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IMMUNOTHERAPY IN TREATMENT OF ANAPLASTIC THYROID CANCER: A CASE REPORT

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Abstract

This case report describes a 55-year-old woman with diagnosed anaplastic thyroid cancer (ATC). Initially, the patient was treated surgically, followed by rapid progression. After that radiation therapy was performed, and the patient immediately progresses again.

It was decided that the patient should start chemotherapy while waiting for molecular tests due to the rapid growth of the cancer. After six cycles of chemotherapy in which the disease was stable progression occurred again immediately after discontinuation of chemotherapy.

Molecular test shows PD-L1 positive patient with CPS score of 20% and she was put on immunotherapy with pembrolizumab. After 1 year of immunotherapy treatment, PET CT scan showed metabolic and morphological regression of tumor mass in the neck and cervical lymph nodes. The patient had a good quality of life with no side effects throughout the immunotherapy.

In this case, we want to emphasize that immunotherapy can also be considered as choice of treatment in anaplastic thyroid carcinoma who represents carcinomas with high lethality rate.

Keywords: thyroid anaplastic carcinoma, immunotherapy, PD-L1, pembrolizumab

Introduction

Anaplastic thyroid cancer (ATC) is a rare carcinoma with an annual incidence of 0.1–0.3/100,000 in Europe [1]. This malignant disease has nearly 100% disease-specific mortality and overall survival of 3–5 months from the moment of diagnosis. A greater mutation burden, activation or deactivation, can lead to the transition from normal thyroid to differentiated (DTC) to poorly differentiated thyroid carcinoma (PDTC) and finally to anaplastic thyroid cancer, also ATC may arise de novo [2].

At the initial time of diagnosis in most of ATC patients are detectable: local infiltration of the trachea, esophagus, blood vessels, and muscles, and distant metastases of the lung, bone, and brain which are all surgical contraindications [3].

Surgery-based treatment provides survival benefits to ATC patients with tumor lesions restricted within the thyroid. Selection of treatment options also included local radiotherapy, systemic chemotherapy, targeted therapy and immunotherapy. Radiotherapy is preferred option to ATC patients in R0/R1 resection and nonsurgical cases or in palliative intent. External beam radiotherapy is used as highly heterogenic in dose management, division, equipment, technique and combination treatment [4].

Chemotherapy is a widely used systemic treatment to prolong the survival but resistance of chemotherapy is a common cause of treatment failure in ATC patients, leading to the mean progression-free survival (PFS) of less than 3 months. Recommended and commonly used chemotherapy protocols for ATC are cisplatin plus doxorubicin, paclitaxel plus carboplatin, docetaxel plus doxorubicin, doxorubicin alone or paclitaxel alone [5].

Targeted therapy dabrafenib and trametinib are recommended to ATC patients carrying BRAF V600E mutations, although this specific population only accounts of 20–50% of all ATC patients [6].

The application of immune checkpoint inhibitors like anti-PD-1 (Programmed cell death protein 1), anti-PD-L1 has opened up a brand-new path for thyroid cancer treatment. The FDA granted approval for the anti-PD-1 antibody pembrolizumab for thyroid cancer treatment in 2020, and clinical trials have

substantiated the therapeutic efficacy of the anti-PD-1 antibody spar talizumab in locally advanced or metastatic ATC [7,8].

Case Report

A 55-year-old woman, with Macedonian origin was diagnosed with anaplastic thyroid cancer with fine needle aspiration (FNA) biopsy of the thyroid gland. Computed tomography (CT) scan of head and neck showed, in projection of left thyroid lobe, heterogeneous change in diameter 3.5 x 3.5 cm, with infiltrative growth, CT of thorax was without malignant findings.

At the time of diagnosis, she was stage IV according American Joint Committee on Cancer (AJCC), 2017. Surgical treatment, total thyroidectomy was performed on April 2023. Pathological diagnosis was poorly differentiated (G3) anaplastic thyroid carcinoma originating from a previously follicular type of papillary thyroid cancer with stage IVA: pTNM=pT3a pNx pMx (AJCC) [9.10].

