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Case Report

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Complex Treatment of Rare Aggressive Salivary Duct Carcinoma-A Clinical Case From Our Practice

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Abstract

Salivary duct carcinoma (SDC) is a rare, aggressive salivary neoplasm. We present a 64-year-old woman with locally advanced salivary duct carcinoma of the left parotid gland with metastatic involvement of the left cervical lymph nodes. A radical left-sided parotidectomy with left-sided cervical lymphatic dissection was performed. Given the advanced disease/pT4 pN2b M0, as well as the aggressive nature of the proven carcinoma, the patient was referred for postoperative combined chemoradiotherapy (Ch-RT). Despite aggressive complex local treatment, on the background of achieved local and regional tumor control, at the sixth month after its completion, PET/CT proved metabolically active accumulation in the left extra-regional axillar lymph nodes and in the left occipital implantation metastases.

Strict pathohistological and differential diagnosis of this rare, aggressive tumor requires immunohistochemical analysis of androgen receptors (AR), which are usually positive. In case of distant metastatic dissemination, it is necessary to carry out AR target therapy.

Keywords: Salivary duct carcinoma, Immunohistochemical analysis, Postoperative combined chemo-radiotherapy, Androgen receptors target therapy

1. Introduction

Salivary duct carcinoma (SDC) is a rare, aggressive salivary malignancy [1]. It is diagnosed more often in the major salivary glands than in the submandibular and minor salivary glands [2-5]. SDC is most frequently seen in men aged 50 or older [6-8] and is one of the more rare malignant salivary tumors. Though described as early as 1968, SDC was only recognized as a distinct tumor type by the World Health Organization in 1991 [9]. The diagnosis in a locally advanced stage, the high frequency of relapses and metastases in extra-regional lymph nodes are characteristic [10-15]. The clinical and pathologic findings of SDC have been well described, and several authors recommend aggressive multimodal approaches such as adjuvant radiotherapy or chemoradiotherapy [16–18]. We present a rare SDC in which the combination of surgery and postoperative chemoradiotherapy (Ch-RT) achieved local tumor control despite locally advanced clinical stage. The surprise was the follow-up PET/CT performed 6 months after completion of combined Ch-RT, which showed rare implantation metastases in the occipital cervical region and in the extra-regional left axillary lymph nodes, representing distant spread of the disease.

2. Clinical Case

It concerns a 64-year-old woman with a painless swelling in the neck area on the left in 2022. One year later, a CT scan of the neck revealed a mass in the left salivary gland with multiple left-sided cervical lymph nodes. In August 2023, a left-sided parotidectomy was performed with an extended dissection of the left cervical lymph nodes. Histological result - Massive infiltration from low differentiated /G3 large duct parotid carcinoma with perineural invasion and multiple tumor emboli in lymphatic and blood vessels (Figure 1A, B, C) and bundles of lymph nodes with metastases from the described carcinoma (Figure 2). Lymphatic metastases include level V of the cervical lymph nodes on the left, as well as a lymph node of the hypoglossal nerve on the left and lymph nodes of the ductus thoracicus. The immunohistochemical (ICH) examination proved the above-described diagnosis by the positive expression of the tumor cells for CK7 (Figure 3A), as well as for androgen receptors/AR (Figure 3B) and focally positive expression for GATA 3 (Figure 3C). Negative ICH expression was reported for HER 2 (1+), estrogen receptor (ER), napsin A, thyroglobulin and p63. Given the advanced disease/pT4 pN2b M0, as well as the aggressive nature of the proven carcinoma, the patient was referred for postoperative combined RT-Ch. Intensity modulated radiation therapy (IMRT) using the Volumetric Modulated Arc Therapy (VMAT) method in the tumor bed with a daily dose (DD) 2Gy up to a total dose (TD) 66 Gy, and in the left-sided lymph nodes with a DD 1.82 Gy up to a TD 60 Gy with weekly infusions of Cisplatin was performed (Figure 4, Figure 5 and Figure 6).

