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Treatment and Survival in Anaplastic Thyroid Carcinoma: Our Single Center Experiences

Anaplastik Tiroid Karsinomunda Tedavi ve Sağkalım. Tek Merkez Deneyimlerimiz

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ÖZET

Amaç: Anaplastik tiroid karsinomu en agresif tiroid malignitelerinden biridir ve %1-5 oranında görülür. Multimodal tedaviye rağmen prognozu kötüdür ve ortalama sağ kalım süresi altı aydır. Birçok hasta postoperatif takip sürecinde taburcu edilemeden kaybedilmektedir.
Gereç ve Yöntem: Bu retrospektif çalışmada, son 20 yılda (2004-2024) Necmettin Erbakan Üniversitesi Tıp Fakültesi'nde cerrahi tedavi görmüş ve anaplastik tiroid karsinomu tanısı almış 13 hastanın demografik verileri, tümör özellikleri, tedavi yöntemleri ve sağ kalım sonuçları değerlendirilmiştir.
Bulgular: Hastaların ortalama yaşı 77,23 yıl (69-89) ve erkek-kadın oranı 7:6 idi. Ortanca sağ kalım süresi 140 gündü (10-700). Yaş ve sağ kalım süresi arasında korelasyon saptanmadı (p=0,26). Evre 4B ve evre 4C hastaları arasında sağ kalımda anlamlı bir fark yoktu(p=0,45). Kemoterapi veya radyoterapi gören hastaların sağ kalım süreleri, görmeyenlere kıyasla önemli ölçüde daha uzundu (p=0,017).
Sonuç: Anaplastik tiroid karsinomu, tedavi seçeneklerinin sınırlılığı nedeniyle prognozu zayıf bir malignite olmaya devam etmektedir. Cerrahi önceki yıllarda öne çıkarken, son yıllarda kemoterapi, radyoterapi ve immünoterapinin daha yaygınlaştığı gözlenmiştir. Daha etkili tedavi stratejileri belirlemek için BRAF mutasyonu ve immünoterapi denemeleri de dahil, daha büyük kohortlar ve moleküler analizler içeren çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Anaplastik tiroid karsinomu, tiroidektomi, tiroid kanseri tedavisi

ABSTRACT

Aim: Anaplastic thyroid carcinoma is one of the most aggressive forms of thyroid malignancies, accounting for 1-5% of thyroid cancers. Despite multimodal treatment approaches, prognosis remains poor, with a median survival of approximately six months. Many patients die during postoperative follow-up before discharge, after the initial surgical treatment.
Materials and Methods: This retrospective study analyzed 13 patients diagnosed with anaplastic thyroid carcinoma who underwent surgical treatment at Necmettin Erbakan University Faculty of Medicine over the past 20 years (2004-2024). Patient demographics, tumor characteristics, treatment modalities, and survival outcomes were evaluated.
Results: Mean age was 77.23 years (69-89), male-to-female ratio was 7:6. Median survival time was 140 days (10-700), with no significant difference by gender (p=0.595), age (p=0.26), or cancer stage (4B vs 4C, p=0.45). Patients who received chemotherapy or radiotherapy had significantly longer survival compared to non-recipients (p=0.017).
Conclusion: Anaplastic thyroid carcinoma remains a highly aggressive malignancy with limited treatment options and poor survival. Although chemotherapy and radiotherapy show promise, small sample size limits definitive conclusions. Surgical therapy dominated earlier cases, while recent approaches favor combined regimens including immunotherapy. Future studies with larger cohorts and molecular analyses, including BRAF mutation and immunotherapy trials, are needed to refine treatment strategies.

Key words: Anaplastic thyroid carcinoma, thyroidectomy, thyroid cancer treatment

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INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is the most aggressive and high-mortality type among all thyroid cancers. It constitutes approximately 1-5% of thyroid cancers and usually appears in older age. A rapidly growing neck mass, difficulty swallowing, hoarseness, and difficulty breathing are the most common presenting symptoms(1). ATC, unlike differentiated thyroid cancers (papillary and follicular), originates from anaplastic follicular epithelial cells and shows rapid progression. In the majority of cases, the disease is already locally advanced or has metastasized at the time of diagnosis. Diagnosis is usually made through fine needle aspiration biopsy; however, in some cases, evaluation of morphological and immunohistochemical findings may be necessary for a definitive diagnosis(1). Available treatments are scarce, and a multimodal approach involving surgery, radiation therapy, and chemotherapy is commonly employed. However, due to the aggressive nature of ATC, treatment outcomes are generally not promising. In this type of cancer, which requires a multidisciplinary approach, early diagnosis and rapid treatment planning are of vital importance(2).

