CASE REPORT
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# Pleomorphic Adenoma of the Submandibular Gland in Children: Case Report and Review of the Literature

Diogo Cunha-Cabral[1,2], Pedro Marques Gomes[1], André Alves Carção[1], Beatriz Fevereiro[3], Duarte Rosa[3], Joana dos Santos[4], Delfim Duarte[1], José Ferreira Penêda[1]

[1]Department of Otorhinolaryngology, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Porto, Portugal
[2]Division of Biomedicine, Department of Anatomy, University of Porto Faculty of Medicine, Porto, Portugal
[3]Department of Radiology, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Porto, Portugal
[4]Department of Pathology, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Porto, Portugal

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## ABSTRACT

Salivary gland tumors, especially those affecting the submandibular gland, are extraordinarily rare neoplasms in children. As a result, there is not a lot of available information regarding the diagnostic approach and treatment of pleomorphic adenomas in this location in the pediatric population. With this work, by presenting our own case of a pleomorphic adenoma of the submandibular gland in a 10-year-old boy and by reviewing the published case reports of pleomorphic adenomas of the submandibular gland in pediatric age, we aim to help improving the management of children with these tumors.

**Keywords:** Benign mixed adenoma, children, fine needle aspirate, pleomorphic adenoma, submandibular gland

## Introduction

Submandibular triangle masses in children may have infla mmatory/infectious, congenital, or neoplastic etiologies. Among the neoplastic ones, those from vascular origin, namely hemangiomas, predominate. When compared to these vascular lesions, submandibular gland tumors are relatively rare.[1,2]

In fact, all salivary gland tumors are uncommon in the pediatric population, corresponding to between 1% and 8% of all head and neck tumors in this age group.[1,3,4] Regarding their location, they occur more frequently in the parotid gland (56.7%-61%), followed by the submandibular gland (18%-31%). Amid minor salivary glands, the palatal ones appear to be the most affected.[1,5]

When considering solely submandibular gland's tissue tumors, the pleomorphic adenoma (PA) is the most common neoplasm.[1,6,7] Pleomorphic adenoma, also known as benign mixed adenoma, is a benign salivary gland tumor formed by epithelial and stromal components that may assume a variety of patterns.[8] Experience from PA behavior in other glands and adults reveals that these neoplasms may recur after treatment and may even show malignant transformation.[5,9]

Given the low incidence of the salivary gland tumors in children, namely the ones affecting the submandibular gland, the PA of the submandibular gland may be considered as rare in the pediatric age group.[7,10] As a result, there is not a lot of accumulated experience in managing these cases and there is much still to be known about the recurrence rates and the risk of malignant transformation of these tumors.[5,9,10]

With this work, by presenting the first reported case of a pediatric submandibular PA in Portugal and by reviewing the previously published case reports on this subject, we aim to help improving the diagnostic approach and management of the children with this pathology.

We conducted a review of the literature in March 2022 using PubMed (Medline), Scopus, and Web of Science databases. On the former, the following query was used: (pleomorphic adenoma [MeSH Terms]) AND (submandibular gland) AND (children). Similar terms were used in the 2 other databases.

**Corresponding author:** Diogo Cunha-Cabral, e-mail: diogo.cabral08@outlook.com/dcabral@med.up.pt
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Case reports and case series were retrieved, and we further searched their references for other relevant publications.

To allow an updated review of the diagnostic approach and treatment of PAs of the submandibular glands in the pediatric population, we only selected publications from after the year 2000.

There were only included articles written in English or Portuguese. Publications lacking clinical data were excluded.

Informed consent was obtained from our patient legal representative.

### Case Presentation

A 10-year-old, previously healthy boy was referred to our department because of a 2-month history of a right-side submandibular swelling. An ultrasound ordered by his family doctor revealed a nodular hypoechoic lesion, measuring 20 × 26 mm, within the submandibular gland tissue.