Four months after completion of combined chemo-radiotherapy, local tumor control was established, but after 6 months, solid non-painful lesions were found in the left occipital region (Figure 7A) and in the left preauricular region, which were scanned without contrast (Figure 7 B, C). The patient was referred for PET/CT, which proved metabolically active metastatic lesions, including in the left axillary region (Figure 8A,B). Surgical excisions of the above-described metastatic lesions in the left preauricular region, left occipital region, and left axilla were performed, followed by pathohistological verification. The patient was directed to continue the treatment with AR targeted therapy, given the positive immunohistological AR tumor expression.

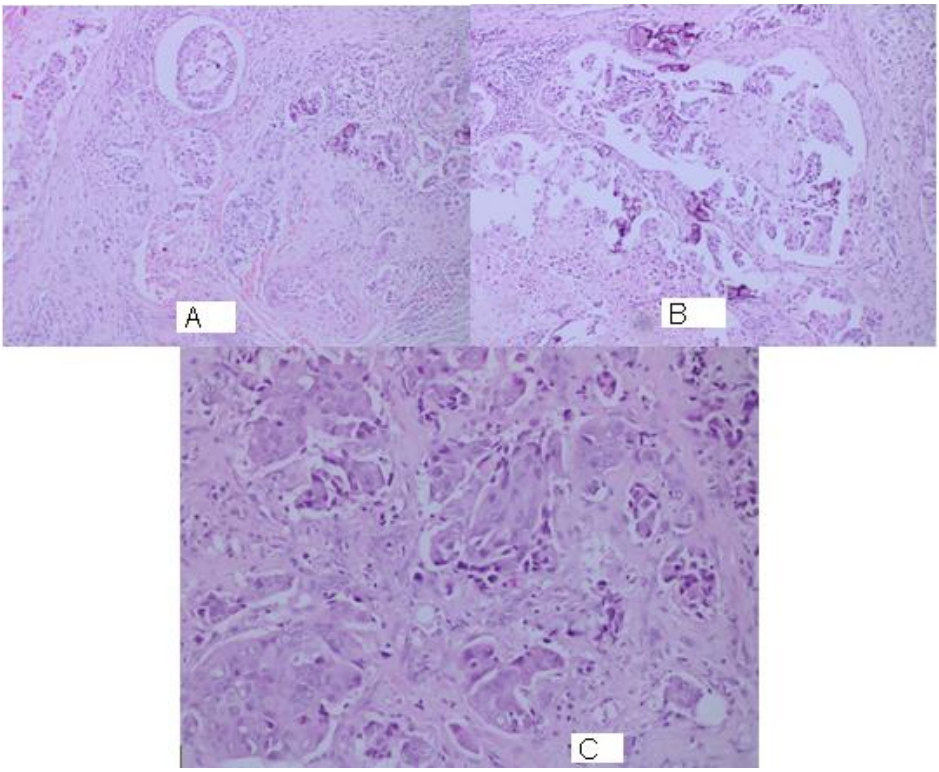

Figure 1: Histological findings of large duct parotid carcinoma - Massive infiltration from large duct parotid carcinoma with perineural invasion and multiple tumor emboli in lymphatic and blood vessels: A , B- HEx100, C- HE x 200.

