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Epidemiological, Clinical and Therapeutic Profiles of Anaplastic Thyroid Carcinoma at the Mohammed VI University Hospital from 2020 to 2025

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Abstract | **Original Research Article**

Introduction: Anaplastic thyroid carcinoma is a rare, highly aggressive, and undifferentiated thyroid tumor, accounting for approximately 2% of all malignant thyroid neoplasms. Its prognosis is poor, with a median survival of around 4 months. ***Objective:*** The aim of this study was to report the clinical characteristics and to discuss the therapeutic modalities in patients treated for anaplastic thyroid carcinoma. ***Methods:*** We conducted a retrospective study of 10 cases of anaplastic thyroid carcinoma treated between January 2020 and January 2025 in the Oncology-Radiotherapy Department of Mohammed VI University Hospital, Marrakech. ***Results:*** The mean age of patients was 66.1 years, with a female predominance (sex ratio 4:1). The main reason for consultation was the appearance of a rapidly enlarging anterior cervical mass, associated with dyspnoea in 80% of cases. At diagnosis, 50% of patients were at stage IV-B, with locoregional invasion involving the trachea in 90% of cases. Metastatic disease was present in 40% of patients, 80% of which were pulmonary. Total thyroidectomy with bilateral lymph node dissection was performed in 60% of cases, combined with tracheotomy in 40%. Adjuvant chemotherapy was administered in 60% of cases, with concomitant radiotherapy in 30%. The most frequently used protocol was paclitaxel–carboplatin (30% of cases). Decompressive radiotherapy was delivered in 40% of cases. The mean overall survival was estimated at 5.7 months. ***Conclusion:*** Anaplastic thyroid carcinoma is a rare and highly aggressive thyroid malignancy with a dismal prognosis. Early diagnosis and multimodal management are essential to improving patient survival.

Keywords: anaplastic thyroid carcinoma, aggressive tumor, thyroid cancer, undifferentiated carcinoma, neck mass.

INTRODUCTION

Anaplastic thyroid cancer is an undifferentiated carcinoma originating in the thyroid gland. It is the rarest form of thyroid cancer, accounting for 0.2% to 2% of all malignant tumours of the thyroid [1]. Its prognosis is very poor as it is considered one of the most aggressive tumours in humans, with a median survival of 4 months and a one-year survival rate of 20% [2]. Longer-term survival is rare, with a disease-specific mortality rate close to 100% at 5 years [3]. It mainly affects middle-aged individuals, estimated to be between 62 and 65 years old [4].

All patients are classified as stage IV according to the American Joint Committee on Cancer (AJCC) TNM classification, with the following subgroups: stage IV-A (tumours confined to the thyroid), stage IV-B (locoregional spread) and stage IV-C (distant metastases) [5].

Given the aggressiveness of anaplastic thyroid carcinoma, early diagnosis and rapid multimodal management are rare and would allow for potentially curative local treatment consisting of surgery followed by concomitant radiotherapy and chemotherapy [6].

Inoperable and/or metastatic anaplastic thyroid carcinomas are treated with taxane-based chemotherapy combined with platinum salts or anthracyclines, combined with radiotherapy for local control in the cervical region, with tumour regression in a minority of patients and a lesser overall survival benefit [6].

The use of targeted therapies and immunotherapy in personalised treatment approaches based on molecular analysis, including prior to surgery,

has led to improved progression-free survival and overall survival in patients, as reported in major American centres, and offers hope in the management of this disease [7,8].

Our study aims to report on the clinical aspects and discuss the therapeutic modalities of patients treated for anaplastic thyroid carcinoma at the Oncology-Radiotherapy Department of the MOHAMMED VI University Hospital in MARRAKECH.

Materials and Methods

This is a retrospective study of a series of 10 cases treated for anaplastic thyroid carcinoma over a five-year period from January 2020 to January 2025 in the Oncology-Radiotherapy Department of the MOHAMMED VI University Hospital in MARRAKECH.

Patient data were collected from patient records based on a data sheet that included epidemiological parameters (age, sex, etc.); clinical parameters (medical history, duration of disease, functional signs, physical examination data, etc.); paraclinical parameters (biological, radiological, isotopic, etc.); therapeutic and evolutionary (follow-up, modalities, rhythm). The diagnosis suggested by the histological anatomopathological study was always verified and confirmed by an immunohistochemical study. All our patients received multidisciplinary care in consultation with surgeons, oncologists, radiologists and radiotherapists.

