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Original Research Article

Evaluation 172 patients of submandibular gland swelling with a case of adenocarcinoma, not otherwise specified: a needle in a haystack

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ABSTRACT

Background: Aim of the study was to assess the patients of submandibular gland pathology and to describe a case of adenocarcinoma, not otherwise specified (ANOS) of the submandibular gland in terms of clinical presentation, diagnosis, line of management and prognosis.
Methods: The study was conducted as a retrospective review of all the patients who underwent submandibular gland excision in the last 6 years at the department of otorhinolaryngology, M.D.M. hospital, Dr. S.N. Medical college, Jodhpur. The records were assessed and statistically evaluated.
Results: Out of 172 cases of submandibular gland excision, only 1 case of ANOS was seen. The rest included 134 cases were of chronic non-inflammatory process, 24 cases of sialolithiasis, 10 cases of metastasis from oral cavity cancer and 3 cases of primary squamous cell carcinoma. Fine needle aspiration cytology (FNAC) was not diagnostic in ANOS. Excision of the gland with primary closure was done. Adjuvant radiotherapy was given.
Conclusions: ANOS has a rare occurrence in submandibular gland swelling and it is also very tricky to diagnose it. The nature of this malignancy is invasive and nodal metastasis is present. Surgical excision and post-op evaluation can be life-saving.

Keywords: Adenocarcinoma, not otherwise specified, Submandibular gland swelling, Sialolithiasis, FNAC

INTRODUCTION

Submandibular gland is the second largest salivary gland in human body. Swelling in the submandibular gland region is mainly due to inflammatory pathologies. Parotid gland is the commonest site for salivary gland tumors (65-80%) followed by submandibular gland (7-11%), sublingual gland (1%) and minor salivary glands (9-23%). Benign tumours 54-79% are more common than malignant tumors in salivary gland tumors. The percentage of malignant tumours, however, varies greatly by site. Malignant tumors comprise 15-32% of parotid tumors, 41-45% of submandibular tumors, 70-90% of sublingual tumors.[1]

Malignant salivary gland neoplasms account for 0.5% of all malignancies and approximately 3% to 5% of all head and neck cancers.[2,3] The term adenocarcinoma, not otherwise specified (ANOS) is simply given to all those gland-forming malignancies that does not fall under the diagnostic criteria of other "named" salivary malignancies. Adenocarcinoma NOS of salivary glands is a rare cancer with an incidence of merely 2.5 to 3.0 cases per 100,000 per year in the western world.[2] The clinical symptoms of adenocarcinoma NOS in the major salivary gland often is a firm and asymptomatic painless solitary mass.[4]

Though FNAC is quiet helpful in establishing the diagnosis in all the salivary gland tumors but sometimes

the tumor cells may mimic multiple other conditions. And to add, the diagnosis of this subtype of tumor may be even more difficult as ANOS could exhibit heterogenisity in terms of histology and present with glandular or solid structure and be accompanied by focal papillary or cystic pattern. There are a very limited or no cases reported of ANOS of submandibular gland in Rajasthan and hence we present this case not only because of its rarity but also for the difficulty faced by the clinicians in its diagnosis.

METHODS

The study was conducted in the department of otorhinolaryngology, MDM hospital and it includes the patients with submandibular gland swelling who have undergone submandibular gland excision in the last 6 years from June 2016 to June 2022.

Study design

It was a retrospective descriptive study.

Study location

The study was conducted at the otorhinolaryngology department, M.D.M. Hospital, Dr. S.N. Medical College, Jodhpur, Rajasthan, India.

Inclusion criteria

Patients with submandibular gland swelling who underwent gland excision were included.

Exclusion criteria

Patients who were unwilling for surgical management were excluded.

Methodology

Since it is a retrospective observational study based on records of patients already operated, history was sought for age, gender, clinical presentation, diagnosis, surgical management, adjuvant chemo/radiotherapy and prognosis from the records of patients kept in M.D.M. Hospital, Jodhpur. All the patients were clinically assessed and then they underwent FNAC and then were proceeded for submandibular gland excision via transcervical approach. The sample was sent for final histopathology post-operatively.

RESULTS

A total of 172 patients underwent submandibular gland excision in the last 6 years with a male: female ratio 2.7:1. The median age was 56 years. Most common presentation was painless lump in submandibular region. Out of these, the leading cause was non-specific inflammatory process and only 1 case of adenocarcinoma NOS came into light (Figures 1 and 2).

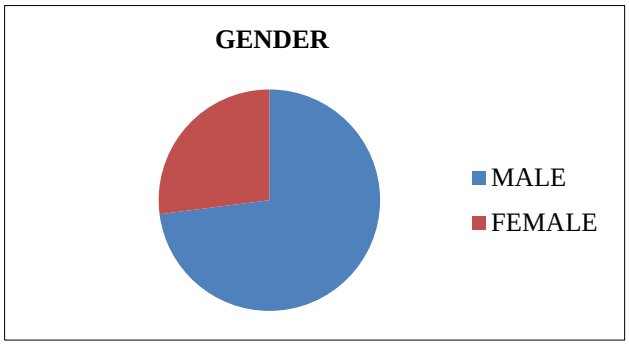

Figure 1: Depicting gender predisposition.