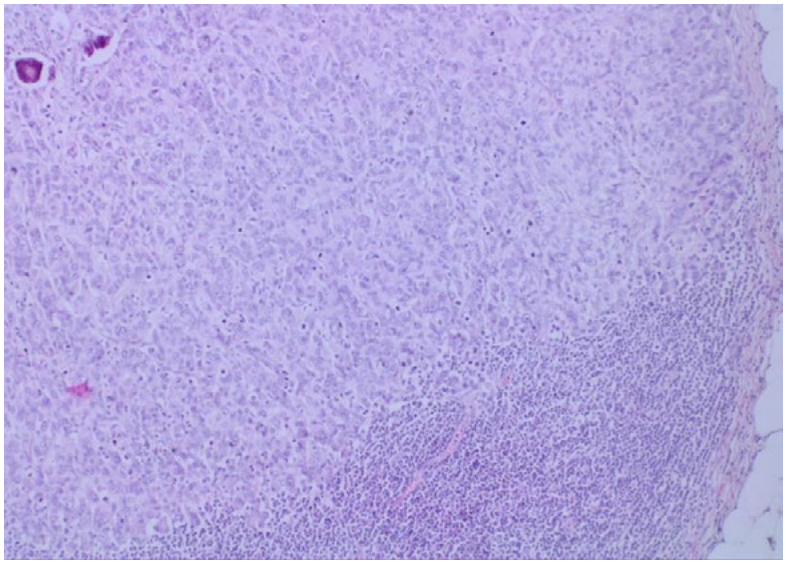

Figure 2: Histological findings of metastatic lymph node/ HEx100

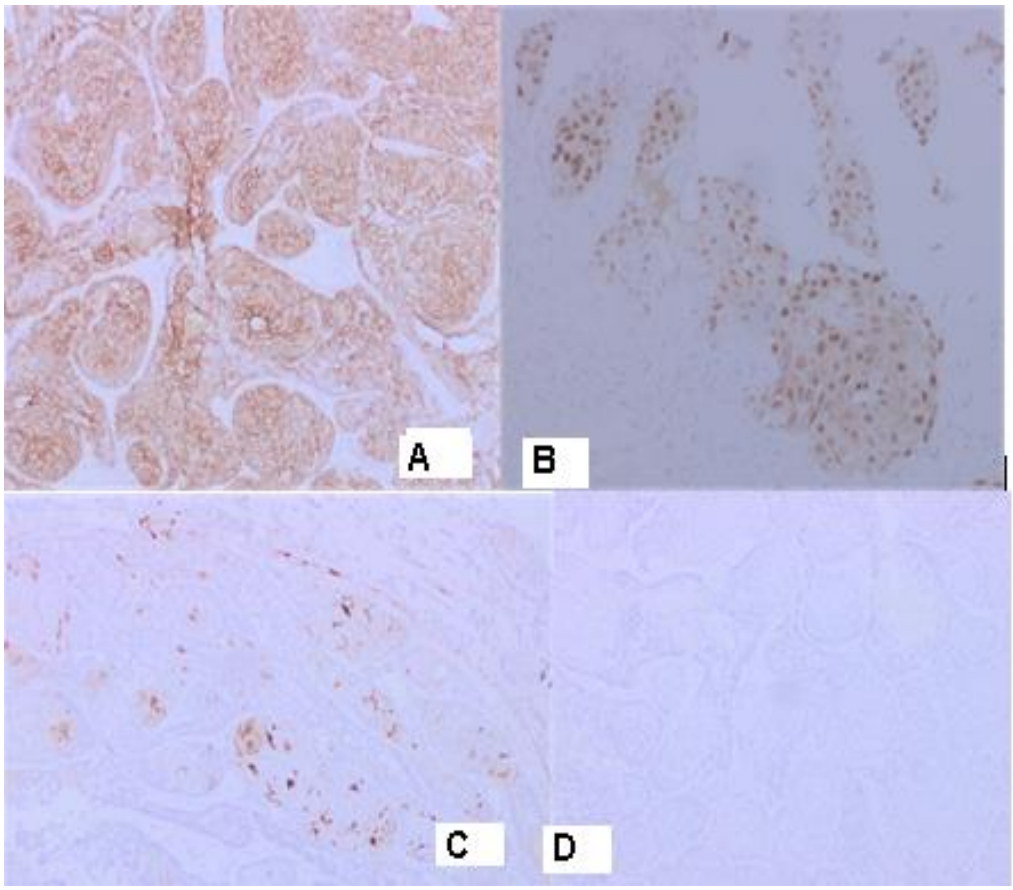

Figure 3: Immunohistochemical analysis– A) Positive ICH expression for CK 7; B) Positive expression for AR; C) Focally positive expression for GATA; D) Negative expression for p 63

