Table/Fig-5b] showing the hypercelluar and hypocellular areas of spindle cells in three cases of haemangioma. In present study,

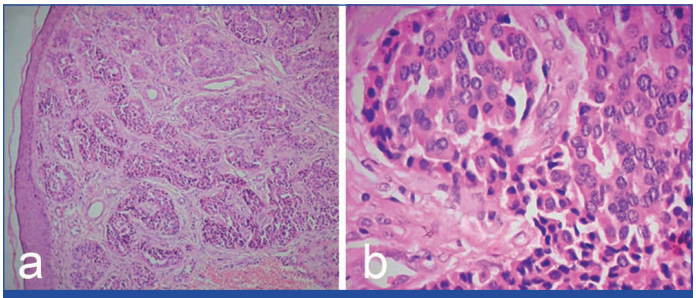


[Table/Fig-4]: a) Paraganglioma showing nest and zellballen pattern of chief cells seperated by vascular septa (H&E,10 X); b) Showing cells with eosinophilic granular cytoplasm (40X H&E); c) Chromogranin positive in tumour cells consistent with Paraganglioma (40X H&E).



[Table/Fig-5]: a) Haemangioma showing capillary sized blood vessels of varying sizes lined by endothelial cells (H&E, 20X); b) Schwannoma showing hypercelluar and hypocellular areas of spindle cells (H&E, 20X).

there was single case of middle ear adenoma. Histopathological findings of Middle Ear Adenoma (MEA) revealed sheets, nests, trabeculae of cuboidal cells with indistinct cell borders with dense eosinophilic cytoplasm and nuclei were round to oval with minimal pleomorphism, eccentric nucleus [Table/Fig-6a,b].



[Table/Fig-6]: a) Middle ear adenoma showing sheets, nests, trabeculae of cuboidal cells (H&E, 10X); b) Middle ear adenoma showing cells with indistinct cell borders with dense eosinophilic cytoplasm, nuclei are round to oval with minimal pleomorphism, eccentric nucleus and salt and pepper chromatin (H&E, 40X).

DISCUSSION

Middle ear tumours are relatively uncommon lesions present as mass in the ear, discharge, hearing loss, tinnitus, CSOM. Primary tumours from middle ear present as polyp in external auditory canal or extend intracranially or into the portions of temporal bone or skull base. In the present study 5 year duration, 560 ear biopsy specimens, only 26 were middle ear tumours accounting for 5% of all ear biopsies. Peak incidence of benign tumours was seen in the 5th decade which is similar to other studies [6,7]. The peak incidence of malignant tumours was seen in the 6th decade which is similar to other studies [5]. Male: Female ratio of benign tumours was 1:3.33 and of malignant tumours was 1:1.

In this study, most common benign middle ear tumour was paraganglioma 13 (50%) predominantly seen in females in the right ear as compared to other studies [5-9]. Paraganglioma is the most common primary middle ear tumour and the second most common tumour of the temporal bone. Glomus tumours originate in the paraganglia present throughout the temporal bone, including on the jugular dome, the promontory of the middle ear, and along the jacobson/tympanic branch of glossopharyngeal nerve (12%) and arnold nerve/auricular branch of vagus nerve (3%) [10].

Paraganglioma are subclassified according to size. These are benign slow growing and extremely vascular tumours but locally destroying the skull base structures. They can paralyse the face, spread along paths of least resistance and spread even to the brain if not treated. The most common presenting symptoms are conductive hearing loss, pulsatile tinnitus mass in the ear, blood stained discharge as compared to studies [8-11]. Large glomus tumours may also cause vertigo, facial palsy, and even sensory neural hearing loss. In rare cases, they may produce hormones, such as adrenalin, causing rapid heartbeat, headaches, flushing, sweating, and diarrhoea mimicking symptoms of hyperthyroidism and lead to confusion in diagnosis, which may be differentiated with blood investigations [12].

On otoscopy seen as presence of reddish pulsatile mass behind the tympanic membrane. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scans are the primary imaging modalities used in evaluating the size and extent of glomus tumours [13]. Microscopically jugulotympanic paragangliomas had zellballen pattern or nests of chief cells with eosinophilic cytoplasm surrounded by sustentacular cells interlaced with a rich network of capillaries and venules [14]. All 13 cases in present study showed histological features of paragangliomas confirmed with IHC using chromogranin, synaptophysin. Total 11 out of 13 cases showed intense cytoplasmic positivity with chromogranin and synaptophysin.

The three treatment modalities available for these tumours are observation with regular CT monitoring, surgical excision, and radiotherapy. The preferred treatment modality for glomus tumours is surgical excision of the tumour but because of its location and extreme vascularity, resection of this tumour can be complicated and challenging [15]. To reduce bleeding complication during surgery preoperative embolisation is done. Most promising results have been shown by radiotherapy, particularly gamma knife radiosurgery, with good tumour growth control and less risk of cranial nerve injury [15].

In present study, three cases of haemangioma were diagnosed which showed slit like vessels lined by endothelial cells. Total 15 cases of isolated middle ear haemangiomas have been reported in the literature till date [16]. A study reported that vascular lesions of temporal bone constitute both haemangiomas and vascular malformations [17]. The extensive blood supply surrounding scarpa's ganglion and the geniculate ganglion makes this region more susceptible to these tumours [17].

