Acta Otorrinolaringol Esp. 2009;**60(2):**120-5

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

Tumoral pathology of salivary glands. Our experience

María Teresa Lahoz Zamarro,[a,*] Agustín Galve Royo,[b] and Fernando Galve Royo[b]

[a]*Servicio de Otorrinolaringología, Hospital Obispo Polanco, Teruel, Spain*
[b]*Medicina de Familia, Teruel, Spain*

Received June 23, 2008; accepted October 28, 2008

KEY WORDS
Major and minor salivary gland tumours;
Parotid gland;
Submaxillary gland

Abstract
Introduction and objectives: We report a descriptive epidemiologic study of 63 patients with major and minor salivary gland tumours diagnosed at our centre over the last 10 years.
Methods: The data collected from all patients included gender, age, location, histopathology, diagnostic procedures, treatment, and follow-up.
Results: Among the 38 males and 25 females, we found 39 with benign tumours and 24 with malignant tumours. Most of these tumours (42; 67%) arose in the parotid gland, 12 (19%) in the submaxillary gland, 7 (11%) in the palate, and 2 (3%) in external auditory canal. The mean age was 54 years for benign tumours and 80 years for malignant ones. The most common benign tumours found were pleomorphic adenomas (67%) whereas squamous cell carcinoma (54%) followed by lymphomas (25%) were the most frequent among malignant tumours.
Conclusions: We have found 2 main differences with previously reported studies: the elevated mean age of patients with malignant tumours and, probably as a result of this advanced age, the high incidence of squamous cell carcinoma due to metastatic dissemination of skin cancers.

PALABRAS CLAVE
Tumores de glándulas salivales mayores y menores;
Glándula parótida;
Glándula submaxilar

Afección tumoral de las glándulas salivales. Nuestra experiencia

Resumen
Introducción y objetivos: Presentamos un estudio epidemiológico descriptivo de 63 pacientes con tumores de glándulas salivales mayores y menores diagnosticados en nuestro hospital en los últimos 10 años.
Métodos: Hemos recogido, de todos los pacientes, edad, sexo, localización, histopatología, métodos de diagnóstico, tratamiento y supervivencia.

*Corresponding author.
E-mail address: agalveroyo@hotmail.com (M.T. Lahoz Zamarro).

0001-6519/$ - see front matter

Resultados: Se trata de 38 varones y 25 mujeres, con 39 tumores benignos y 24 malignos. En su mayoría aparecieron en la glándula parótida (42; 67%), 12 (19%) en la submaxilar, 7 (11%) en el paladar y 2 (3%) en el conducto auditivo externo. La media de edad era 54 años en los pacientes con tumor benigno y 80 en aquellos con tumor malignos. Los más frecuentes fueron: adenoma pleomorfo, que representa el 67%de los tumores benignos, y carcinoma epidermoide (54%) entre los malignos, seguido por linfoma (25%).
Conclusiones: Encontramos dos diferencias principales con la literatura revisada: la elevada media de edad de los pacientes con tumores malignos y, probablemente debido a ello, la gran incidencia de carcinomas escamosos por diseminación metastásica de cánceres cutáneos.

Introduction

Salivary gland tumours represent 3% of head and neck tumours. The average age of onset is 45 years, with a higher frequency in the fifth and sixth decade and a higher age for malignant tumours than for benign. The usually long time between the onset of clinical signs and the first consultation is characteristic.

The parotid gland is the most common location, followed by the submandibular gland and accessory salivary glands, without any aetiological factor being identified.

Three quarters of the tumours are benign; the pleomorphic adenoma is the most frequent. Malignant tumours of the submaxillary and the accessory salivary glands have a much worse prognosis than that of parotid tumours.

Methods

We conducted a study of tumours of the salivary glands observed in our department between 1997 and 2007. First we carried out a general study and then separated the cases depending on the involvement of the parotid or submandibular glands or the accessory glands of the soft palate. We present the clinical data of 63 patients and for all of them we collect age, gender, location, histopathology, diagnostic methods, treatment, and survival. This is a descriptive epidemiological study in which we present the number and percentages of patients.