The physical examination showed a rounded, firm but mobile mass in the right submandibular gland that was painless to the touch. No other changes were noticed, as such cervical lymphadenopathy or marginal mandibular or hypoglossal nerves palsies.

A magnetic resonance imaging (MRI) with contrast was conducted for further characterization (shown in Figure 1). It demonstrated a rounded and well-demarcated mass centered to the right submandibular gland, measuring 20 × 19 mm. The hypothesis of PA was raised given its typical homogenous hyperintensity on T2 weighted (W) images and diffuse contrast enhancement in T1W. Fine needle aspiration biopsy guided by ultrasound was performed for diagnostic confirmation. Its results were indicative of PA, corresponding to a IVa category of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).[11]

The patient was subjected to total submandibular gland excision. The gross examination revealed a salivary gland with a well-circumscribed lesion measuring 40 × 35 × 23 mm. The cut surface was tanned, with white areas (shown in Figure 2A). On histologic examination, the tumor was capsulated and composed of 3 components: epithelial, myoepithelial, and stromal (shown in Figure 2B). There was a byphasic population of plasmocytoid and epithelioid myoepithelial cells and few epithelial cells arranged in tubular structures. The stroma was variable, with myxoid and chondroid areas. These features were consistent with the diagnosis of PA. The entire tumor capsule was preserved.

There were not early or late postoperative complications.

**Main Points**

- Pleomorphic adenoma of the submandibular gland is extremely rare in children.
- Pleomorphic adenoma usually presents as a painless submandibular mass.
- Magnetic resonance imaging and fine needle aspiration cytology together can make an accurate diagnosis of pleomorphic adenoma.
- Total submandibular gland excision is the preferred treatment of pleomorphic adenoma of the submandibular gland in children.

## Results

After a careful review of the available literature, we selected 11 articles. A total of 7 publications were included this review, after exclusion of 1 case report because it was published before the year 2000 and 3 for being written in Japanese. Of the included ones, 6 were single case reports and 1 consisted of a case report and a review of 22 cases of PAs of the submandibular gland in the Japanese Literature.[12]

Table 1 summarizes the studies included in this work.

## Discussion

### Clinical Presentation

The mean age at diagnosis of the case reports included in our study was 10.8 (±3.25) years, excluding the case of congenital PA reported by Azma et al.[13] This was similar to one reported by Masumoto et al[10] in a review of Japanese cases which was of 12.0 (±2.70) years.

All the cases included in our study presented as painless submandibular masses. These were mainly characterized as firm and mobile, which was also the case of our patient. In 2 cases, however, the submandibular masses were described as hard. Azma et al[13] also reported a bulging of the oral floor caused by the tumor. No other signs and symptoms were reported, namely cervical lymphadenopathies. Despite the close anatomical relations of the submandibular gland with the hypoglossal nerve and with the marginal mandibular nerve, none of the patients presented palsies of these nerves.

Regarding the duration of the symptoms, excluding the case that was diagnosed in the newborn, it was on average 11.2 (±7.16) months. This is similar to the one reported by Fu et al[5] for the duration of symptoms of PA affecting all the salivary glands. These intervals are relatively shorter to the ones of PA affecting the adult population. Fu et al[5] purposed that this may result from an extra attention from the parents for lesions in their children. Other factor might be that smaller tumors can be more easily noticed in children than in adults.

As aforementioned, the PA of the submandibular gland is extremely rare in children. As a result, there is not much information regarding its clinical features.[9,10] In this work, we reunite clinical information of several cases of PA of the submandibular gland in pediatric population. Although other authors had already reviewed the clinical features of PA affecting all salivary glands, none has done it specifically for PA of the submandibular gland.

### Diagnostic Approach

***Imaging*** Given the heterogeneity of lesions that may affect the submandibular triangle, imaging is crucial for the diagnostic approach of masses located in this region.

When our patient was referred to our department, he had already done an ultrasound (US) of the submandibular triangle.

