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Case Report

Secondaries in the neck-submandibular gland carcinoma pleomorphic adenoma with salivary gland

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ABSTRACT

Carcinoma ex pleomorphic adenoma (CA-ex-PA) represents a highly uncommon form of malignancy within the minor salivary glands of the oral cavity. CA-ex-PA is characterized as a carcinomatous transformation, occurring either as primary lesion or as recurrence of PA. PA can develop into different forms of malignancies like CA-ex-PA, carcinosarcoma or metastasizing PA. This particular type of tumor is predominantly prevalent among women aged between 30 and 60 years. A 55-year-old woman presented with symptoms including swelling on the right side of neck below the jaw, which is suspected to have metastasized from an unknown origin. Intraoperatively submandibular gland excision and right radical neck dissection along with internal jugular vein (IJV) was done to ensure definitive diagnosis. Histopathological results revealed that she was affected with CA-ex-PA stage pT3N2a. After the surgery patient was sent for radiotherapy as a part of her treatment plan and made an uneventful recovery. On the follow-up, the patient has shown no signs of recurrence and has no adverse or anticipated events. CA-ex-PA is a rare, aggressive cancer that can lead to death. Preoperative diagnosis of submandibular gland tumors requires comprehensive clinical history, suspicion of malignancy and radiographic analysis. In order to manage CA-ex-PA and prolong survival rates, prompt diagnosis, a multidisciplinary approach, surgical resection and radiation therapy are essential. Consistent follow-up is also crucial.

Keywords: CA-ex-PA, Submandibular gland excision, Right radical neck dissection, Radiotherapy

INTRODUCTION

The most prevalent forms of malignant tumours within the salivary glands include malignant PA, adenoid cystic carcinoma, mucoepidermoid carcinoma and adenocarcinoma.[1] PA presents three distinct morphological variants, each marked by malignant transformations. These include Ca ex PA, true malignant mixed tumour (carcinosarcoma) and metastasizing PA which is an uncommon type of cancer that primarily impacts the major salivary glands, with a particular focus on the parotid and submandibular glands.[2] A variety of terms, such as non-invasive (intracapsular) carcinoma, intracapsular (*in situ*) carcinoma, precancerous foci, intraductal carcinoma and intraductal precursor, have been used to identify and describe the existence of early Ca ex PA.

Traditionally, a PA is recognized as a well-encapsulated tumour characterized by the presence of epithelial and myoepithelial cells.[3] It is suggested that cytological examination may serve as a valuable tool in its early detection.[4] Salivary gland tumours are infrequently encountered neoplasms. The majority of these tumours are confined to specific areas within the parotid glands, subsequently followed by the submandibular, sub lingual and minor salivary gland regions.[5] The primary form of treatment involves surgical resection of the tumour, accompanied by a neck dissection. The best course of action is to perform a thorough local excision with

adequate safety measures and then continue to monitor the patient on a regular basis.

The selection of surgical procedures is influenced by various factors, including the position, dimension and histological characteristics of the tumour. The administration of adjuvant radiotherapy is recommended for individuals at an elevated risk of recurrence, characterized by factors including significant tumour stage, positive resection margins and a high histological grading.[6] The employment of adjuvant radio therapy has considerably enhanced the rates of local control and overall survival (OS) among patients with cancers of the head and neck.[7] Here, we present a rare case of carcinoma PA in female patient followed by the sub mandibular excision with right radical neck dissection.

CASE REPORT

A 55-year-old female presented with complaints of swelling in the right side of neck below the jaw with metastasis of unknown origin (MUO) of neck. The patient was admitted here for further management. On physical examination the patient was conscious, blood pressure was 110/71 mmHg, heart rate was 88 beats per minute, normal respiratory rate, body temperature was 98.6°F and 99% SpO_2 on room air and on examination the abdomen was soft with bowel sounds. Blood, serum and urine investigative results were within normal range. Upon thorough examination of the tongue and associated oral cavity sites, no abnormalities were observed. The endoscopic examination of the pharynx and larynx also demonstrated normal findings.

Computed tomography (CT) showed various nodules at the right cheek with malignancy and enlarged submandibular gland with a lymph node mass of 6×4 cm extended to level 2 and 3 infiltrating in IJV (Figure 1). There was no facial weakness on examination. In order to ensure a definitive diagnosis, intraoperative sub mandibular gland excision and right radical neck dissection along with IJV was done on the following day of admission. Due to the spread of lymph node to the IJV, IJV was sacrificed. During the surgery, complete right side lymph nodes were dissected, hemostasis was achieved, drains were placed.