After surgery cancer progression had occurred and patient received radiation therapy in private hospital. Intensity- modulated radiation therapy was performed up to total tumor dose of 45 Gy, 2,5 Gy per fraction in 18 fractions in May, 2023. (figure1)

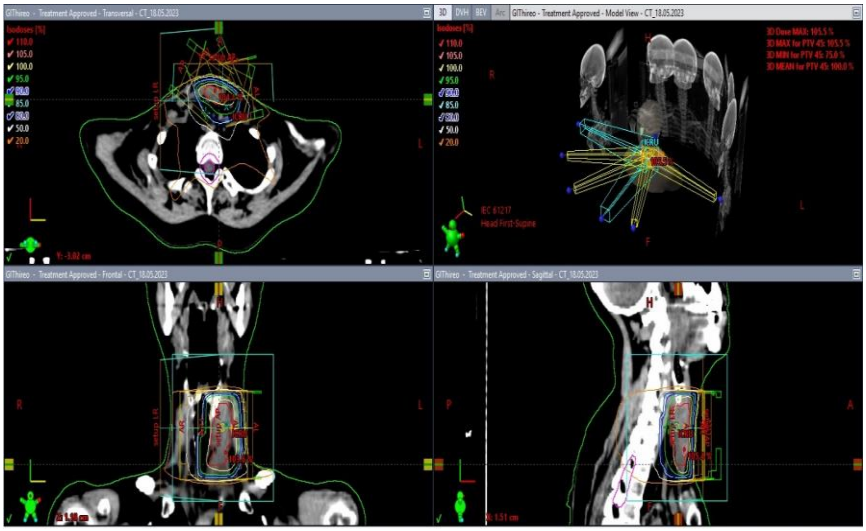

Figure 1. Radiation therapy planning for treatment of patient study in transversal, sagittal and coronal view.

New CT of head, neck and thoracic region was performed on 16 Jul 2023 after radiotherapy. Results showed large tumour in left neck region starting from cervical vertebrae 4 to upper anterior mediastinum with dimensions 122x52x48 mm with reduction of airway and cutaneous extension, metastatic lymph node in left supraclavicular region from 12 mm, and in the medial part of the right supraclavicular region with dimensions 25x15 mm. (Figure 2)

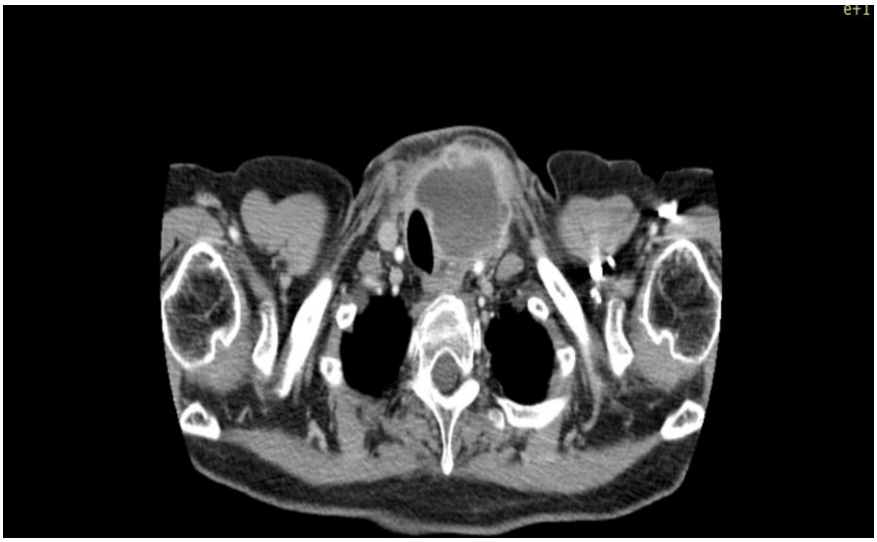

Figure 2. CT of head, neck and thorax performed on 16 Jul 2023.

