Review Article

Oncocytoma: A Mystifying Parotid Gland Tumour

Al Mamun MA[1], Islam MR[2], Majumder RA[3], Amin MN[4], Anowar MA[5], Mahbub MR[6], Ashaduzzaman M[7]

ABSTRACT

Oncocytoma is a rare salivary gland tumor consisting of oncocytes with many hyperplastic mitochondria. It usually occurs in the parotid gland. Very few cases of parotid oncocytoma have been reported in literature. Because of its rarity (<1-2% of salivary gland tumors) and clinical presentation of the tumor. Clinical diagnosis is often challenging due to the likeness of oncocytoma to other benign and low-grade malignant salivary gland tumors there is a tendency among the clinicians to misdiagnose it as pleomorphic adenoma, hemangioma, or other forms of oncocytosis. Previously published articles had all agreed on the reality of this lesion occurring over the parotid gland. The paper aims to review previously published cases of oncoytoma to provide a better insight regarding demographic, clinicopathological, radiological and histological features of this rare tumor of parotid gland. A systemic review of English literature was performed after using a sensitive search strategy involving two different databases: google scholar and PubMed. A total number of 9 cases were included. The tumour is mostly presented in old age as a slowly growing tumour (mean duration 3.17 years) and showed a slightly higher female predominance (Female:Male=1.25:1). They were mostly located over superficial lobe,100%. Conventional histological variant has only been reported. Complete surgical excision was performed for all the cases without any reports of recurrence or malignant transformation. Imaging studies diagnosed the lesion as a benign tumor. Only histopathological examination can confirm it. Definitive histology examination concludes to oncocytoma. Furthermore, our aim is to bring to the forefront how these lesions require a comprehensive workup and how to choose the best treatment strategy.

Keywords: *Oncocytoma, parotid, hemangioma, pleomorphic adenoma, superficial parotidectomy*

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INTRODUCTION

Salivary gland neoplasm represents the most complex and diverse group of tumors encountered by head and neck surgeons. Their diagnosis and management are complicated by their relative infrequency (1% of head and neck tumors), the limited amount of pretreatment information available, and wide range of biological behavior seen[1]. The parotid gland is the most frequent site (80%) for all salivary gland tumours. Oncocytoma are rare tumors. Most oncocytomas arise in the parotid gland. Oncocytomas are benign epithelial tumors that most commonly occur between

1. Dr. Md. Abdullah Al Mamun, Assistant Professor, Department of Otorhinolaryngology and Head-Neck Surgery, Mugda Medical College & Hospital, Dhaka-1214.
2. Dr. Md. Rabiul Islam, Associate Professor and Head, Department of Otorhinolaryngology and Head- Neck Surgery, Mugda Medical College & Hospital, Dhaka-1214.
3. Dr. Riashat Azim Majumder, Medical Officer, Department of Otorhinolaryngology and Head- Neck Surgery, Mugda Medical College Hospital, Dhaka-1214.
4. Dr. Mohammad Nurul Amin, Assistant Professor, Department of Endocrinology, Mugda Medical College & Hospital, Dhaka-1214.
5. Dr. Md. Asif Anowar, Assistant Professor, Department of Otorhinolaryngology and Head-Neck Surgery, Nilphamari Medical College Hospital, Nilphamari-5300.
6. Dr. Md. Rashid E Mahbub, Assistant Professor, Department of Otorhinolaryngology and Head-Neck Surgery, Rangpur Medical College Hospital, Rangpur-5400.
7. Dr. Mohmmad Ashaduzzaman, Assistant Professor, Department of Hepatology, Mugda Medical College & Hospital, Dhaka-1214.

Address of correspondence: Dr. Md. Abdullah Al Mamun, Assistant Professor, Department of Otorhinolaryngology and Head-Neck Surgery, Mugda Medical College & Hospital, Dhaka-1214. Email: mamunmail24@gmail.com

the sixth through the eighth decades of life with a slightly higher incidence in women. They often present as solitary slow growing painless masses, which are firm, multilobulated and mobile entities upon clinical examination and may rarely be bilateral[2]. It is important to note that even though oncocytoma of the parotid is the most common of salivary gland tumours, is only 1-2% of head and neck tumours[3] and with the associated vague complaints by patients and ambiguous fine needle aspiration cytology (FNAC), there is a tendency to either entirely miss it or diagnose it wrongly. Diagnosis is suggested by imaging. Computed tomography (CT) and magnetic resonance imaging (MRI) are the image modalities of choice and on CT, the most common finding is a well-defined homogeneous parotid mass.[4-6] On MRI, these tumors appear hypodense on T1 and T2 sequences. The preferred treatment is complete surgical excision and total parotidectomy Diagnostic confirmation is histological after parotidectomy[3,4]. In addition, a follow-up MRI at 12 and 24 months are recommended to assess patient progression.