Results

Our series consists of 10 cases, predominantly female, with 80% women and 20% men. The average age for both sexes is 66.11 years, ranging from 51 to 80 years. The most common reason for consultation was a rapidly developing anterior cervical swelling associated with dyspnoea in 80% of patients, followed by dysphagia in 20% of cases.

No history of accidental or iatrogenic radiation exposure was found, and no cases of familial thyroid carcinoma were reported. A goitre prior to diagnosis was found in 20% of cases and alcohol and tobacco intoxication in 10% of cases.

Clinical examination revealed a solitary thyroid nodule (20%) and a multinodular goitre (80%); associated with cervical lymphadenopathy greater than 1 cm in diameter in 70% of cases. Cervical ultrasound performed in all patients revealed a heterogeneous multinodular goitre in 80% of patients and a single nodule in 20%, whose malignant characteristics included hypoechoic lesions with irregular contours and microcalcifications, and hypervascularisation on colour Doppler, classified as EUTIRADS 5 in 80% of cases and EUTIRADS 4 in 20% of cases. The ultrasound size of the nodules ranged from 20 to 150 mm in long axis, with an average of 67.76 mm. Ultrasound-guided thyroid fine needle aspiration was performed in all patients presenting with suspicious carcinomatous lesions of papillary origin in 70% of cases; vesicular in 20% of cases; and poorly differentiated in 10% of cases.

A cervical CT scan was performed in 80% of patients, revealing a plunging goitre with signs of compression in 50% of cases. The tumour was compressing the trachea and larynx in 90% of cases and the pharynx and oesophagus in 50% of cases. Cervical CT also revealed the presence of lymph nodes larger than 1 cm, with irregular contours, a round appearance and loss of central fatty hilum, which were suspicious in 70% of patients.

A staging assessment consisting of a thoraco-abdominal-pelvic CT scan was performed immediately in all patients, revealing synchronous metastases in 40% of cases, with 80% of these located in the lungs and 20% in the liver.

At the time of diagnosis, we used the TNM classification from the AJCC, 8th edition, 2017. The tumour was classified as T3a in 20% of cases, T3b in 40% of cases, T4a in 30% of cases and T4b in 10% of cases. In our series, 30% of cases were classified as N1a and 20% as N1b. Forty percent of patients had lung metastasis (M1) from the outset. Thus, 40% of patients were classified as stage IVC, 50% as stage IVB, and 10% as stage IVA.

Surgery was the treatment of choice depending on whether the tumour was resectable or not. Total thyroidectomy combined with bilateral lymph node dissection was performed in 60% of cases and lobectomy with unilateral lymph node dissection in 10% of cases.

Surgery was considered macroscopically complete in 30% of cases and incomplete in 40% of cases, leaving part of the tumour in place near the recurrent nerve in two cases and near the carotid artery in two cases. Incomplete surgery was associated with a tracheotomy in 40% of cases. Thus, 50% of patients in our series had a permanent tracheotomy.

The anatomopathological study of surgical specimens showed anaplastic carcinoma in all patients, with spindle cells in 60% of cases, pleomorphic cells in 20% of cases and squamous cells in 20% of cases; this was associated in 50% of cases with tumour necrosis and neutrophilic infiltrate in 20% of cases. Breach of the thyroid capsule was observed in 90% of patients and was associated with extension to the perithyroid tissues. Vascular emboli were observed in 40% of cases. Lymph node invasion was found in 70% of cases.

Immunohistochemistry revealed positive results for the following markers: pan-cytokeratin in

30% of cases, PAX 8 in 15% of cases, thyroglobulin in 15%, TTF1 in 10%, TP53 in 10%, vimentin in 10% and PS100 in 10%.

Following a multidisciplinary consultation meeting, 30% of patients received adjuvant radiotherapy and 60% received adjuvant chemotherapy. The standard radiotherapy protocol was five sessions per week at a dose of 2 Gy per session on the cervical region (thyroid bed and lymph node areas) and upper mediastinum. The total dose was between 60 and 70 Gy, requiring between 30 and 35 sessions.

Table I: Therapeutic Approaches and Average Survival

Treatment	Mode	Protocol	Number	Average survival (months)
Palliative	Decompressive radiotherapy	30Gy in 10 fractions of 3Gy	4*	2
Adjuvant to thyroidectomy	Radiotherapy	60Gy in 30 fractions of 2Gy	2	5
	Chemotherapy	Paclitaxel-Carboplatin	3	4
		Doxorubicin-Cisplatin	1	5
	Concomitant chemoradiotherapy	70Gy in 35 fractions of 2Gy	2	7

* Of the four patients, two received decompressive radiotherapy after progression under adjuvant chemotherapy.