A well-defined grey-white lesion that spread into the muscle with a coverage of 5.5×6.5×4.5 cm was identified in the section that was cut from the dissected specimen, which measured 11.5×7×5 cm. The attached skin ellipse was measured about 5.5×5.5×0.3 cm. Additionally, a salivary gland of 3.8×2×1.2 cm along with lymph nodes were identified. A well-defined grey-white lesion measuring 4×3.5×3.5 cm was found within the right submandibular gland, which measured 7×4.5×3.5 cm. A sclerotic nodule measuring 1.2×1.3 cm, 3 cm-diameter dilated vessel and an adjacent salivary gland measuring 2×2×1 cm was also identified. This dissected specimen was sent to histopathology lab for the precise conformation.

Histopathological examinations revealed that the smaller nodule of right submandibular gland was consistent Ca ex PA with salivary duct (Figure 2 and 3) tumour is uni focal measuring 4 cm in maximum dimension, lymph vascular invasion and perineural invasion was also identified. Resected margin was free of tumour and extra nodular extension was identified (Figure 4 A-C). Right neck nodes with jugular vein of larger nodule with a largest metastatic deposition of 6.5 cm was identified. It was also noted that, skin, adjacent salivary gland and separately received vessel were free of tumour. Infiltrating tumour arranged in lobules, sheets and cells showed moderate pleomorphism with vesicular nucleus, prominent nucleoli and moderate eosinophilic cytoplasm with extensive areas of necrosis was noted (Figure 5 A-C). Final diagnosis was Ca ex PA, stage pT3N2a. Postoperatively patient was hemodynamically stable, drains were removed and sent for the radiotherapy as a part of treatment plan. Here our patient was exposed to an external beam radiation dose of 50 GY (range, 45-71 GY) in ten fractions sequentially boost given to the dissected area with a dose of 15GY as advised by radiation oncologist. Patient found stable and was discharged from the hospital. On the follow up the patient has shown no signs of recurrence and has no adverse or anticipated events and successful recovery.

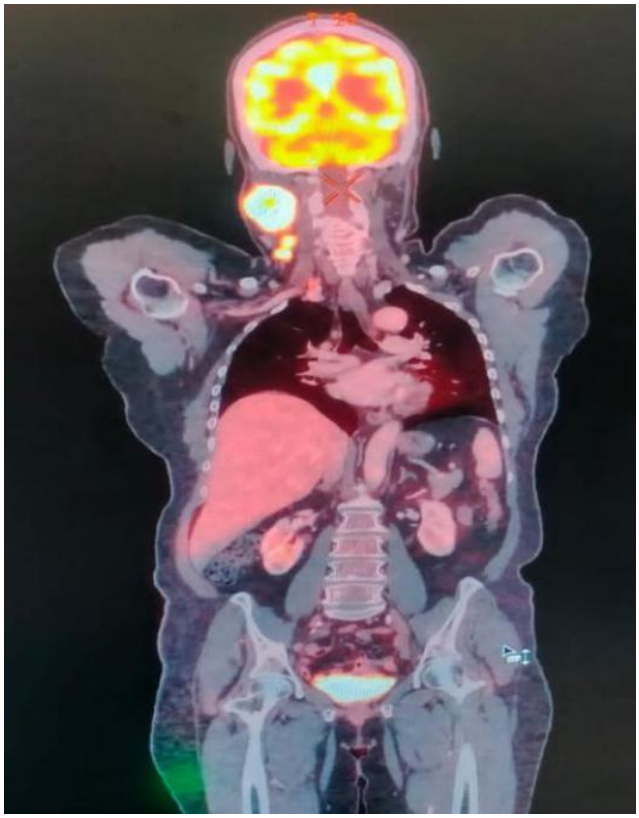

Figure 1: PET-CT image showing right check with malignancy and enlarged submandibular gland with lymphnode.