Results

In that time we have diagnosed 63 salivary gland tumours, 2 of them in ectopic glands; 39 were benign and 24 malignant. The majority (42) appeared in the parotid, followed by the submaxillary (12) and soft palate (7). The 2 ectopic tumours appeared in the external auditory canal (Figure 1).

The mean age of patients with benign tumours was 54 years, compared with 80 years in patients with malignant tumours. By glands, ages were 57 and 80 years, respectively, in the parotid; 50 and 83, in the submaxillary, and 49 and 75 years in the soft palate (Figure 2). With regard to gender,

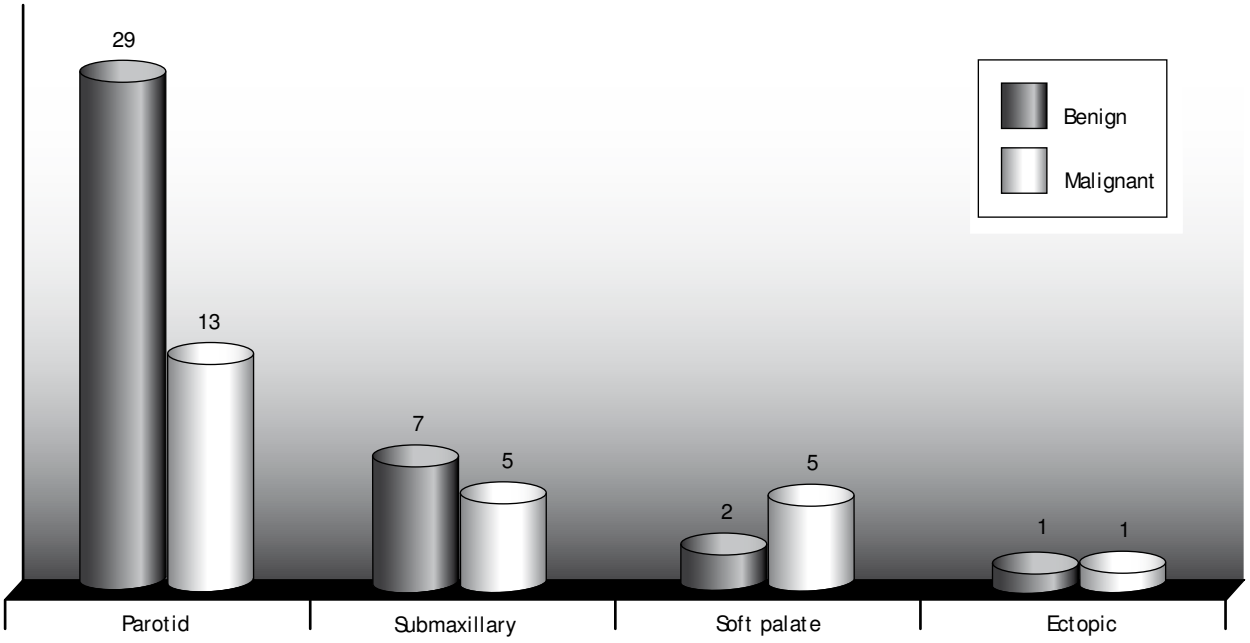

Figure 1 Location of the tumours of the salivary glands.

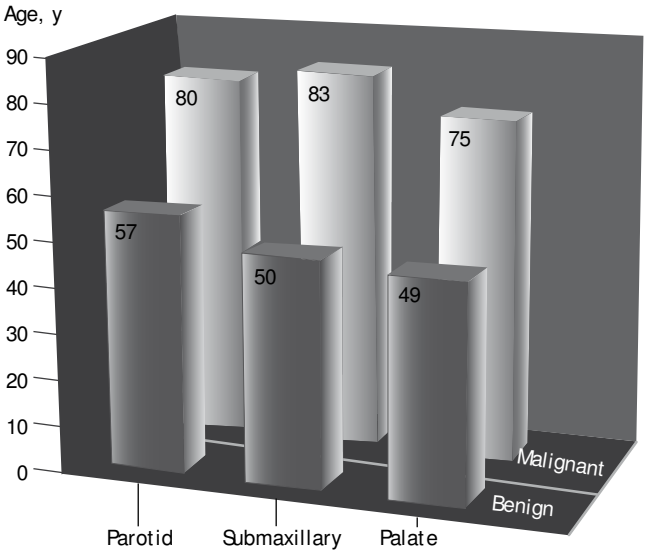

Figure 2 Mean age of patients with benign and malignant tumours.