The longest median survival was 9 months, observed in a 63-year-old patient in good general health with an unresectable tumour, who underwent a protocol of 3 courses of doxorubicin-cisplatin followed by radiotherapy and then 4 courses of doxorubicin-cisplatin.

Two patients (10%) received adjuvant chemoradiotherapy with paclitaxel-carboplatin concomitantly.

The most commonly used chemotherapy protocol was paclitaxel-carboplatin in 30% of cases. Decompressive radiotherapy was performed in 40% of cases at a dose of 30 Gy in 10 fractions of 3 Gy, with an estimated average survival of 5.7 months.

DISCUSSION

Anaplastic thyroid carcinoma represents the final form of dedifferentiation of follicular thyroid tumours. They account for less than 2% of all thyroid cancers and their annual incidence is estimated at two cases per million inhabitants per year [1,3]. Its incidence is declining thanks to the early management of nodules that appear suspicious on ultrasound [9]. It is largely predominant in older individuals, with peak incidence during the seventh decade of life. However, it can also affect younger individuals [6]. It is frequently found to be more prevalent in women [9].

Our series of 10 cases over a 5-year period reports an incidence of 1.6% of all thyroid cancers, which is close to that reported in the literature, and notes a female predominance with a female/male sex ratio of 4/1. This result is similar to those of African [3] and global [4] series. The average age in our study of 66.11 years is also close to that of other studies [2-4], which is in the seventh decade.

Our study reports rapid onset of anterior cervical swelling associated with dyspnoea as the main reason for consultation in 80% of patients, followed by dysphagia in 20% of cases. This is consistent with other authors who report rapid or explosive transformation of an old goitre revealed by increased volume, tracheal compression and dysphonia often preceding progressive dysphagia as the main clinical signs indicative of anaplastic thyroid carcinoma [10].

The average ultrasound size of the nodules was 67.76 mm in our series. This is close to the data from other authors who report an average tumour size of 8 cm.

Several studies have found extracapsular and lymph node invasion as well as distant metastases at the time of diagnosis. Lymph node metastases are present in more than half of cases. Distant metastases are detectable in 20 to 50% of patients and develop rapidly, in the lungs (80% of cases), and sometimes in the bones and brain [6].

The results of our study are similar to those reported by the authors, showing capsular invasion in 90% of patients, lymph node involvement in 70% of cases and synchronous metastases in 40% of cases, with lung metastases being the preferred site in 80% of cases.

Under microscopic examination, the histological appearance is highly variable. The tumour cells are very atypical and poorly differentiated or even undifferentiated. Nuclear atypia is significant. Cell proliferation is high, with a high mitotic index (>1 mitosis per HPF) and high KI-67 (>30%) [24]. On immunohistochemistry, tumour cells have the following profile: p53+, thyroglobulin-, TTF1-, PAX8+, CD45- (which differentiates an anaplastic tumour from a lymphoma) and cytokeratins are often present [11]. It is also worth noting the high prevalence of TERT, p53 and BRAF gene mutations (found in 70% of cases) [12]. To date, no specific genomic alterations have been found in anaplastic carcinoma.

Our series found similar results in terms of histology. However, the immunohistochemical profile differs slightly for certain positive markers, including thyroglobulin found in 15% of cases and TTF1 in 10% of cases, but is consistent with the results reported in the literature for other markers, including pan-cytokeratin in 30% of cases, PAX 8 in 15% of cases, TP53 in 10%, vimentin in 10%, and PS100 in 10%.

This immunohistochemical difference has been found by some authors, who explain it by the presence of a contingent of differentiated cells commonly found in anaplastic cancers, which suggests the transformation of a differentiated cancer [13]. Conversely, a diagnosis of anaplastic cancer should be made as soon as a contingent of undifferentiated cells is present in a papillary or vesicular tumour [14].

After staging with a thoraco-abdominal-pelvic CT scan, anaplastic carcinomas, given their high aggressiveness, are classified immediately as stage IV (A, B or C) (AJCC). Lesions that have not spread beyond the thyroid parenchyma and in the absence of lymph node or distant involvement are classified as stage IVA (T1-T3a, N0, M0). Lesions that have spread beyond the thyroid capsule (T3b, T4) or have caused locoregional lymph node involvement (>=N1) without distant metastases are classified as stage IVB. In the event of distant metastasis, the lesion is classified as stage IVC [5].

