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RESEARCH ARTICLE

POSTOPERATIVE RADIOTHERAPY IN SALIVARY DUCTCARCINOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Salivary duct carcinoma(SDC) is a rare and aggressive tumor of the salivary glands that often occurs in men between the fifth and sixth decades of life. standard treatment is based on wide surgical resection of the primary tumor with lymph node dissection, followed by postoperative radiotherapy. The place of chemotherapy in the treatment of SDC remains unknown. In this publication, authors report a case of SDC of the left parotid gland. A 28-year-old male suffered from a painful neck mass associated with hearing loss that had been evolving for 6 months. The patient initially had a cervical CT scan and a parotid MRI, which showed a tumor of the left parotid gland. He initially had a total parotidectomy preserving the facial nerve with an ipsilateral neck dissection, as the intraoperative histological examination was in favor of malignancy. The final analysis of the surgical specimen concluded to a ductal carcinoma of the parotid with lymph node metastasis. Adjuvant radiation therapy has been indicated. The evolution was unfavorable due to the appearance of multisite metastases after one year.

Introduction:-

Salivary duct carcinoma (SDC) is a rare and one of the most aggressive subtypes of salivary gland cancer that histologically resembles mammary ductal carcinoma **[1,2]**. It occurs most frequently in the parotid gland and shows an aggressive behavior with early cervical nodes involvement and distant metastasis, the prognosis of SDC is highly unfavorable **[1]**. The mainstay of treatment in SDC is wide surgical resection followed by adjuvant radiation therapy **[1,2].** We describe a case of SDC recently treated in our institution and discuss the role of radiotherapy in the management of SDC.

Case Presentation:

A 28-year-old Moroccan male with a past of 17 pack-year history of tobacco smoking presented to the Oral and Maxillofacial Surgery Department for progressive swelling of the left parotid region for 6 months associated with moderate pain and hearing loss. He did not have peripheral facial paralysis or other localized or constitutional symptoms.

A cervical computed tomography (CT) was requested at first which identified two left parotid nodules with a necrotic center, enhancing in the periphery after contrast injection, and measuring 26*18 mm and 15*15 mm associated with a left spinal lymph node measuring 11 mm on the short axis. Then a parotid MRI was performed, it

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showed multiple left parotid nodules measuring 6*3,5*2,5 cm. The lesion appeared isointense on T1-weighted images and had intermediate to high signal intensity on T2-weighted images with intense and heterogeneous contrast enhancement on T1 following administration of gadolinium (Figure 1).