There were three cases of schwannoma with female preponderance and facial palsy in 50% cases as compared to other study [18]. Middle ear schwannoma arises from the facial nerve, and its branches: the tympanic branch of the glossopharyngeal nerve/ jacobsons nerve and the auricular branch of the vagus nerve/ arnolds nerve, the chorda tympani; the stapedial nerve. In cases of facial nerve schwannoma, High Resolution Computed Tomography (HRCT) scan shows enlargement of the fallopian canal with hypodense lesion in middle ear with ossicular erosion and erosion of stylomastoid foramen which are nonspecific, also seen in paraganglioma and cholesteatoma [19].

In present study, authors encountered one rare case of middle ear adenoma with neuroendocrine differentiation which occurred in fifth decade and presented with hearing loss as compared to other studies [20-22]. Middle ear adenomas are rare constituting less than 2% of all ear tumours. Hyams VJ and Michaels L, first described these tumours in 1976. Middle ear adenomas are rare glandular neoplasms that may have originated from the mucosal epithelium of the middle ear or neural crest precursor [20]. In 1980, Murphy GF et al., described a similar tumour named as carcinoid tumour due to the ultrastructural evidence of a neuroendocrine differentiation. In the literature till date, there is still much debate about the true nature of these neoplasms [21].They are same tumours with different degrees of glandular and neuroendocrine differentiation, are named as neuroendocrine adenoma of the middle ear by Derlacki EL and Barney PL, in 1976 [22]. In 1980, although benign, it may show metastasis as described by Mooney EE et al., [23].

The middle ear adenoma neuroendocrine differentiation presents with aural fullness, tinnitus, otorrhea, unilateral conductive hearing loss, otalgia, and facial nerve palsy. They rarely present with symptoms of carcinoid syndrome. On otoscopic examination seen as bulged tympanic membrane with reddish to whitish mass [24]. The patient in current study presented with complaints of fullness, tinnitus and mass in the right ear and hearing loss. In present study, middle ear adenoma is composed of glandular or tubular formation,solid sheets, nests, cribriform pattern, trabeculae of cuboidal cells with indistinct cell borders with dense eosinophilic cytoplasm, nuclei are round to oval with minimal pleomorphism, eccentric nucleus and salt and pepper chromatin consistent with neuroendocrine origin, stroma is fibrotic [21,25].

Tumour cells are characteristically positive for epithelial markers like cytokeratin, predominantly CK7 (89.6%), CAM 5.2. Neuroendocrine markers like chromogranin-A, neuron specific enolase, synaptophysin [23,26]. The main differential diagnosis of middle ear adenoma neuroendocrine differentiation, is paraganglioma. Immunohistochemical staining for cytokeratin can help to differentiate the two lesions. Paraganglioma is negative for cytokeratin

Complete surgical removal of the tumour mass with negative margins and careful long term follow-up is the treatment of choice [23,26]. Majority of these tumours are benign with local recurrence of 12-18% due to incomplete removal of the tumour or the involvement of the ossicular chain. Therefore, careful follow-up is mandatory. Subsequent surgery to remove the other involved structures may result in better clinical outcome [25].

In present study, squamous cell carcinoma was the most common malignant tumour in the middle ear occurring in the 6th decade as compared to study done by Shu MT et al., [4]. Microscopy of all cases showed the features of well differentiated squamous Cell carcinomas. Malignant tumours arising in the middle ear are rare, accounting for only 0.25% of the malignant tumours in this region, and with a low incidence rate of approximately 0.03% [27]. The classical symptoms are mucopurulent or blood stained ear discharge, intractable pain, sudden deafness, facial palsy and rarely other symptoms of inner ear damage. The common age range of presentation is between the 5th-6th decade. The pre-existing CSOM with or without cholesteatoma delays the diagnosis and poses diagnostic and therapeutic problem. As per literature, 75-85% of primary middle ear carcinomas occur secondary to chronic supportive otitis media which may be due to metaplasia of the middle ear mucosa caused by chronic inflammation [28-30]. In the present study, four patients had a history of chronic suppurative otitis media of more than 30 years duration as compared to other studies [31].

Histopathology confirmation of masses and polyps is of clinical significance in early diagnosis and treatment [32]. Squamous cell carcinoma in the early stage is curable and in the advanced stage, surgical resection with radiotherapy and chemotherapy can improve the survival. The factors which favor poor prognosis are involvement of facial nerve, margins, dural involvement, severe pain and regional lymph node involvement. Most of these malignant tumours need to be excised properly but are difficult because of intracranial extension [33].

Limitation(s)

As the study was a retrospective study with a small sample size due to rarity, detailed evaluation could not be done, so, a study with larger number may be necessary for knowing the aetiological risk factors, predisposition and complete understanding of these tumours for better patient outcome.

CONCLUSION(S)

Middle ear neoplasms are important differential diagnoses of middle ear infections and masses. Benign tumours are more common than malignant tumours in the middle ear. Histological diagnosis and confirmation with immunohistochemistry is needed in all middle ear tumours as clinical and radiological findings are non specific. In the majority of the cases, surgical excision with careful follow-up is needed to prevent recurrence. The aetiological factors in primary middle ear carcinomas are unknown but one cause is CSOM can lead to squamous cell carcinoma in elderly patients due to metaplasia in the middle ear caused by inflammation. Future studies with more number of cases and long duration is necessary to provide knowledge about the clinical, biologic behaviour, recurrence and metastatic potential of these middle ear tumours for better management.

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