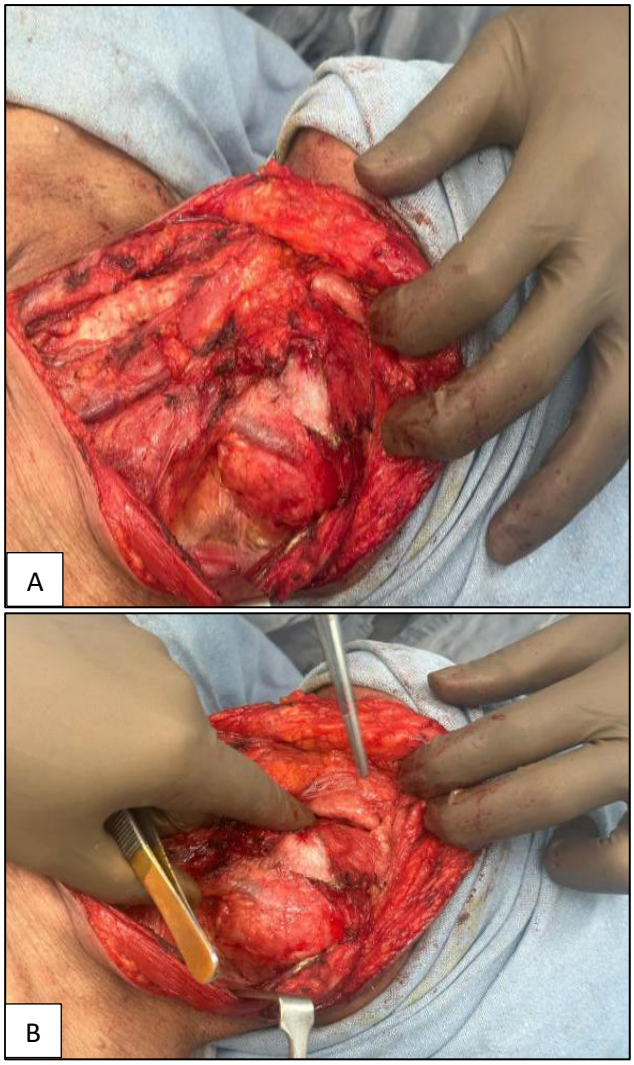

Figure 2 (A and B): Intraoperative pictures showing submandibular gland carcinoma PA of right side of neck below jaw level II and level III.

Figure 3: Postoperative image of the patient's neck.