CASE SUMMARY

A 67-year-old male reported to the Ear, Nose and Throat (ENT) outpatient department of Mugda Medical College Hospital, Dhaka, with a mass at the right parotid region which had an insidious onset but not increasing in size for the last 4 years. The patient had no other significant complaints. On examination, a solitary 4 cm × 3 cm sized right parotid mass. It was a non-tender, non-fluctuant, non-pulsatile swelling with regular margins. It was not adherent to overlying skin or underlying structures. There were no palpable cervical lymph nodes, and no signs of facial palsy were seen. The Stensen's canal orifice was free at the intraoral exam. Ultrasound exam showed a well circumscribed 4x3 cm a lobulated mass of superficial lobe of the right parotid gland. This lesion was hypoechoic and vascularized (Fig. 1). FNAC report was suggestive of pleomorphic adenoma. On contrast enhanced computerized tomography (CECT), A T2W1 hetregenously rounded hyperdense lesion of 4x3x3 cm in the superficial lobe of the right parotid was seen with moderate enhancement observed after intravenous contrast media injection. A fairly large T1W1 hypodense multiple internal necrotic areas were present which according to radiologist could be benign parotid

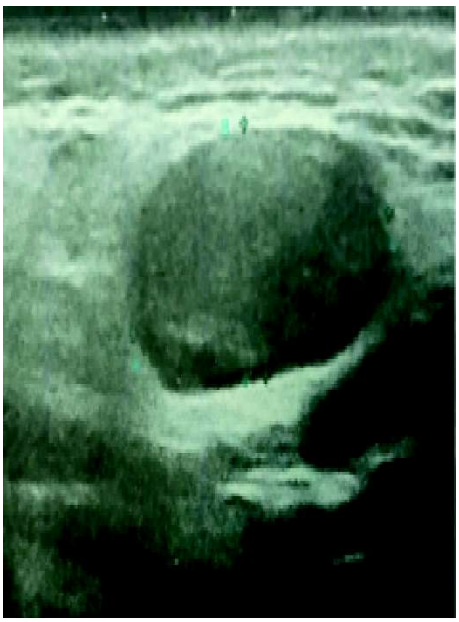

Fig. 1: *Parotid ultrasonography shows a 4 cm × 3 cm well-circumscribed mass of the superficial lobe of the right parotid gland. The mass is hypoechoic.*

neoplasm, hemangioma, or enlarged lymph node. The morphology of the left parotid gland, bilateral submaxillary glands, jugulodigastric and left periparotid nonspecific lymph nodes were also intact (Fig. 2). Magnetic resonance imaging (MRI) showed a hyposignal lesion on T1-weighted imaging of the superficial portion of the right parotid gland with

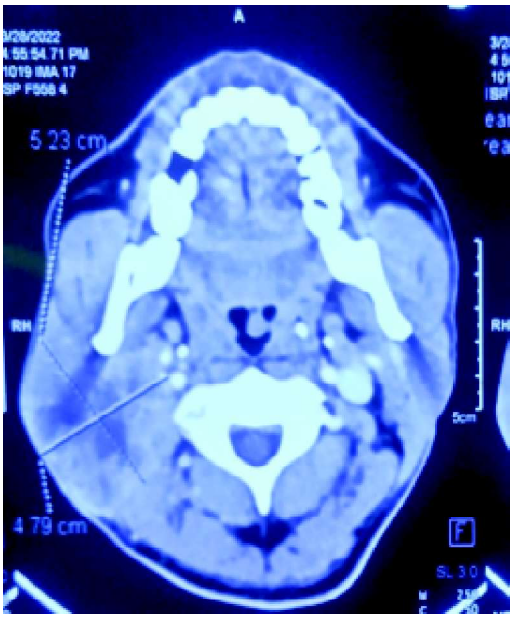

Fig. 2: *Contrast enhanced computerized tomography of the head and neck showing a rounded hyperdense lesion in the superficial lobe of the right parotid.*

homogenous enhancement after gadolinium. The mass was slight hypersignal on T2-weighted imaging. (Fig. 3) Based on the above-mentioned findings, a provisional diagnosis of oncocytoma in the right parotid was made with benign parotid tumour. The patient underwent superficial parotidectomy with complete tumor excision and facial nerve preservation. Frozen section examination was not