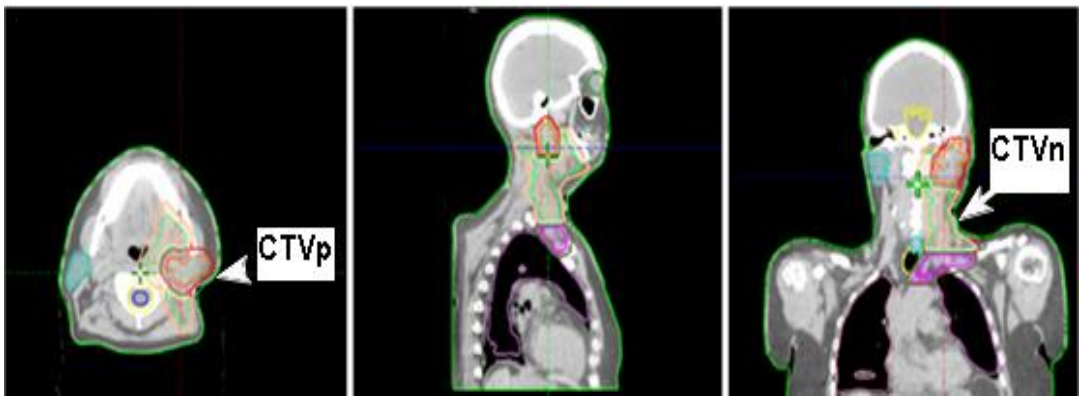

Figure 4: Contouring of the clinical target volumes-tumor bed (CTVp) and left cervical lymph nodes (CTVn).

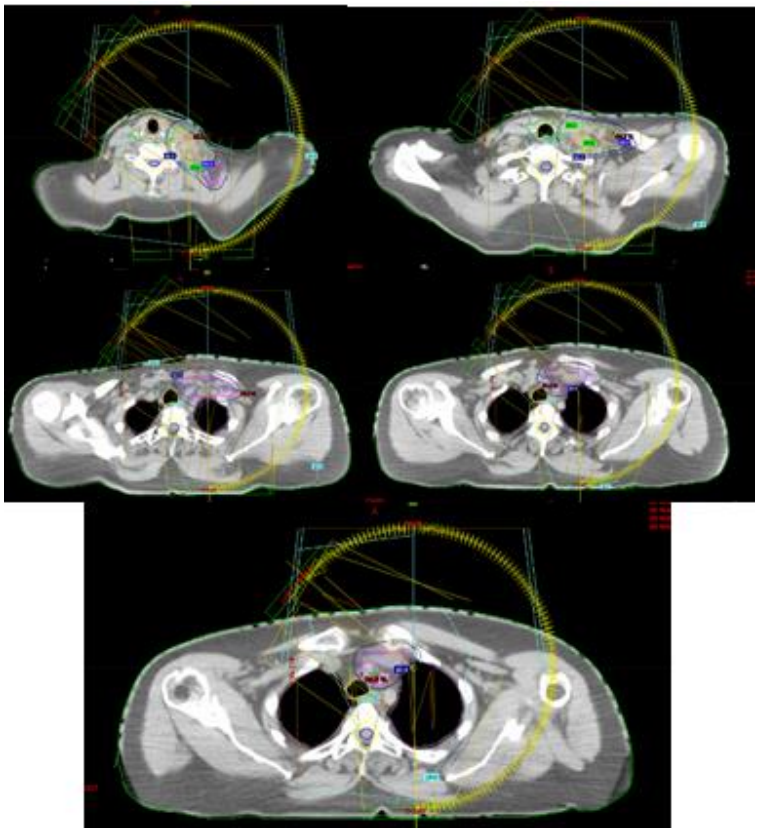

Figure 5: Intensity modulated radiation treatment using the VMAT method in the area of the left-sided lymph nodes, including at the V cervical level with a DD 1.82 Gy up to a TD 60 Gy, and in the area of the VI cervical level with a DD 1.63 Gy up to a TD 54 Gy