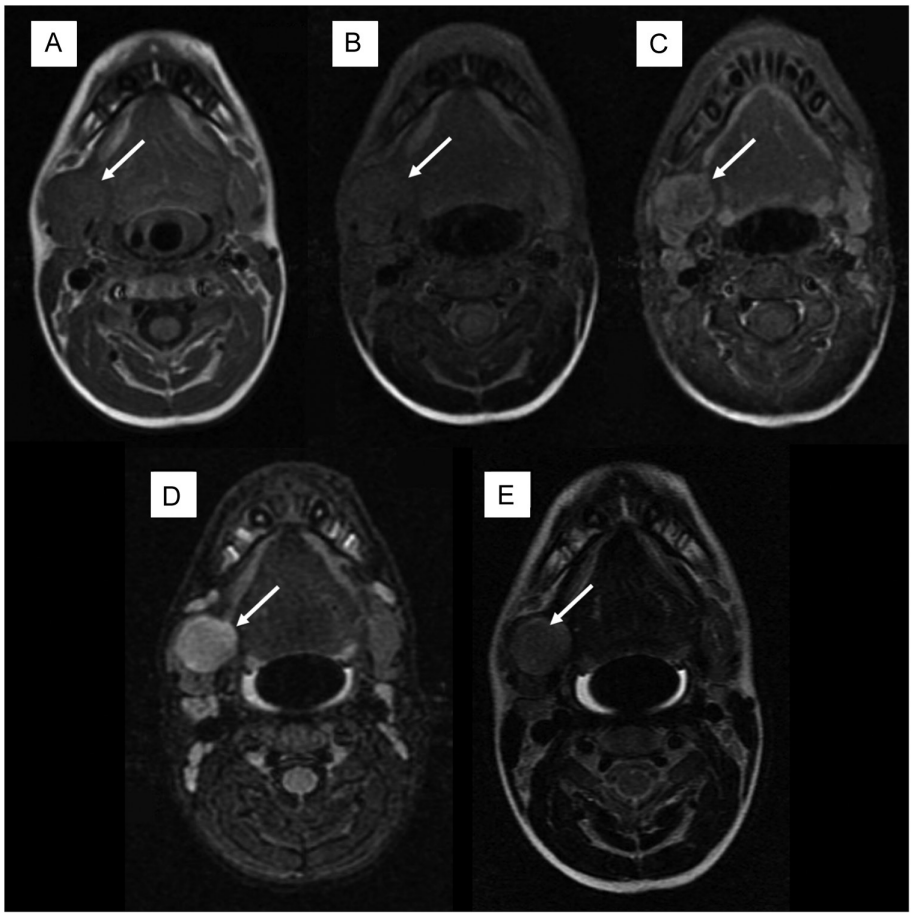


**Figure 1.** Magnetic resonance images. (A) Axial T1W and (B) fat-suppressed T1W sequences demonstrate a rounded and well demarcated mass centered to the right submandibular gland, measuring 20 × 19 mm. (C) After administration of gadolinium, this mass shows diffuse contrast enhancement on T1W sequences. (D) A high homogenously hyperintensity signal is evident on the fat-suppressed T2W sequence using *short tau inversion recovery* technique (E) when compared to T2W images (E).

Three of the reviewed cases also used US examination as the initial imaging method. All three complemented the study with other imaging techniques. In one case, however, the US examination was the only imaging method used.

Ultrasound is the first line image modality when evaluating a patient with a cervical mass, especially in children, since it does not use radiation and is often well-tolerated, thus avoiding the need of sedation.[5,9,14] At US examination, PAs appear as hypoechoic rounded masses with a smooth and lobulated surface. Posterior enhancement of ultrasounds is frequently observed; however, it may be misinterpreted as a cystic mass, which is usually the presentation of some congenital masses, such as second branchial arch cysts. In fact, the acoustic enhancement and the lobulated shape are the most characteristic sonographic findings. Even though calcifications are rare, they may be present in larger tumors.[15] Doppler evaluation will also demonstrate scarce intralesional vascularization.[14]