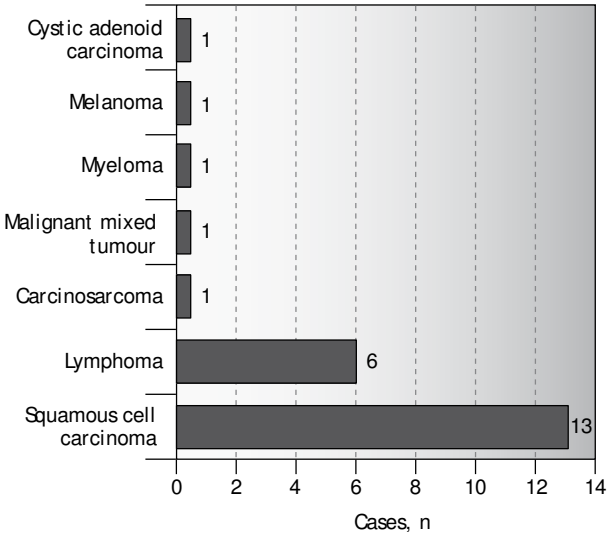

Figure 4 Pathology of malignant tumours.

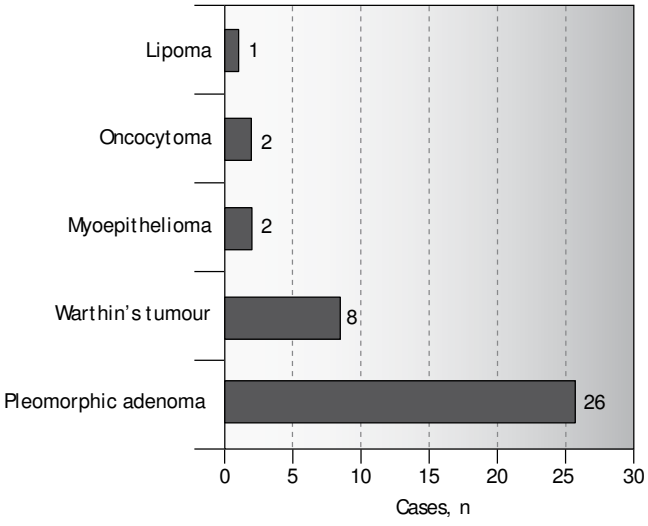

Figure 3 Pathology of benign tumours.

24 males and 15 females had benign tumours and 14 males and 10 females, malignant; in total, 38 versus 25.

Histopathology showed that most were pleomorphic adenomas (26 cases; 67%), followed by Warthin's tumours (8 cases; 20%) and in fewer number, oncocytomas (2 cases; 5%), myoepitheliomas (another 2) and 1 lipoma (3%) (Figure 3). Among the malignant tumours, squamous cell carcinomas were the most frequent (13 cases; 54%), followed by lymphomas (6 cases; 25%), whereas for other types, carcinosarcoma, malignant mixed tumour, myeloma, melanoma, and cystic adenoid carcinoma, there was only 1 patient of each (Figure 4).

The parotid gland was the most affected (67%), with 18 pleomorphic adenomas, 7 Warthin's tumours, 2 myoepitheliomas, 1 oncocytoma, and 1 lipoma, as benign tumours. Among the malignant we highlight 6 squamous cell carcinomas, 5 lymphomas, 1 carcinosarcoma, and 1 malignant mixed tumour.

In the submandibular gland (19%), there were 5 mixed tumours, 1 oncocytoma, 1 Warthin's tumour, and, among the malignant tumours, 4 squamous cell carcinomas and 1 myeloma.