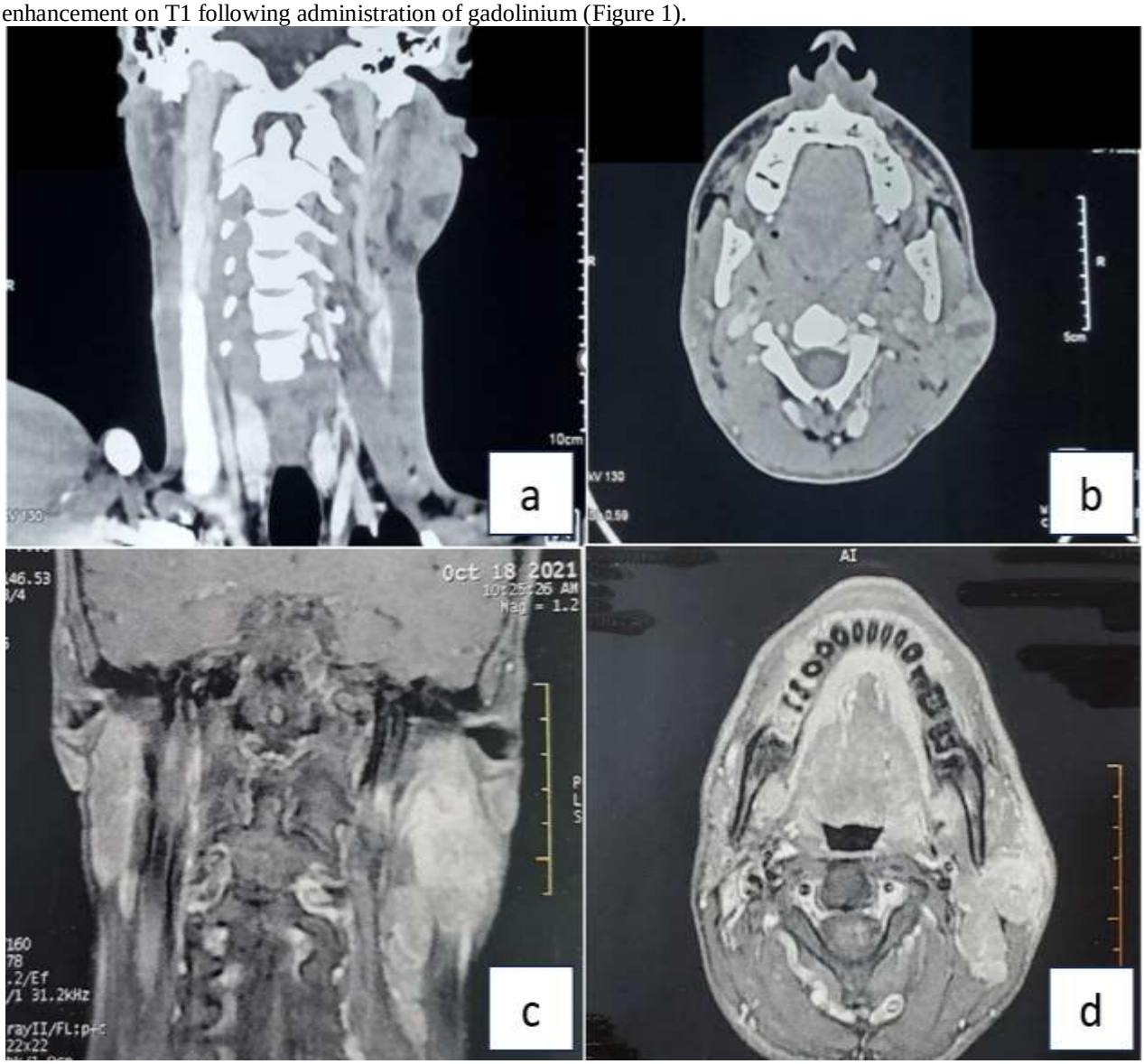

Figure 1:- CT (a,b) and MRI (c,d) images showing a tumor in the left parotid gland.

The patient initially had a total parotidectomy preserving the facial nerve with an ipsilateral neck dissection, as the intraoperative histological examination was in favor of malignancy. On Anatomopathological examination, the macroscopic study revealed a fragmented surgical specimen with, on section, multiple firm whitish tumor nodules measuring 0.5 to 2 cm on the long axis. The microscopic analysis showed an infiltrating, multinodular carcinomatous proliferation with a polymorphic architecture, solid, trabecular and rarely micropapillary. Tumor cells are cuboidal or polygonal with abundant granular eosinophilic cytoplasm and a heavily nucleolated round nucleus. Mitoses were frequent. The stroma was desmoplastic. There were foci of necrosis and lymphovascular invasion. These histological characteristics are specific to SDC which are reminiscent breast ductal carcinoma(Figure2). 28 lymph nodes were involved among 30 removed.