It is well-known that PAs may undergo malignant transformation and the risk of malignancy is inversely proportional to the size of the salivary gland.[14] Unfortunately, sonographic imaging alone cannot distinguish between benign and malignant

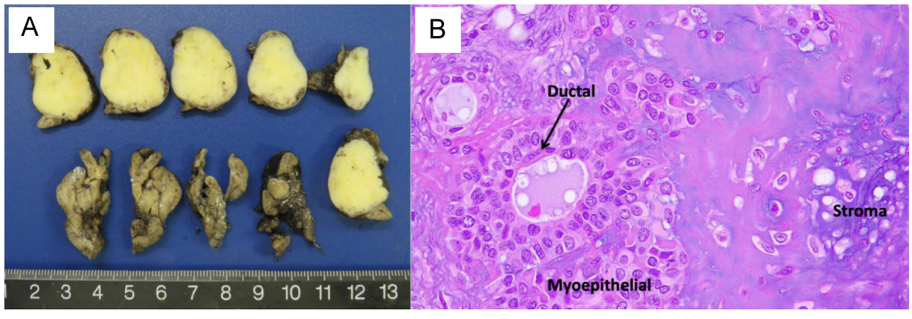


**Figure 2.** Extracted right submandibular gland. (A) Cross section of the right submandibular gland showing a yellowish and well circumscribed lesion. (B) The microscopic examination of the lesion revealed a PA with ductal, myoepithelial, and stromal components—HE, 20×.

**Table 1. Summary of the Case Reports of Pleomorphic Adenomas of the Submandibular Gland in Children Included in This Work**

| Author/ Date | Number of Cases | Age at Diagnosis | Gender | Side | Clinical Features | Duration of Symptoms | Diagnostic Approach | Treatment |
|---|---|---|---|---|---|---|---|---|
| Molina et al[16] | 1 | 16 years-old | Male | Right | Painless, firm, and mobile submandibular mass | 6 months | CT | Complete submandibular gland excision |
| Köybaşı et al[12] | 1 | 7 years-old | Female | Right | Painless, firm, and mobile submandibular mass | 1 year | MRI FNAC | Complete submandibular gland excision |
| Masumoto et al[10] | 1 | 8 years-old | Female | Left | Elastic hard submandibular mass | 1 year | US MRI | Partial submandibular gland excision |
| | 22 | 12 ± 2.7 years-old | 6 male 16 female | 16 right 5 left | NA | 40.5 ± 39.4 months | NA | Complete submandibular gland excision—9 Tumor resection and partial submandibular gland excision—3 Tumor resection—8 |
| Braich et al[17] | 1 | 12 years-old | Male | Right | Round, well-demarcated, smooth submandibular mass | 4 months | CT | Tumor resection |
| Azma et al[13] | 1 | 1 day-old | NA | Left | Mobile hard submandibular mass with extension to the oral cavity | NA | US CT Open biopsy | Tumor resection |
| Satta et al[18] | 1 | 12 years-old | Female | Left | Painless submandibular mass | 9 months | US | Complete submandibular gland excision |
| Rachida et al[19] | 1 | 10 years-old | Female | Left | Painless, firm, and mobile submandibular mass | 2 years | US MRI FNAC | Complete submandibular gland excision |

CT, computed tomography; FNAC, fine needle aspiration cytology; MRI, magnetic resonance imaging; NA, not available; US, ultrasound.

forms of this tumor and is usually used as a preliminary imaging method.[14,15]

To obtain a detailed characterization of the submandibular mass in our patient, we performed a contrasted MRI with sedation. Among the reviewed cases, two also had an MRI after an initial US. In one case, the MRI was the initial and only imaging method used.