After this disease progression patient was referred to the Next Generation Sequencing (NGS), but due to the rapid growth of the tumour she started with chemotherapy according to chemotherapy protocol for anaplastic thyroid carcinoma carboplatin AUC 5 with docetaxel 75 mg/m². Six cycles of chemotherapy were given on 21 days starting from 21 Jul 2023 till 16 Nov 2023 with corticosteroid premedication and post medication. Before every cycle laboratory testing was performed.

During the chemotherapy on clinical examination patient expired reduction of tumour mass and right after the new cycle of chemotherapy increase of tumour mass. NGS has shown negative results for BRAF V 600 mutation and NTRK gene fusion but high CPS= 20 %.PET CT (Positron Emission Tomography) was performed on 13 December 2023, one month after completing chemotherapy: A metabolically active lesion with malignant features in the left cervical region propagating into the upper mediastinum with central necrosis (SUV max=12.4, d= 30x35x130 mm). No scan graphic signs of distant metastases. (Figure 3)

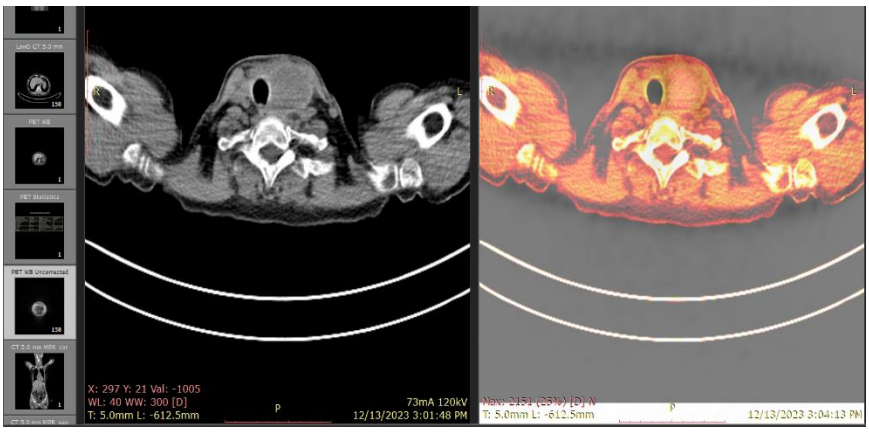

Figure 3. PET CT on 13 December 2023.

According to CPS score 20%, on 28 Dec 2023, patient started with immunotherapy Pembrolizumab 200 mg on 21day. During the first two cycles there was no clinical improvement. Next evaluation of the disease was again with PET CT (May 2024): partial metabolic and morphological regression of a tumor located from level 3 of the neck to the superior and anterior mediastinum necrosis (SUV max=5.1, d= 21x30x90 mm). The patient continued treatment with immunotherapy every 3 weeks.

On clinical examination we noticed clinical regression on palpation. Next PET CT evaluation was done in December 2024. Compared to the previous scan, morphological and metabolic regression of the tumor mass in the neck left and of the lymph nodes left cervical is visible (SUV max=3.2, d= 14x10x10 mm). (Figure 4).