In conclusion, ATC is a rare but poorly prognosed type of thyroid cancer. In the literature, it has been reported that the survival durations of patients with ATC are generally short, with an average survival time of around 6 months (3). Therefore, more research is needed to develop more effective methods for the diagnosis and treatment of ATC.

MATERIALS AND METHODS

This study presents a retrospective evaluation of anaplastic thyroid carcinoma (ATC) cases managed surgically at the General Surgery Department of Necmettin Erbakan University Faculty of Medicine over a 20-year period (2004–2024). A total of 13 patient files were reviewed to assess clinical and demographic characteristics, diagnostic tools, tumor stage, treatment modalities, and survival rates. Data were sourced from the hospital's digital medical record system (HBYS), including surgical notes, pathology reports, and follow-up documentation. Patient variables such as age, sex, presenting symptoms, diagnostic approaches (e.g., FNAB and imaging), tumor dimensions, metastatic status, surgical margins, and adjuvant treatments were recorded. All procedures adhered to ethical standards and patient confidentiality was preserved. Statistical analyses were performed using SPSS and Microsoft Excel, employing descriptive measures such as means, standard deviations, and percentages. Patients included had confirmed ATC diagnoses and received surgical intervention; those with incomplete data or different histopathological diagnoses were excluded. The aim was to enhance existing literature by providing detailed insight into the clinical and surgical management of ATC in our institution.

RESULTS

Following the retrospective analysis, data from 13 patients were retrieved. Among them, 7 were male and 6 were female. The mean age across all cases was 77.23 years, with a range from 69 to 89. Female patients had an average age of 76.86 years, while males averaged 77.67 years, showing no significant difference (p= 0.84). 3 cases had hypertension at the time of surgery, 2 cases had hypertension and type 2 diabetes, and 1 case had asthma. 7 cases had no known comorbidities. The comorbidity statuses of female and male cases were similar (p=0.203).

Survival times were calculated from the day of the operation when they were diagnosed with anaplastic thyroid cancer histopathologically to the day the cases exited. The median survival time was 140 days (10-700). The survival times between female and male cases were similar (male: 167.14, female: 108.67, p: 0.595). There was no significant relationship between the ages of the cases and their survival durations (correlation coefficient: -0.33, p: 0.26). 10 cases were stage 4B, and 3 cases were stage 4C. There was no difference in average survival times between the stage 4B and 4C groups. (4B: 151.3 days, 4C: 103 days, p: 0.45)

The first case involved a 69-year-old man who underwent surgery for a neck mass. Histopathological evaluation confirmed the diagnosis of anaplastic carcinoma. The tumor, measuring 4.5 by 4 cm, was situated in the left thyroid lobe. Capsule invasion and extrathyroidal invasion were present. The disease stage was evaluated as 4B. The patient had no known comorbidities. After the operation, she received 3 cycles of cisplatin+etoposide chemotherapy. Due to regrowth of the mass and associated pressure effects, a debulking surgery was carried out four months after the first intervention. In the 6th month, a debulking and tracheostomy procedure were performed again. Later, the patient underwent debulking surgery two more times at approximately one-month intervals, but due to tracheal invasion and respiratory problems, he passed away 222 days after the first operation.

Case 2 was an 82-year-old woman. The histopathological examination of the patient operated on due to thyroid cancer was reported as anaplastic carcinoma. The tumor was located in both lobes and had a largest diameter of 4.2 cm. Capsule invasion and extrathyroidal invasion were present. The disease stage was evaluated as 4B. Around six weeks after the initial surgery, the patient developed a recurrent neck mass exerting compressive effect. A simultaneous debulking procedure and tracheostomy were carried out. Unfortunately, the patient passed away on postoperative day two, corresponding to the 53rd day after the first surgery.

Case 3 was an 84-year-old male. The patient, who underwent Fine Needle Aspiration Biopsy (FNAB) due to a thyroid nodule, was initially reported as benign in the

cytological examination. However, anaplastic thyroid cancer was detected in the paraffin block examination of the total thyroidectomy material. The tumor size was 7.5x6.5 cm. There was extrathyroidal invasion. The disease stage was evaluated as 4B. The patient had a known history of hypertension. Due to compressive symptoms, a second surgical intervention involving debulking was carried out one month following the initial procedure. The patient passed away three days after the second surgery.

Case 4 involved a 75-year-old female patient who underwent total thyroidectomy following a preoperative FNAB that indicated a possible follicular neoplasm. The histopathological diagnosis after the operation was reported as anaplastic thyroid carcinoma. The tumor, measuring 5x2.5 cm, showed extrathyroidal extension. Stage 4B was diagnosed. The patient, who had hypertension, was advised to begin chemotherapy after surgery based on pathology findings, but she opted out of treatment during the planning phase. Later, the patient, who attended outpatient clinic follow-ups, was lost 246 days after the operation.