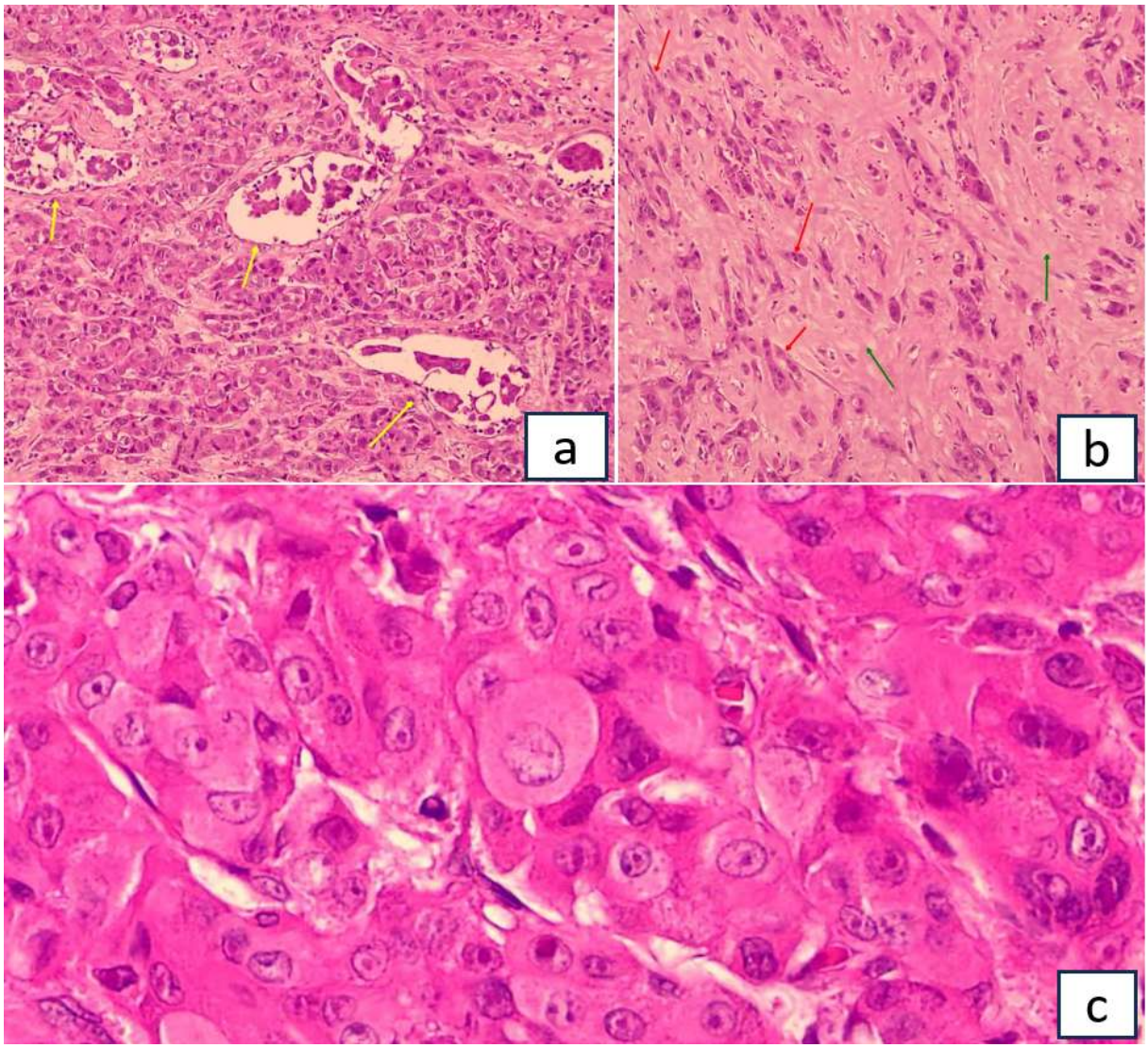

Figure 2:- Histological analysis in favor of SDC (a: micropapillary (yellow arrow) and solid architecture, b: desmoplastic stroma (green arrow) and trabecular architecture (red arrow), c: cytonuclear atypia).

Postoperative Cervical-thoracic-abdominal-pelvic CT showed a suspicious soft tissue lesion in the left cervical region at the height of second cervical vertebrae measuring 18*12 mm, without distant metastasis. The medical report was then discussed in Multidisciplinary meeting hence the decision to complete with a cervical ultrasound. The latter revealed multiple lymph nodes around the upper and middle left internal jugular chain, the largest measuring 15*9 mm. A revision surgery was required, an ipsilateral radical neck dissection was then performed. Histological examination revealed 26 positive lymph nodes for salivary duct carcinoma among 35 removed. The final pathological staging was T3N2bM0.

36 days after surgery, post-operative radiation therapy was applied. External beam radiotherapy was prescribed to the parotid bed at a total dose of 60 Gray in 30 fractions, 2.0 Gy per day, delivered once daily, five days a week; and 54 Gray to the ipsilateral and contralateral cervical lymph node chains in 30 fractions simultaneously, 1,8 Gy per day, delivered once daily, five days a week, over 7,3 weeks, using volumetric modulated arc therapy technique with simultaneous integrated boost (VMAT- SIB) (Figure 3). We were able to respect the constraints of the organs at risk such as the spinal cord, contralateral parotid, oral cavity, eyes, mandible and temporomandibular joint, brachial plexus, esophagus and larynx and at the same time deliver the expected radiation dose to the target volumes. the patient received the total planned dose with good overall tolerance. Weekly consultation during radiotherapy did not reveal any acute toxicities except grade II radiation dermatitis and also grade II radiation esophagitis, which were

treated symptomatically with a good outcome. The patient was presented three months after the end of treatment, he reported a grade II xerostomia without evidence of disease recurrence.