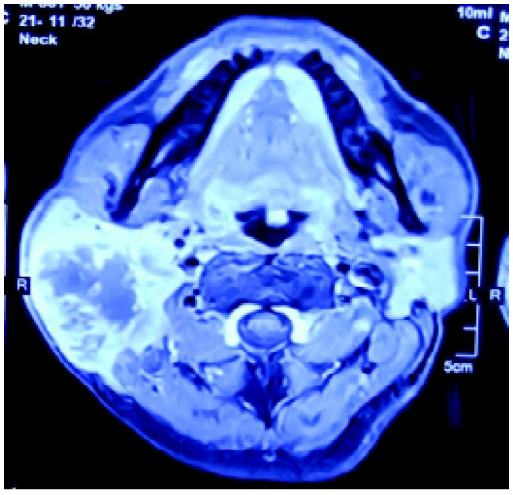

Fig. 3: *MRI in T1-weighted sequences shows mass of the superficial lobe of the right parotid gland; with homogenous enhancement after gadolinium injection.*

contributive. We decided not to complete parotid excision and waited for definitive histology. complications were observed after surgery, particularly no facial nerve palsy. (Fig.-4) (identification and preservation of the facial nerve). Excised mass was sent for histopathological examination, which confirmed it as oncocytoma

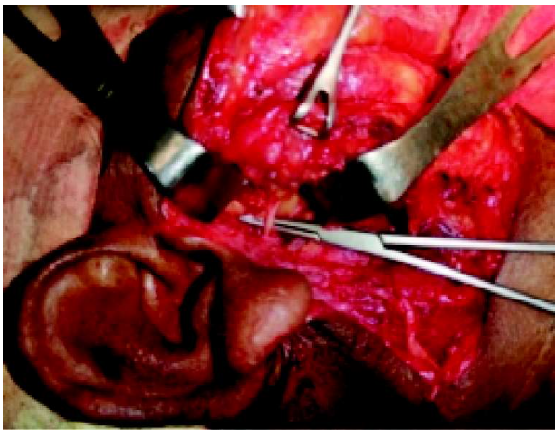

Fig. 4: *Identification and preservation of the facial nerve and its terminal branches.*

(oxyphilic adenoma). Grossly, the resected specimen measured 4 cm×3 cm×2 cm in size (Fig. 5). Macroscopically, the tumor was a nodular, circumscribed lesion measuring 2 cm × 2 cm × 1.5 cm in size and irregular nodular grayish white tissue with fibrofatty tissue in color. Microscopic findings

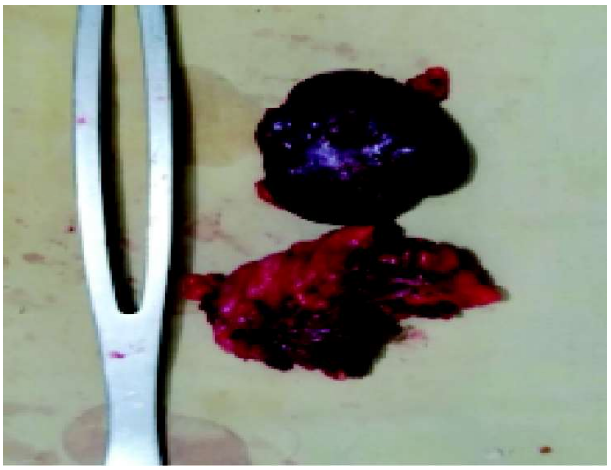

Fig. 5: *Resected right parotid region tumour.*

show capsulated tumor composed of lobules of oncocytic cells are arranged in sheets and trabecular form (Fig.-6). The cells were large and round with abundant granular eosinophilic cytoplasm (Fig.-7). No mitotic figures were noted. These features are confirmed the diagnosis consistent with salivary gland tissue oncocytoma. The patient has been on follow up and has remained disease free with no local or remote recurrence of the disease at present.