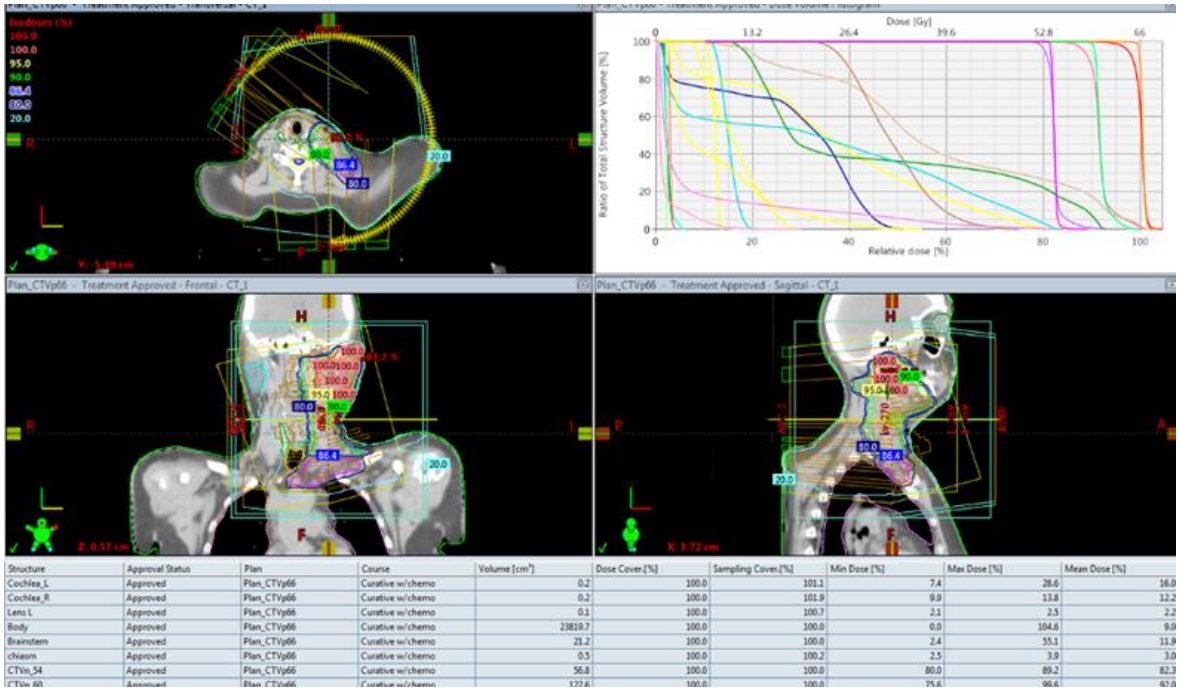

Figure 6: Intensity modulated radiotherapy using the VMAT method in the tumor bed area with a DD 2Gy up to a TD 66 Gy, and in the left-sided lymph nodes area with a DD 1.82 Gy-1,63 Gy up to a TD 60 Gy-54 Gy.