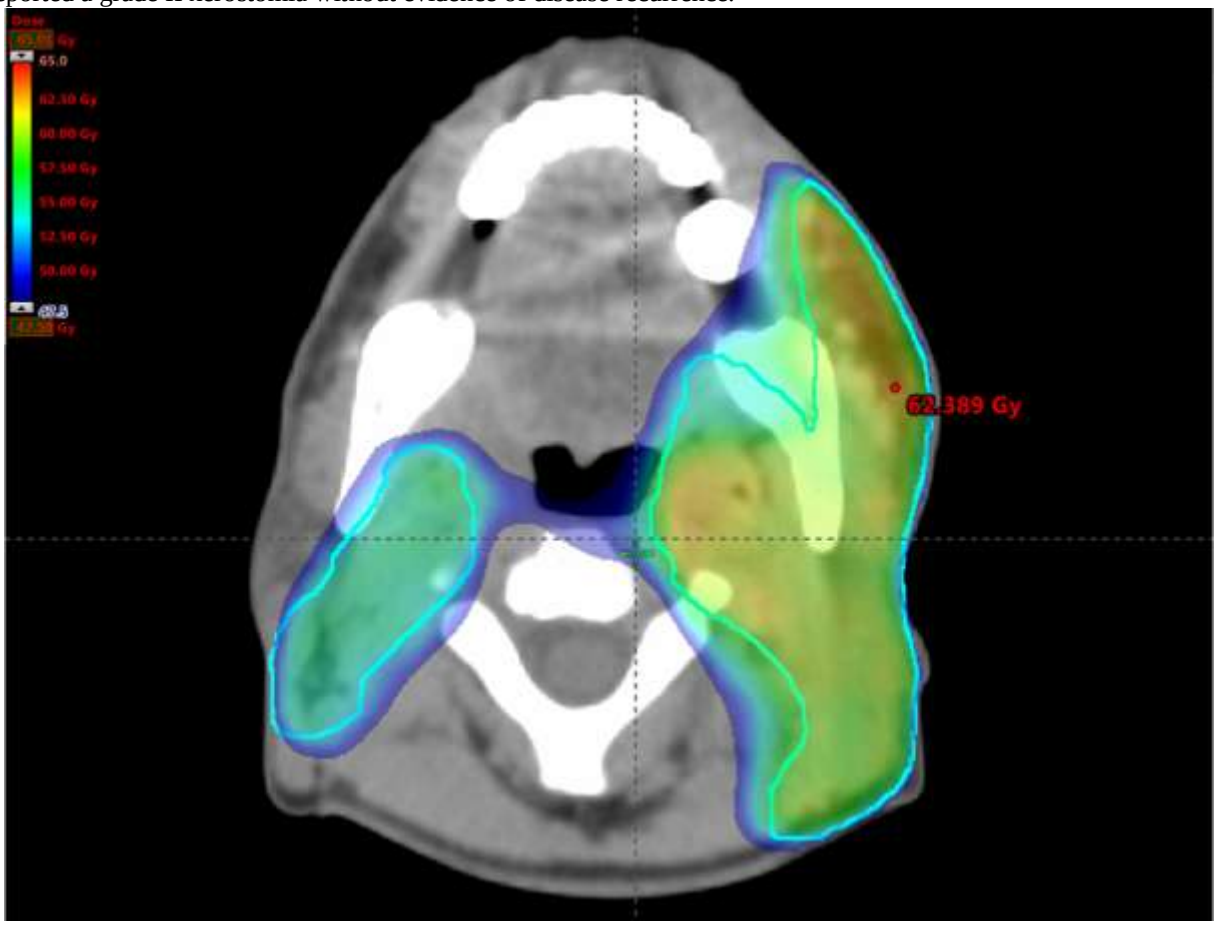

Figure 3:- Radiotherapy of the left parotid bed and the ipsilateral and contralateral cervical lymph node chains.

He did not receive adjuvant systemic treatment because the Human Epidermal Growth Factor Receptor-2 (HER2) analysis did not find any amplification. One year after the end of treatment, the patient reported headaches and left axillary lymphadenopathy. An axillary ultrasound and a whole-body CT scan were performed. They showed a cerebral, pulmonary and lymph node relapse. For which he received chemotherapy with carboplatin docetaxel.