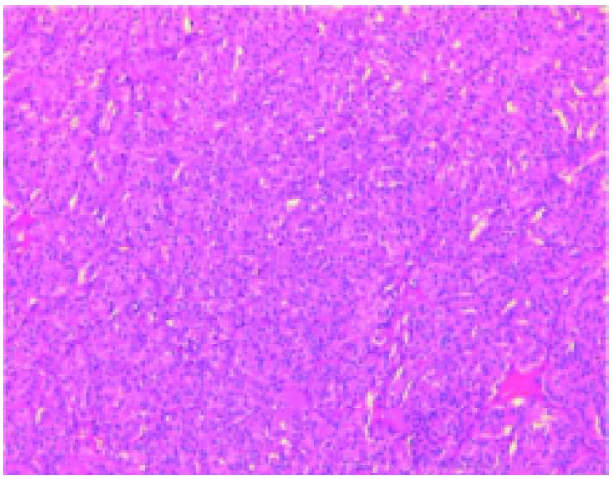

Fig. 6: *Sheets or trabeculae, patterns of monotonous large polygonal cells with well-defined cell borders, deeply eosinophilic and granular cytoplasm (H&E, ×100).*

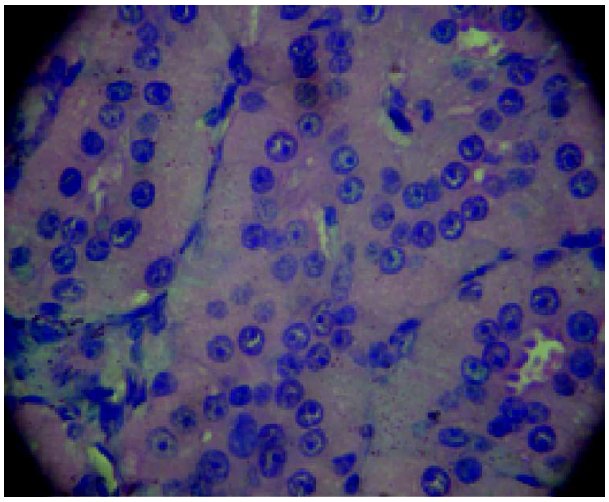

Fig. 7: *Large round oncocytes with abundant granular eosinophilic cytoplasm.*

METHODS

An extensive search of two medical databases (Google Scholar and PubMed) was performed between October and December 2022. The databases were searched for full length articles and abstracts published in the English language and confined to human subjects, using the following Medical Subject Headings (MeSH): ''Oncocytoma'' AND/ OR ''Oncocytosis'' AND/OR ''Parotid tumour''. Included articles were either an isolated case report or a single case report with review of literature and only reported a lesion confined to the parotid. Case reports with a lesion extending to surrounding structures such as the facial nerve, neck lymph node, neck great vessels, skin were excluded. No age, race or demographic filters were applied. Information from the included articles were collected on the basis of general outline of oncocytoma parotid, age, sex, other organ involvement, pathology and pathogenesis, clinical presentation, FNAC findings, ultrasonographs and radiological findings, operative surgical procedure, postoperative adjuvant therapy and recurrence of tumour and reflected in our discussion.

RESULTS

A total of nine cases were included in the current review. From the included article general outline of oncocytoma, age, sex, clinical presentation, pathogenesis, cytological, histopathological and treatment findings were documented. The cases were reported from eight different countries: India, UK, USA, German, Cyprus, Taiwan, Japan, Korea Out of nine included cases five were female (55.56%) and 4(44.44%) were male. The ages range was 35-70 years (52.22 mean) The mean duration of lesion was 3.17 years (6 months to 10 years, SD 2.87).The mean largest dimension of the lesion was 29.63 mm(17-39 mm, SD 8.7). The tumour was involved in one gland, either right (5 cases) or left parotid gland (4 cases).[4] Among the nine lesion 3 involved upper quadrant, 6 involved mid and lower quadrant of parotid gland of superficial lobe.[6,7] All cases with the exception of one presented symptomatically with a painless lump. Hamada et al. reported intermittent pain over the lump. There were reports of neurological symptoms such as facial palsy of one case.[3] A majority of the lesions were firm, nontender and or mobile. Tenderness over the tumor site was reported from one case and a soft/soft firm lesion on palpation was reported twice[8-10]. Overlying skin ulceration was not noted it in any tumor. The observations imply a good encapsulation of the tumor in all cases. Various preoperative differentials were considered by the authors these included pleomorphic adenoma, Warthin tumour, low grade adenocarcinoma[9,10]. For diagnostic purpose FNAC is the procedure of choice. For its overlapping morphological features diagnosis by cytology alone often become difficult[11-14]. All cases FNAC diagnosis were parotid gland origin tumor like pleomorphic adenoma, oncocytosis or oncocytoma[15-17]. Histopathology remains the gold standard to clinch the precise diagnosis. In our review of literature of nine cases by histopathological diagnosis all cases were final diagnosis as oncocytoma of parotid gland. In case of treatment complete surgical excision was employed in all nine cases of review literature with superficial parotidectomy or total conservative parotidectomy. No adjuvant treatment like chemotherapy or radiotherapy was employed because of benign nature of this disease. No recurrence or malignant transformations were reported in nine cases of review of literature.