In the soft palate (11%), the 2 benign tumours were pleomorphic adenomas, and the malignancies included 3 squamous cell carcinomas, 1 melanoma, and 1 lymphoma.

The ectopic tumours (3%) were 1 pleomorphic adenoma and 1 adenoid cystic carcinoma.

Diagnosis was made by fine needle aspiration (FNA) and in cases of doubt, we requested an ultrasound or a computed tomography (CT) (Figure 5). There were 3 failures in the FNA, in one case a pleomorphic adenoma was diagnosed when in fact it was a chronic sialoadenitis; in another, the diagnosis was sialoadenitis while the CT and the intervention discovered a malignant tumour of the deep lobe of the parotid gland. In the third case, the FNA diagnosis was squamous cell carcinoma but the post-operative analysis revealed lymphoma.

Of the 39 patients with benign tumours, 4 refused treatment due to poor general condition or did not accept the procedure. The others were operated on: 7 had total superficial parotidectomies, 15 partial superficial parotidectomies, 4 extracapsular tumour dissections, 7 submaxillectomies, and 2 resections of tumours from velum of the soft palate. As a complication, we had Frey's syndrome in 2 cases of superficial total parotidectomy, and 2 salivary fistulas that resolved spontaneously.

We have had a recurrence of pleomorphic adenoma in the parotid gland and another in the submaxillary gland; the latter is a multifocal tumour in a 30-year-old patient who has been operated on 3 times, and multiple tumour nodules have been found in each operation (Figure 6).

Of the 24 patients with malignant tumours, 13 affected the parotid gland. The 5 patients with lymphoma received chemotherapy, and one who had been diagnosed

by FNA with squamous cell carcinoma, underwent a total parotidectomy. In the rest we performed 7 total parotidectomies and 1 superficial parotidectomy. Within the total parotidectomies, in 4 it was necessary to remove the superjacent skin and perform rotation flaps to close the skin defect. We also carried out cervical dissection in 3 cases and 6 patients received radiation therapy. In the 5 patients with submaxillary tumours, we performed 3 submaxillectomies with wide resection margins, 1 patient received chemotherapy and another did not agree to be operated on. Of the 5 malignant tumours of the soft palate, we performed 2 surgical resections, 1 patient was not treated due to advanced age and another 2 were referred to another facility. The carcinoma of the external auditory canal was also resected with wide margins.

Regarding the survival of patients with malignant parotid tumours, 3 are well and free of disease and 2 with disease. The remaining 8 have died: 3 due to locoregional recurrences, 2 due to lung and bone metastases, and 3 due to intercurrent disease.

Of the 5 patients with malignant submaxillary tumours, it has not been possible to follow up one and the other 4 have died: one of them due to local recurrence; 2 presented pulmonary and mediastinal metastases; and the last due to intercurrent disease.

Of the 5 patients with malignant soft palate tumours, 3 have died: one due to local recurrence, another one due to lung metastasis, and the third due to intercurrent disease; the other 2 are alive, one with lung and mediastinal metastases.

Considering all malignant tumours, the 5-year survival has been of 35%, of which 21%died from causes unrelated to the disease, and 25%presented metastasis.

According to the locations, the 5-year survival of patients with parotid tumours was 38%, compared to 0% of the submaxillary gland and 40%of patients with tumours of the soft palate.

Discussion

In our study, the first difference we found with the published literature is the high average age of our patients with malignant tumours. In the literature, the average age is 40 years for benign tumours and 55 years for malignant tumours,[1,2] compared to our values of 50 and 80, respectively.[3] This would explain the differences in histology and survival we have found.

The parotid gland was the most affected, with 67%, similar to the 63%-86%found in the literature, followed by the submandibular with 19%(14%-23%in the literature) and the soft palate with 11%(1%-14%in the literature).