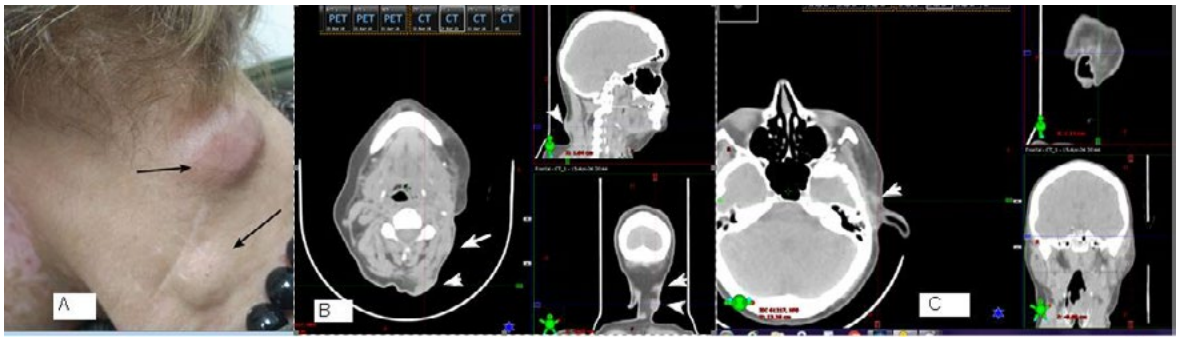

Figure 7: A) Photo- picture of the occipital region; B) C/CT images of the face and neck area after 6 months from the completion of the post-operative combined radiation-chemotherapy- B; C) Well visible soft tissue seals, localized in the left preauricular region and posterior occipital below the skull base with the appearance of implantation metastases. An excisional biopsy is required for histological verification. (Lesions are indicated by the white arrows).

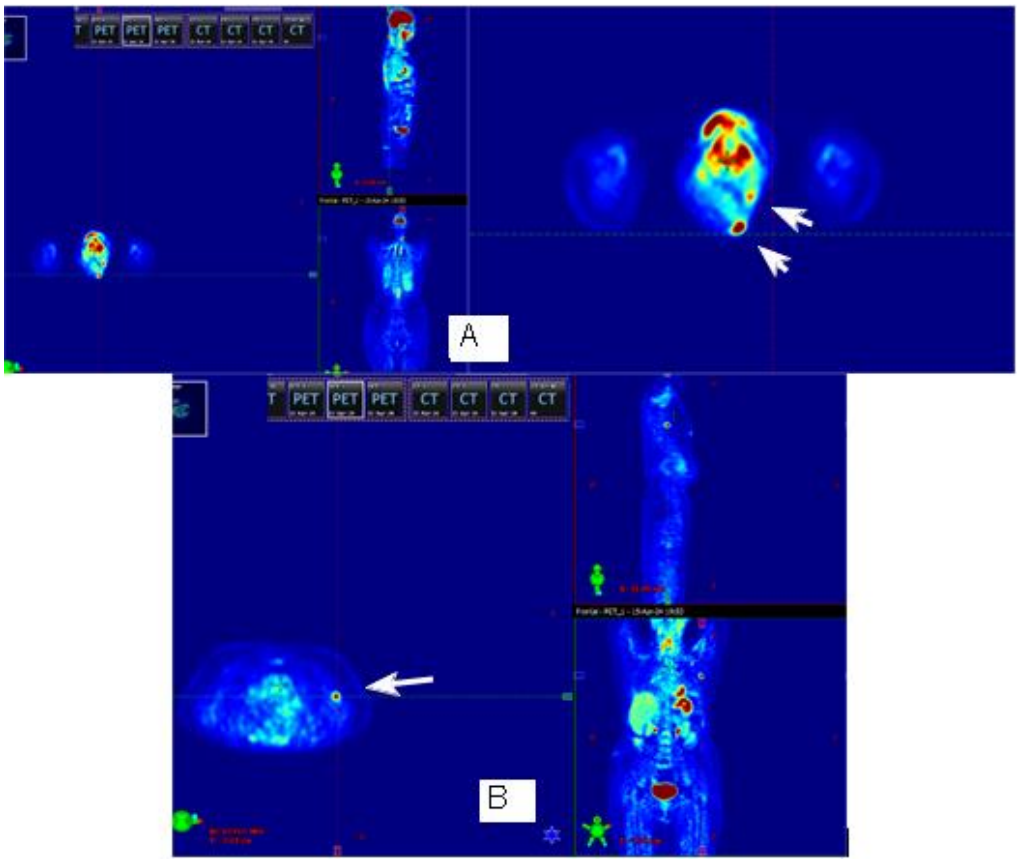

Figure 8: PET/CT after 6 months from the completion of the post-operative combined chemoradiotherapy: A) Increased accumulation of the radioactive isotope in two lesions localized in the left occipital region B) Increased accumulation of the radioactive isotope in the left axillary region. (White arrows indicate the implantation metastasis in the left occipital region and the lymphatic metastasis in the left axilla).