DISCUSSION

Salivary gland tumors account for 3% of head and neck lesions and approximately 80% of these occur in the parotid gland[5,6]. The majority of parotid gland tumors are located in the superficial lobe and some investigations have reported that 2–4% of parotid tumors originate from the deep lobe. A total of 80-90% of these are benign, mixed tumors and the others

are adenoid cystic, mucoepidermoid, acinic cell carcinomas and lipomas[7].

The word "oncocyte" was first introduced in 1931 by Hamperl[3]. Oncocytomas are rare tumors that account for 0.1-1.5% of salivary gland tumors and 2.3% of benign epithelial salivary gland neoplasms[3,4,8]. Oncocytomas were first described by Jaffe in 1932[4]. The parotid is the most commonly involved gland accounting for 78-84% of salivary gland oncocytomas[4]. Oncocytomas are benign epithelial tumors characterized by oncocytes with eosinophilic granular cytoplasm that contains mitochondria. Oncocytic cells are thought to originate from the transformation of epithelial cells of salivary gland ducts or acini[9]. They occur most commonly in the sixth to eighth decades and are slightly predominant in female gender[4].

Although malignant transformation of this tumor is unusual, clinical follow-up is important because malignant oncocytoma may not be correctly diagnosed owing to histological similarities with benign oncocytoma[10]. The correlation of certain viruses, such as Epstein–Barr virus, HIV, human herpesvirus 8, human T lymphotropic virus 1, and human papillomavirus with parotid neoplasia has been documented. Vlachaki et al. described the case of a 74-year-old female patient with left parotid oncocytoma and a previous history of immune thrombocytopenia and chronic HBV infection[6]. In our case, there was no history of viral infection or thrombocytopenia in the patient.

Oncocytes are seen in various organs such as salivary glands, thyroid, parathyroid, pituitary, nasal cavity, sinuses, ocular carbuncle, lacrimal glands, buccal mucosa, eustachian tube, larynx, esophagus, liver, pancreas, and kidney[11].

Clinical presentation of oncocytomas is similar to other benign salivary tumors with no specificity. They present as lobulated and mobile mass.[8] Bilateralism is observed in 7% of cases[12]. The newest World Health Organization (WHO) classification describes three entities: nodular oncocytic hyperplasia, oncocytoma and oncocytic carcinoma[13]. In previous cases, as revealed by electron microscopy, the oncocytes contained unusually large number of mitochondria[13-15]. Oncocytic cells are thought of as metaplastic cells formed in response to adverse changes, with the normal cells losing their original specialization. Aging is also thought to cause a functional exhaustion of mitochondrial enzymes, and a compensatory hyperplasia of mitochondria can occur, which, in turn, is responsible for the oncocytic change. Indeed, solitary oncocytes appear most often as incidental findings in aging salivary tissue, with studies showing up to 80% presence in persons older than 70 years of age[11]. In our case, the age of patient was 67 years which points toward the progressive degeneration of salivary epithelial cells which lead to oncocytic changes[16].

Areas of oncocytic metaplasia can be seen in a host of salivary gland tumors such as basal cell adenoma, pleomorphic adenoma, myoepithelioma, cystadenoma, canalicular adenoma, polymorphous low-grade adenocarcinoma, Warthin's tumor, acinic cell carcinoma and mucoepidermoid carcinoma[16,17]. However, oncocytes also give rise to neoplasms such as oncocytoma and its malignant counterpart, the oncocytic carcinoma[18]. Histopathological findings in our case are typical of a benign oncocytic neoplasm which points toward the fact that prolonged follow up may not be necessary.

Fine needle aspiration is the procedure of choice for making a diagnosis in the majority of cases although its sensitivity is reported to be only 29%[16]. FNAC has increasingly been used as a primary screening tool for salivary gland lesions with high levels of sensitivity and specificity. However, as salivary glands are notorious for having overlapped morphological features, diagnosis by cytology alone often becomes difficult[2]. The situation may slightly improve using multiple passes from the swelling.