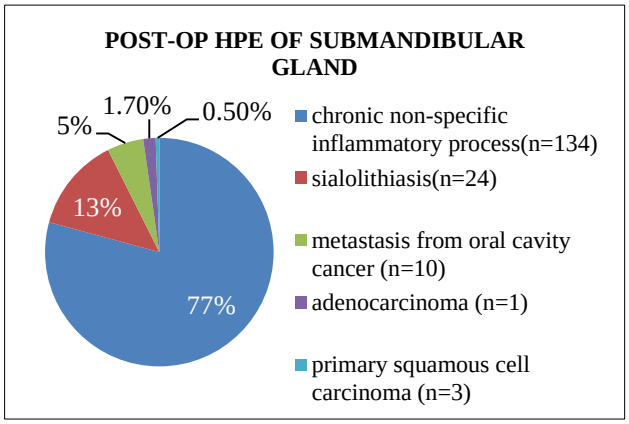

Figure 2: Depicting post-op HPE of submandibular gland swelling.

Case description

A 30-year-old female presented in our department in the M.D.M Hospital, Jodhpur with the chief complaint of painful swelling in right submandibular region for two months which was gradually increasing in size. On examination a 2×2 cm hard bimanually palpable swelling over the right submandibular area was seen. Ultrasonography (USG) neck was suggestive of sialadenitis and no calculus was seen. FNAC was suggestive of pleomorphic adenoma, however looking at the hard consistency of the swelling a repeat FNAC was done after seven days. It was also reported as pleomorphic adenoma.

The patient was unwilling for surgery. The patient reported back to us 15 days later as the swelling had increased and the examination showed a 3.5 x 2 cm hard swelling with a small 1×0.5 cm hard level 1A lymph node (Figure 3). Magnetic resonance imaging (MRI) neck was done and it showed that the submandibular gland was replaced by the tumour with invasive margins suggesting capsular breach and extra glandular spread of the mass. The mass was abutting the mandible, mylohyoid muscle and hyoid bone. Level IA node was seen with central necrosis suggestive

of metastatic lymph node (Figures 4 and 5). Repeat FNAC at this stage was reported as acinic cell carcinoma. X-ray chest was normal. The patient was taken for surgery.

During the surgery it was seen that the tumor was adherent to the anterior belly of digastric, mylohyoid muscle and the hypoglossal nerve was encased by the tumor. The level IA lymph node (0.5×1 cm) was hard and level II A lymph node (2.5×5 cm) was oval firm and an adherence to IJV was noted. Submandibular gland along with anterior belly of digastric and a cuff of mylohyoid muscle was excised+modified neck dissection type 2 was performed (Figure 6). Hypoglossal nerve was sacrificed.

Figure 3: Patient showing submandibular region swelling

Figure 4: MRI showing submandibular region swelling with capsular breach.

Figure 5: MRI showing submandibular gland swelling with capsular breach.

Figure 6: Intra-perative picture showing submandibular gland tumor.

The postoperative HPE was reported as poorly differentiated adenocarcinoma NOS. All margins were free of tumor. The closest cut margin was 1mm posteriorly. Lymphovascular and perineural invasion was present**.** 3 out of 32 dissected lymph nodes were positive for mets and showed perinodal extension. The mylohyoid and anterior belly of digastrics muscle were free of tumor. The patient was sent for post-operative CT+RT and radiation dose 60 Gy/30 Fr was given from 14.3.2016 to 29.4.2016. Till last follow up, the patient was free of disease.

DISCUSSION

Adenocarcinoma, not otherwise specified (NOS) is a salivary gland carcinoma that shows glandular or ductal differentiation but lacks the prominent features that characterize other, more specific types of carcinoma.

The relative frequency of adenocarcinoma NOS is quite variable but its incidence has greatly reduced since after the 2nd World Health Organization (WHO) classification of salivary gland tumors in 1992 as it entails 14 recognized diagnostic entities as opposed to the 1st classification that described only 5 types of carcinomas.[5] Moreover, the 3rd classification added 3 more entities. In a review of 5416 salivary tumors recorded at Shanghai Ninth People's Hospital (1975–2003), ANOS represented 10% of salivary malignancies and in which only 0.24% (13/5416) were in submandibular gland.[6] In a study of 633 salivary gland tumors at Mount Sinai Medical Center (1989–2003), ANOS constituted 8% of salivary gland malignancies and none of them were seen in submandibular gland. This clearly shows the rarity of ANOS in submandibular gland. Similarly, in our study only 1 case was diagnosed with ANOS submandibular gland out of 172 cases who went under submandibular gland excision from 2016-2021.