Case 5 was a 69-year-old male. He was taken for surgery based on a preoperative diagnosis of papillary thyroid cancer. During the operation, a mass with an irregular appearance invading the carotid artery and trachea was observed, leading to the consideration of anaplastic thyroid cancer and subsequent debulking surgery. Histopathological analysis of the resected tissue confirmed the diagnosis of anaplastic thyroid carcinoma. In the patient who underwent systemic screening after the diagnosis, PET-CT revealed both lungs, the liver, inguinal lymph nodes, and multiple bone metastases. The patient was classified as stage 4C. The patient, who was started on adriamycin treatment by medical oncology, was lost 120 days after the operation.

Case 6 was an 82-year-old woman. The patient underwent surgery based on a preliminary diagnosis of anaplastic thyroid carcinoma, during which both debulking and tracheostomy were carried out simultaneously. In the patient's preoperative systemic scan, multiple metastases were present in the lungs. The patient was classified as stage 4C. The patient, who remained on mechanical ventilation in the postoperative ICU, died on the tenth day following surgery.

Case 7 involved an 82-year-old male. He had undergone total thyroidectomy and right lateral neck lymph node dissection three years earlier for papillary thyroid carcinoma. Recently, bilateral vocal cord paralysis had developed, necessitating a tracheostomy. During the procedure, suspicious tissue observed in the thyroid bed was excised as a potential recurrence. Histopathology confirmed anaplastic thyroid carcinoma. The patient died on the tenth postoperative day.

Case 8 was a 70-year-old male. The patient, who was taken for surgery with a pre-diagnosis of thyroid cancer and planned to undergo total thyroidectomy and right lateral neck lymph node dissection, was found to have an irregularly appearing mass highly invasive to the surrounding muscle tissues in the thyroid bed and right lateral neck region during the operation. Considering the possibility of anaplastic cancer, isthmectomy was performed to prevent the development of respiratory obstruction. The histopathological examination of the resection resulted in anaplastic thyroid cancer. The patient passed away at home 22 days after the operation while in the examination stage for medical oncological treatment.

Case 9 involved a 75-year-old man who underwent surgery with a preliminary diagnosis of thyroid cancer. Intraoperatively, a mass was identified that occupied the entire right lobe and had infiltrated the trachea, esophagus, and recurrent laryngeal nerve. It was considered inoperable in its current state. A right subtotal hemithyroidectomy was performed for the palliation of the mass compression. The postoperative histopathological diagnosis came back as anaplastic thyroid carcinoma. The tumor size was 6.5x3.5 cm. Taxane+carboplatin chemotherapy was administered. Additionally, due to the presence of a macroscopic tumor load in the invaded tissues, the patient received 68 Gy to the thyroid and 60 Gy to the neck, totaling 23 fractions of radiotherapy. Later, the patient discontinued treatment at her own request. The patient, who attended outpatient clinic check-ups at infrequent intervals, passed away at home 700 days after the operation.

Case 10 refers to an 83-year-old female who initially presented with multinodular goiter and cervical lymphadenopathies. Although the Fine Needle Aspiration Biopsy (FNAB) yielded nondiagnostic results, imaging studies showed multiple lymph nodes with suspicious malignant features. Additionally, a lateral neck thyroglobulin washout test was positive. These findings led to a diagnosis of thyroid cancer, and the patient subsequently underwent total thyroidectomy with bilateral lateral neck dissection. Histopathological evaluation confirmed a 6.5 × 5.5 cm anaplastic thyroid carcinoma in the right lobe. During the early postoperative phase, she developed cervical swelling and respiratory distress and ultimately died 40 days after surgery due to respiratory failure in the intensive care unit.

Case 11 involved a 74-year-old female who presented with cervical swelling and compressive symptoms. FNAB of the thyroid nodule indicated a suspicion of malignancy. Given the detection of metastatic lesions in the lungs and brain, total thyroidectomy was performed with a presumptive diagnosis of thyroid carcinoma. As a result of the histopathological examination, it was interpreted as anaplastic thyroid carcinoma measuring 4.5x4 cm. Due to distant metastases, it was evaluated as stage 4C. The patient who received

Table 1. Case Characteristics and Treatment Overview

	Age	Gender	Stage	Survival (Day)	Adjuvant chemotherapy	Radiotherapy
Case 1	69	M	4B	222	Cisplatin + Etoposide	
Case 2	82	F	4B	53		
Case 3	84	M	4B	33		
Case 4	75	F	4B	246		
Case 5	69	M	4C	120		
Case 6	82	F	4C	10		
Case 7	82	M	4B	10		
Case 8	70	M	4B	22		
Case 9	75	M	4B	700	Taxane + Carboplatin	+
Case 10	83	F	4B	40		
Case 11	74	F	4C	179	Taxane + Carboplatin	
Case 12	89	M	4B	63		
Case 13	70	F	4B	124		

taxane+carboplatin chemotherapy passed away at home on the 179th postoperative day.