3. Discussion

Salivary duct carcinoma (SDC) is the most aggressive tumor of the 21 subtypes of primary salivary gland carcinoma in the latest World Health Organization classification, showing high rates of local recurrence and distant metastases (DM) [19,20]. SDC is defined as an aggressive epithelial malignancy resembling high-grade mammary ductal carcinoma characterized by tumor cell proliferation with comedonecrosis and a cribriform growth pattern [19]. Although SDC histologically resembles breast carcinoma, it generally shows more marked cellular atypia and more mitoses than the latter [21].In terms of risk factors for DM, multiple pathological lymph nodes (LNs), lymphovascular invasion, and extracapsular extension have been known to be major factors [22,23].

The pathohistological examination of the presented clinical case

shows low-differentiated large duct carcinoma with perineural invasion and multiple tumor emboli in lymphatic and blood vessels (Figure 1/A, B, C) and bundles of lymph nodes with metastases from the described carcinoma (Figure 2). Exact pathohistological verification and differential diagnosis of this rare aggressive tumor requires immunohistochemical analysis of AR and GATA3 expression. The diagnosis of SDC should be based primarily on the morphologic features with the support of AR immunohistochemistry [24]. Immunohistochemically, a strong and diffuse AR expression is a characteristic feature and a practical tool in the diagnosis of SDC, especially when paired with positive staining for GATA3 [25,26]. The p63 expression is helpful for differentiating mucoepidermoid carcinoma from SDC, which is usually negative for p63 [27]. Figure 3 shows the immunohistochemical analysis regarding the positive expression for CK 7, AR and GATA3, as well as the negative expression for p63.

SDC is typically managed by similar treatment approaches as other high-grade salivary gland tumors [28-30]. The major therapeutic approach for SDC is adequate and appropriate surgical resection [31]. In the presented clinical case, a left-sided parotidectomy with an extended dissection of the left cervical lymph nodes was performed. After gross total resection, it is unclear if the indications for adjuvant radiotherapy (RT). Additionally, NCCN guidelines reference tumor spillage as an indication to consider adding RT [32]. Postoperative radiation therapy is an effective and appropriate therapeutic option according to the NCCN guidelines, regardless of the T stage and margin status [33]. Postoperative radiotherapy to the tumor bed and ipsilateral neck is usually recommended [34]. Given the advanced disease/pT4 pN2b M0, as well as the aggressive nature of the proven carcinoma, the patient was referred for postoperative combined Ch-RT. Despite aggressive local treatment, including radical surgery, followed by postoperative combined Ch-RT to high cancericidal doses in the area of the tumor bed and left cervical lymph basin, against the background of achieved local and regional tumor control, at the sixth month post-treatment PET/CT demonstrated metabolically active accumulation in the left axilla and implantation metastases in the left occipital region. The patient was referred for surgical extirpation of the metabolically active PET/CT accumulation, which was histologically verified. Several authors reported that the presence of androgen receptor or human epidermal growth factor receptor-2 is common in SDC [35-37]. Thus, androgen deprivation therapy or targeted therapy with trastuzumab in patients with recurrent or disseminated disease may be beneficial [38]. The latest NCCN guidelines include AR therapy and anti-HER2 therapy as therapeutic options for AR-positive and HER2-overexpressing tumors, respectively [33]. The patient was directed to continue the treatment with AR targeted therapy, given the positive immunohistological AR tumor expression.

4. Conclusion

Salivary duct carcinoma (SDC) is a rare, aggressive parotid neoplasm. Exact pathohistological and differential diagnosis of this rare aggressive tumor requires immunohistochemical analysis of AR and GATA3 expression. Basically, this rare tumor is diagnosed in advanced local status with metastases in the ipsilateral cervical lymph nodes. Achieving local tumor control after radical surgery for the primary parotid tumor with cervical lymphatic dissection requires postoperative high-tech radiation therapy with radical doses combined with Ch. In locally advanced tumors, the risk of extra-regional lymph metastases is extremely high. Therefore, in case of positive immunohistochemical AR tumor expression, long-term systemic treatment with AR target therapy is necessary.

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