In the parotid the majority of tumours were benign, in the submaxillary gland the proportion was similar and in the minor salivary glands, malignancies predominated.[1]

We concur with the publications in that the most common benign tumour is usually pleomorphic adenoma, followed by Warthin's tumour. However, the differences in the pathology of the malignant tumours from that published in the literature is noteworthy. Among the 24 tumours, we do not have any of the most frequent ones, namely mucoepidermoid carcinoma,[4] and adenocarcinoma.[5] In our study, the vast majority are squamous cell carcinomas (54%), and almost all in elderly patients who had been operated on for epitheliomas of the face and scalp, so we consider them to be metastatic.[6] This would be explained by the considerable ageing of the population in our setting: as we have stated, the average age in malignant tumours was 80 years compared with 55 in the literature.[2] Bron et al,[7] in a review of 232 parotidectomies carried out in Australia,

Figure 5 Computerized tomography of the parotid displaying an expansive lesion of 2.5 cm and lobed contour, located behind the ascending branch of the mandible and in front of the mastoid in the deep parotid space.

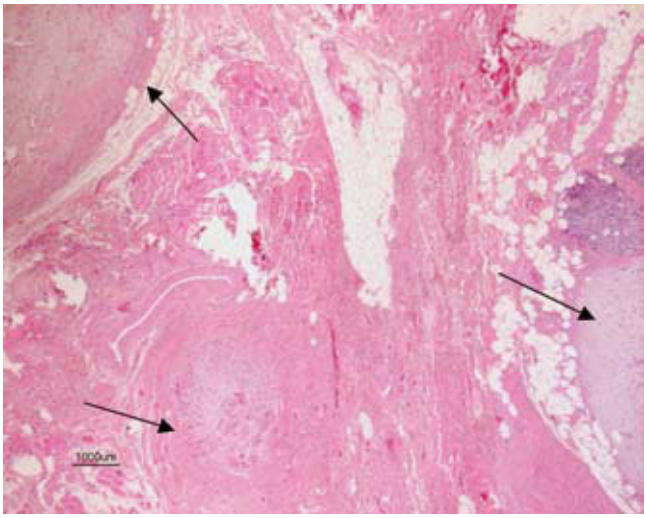

Figure 6 Pathological anatomy: three foci of multifocal pleomorphic adenoma of the submaxillary gland (arrows), separated by healthy glandular tissue (HE, ×100).

also found a majority of squamous cell carcinomas (55%), which they attributed to the high incidence of skin cancer in their environment, with a worse survival for these than for rest of the tumours in their study; moreover, they also found that melanomas were the most common cause of distant metastases.[8]

Our diagnosis was reached by FNA.[9-11] The false positives should be borne in mind, as in salivary glands these vary between 0% and 4%. In our study, there were 3 failures. One patient was diagnosed with pleomorphic adenoma of the submaxillary gland and, after surgery, the pathology report was chronic sialoadenitis. The other 2 patients were cases of malignant tumours, one diagnosed as poorly differentiated squamous cell carcinoma in both the prior FNA and the intra-operative biopsy. A total parotidectomy with cervical dissection was carried out, but the final report was lymphoma. The other was diagnosed on 2 occasions as having acute sialoadenitis, but as the clinical presentation did not coincide, a CT was performed and a tumour of the deep lobe of the parotid gland diagnosed; a subsequent guided FNA, confirmed malignancy.

In view of the risk of damaging the facial nerve, we only performed biopsies in lymphomas when a complete pathology analysis was necessary to initiate chemotherapy.

The diagnostic imaging techniques are not mandatory; we only performed them in cases of doubt or for a diagnosis of extension. Ultrasound is capable of distinguishing between benign and malignant lesions in 96% of cases and, for some authors, it diagnoses a pleomorphic adenoma in 85% of cases.[12]

MRI is the technique of choice to determine the involvement of parapharyngeal, nerve, or cutaneous soft tissue and, together with CT, would enable us to know the exact location of the tumour[13] and the existence, possible but rare, of multiple intraparotid tumour nodules or in the contralateral gland.[14]