Magnetic resonance imaging not only overcomes US limitations for allowing tissue characterization, but also provides accurate anatomic description and in-depth analysis for surgical planning.[14] However, due to long acquisition times, sedation is often necessary in the pediatric population to guarantee image quality.[9]

Magnetic resonance imaging features vary accordingly to the tumor size. Smaller lesions (<2 cm) appear as rounded well-circumscribed masses, with low signal intensity on T1W images, a typical hyperintensity on T2W and moderate homogeneous contrast enhancement. Lesions greater than >2 cm usually present lobulated borders, heterogeneity (due to necrotic and myxoid components) with inhomogeneous hyperintensity on T2W and enhancement T1W with contrast scans.[14]

The presence of characteristic MRI features demonstrated a 95% specificity with an 86% positive predictive value for PA, which might be particularly interesting when preoperative FNAC is not easily available.[20] Furthermore, FNAC is sometimes inconclusive due to sampling of "non-target" intralesional

tissue, such as areas of necrosis or hemorrhage. Ordering an MRI evaluation previously to FNAC may improve diagnostic accuracy by mapping the ideal tissue sampling areas.[14]

In addition, recent studies suggest that the quantitative analysis of glandular lesions' contrast enhancement using dynam ic-contrast-enhanced and diffusion-weighted MRI sequences can contribute to the specificity of the histological diagnosis and possibly avoid histological characterization. However, these results are not completely validated to become part of the routine examination of every salivary gland in daily practice.[21,22]

Computed tomography (CT) was the only imaging method used to characterize the submandibular mass in 2 of the reviewed cases. In 1 patient, CT scan was chosen to complement the study of the tumor after an initial US.

Although CT is a widely available method with good spatial resolution and shorter acquisition times compared to MRI, it has the downside of using ionizing radiation, especially relevant in children, and a limited role in characterization of soft tissue lesions.[23]

### Fine Needle Aspiration Cytology

Fine Needle Aspiration Cytology (FNAC) represents one of the most controversial topics when discussing the diagnostic approach of salivary gland masses in children.

We performed US-guided FNAC in our patient, using the same sedation that was required to perform the MRI. The results of the collected samples suggested the diagnosis of PA. In 2 of the reviewed cases, FNAC of the submandibular mass was also performed and in both the results were of PA of the submandibular gland.

The role of FNAC in the diagnosis of salivary gland masses in adults is already well established.[9,10,24] In the adult population, this technique has a sensitivity and specificity greater than 90%, making of it a widely accepted method for the diagnostic approach of salivary gland tumors.[5,12,24,25] The use of the MSRSGC in adults has shown an high sensitivity for salivary gland tumors diagnosis.[26]

When considering the use of FNAC in children for the study of salivary gland tumors, including those affecting the submandibular gland, there are diverging opinions.[9,10,16] Several studies reported identical sensitivity and specificity of the FNAC in the pediatric population when compared to adults and considered the MSRSGC as a useful and reliable classification system in children.[26-28] However, there are some limitations related to its use.[24] The need of sedation to perform it in most children is one of the pointed downsides of FNAC. Also, the possibility of having an insufficient sample of cells for the diagnosis is another justification for not using FNAC.[9,10,19]

The use of FNAC is not mandatory for the diagnosis of PAs of the submandibular gland, however, it can be considered as a reliable diagnostic tool in cases of doubt between inflammatory and neoplastic etiologies of submandibular masses in children.[29] As aforesaid, the MRI may help identifying the ideal location for sampling the tumor, being possible to perform both procedures using the same sedation. When each of these 2 diagnostic methods demonstrate typical findings of PA, they can give an accurate diagnosis of PA.[30]

Open biopsy is not recommended in the study of submandibular gland masses because of the associated risk of nerve damage and tumoral seeding.[29]

### Treatment

The recommended treatment for the submandibular gland PA in children is submandibular gland excision. In 5 of the reported cases, as also in ours, this was the treatment of choice. Among the cases reviewed by Masumoto et al[10], 3 underwent tumor resection with partial submandibular excision and 8 had their tumor resected with preservation of the submandibular gland. Braich et al[17] and Azma et al[13] also reported cases in which it was only performed resection of the tumor.