8 months later, he presented with intracranial hypertension syndrome, the brain CT revealed multiple infra and supra tentorial metastasis for which a whole brain radiotherapy was administrated with corticotherapy (Figure 4). A second line of systemic therapy with vinorelbine was indicated.

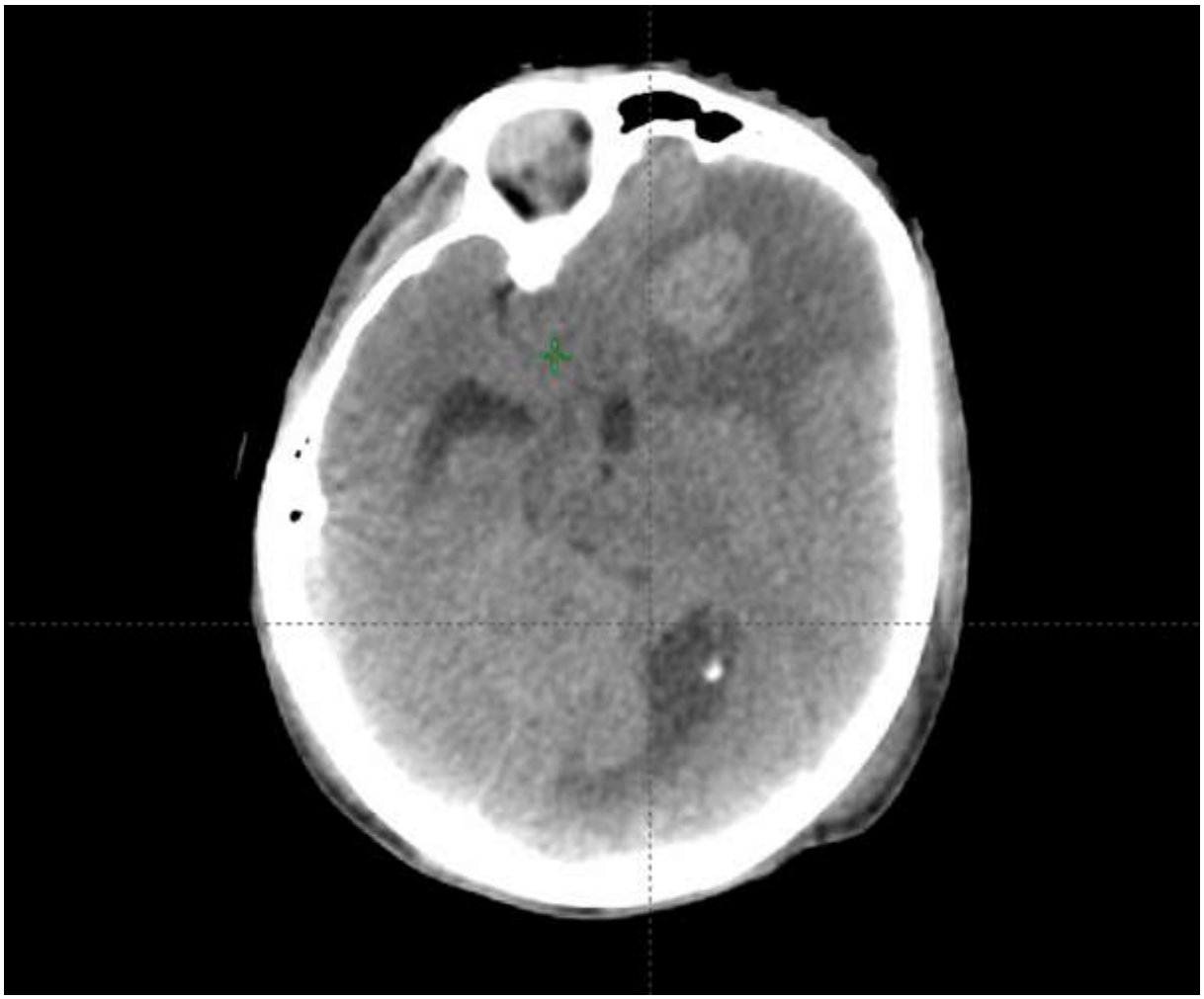

Figure 4:- CT image showing brain metastasis.