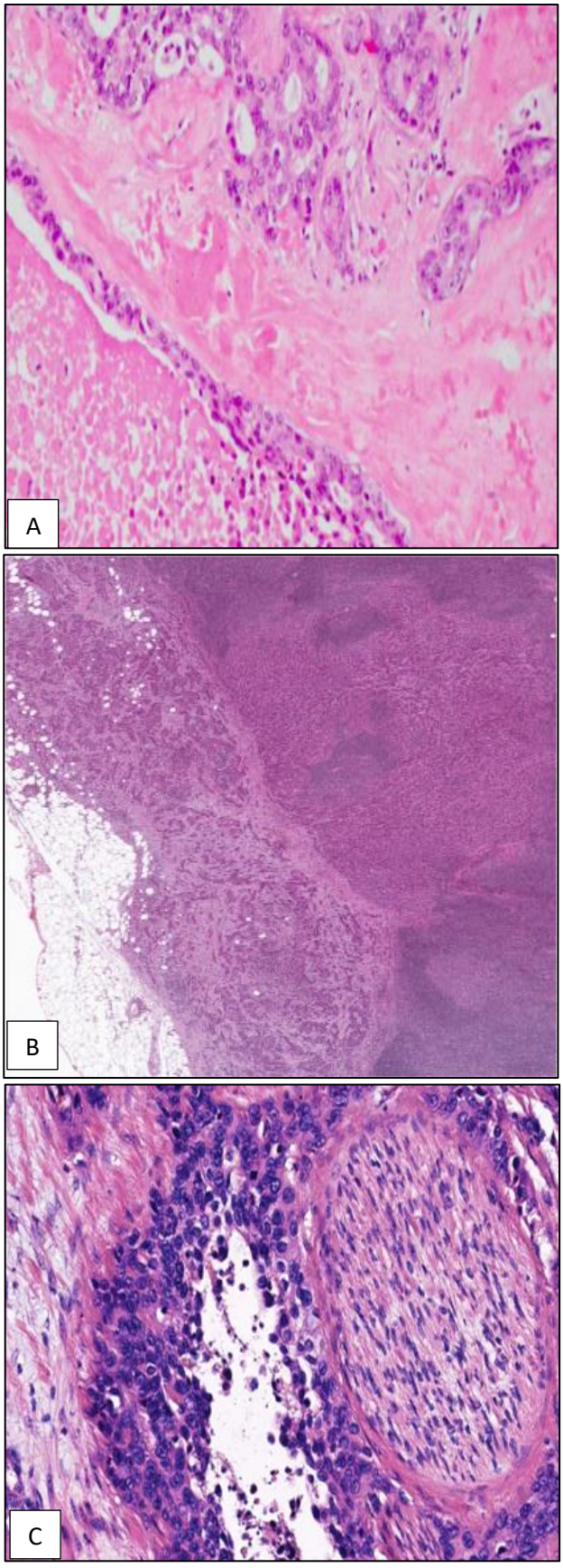

Figure 4 (A-C): Histopathology images show cells arranged near are carcinoma PA, extra nodular extension and perineural invasion in carcinoma PA.

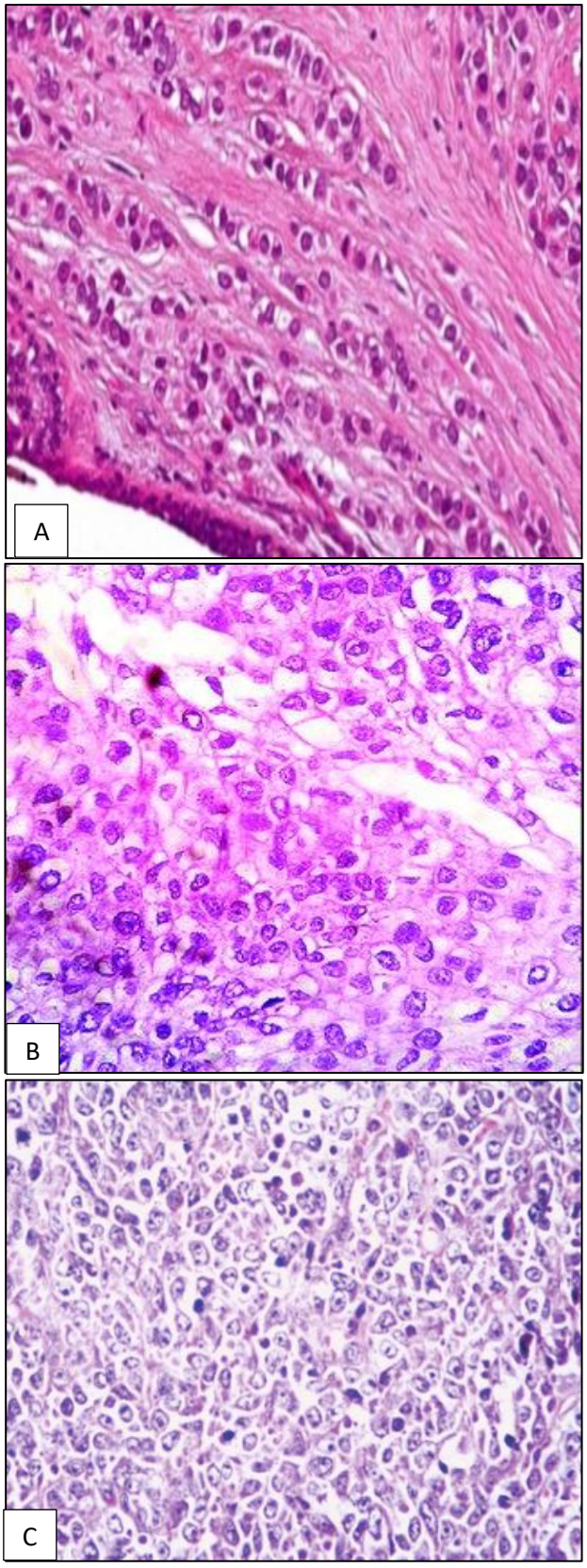

Figure 5 (A-C): Histopathology images show infiltrating tumour arranged in lobules, sheets and cells, moderate pleomorphism with vesicular nucleus and prominent nucleoli and moderate eosinophilic cytoplasm with extensive areas of necrosis.