Four-fifths of the parotid parenchyma are located above the facial nerve in the superficial lobe, which is where 90% of all malignancies settle. Fifty years ago, treatment consisted of the enucleation of the tumour, but recurrence rates were 20% to 45%, given that microscopic tumour portions pierced the capsule, and excision was thus incomplete. Therefore, this is no longer done and instead there are 3 techniques: total parotidectomy, superficial parotidectomy, either total (TSP) or partial (PSP), and extracapsular dissection. Total parotidectomy removes all glandular tissue lateral and medial to the facial nerve. Superficial parotidectomy removes just the tissue which is lateral to the nerve, either in its entirety, after dissection of all branches of the facial nerve (TSP) or dissecting only the corresponding branch of the facial nerve and removing a generous margin, of at least 2 cm, but without sacrificing the normal parotid tissue distant from the tumour (PSP).[15] This technique has reduced relapses to 14%[16] It would be indicated for low-grade, mobile benign or malignant tumours of less than 4 cm. In extracapsular dissection, no dissection of the facial nerve is performed. It is distinguished from enucleation by meticulous haemostasis and the dissection of a small layer of parenchyma just outside the tumour capsule. Special care has to be taken with tumour lobes and their possible relationship with the branches of the facial nerve, and therefore this technique should be performed on tumours that are mobile within the gland and with a thin glandular cover. Nevertheless, there are numerous surgeons who criticise this procedure.

Only in a small number of publications[17] has the capsule of pleomorphic adenomas been studied thoroughly, despite their importance, and these show that in 45%-55% of superficial parotidectomies, capsular dissection, or partial enucleation areas appear, predominantly along the facial nerve, without implying a higher number of relapses. Witt[18] also proved that a partial parotidectomy does not mean more recurrences and that it does decrease the incidence of facial paresis and Frey's syndrome, but recommends that the margins are wide. The 2 cases of Frey's syndrome which we had appeared in 2 patients undergoing complete superficial parotidectomy, a complication that has not been repeated since we used a rotated sternocleidomastoid muscle flap interposed between the nerve and the skin.[19]

The rate of facial paresis after parotidectomy varies from 9% to 64%, while total palsy occurred in 0% to 5%. This incidence is much greater in the case of reinterventions, always involving the possibility of permanent paralysis.[20,21]

The treatment is surgical, but despite complete resection, there is a high risk of local recurrence[22] (16%-27%) and distant metastases (13%-26%). Among the poor prognostic factors, we noted lymph node involvement and, to a lesser extent, advanced stages, high degree tumours, and perineural invasion. Submandibular and minor salivary glands tumours also have a worse prognosis than those of the parotid gland. In the literature, 5 year survival rates are 65%[23,24]; our numbers have been worse, but we must take into account the high age of our patients and that 21% of them died for reasons unrelated to the disease.

There is around 10% of occult lymph node involvement and in the literature the benefits of prophylactic cervical dissection are not clear[25]; it is generally recommended in cases of positive nodes and radiation therapy in cases of poor prognosis. Chemotherapy is often used as a palliative treatment.

Conclusions

In this review of 63 benign and malignant tumours of the salivary glands we agree with the literature consulted on the higher frequency of benign tumours and more common involvement of the parotid gland.

We highlight the advanced age of patients with malignant tumours, mostly metastases of squamous cell carcinomas of the face and scalp.

Survival has been low, both due to the advanced age and also because the majority were metastatic tumours.

Conflict of interests

The authors have indicated there is no conflict of interest.

References

1. Al-Kateeb TH, Ababnek K T. Salivary tumours in north Jordanians: a descriptive study. Oral Surg Oral Med Oral Pathol Oral Radiol Endodod. 2007;103:53-9.