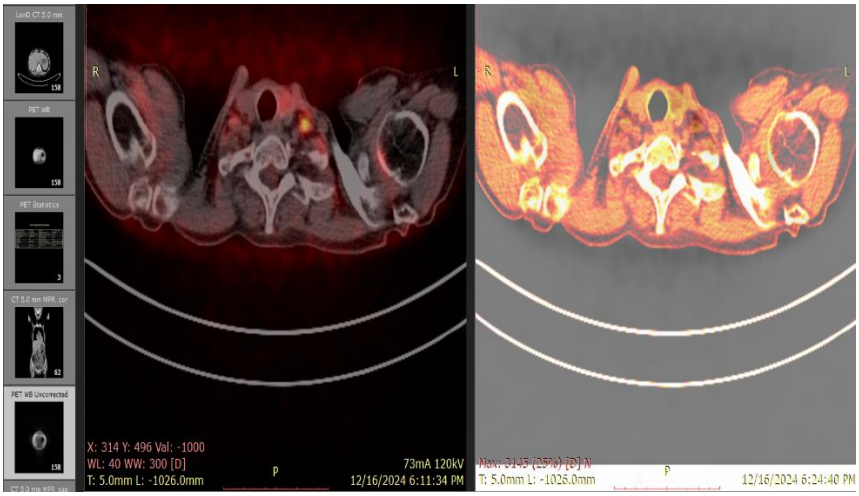

Figure 4. PET CT on 16 December 2024.

No side effects were reported during the treatment and the patient is in good general condition and is continuing treatment with Pembrolizumab. (Figure 5,6).

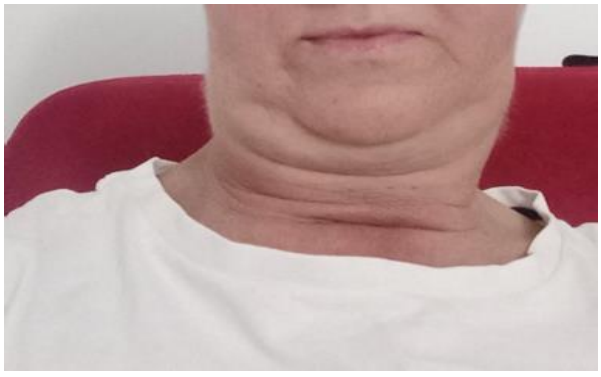

Figure 5. Before treatment.

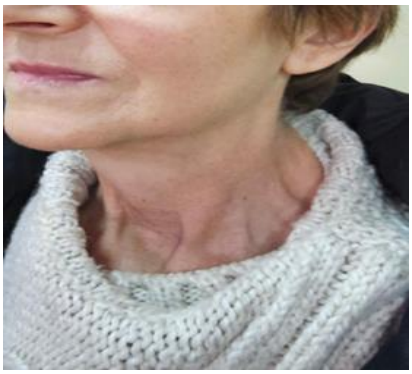

Figure 6. After 12 months treatment with Pembrolizumab

Discussion

ATC's treatment approach progresses toward personalized treatment with the possibility of NGS from chemotherapy and radiotherapy to targeted therapy. PD-1 inhibitors have been used to treat many cancers, such as metastatic and advanced stage of melanoma, NSCLC and renal carcinoma. Owing to their efficacy in suppressing tumor growth and inducing tumor cell apoptosis, the Food and Drug Administration has approved many PD-1 inhibitors for the treatment of a variety of cancers [14].

The induction of an immune checkpoint receptor on cancer cells could evade immune attack, resulting in tumor proliferation, invasion, and metastasis [15]. PD-1 and CTLA-4 are the most well-studied immune checkpoint receptors at present. ATC has a relatively high frequency of PD-L1 amplification among most solid tumors, which means that ATCs may be more sensitive to PD-L1 inhibitors than solid tumors with a lower frequency of PD-L1 amplification [16].

Despite the success of immune checkpoint inhibitors in many solid tumors, there are many patients who still do not respond to immunotherapy or develop therapeutic resistance. One of the main reasons for low response rates is considered insufficient immune activation and combination of checkpoint blockers has been proposed to increase the response rates [17,18].

Consistent with current research and the high mortality rate of ATC adjuvant postoperative immunotherapy treatments study are ongoing for this type of cancer.

Conclusion

ATC is still a challenge for clinical experts due to its dedifferentiated phenotype and aggressive features. Surgery-based treatment, chemotherapy and radiotherapy do not provide satisfactory treatment results. Although immunotherapy has been shown as a promising strategy for this cancer with high mortality rate, there are many concerns regarding this treatment that need to be resolved, and this case serves as an example of possible further successful treatments for ATC.

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