Therapeutic intervention

Patient was treated conservatively with analgesics and antibiotics, tablet monocef (oral, 200 mg, twice daily), tablet paracetamol (oral, 325 mg, twice daily), tablet aceclofenac (oral, 100 mg, twice daily), tablet pantoprazole (oral, 40 mg, once daily), tablet zincovit (oral, once daily).

DISCUSSION

Ca ex PA characterizes a spectrum of incidence, ranging from 5 to 15%, in contrast to the widely accepted range of 12% for all salivary gland malignancies. This discrepancy is attributed to the potential presence of a small residual PA component and the diversity of carcinoma sub types. Numerous research studies view Ca ex PA as a highly aggressive carcinoma, characterized by a poor prognosis.[8] It is frequently associated with the development of metastasis and contributes significantly to disease-related mortality. Previous research has identified a number of clinicopathological factors that exhibit a negative correlation with the prognosis of Ca ex PA. These factors encompass advanced stage, involvement of lymph nodes, extent of invasion, type of tumor and grade.[9] The most frequently observed initial indication of Ca ex PA is a persistent mass within the salivary glands, which is frequently asymptomatic initially, preceding a rapid expansion in size. This expansion can lead to discomfort or pain in some cases. Nonetheless, the clinical manifestation may imitate that of a benign parotid adenoma, complicating the accurate diagnosis of Ca ex PA.[10]

In our case, the patient had swelling at right side of the neck below the jaw which was diagnosed as submandibular swelling MUO of neck. MUO constitutes a diverse collection of malignant tumors characterized by the presence of lymph node or distant metastasis.[11] Our patient's CT revealed the presence of malignant multiple nodules at the right side and an enlarged submandibular gland accompanied by a lymphnode mass. In individuals diagnosed with salivary gland cancer, positron emission tomography/ CT (PET/CT) plays a crucial role as a diagnostic tool for determining the extent of the disease and providing prognostic insights, which helps in deciding the appropriate treatment methods.[12, 13]

Our patient underwent sub mandibular gland excision and right radical neck dissection along IJV. Due to the attachment of lymph node to IJV, salivary gland and complete right side lymph nodes were dissected. During surgical procedure encompassing skin incisions and tumour excision, it is crucial to thoroughly assess the anatomical orientation of the adjacent blood vessels.[14] Small nodule of right submandibular gland was consistent with CA-ex-PA of salivary duct carcinoma and Surgical resection remains the mainstay of treatment for Ca ex PA. [15]

The primary therapeutic approach for Ca ex PA involves a complete removal of the tumor. In preference, radical resection should be pursued whenever feasible. The extent to which the tumor resected will significantly impacts the prognosis. The surgical extent must be tailored to each case, taking into account the tumor's location and the proximity of adjacent anatomical structures. A neck dissection may be required if the lymph nodes demonstrate signs of metastasis.[16] The procedure of neck dissection is recommended to majority of the patients with cervical cancer who have undergone primary axillary surgery, with the exception of instances involving intracapsular or minimally invasive disease. This procedure can be executed in three different forms like functional, modified, or radical.[17]

In our case, patient under went radiation therapy after the surgery. Postoperative radiation therapy is commonly administered to patients with an excisional cancer and positive surgical margins, particularly when the tumor exhibits advanced stage, high histological grade, residual tumor volume and close margin, in addition to neural or perineural invasion, lymph node involvement and lympho vascular invasion. The incidence of recurrence can be reduced when surgery is supplemented with radiotherapy, as opposed to surgery performed in isolation.[18] Multiple research studies have indicated that adjuvant radiotherapy can enhance the control of local tumors and increase the survival rates of patients. Furthermore, it acts as a salvage treatment option for individuals who have insufficient surgical margins.[19]

CONCLUSION

Ca ex PA represents a rare and highly aggressive form of cancer. It is frequently linked with the development of regional metastasis; sometimes this condition invariably results in the death of patient. The preoperative diagnosis of submandibular gland tumors presents significant challenges. Hence, it is crucial to consider a comprehensive clinical history, along with a suspicion of malignancy concerning a persistent salivary gland mass, in conjunction with radiographic analysis.