Case 12 involved an 89-year-old male who underwent total thyroidectomy based on an initial clinical impression of thyroid cancer. Histopathological analysis confirmed anaplastic thyroid carcinoma, and the patient began radiotherapy. Despite treatment, he passed away 63 days postoperatively due to complications.

Case 13 involved a 70-year-old female patient who had previously undergone surgery for medullary thyroid carcinoma at another medical center three months earlier. She presented with a recurrent cervical mass, for which a debulking procedure was performed. Histopathological analysis revealed anaplastic thyroid carcinoma arising from malignant dedifferentiation of a pre-existing differentiated epithelial tumor. Chemotherapy was initiated under the care of the medical oncology team. However, she died 124 days after surgery due to respiratory complications in the emergency department.

The age, gender, survival duration, and non-surgical adjunctive treatment statuses of all cases are summarized in the table (Table 1).

DISCUSSION

Anaplastic thyroid carcinoma (ATC) is the rarest but most aggressive form among thyroid cancers. Although it constitutes 1-2% of thyroid cancers, it is responsible for 50% of deaths related to thyroid cancer. The average age of the patients is 71, and the incidence is approximately 1-2 per million annually (4,5).

This retrospective analysis evaluated the clinical profiles, therapeutic strategies, and survival times of 13 patients diagnosed with ATC. The mean patient age was 77.23 years, aligning with prior literature that highlights the predominance of advanced age. Regarding gender, the distribution between males and females showed no statistically significant difference, a finding consistent with several previous reports, although some studies have noted a male predominance(6).

When looking at treatment approaches, surgical intervention has been applied to all patients, and additionally, adjuvant treatments such as chemotherapy and radiotherapy have been used in some patients. Survival outcomes differed significantly between patients who underwent chemotherapy or radiotherapy and those who did not receive these treatments. (average survival 72 days - 367 days, p=0.017) This duration may indicate that chemotherapy and radiotherapy have a significant impact on survival, or it could be due to cases that were exposed to early death during the examination and preparation phase after surgery and did not have time to receive chemoradiotherapy, resulting in a higher outcome in favor of chemotherapy and radiotherapy. The small number of cases also makes it difficult for us to provide an objective interpretation on this matter. In our study, there was also no difference in survival between stage 4B and stage 4C patients.Although it is anticipated that patients with stage 4C disease and systemic metastases would have poorer survival outcomes, we attribute our findings to the limited number of cases analyzed. Studies with larger cohorts may yield alternative results. In anaplastic thyroid carcinoma, the most influential factor for improving survival has been identified as achieving total tumor resection, regardless of the use of adjunctive chemotherapy or radiotherapy(7).

In the treatment of anaplastic thyroid cancer, despite the use of different methods together, 80% of patients are lost within 1 year following the diagnosis(8). Additionally, patients who are lost before 3 months are classified as "early death" (9). When the survival durations were examined, the average survival duration was determined to be 133.69 days. This duration is consistent with the reported 5-month median survival time in the literature (10). Early death was observed in 7 cases (53%), and the rate observed in our cases is consistent with the literature (60%) (9). Of the 7 cases of early death, 6 were patients over the age of 80. A 70-year-old patient who experienced early death was also unresectable, so

R0 or R1 resection could not be performed, and R2 resection was done with gross tumor tissue left behind. It is thought that advanced age and incomplete resection are factors in the early death.

In the treatment of ATC, there are various approaches such as surgery, radiotherapy, chemotherapy, targeted therapies, and immunotherapy. It is known that radical surgical excision contributes to overall survival on average, but surgery has limited applicability due to the rapid progression of the tumor (11). Radiotherapy is used to achieve local control, while chemotherapy is often administered in combination with radiotherapy(12). Targeted therapies are also used in cases with positive BRAF mutations(13).

This study is limited by its retrospective nature and the relatively small patient cohort. Additionally, our study is single-centered, and difficulties were encountered in accessing records for some cases. In many older cases, due to the technical limitations of the time, there are no records indicating that certain immunohistopathological (BRAF) examinations were conducted. However, due to the rarity of ATC, such studies make significant contributions to the literature. Additionally, all the cases in the study reflect the Turkish patient population and, being a single-center study, it involves a standardized surgical procedure. In the future, conducting prospective studies with larger patient populations will help in the development of treatment and management strategies for ATC.

CONCLUSIONS

Considering the aggressive nature of ATC and the limited treatment options, although combined multidisciplinary treatment approaches are available, treatment success and survival rates remain quite low. The presence of BRAF mutation in treatment and immunotherapy studies may yield promising results in treatment. There is a need for more comprehensive research to develop new treatment strategies and enhance the effectiveness of existing treatments.

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