Diouf et al. reported a case of oncocytoma of the left parotid gland in a 69-year-old woman in whom FNAC was for a pleomorphic adenoma. Through this case, they highlighted the importance of histopathology in the positive diagnosis of parotid oncocytoma as well as in its differential diagnosis and also the place of FNAC[17].

Histopathology remains the gold standard to clinch the precise diagnosis. Chakrabarti et al. presented a case of a cytologically diagnosed oncocytic lesion with a possibility of oncocytoma. However, on subsequent histopathology, the lesion was diagnosed as diffuse hyperplastic oncocytosis. In our case, the FNAC was clearly suggestive of pleomorphic adenoma and after histopathological examination, oncocytoma was confirmed[18]. The ultrasound features of parotid oncocytomas are not specific and

include a hypoechoic mass with well-defined margins, like other benign parotid tumors such as pleomorphic adenomas[19].

CT and conventional MRI are presently the image modalities of choice used in the evaluation of both palpable and non-palpable neck lesions[20]. It is important to decide whether a mass is superficial or deep and if it affects the facial nerve. A frequently used landmark is the retromandibular vein. The facial nerve lies laterally and obliquely to this vein and can be seen on CT and MRI studies. Other considerations for the selection of additional imaging studies include involvement of adjacent tissues, perineural involvement and lymphadenopathy[1].

Technetium-99m pertechnetate scintigraphy (salivary scintigraphy) is useful to evaluate parotid gland masses. There are two ways to explain the mechanism of increasing the uptake of technetium-99m pertechnetate by oncocytoma. There is accumulation in cystic spaces due to the absence of intralobular duct. Another theory is that technetiun-99m pertechnatate can concentrate inside the tumor because the cells cannot excrete so much, meaning that the uptake is prolonged [9].

CT has been established as the first-line image modality in the assessment of major salivary gland tumors [8]. Oncocytomas and Warthin's tumors have very similar imaging features; thus, they are indistinguishable in standard CT and MR images[21]. The common CT finding of the parotid oncocytomas described in the literature is a well-defined parotid mass showing homogeneous enhancement. The reports on MRI imaging of parotid oncocytomas describe these tumors as appearing hypodense on both T1 and T2 sequences. This has been attributed to the high cellularity and low water content displaying homogeneous contrast enhancement[4,7-9]. Due to their low prevalence, only few case reports on the MRI features of parotid oncocytomas are available in the published literature[8,10]. In the literature, MRI characteristic of parotid oncocytoma is well-defined parotid mass with homogeneous enhancement. The important differential diagnoses for well-defined enhancing parotid tumors seen on MRI include the Warthin's tumor and basal cell adenomas[9].

Complete surgical excision with radical or superficial parotidectomy are the treatments of choice[6,8,9]. The extent of the excision is dictated by preoperative clinical and radiological (CT, MR) examinations and intraoperative findings[9]. In addition, radiotherapy may play an important role in the management of locally advanced, unresectable, or recurrent salivary gland cancers when surgery is not feasible. Although radiotherapy can be very effective in achieving tumor shrinkage and providing symptomatic relief, curative non-operative approaches have been challenging[22]. There is no need for adjuvant treatment such us chemotherapy and/or radiotherapy because of benign nature and slow growth rate of the tumour[23].

The use of systemic chemotherapy in advanced salivary gland cancer has in general been confined to those patients with advanced and incurable disease. Literature has reported results from clinical trials using a number of different chemotherapeutic agents often found in mixed populations, including patients with different histologic subtypes. Cisplatin based regimens have been the most frequently explored, but the response rates have been modest, and the impact on survival rate has been impossible to discern[9,24].

Perhaps of greater interest in recent years has been the attempt to use our increasing understanding of the biology of these tumors to identify specific molecular targets that might be amenable to molecularly targeted therapies. Although potential molecular targets have been identified, the results using this approach have been disappointing[24-27]. The recurrence rate has been reported to be 20–30%[6,9] or less than 20%[10] in incomplete excision or multinodularity cases. Interestingly, malignant differentiation and metastasis are rare[6,9].

CONCLUSION

Parotid oncocytoma is benign epithelial tumor that frequently occurs between the sixth and the eighth decades of life. Clinical presentation is not specific with a parotid gland swelling and solid solitary mass on palpation. Oncocytoma should be assessed using MRI studies to evaluate the extending of the tumor. Upon histological verification, a surgical approach should be considered to eradicate the tumor and remove the parotid gland. Follow-up MRI studies are recommended at 12 and 24 months after treatment since most head and neck tumors recur within the first 2 years.

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