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REFERENCES

1. Young A, Okuyemi OT. Malignant Salivary Gland Tumors. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2024.
2. Song JS, Kim Y, Lee YS, Choi SH, Nam SY, Kim SY, et al. Frequent apocrine changes in pleomorphic adenoma with malignant transformation: a possible pre-malignant step in ductal carcinoma ex pleomorphic adenoma. J Pathol Translational Med. 2023;57(3):158-65.
3. Matsushima M, Ohara R, Ishida M, Kanao K, Shimokawa R, Nakajima Y. Carcinoma ex pleomorphic adenoma of the submandibular gland with renal metastases composed exclusively of metastasizing pleomorphic adenoma. Int Cancer Conference J. 2012;1:116-20.
4. Shoukair FL, Maly A, Haran TK, Hirshoren N, Abu Tair J. Maxillofacial diagnostic features of the enigmatic metastasizing pleomorphic adenoma. Int J Oral Maxillofacial Surg. 2020;49 (7):841-7.
5. Galdirs TM, Kappler M, Reich W, Eckert AW. Current aspects of salivary gland tumors-a systematic review of the literature. GMS Interdisciplinary Plastic Reconstructive Surg DGPW. 2019;8:Doc12.
6. Katano A, Yamashita H. Adjuvant Radiotherapy for Major Salivary Gland Malignancies: Impact on Locoregional Control and Survival Outcomes. In Vivo. 2023;37(6):2792-5.
7. Sayan M, Vempati P, Miles B, Teng M, Eric G, Elizabeth GD, et al. Bakst. Adjuvant Therapy for Salivary Gland Carcinomas Anticancer Res. 2016;36(8):4165-70.
8. Grace PL, Guan J, Wang XY, Zhang GL, Ning SB, Dai XP, et al. Submandibular gland carcinoma ex pleomorphic adenoma clinically mimicking a benign lesion. Oral Maxillofac Surg Cases. 2020;6(3):100166.
9. Zhao J, Wang J, Yu C, Guo L, Wang K, Liang Z, Lou J. Pronostic factors affecting the clinical outcome of carcinoma ex pleomorphic adenoma in the major salivary glands. World J Surgical Oncol. 2013;11(1):180.
10. Kim J, Kim M, Choi S. High grade carcinoma ex pleomorphic adenoma of parotid gland: a case report. J Kor Asso Oral Maxillofacial Surgeons. 2020;46:348-352.
11. Nassenstein K, Veit-Haibach P, Stergar H, Gutzeit A, Freudenberg L, Kuehl H, et al. Cervical Lymph Node Metastases of Unknown Origin: Primary Tumor Detection with Whole-Body Positron Emission Tomography/Computed Tomography. Acta Radiologica, 2007;48(10):1101-8.
12. Nakajima R, Patel SG, Katabi N, Flukes S, Mauguen A, Ganly I, Schöder H. Diagnostic and Prognostic Utility of 18F-FDG PET/CT in Recurrent Salivary Gland Cancers. AJR Am J Roentgenol. 2021;216(5):1344-56.
13. Bansal A, Dhamija E, Chandrashekhara SH, Sahoo RK. Role of CT in the detection and management of cancer related complications: a study of 599 patients. E-cancer Med Sci. 2023;17:1529.
14. Shudo A. Large Pleomorphic Adenoma of the Submandibular Gland Causing Internal Jugular Vein

Compression: Case Report. SN Comprehensive Clin Med. 2020;2:2493-9.
15. Fuad AMA, Guan LS, Yunus MRM. Never too young for a salivary gland carcinoma ex-pleomorphic adenoma. Egypt J Otolaryngol. 2024;40:15.
16. Antony J, Gopalan V, Smith RA, Lam AK. Carcinoma ex pleomorphic adenoma: a comprehensive review of clinical, pathological and molecular data. Head Neck Pathol. 2012;6(1):1-9.
17. Niki-Yonekawa A, Morita Y, Kusuyama Y, Ueno Y, Kishimoto S, Morita N, et al. Carcinoma ex pleomorphic adenoma in an elderly patient: A case report and literature review. Oral Maxillofacial Surg Cases, 2022;8(3):2214-5419.
18. Khanna D, Chaubal T, Bapat R, Abdulla AM, Philip ST, Arora S. Carcinoma ex pleomorphic adenoma: a case report and review of literature. Afr Health Sci. 2019;19(4):3253-63.
19. Wakasaki T, Kubota M, Nakashima Y, Tomonobe E, Mihara T, Fukushima J. Invasive myoepithelial carcinoma ex pleomorphic adenoma of the major salivary gland: two case reports. BMC Cancer. 2016;16:827.

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