Adenocarcinoma NOS affects patients primarly in the sixth and seventh decades. Although it appeared to be a slight female predilection, the recent study by Jiang Li et al reported a significant male predominance (4:1) which is similar to the results of Ihrler et al, and Wahlberg et al, while the study by Ellis and Auclair demonstrated that ANOS were more common in women.[6-8]

Our patient presented with a solitary painful swelling in the submandibular region but on the other hand, in a study done by Spiro et. al., the clinical symptoms of adenocarcinoma in the major salivary gland were described as a firm and asymptomatic, painless solitary mass. About 25 percent of patients experienced pain or the effects of nerve involvement. The pain in our case can be explained by the hypoglossal nerve involvement however Adenocarcinoma NOS of intraoral minor salivary gland present mostly as an asymptomatic submucosal mass, but they may also cause mucosal ulcerations (36%) or bone destruction (25%).[9]

As per Tran et al, salivary gland tumors not uncommonly pose problems in diagnosis due to their rarity, broad morphologic spectrum, complex cytoarchitecture, and morphologic overlap among the different tumor types. In the absence of more definitive diagnostic features, only a descriptive diagnosis of "salivary gland neoplasm" can be made, and complete excision or a larger size biopsy is required to arrive at a definitive diagnosis.[10] The difficulty in diagnosis is mainly due to the innocuous presentation and the high incidence of false negative FNAC. The most common pathology is pleomorphic adenoma or chronic non-specific adenitis and this can lull the clinician into complacency. So a wide index of suspicion is necessary while evaluating any submandibular region swelling. The presence of pain or any LAP should alert the clinician for a more thorough examination. Radiologically USG & MRI should be done in all cases. Inspite of all these tests, we were able to get a positive FNAC report on the 3rd attempt when the tumor had spread and metastasis has appeared. ANOS in our case could only be diagnosed after complete surgical excision of the tumor and its histopathological evaluation.

Few publications have described the histology of ANOS in detail. Among these, the Armed Forces Institute of Pathology (AFIP) presented the microscopic findings in greatest detail. Apart from the glandular structures, they demonstrated that cystic and papillary formations were occasionally present. The AFIP also reported that ANOS could exhibit foci of adenoid cystic carcinoma, acinic cell carcinoma, and epithelial myoepithelial carcinoma.[7,11,12]

The biologic aggressiveness of adenocarcinoma can be classified from low grade to high grade according to the degree of cellular differentiation and also related to the place of origin along the salivary gland unit. Tumour with less than 50 percent of glandular or acinar differentiation can be graded as high grade. Otherwise, tumours contain one or more of the several feature such as nuclear atypia, high mitotic rate, necrosis, perineurial invasion, bony invasion, angiolymphatic invasion are also regarded as high grade tumours. All of the adenocarcinoma NOS arise from the relatively large duct unit, such as excretory or intermediate (striated) ducts, thus it appears to possess a more aggressive clinical behaviour, having higher chance to develop cervical and distant metastasis.[6,11-13]

Our patient's post-op HPE report suggested poorly differentiated ANOS and as per Matsuba et al, histological grading to distinguish well, moderately and poorly differentiated adenocarcinomas depends mainly on the quantity and quality of acinar formation.[12]

As per Wahlberg et al, among all the salivary gland malignancies, adenocarcinoma NOS has worse prognosis. Also to note, patients with submandibular gland cancer had similar relative survival as compared to parotid cancers in all except for adenocarcinoma NOS in which submandibular gland involvement carries worse prognosis**.** Though the tumor was aggressive in nature in our patient's case and nodal metastasis along with perineural invasion was present, still the patient was free of disease till last follow-up.

According to both Spiro et al, and Matsuba et al, the site of tumour was an important factor that influence the biologic behaviour of adenocarcinoma NOS. The survival rates of adenocarcinoma NOS of submandibular gland is lower than that in parotid glands. Lung is the most common site for distant metastasis. Metastasis to the skeleton, abdomen, skin can also been found.[12] Like other malignancies, both the stage and grade conduct the decision making of treatment plan. Tumour resections the major part of the treatment. Neck dissection should be performed in cervical metastasis cases. Postoperative radiotherapy was proved improving disease control although some investigators believed that adenocarcinoma NOS seemed to be of relatively lower radiosensitivity.[14] Information on the role of chemotherapy is spared.[15,16]

CONCLUSION

ANOS type of submandibular malignancy is not only an infrequent occurrence but also difficult to diagnose. In this case of ANOS, the initial cytological report (FNAC) was suggestive of a benign pathology (pleomorphic adenoma). However, the hard nature of the swelling and presence of a hard level 1A lymph node alerted us to the fact that the disease may not be as innocuous as it appeared and hence the FNAC was done three times. Still, only the post-op HPE could unravel the adenocarcinomatous nature of the malignancy. It is aggressive and progression of the malignancy is fast. Any negligence can be life-threatening.

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