Discussion:-

SDC is a salivary gland neoplasm that is uncommon, extremely aggressive and very rare, accounting for only 1 to 3% of malignant salivary gland tumors **[3-5]**. Kleinsasser et al first characterized it as a separate entity of salivary gland adenocarcinoma in 1968, which had a histological resemblance to breast ductal carcinoma**[6]**. These tumors were classified as a distinct tumor group by the World Health Organization (WHO) in 1991**[7].**It appears mostly between the fifth and the seventh decade of life; with a male predominance **[8,9],** our case was one of the youngest patients reported in the literature. Most SDC arise from the parotid glands, as was the case of our patient, followed by submandibular glands or minor salivary glands **[3].**

The typical presentation of SDC is a rapidly expanding firm mass accompanied by facial weakness or pain **[3]**. In our case, the patient suffered from a painful neck mass associated with hearing loss. SDC is a high-grade salivary gland malignancy that is highly aggressive by developing early regional metastasis, distant metastasis, and a high-grade recurrence. Lymph node involvement, distant metastasis and local recurrence are found in 40-80%, 60-70 % and 11-48% of patients respectively **[3,7,9,10,11]**. Lung, bone, brain, and liver are the most metastatic sites **[5].**

Histopathologically, SDC is similar to breast ductal carcinoma and is made up of intraductal and invasive components. Cribriform, papillary, or solid growth pattern is commonly observed in the intraductal component, often accompanied by comedolike central necrosis. The invasive carcinoma is composed of irregular glands and cords of cells that often result in a prominent desmoplastic reaction. The majority of tumors develop spontaneously, but 20% of cases are caused by preexisting benign pleomorphic adenomas **[4,12].**

The differential diagnosis of SDC mainly includes the papillary cystic and microcystic variants of acinic cell carcinoma, metastatic breast cancer, metastatic prostate carcinoma, mucoepidermoid carcinoma, and oncocytic carcinoma **[10].** The study of the receptors at estrogen and progesterone and research in immunohistochemistry of the HER-2 protein may be useful for the diagnosis **[9-11].**

The rarity of SDC has made it impossible to conduct large randomized trials to establish a standard of care **[9]**. Current management options include surgery, systemic therapy, radiation and targeted therapy. For National Comprehensive Cancer Network (NCCN 2024), no specific recommendations for SDC exist. However, complete surgical resection of the primary tumor with or without neck dissection is recommended for major salivary gland tumors without lymph node involvement (N0). Regarding high-grade tumors (T3/T4) or tumors with lymph node involvement (N+), treatment is based on complete surgical resection with neck dissection**[9,10]**. Our patient was treated with total parotidectomy with ipsilateral radical neck dissection. Concerning postoperative radiotherapy, it should be used in the event of locoregional recurrence risk factors, namely positive or close resection margins, perineural invasion, intermediate or high-grade tumors, T3/T4 tumors, lympho vascular spread, lymph node metastasis **[9,10]**. For SDC, adjuvant radiotherapy is recommended regardless of the stage or the state of the margins **[5].** Retrospective evidences have shown improvement in local control and overall survival in patients receiving adjuvant radiotherapy **[4,7,9,10,13].** A Median total radiotherapy dose of 60 Gray is recommended in various studies.

Regarding systemic therapies, several studies have shown encouraging results with targeted therapy for androgen receptor (AR) and human epidermal growth factor receptor 2 (HER2), and the recent version of NCCN guidelines recommends the evaluation of AR and HER2 status before treatment **[9,10,14].** In our case, there was no amplification of HER2. Chemotherapy has poor efficacy without benefit of its combination with radiotherapy, it is reserved for metastatic forms **[9,10].**

Salivary duct carcinoma is characterized by aggressive growth, and frequent local recurrence and distant failure **[5].** Perineural involvement, lymphovascular spread, multiple lymph node invaded and the presence of extracapsular nodal infiltration, facial nerve involvement, overexpression of "HER-2", size of more than 2 cm and involved margins often are considered as poor prognostic indicators, although findings are inconsistent. The 5-year disease-free survival rate is 30% and the mortality rate reaches 70% **[11,13].**

Conclusion:-

SDC is a rare aggressive salivary gland cancer associated with high morbidity and mortality. It often affects the parotid gland, and occurs in elderly men with an advanced stage at presentation. Surgery and postoperative radiotherapy in SDC patients resulted in good local control. However, the high rate of distant failures poses a significant challenge, which necessitates optimizing adjuvant therapy.

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