2. Ansari MH. Salivary gland tumours in an Iranian population: a retrospective study of 130 cases. J Oral Maxillofac Surg. 2007;65:2187-94.
3. Morais D, Bachiller M, García-Tejeiro M, Ramírez M, Santos J. Carcinoma del conducto de Stenon o Stensen. Acta Otorrinlaringol Esp. 2003;54:663-6.
4. Pinkston JA, Cole P. Incidence rates of salivary gland tumours: results from a population-based study. Otolaryngol Head Neck Surg. 1999;120:834-40.
5. Buchner A, Merrell PW, Carpenter WM. Relative frequency of intra-oral minor salivary gland tumours: a study of 380 cases from northern California and comparison to reports from other parts of the world. J Oral Pathol Med. 2007;36:207-14.
6. Pomar P, Martín C, San Roman J, Tapia M, Fernández M. Metástasis en la glándula parótida. Acta Otorrinolaringol Esp. 2006;57:47-50.
7. Bron L, Traynor S, McNeil E, O'Brien C. Primary and metastatic cancer of the parotid: Comparison of clinical behaviour in 232 cases. Laryngoscope. 2003;113:1070-5.
8. Lahoz Zamarro MT, Martínez Subías J, Muniesa J, Laguía M. Melanoma de paladar duro. Acta Otorrinolaringol Esp. 2001;52:422-5.
9. Amedee RG, Dhurandar NR. Fine-needle aspiration biopsy. Laryngoscope. 2001;111:1551-7.
10. Zbären P, Schar C, Hotz M, Loosli H. Value of fine-needle aspiration cytology of parotid gland masses. Laryngoscope. 2001;111:1989-92.
11. Altuna X, Gorostiaga A, Zulueta A, Algaba J. Evaluation of the fi ne needle aspiration biopsy in the presurgical diagnosis of tumours of the parotid gland. An Otorrinolaringol Ibero Am. 2006;33:495-503.
12. Bjalek EJ, Jakubowski W, Karpinska G. Role of ultrasonography in diagnosis and differentiation of pleomorphic adenomas: work in progress. Arch Otolaryngol Head Neck Surg. 2003;129:937-8.
13. Hernández R, Armengot M, Alba J, Taleb C, Jiménez J, Frías S, et al. Adenoma pleomorfo gigante de lóbulo profundo de la parótida: a propósito de un caso. Acta Otorrinolaringol Esp. 2006;57:56-8.
14. Urquhart A, Hutchins L, Berg R. Preoperative computed tomography scans for parotid tumour evaluation. Laryngoscope. 2001;111:1984-8.
15. García-Ortega F, Carcasés MJ, Martínez S, Bevia MC, Durán R, Malluguiza J. Mioepitelioma en glándulas salivares. Acta Otorrinolaringol Esp. 2001;52:269-72.
16. Guntinas-Lichius O, Klussmann P, Wittekindt C, Sternert E. Parotidectomy for benign parotid disease at a University teaching hospital: outcome of 963 operations. Laryngoscope. 2006;116:534-40.
17. Lam KH, Wei Wi WI, Ho HC, Ho CM. Whole organ sectioning of mixed parotid tumours. Am J Surg. 1990;160:337-81.
18. Witt R. The significance of the margin in parotid surgery for pleomorphic adenoma. Laryngoscope. 2002;112:2141-54.
19. Govindaraj S, Cohen M, Genden E, Costantino P, Urken M. The use of acellular dermis in the prevention of Frey's syndrome. Laryngoscope. 2001;111:1993-8.
20. Makeieff M, Venail F, Cartier C, Garrel R, Crampette M. Continuous facial nerve monitoring during pleomorphic adenoma recurrence surgery. Laryngoscope. 2005;115:1310-4.
21. Zbären P, Tschumi I, Nuyens M, Stauffer E. Recurrent pleomorphic adenoma of the parotid gland. Am J Surg. 2006; 192:270.
22. Lahoz Zamarro MT, Valero Ruiz J, Royo López J, Yus C. Tumour mixto de conducto auditivo externo. Acta Otorrinolaringol Esp. 1990;41:53-6.
23. Hockwald E, Hakan K, Yoo G, Adsay V, Shibuya T, Abrams J, et al. Prognostic factors in major salivary gland cancer. Laryngoscope. 2001;111:1434-9.
24. Rossi M, Frade C, Cabanas E, Dios C, Lozano A, Labella T. Nuestra experiencia en el tratamiento de los tumoures de glándula parótida. An Otorrinolaringol Ibero Am. 2007;34: 257-71.
25. Pogodzinsky M, Sabri A, Lewis J, Olsen K. Retrospective study and review of polymorphous low-grade adenocarcinoma. Laryngoscope. 2006;116:2145-9.