Despite their benign behavior, experience from adults and from PAs of other salivary glands shows that these neoplasms may recur and may even have malignant transformation.[5] In order to avoid these complications, the complete submandibular gland removal is recommended.[5,10,31]

Partial gland excision together with the tumor is defended by some authors as an alternative as it will preserve part of the physiological function of the submandibular gland.[10,32] Yu and Peng[32] demonstrated in a prospective study in adults that the patients that had been subjected to partial removal of the gland had significantly higher resting saliva flows than the ones of the total submandibular gland excision group. In this study, there were not any difference in tumoral recurrence rates between the 2 groups. A factor that may help choosing between both techniques is the location of the tumor within the submandibular gland. A more central location may result in damage of the vascular and ductal systems in case of partial gland removal, favoring a total excision.[32]

Nevertheless, it is not clear yet if there are real advantages of performing partial submandibular gland excision in children. In the authors opinion, total submandibular gland excision is easier and safer to perform as it is a well-documented surgery. The partial gland removal together with the tumor implies the dissection of the gland's tissue, which makes it more unpredictable. Therefore, the lack of evidence regarding the functional benefit of a more conservative approach together with the additional risk of complications favors total submandibular gland removal.

Also, due to the PAs large dimensions and the possibility of existing pseudopods and satellite nodules[18] in the remaining gland that may predispose these patients to increased recurrence risk in the future, total submandibular gland removal is the preferred treatment.

Due to the proximity of the submandibular gland to the mandibular marginal branch of the facial nerve, this is one of the principal structures that may be lesioned during total submandibular gland excision.[24] Although less common, the lingual and hypoglossal nerves may also be damaged when performing this surgery.[17,19,24] In all the reviewed cases, the tumor excision occurred without any surgical complication.

### Prognosis

As aforementioned, PAs of the salivary glands may recur. For the ones affecting the parotid gland, depending on the type of surgery performed and the tumor location, there were recorded rates of recurrence from 2.8% to 46.6%.[9] Given its low incidence, there is not accurate information regarding the recurrence rates of PA of the submandibular gland. In our case series, there was not any recurrence mentioned, however there is not enough information about the period of surveillance for each of the patients. There are reported cases of recurrence for PAs of the parotid gland after 15 years from the surgery, so the absence of recurrent cases of PA may be due to a short surveillance time.[9]

A factor that has an extreme importance in the prevention of tumor recurrence in the parotid gland is the complete removal of the tumor with preservation of the tumor capsule.[5] For this reason, the tumor excision with complete or partial submandibular gland removal instead of the tumor enucleation is the preferred method of treatment of PAs in this anatomical region, as it reduces the chances of damaging the tumor capsule and allows the removal of any satellite nodule of tumor within the gland not detected in imaging. In fact, in the cases reported by Masumoto et al[10], the only 2 cases of recurrence occurred in patients who had underwent tumor enucleation.

The malignant transformation of the PAs of the salivary glands is a complication that is relatively rare. There have been described 10 cases of malignant mixed tumors of the salivary glands in children by Bradley et al and 1 by Masumoto et al.[10,29] There is still some debate to whether these cases resulted from malign degeneration of an initial PA or if there was a concomitant malign neoplasm together with the PA.

## Conclusion

The PA of the submandibular gland is an extremely rare neoplasm in children. Despite its benign behavior, an inappropriate treatment selection may result in recurrence of the tumor. Therefore, a correct diagnostic approach to submandibular triangle masses in the pediatric population is crucial to facilitate its diagnosis and thus helping in the choice of the treatment that will bring the best long-term results.

**Informed Consent:** Written informed consent was obtained from the patient who agreed to take part in the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – D.C., J.P.; Design – D.C., J.P.; Supervision – J.P.; Resources – D.C., P.G.; Materials – D.C., B.F., J.S.; Data Collection and/or Processing – D.C., A.C.; Analysis and/or Interpretation – D.C., P.G., A.C.; Literature Search – D.C.; Writing – D.C., B.F., J.P.; Critical Review – J.P., D.R., D.D.

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