Treatment must be rapid for two reasons: the tumour doubling time is extremely short and the extent of the disease determines the treatment options and survival. No standard treatment protocol has been established [6]. Tracheotomy is very common in these patients, reaching 40% in Tashima's series [15], reflecting the frequent involvement of the airways.

Patients with localised tumours (stages IVA and IVB) may benefit from complete resection if satisfactory tumour removal (R0/R1) can be achieved without causing significant morbidity. Most studies have shown that tumour resection (R0/R1) improves survival rates with or without adjuvant chemoradiotherapy [6]. However, it is unnecessary and harmful in cases of cervical masses infiltrating the oesophagus-trachea axis in elderly patients whose general condition is already compromised. The surgical procedure consists of a total thyroidectomy combined with central neck dissection. Lateral neck dissection is only indicated in cases of suspicious lymphadenopathy confirmed clinically or by imaging [6]. Surgery does not replace complementary treatment with radiotherapy and chemotherapy. According to a meta-analysis including 1,147 patients, adjuvant radiotherapy with or without chemotherapy after thyroid surgery (R0/R1) has been shown to increase survival rates compared to surgery alone [16]. The recommended radiotherapy dose is 45 to 64 Gy at a rate of 2 Gy per session, 5 sessions per week.

For patients with stage IVA and IVB tumours, combining chemotherapy with post-operative radiotherapy improves local control and prolongs survival [17]. According to the latest report from the American Thyroid Association (ATA) 2021, it is recommended that patients in good general health who have undergone R0 or R1 resection should receive concomitant postoperative chemotherapy and radiotherapy [6]. The chemotherapy to be offered to patients in good general health who wish to undergo aggressive treatment is based on taxanes (paclitaxel or docetaxel), with or without anthracyclines (doxorubicin) or platinum (cisplatin or carboplatin) [6]. In the case of a locally invasive tumour deemed inoperable from the outset without distant metastasis, or after R2 resection in a patient wishing to receive aggressive therapy, the use of chemoradiotherapy is indicated and has proven beneficial [18]. If an objective tumour response is achieved, surgical treatment may be added [19]. The theoretical advantage is to limit the development of metastases at a very early stage through systematic treatment and to increase the chances of complete resection. In the case of metastatic tumours in patients in good general health, chemotherapy based on taxanes alone or in combination with anthracyclines or platinum may be offered.

Tumour reduction surgery, as well as a tracheotomy and gastrostomy, are sometimes indicated for palliative purposes in cases of compression of the aerodigestive tract, or for haemostatic purposes [6].

For patients with a BRAFV600E mutation, targeted therapy with dabrafenib-trametinib has proven beneficial and, when combined with chemoradiotherapy, allows for better control of the disease [7,8]. Adjuvant radiotherapy-chemotherapy treatment should be started as soon as the patient has recovered from surgery. Most authors recommend a delay of 2 weeks for chemotherapy and 4 to 6 weeks for radiotherapy. Whether for curative or palliative purposes, the target volume for radiotherapy should include the thyroid gland or tumour bed, bilateral cervical lymph node areas II to V, central lymph node groups VI and the upper mediastinum.

The factors associated with a better 2-year survival prognosis were: age under 65, a tumour smaller than 6 cm located in the thyroid gland with no lymph node or distant metastasis, R0 resection and good general health [20]. Acute cervical symptoms and the presence of distant metastasis were considered poor prognostic factors [21].

Monitoring is clinical, every 3 months, focusing mainly on checking that the airways are clear. Patients who no longer have tumour foci may undergo a brain, chest, abdomen and pelvis CT scan at 1-3 months, then at 6-12 months [20,21]. An 18-FDG PET scan may be performed 3 to 6 months after initial treatment in patients with no clinical signs of disease in order to identify any

small tumour sites and, if necessary, change the treatment strategy. An 18-FDG PET scan may also be requested every 3 to 6 months in patients whose tumour is still present, in order to assess tumour response and identify new tumour sites. Other additional tests are requested depending on the findings. Monitoring must be continued for life.

CONCLUSION

Anaplastic thyroid carcinoma is a rare, highly aggressive thyroid tumour with a poor prognosis, for which early diagnosis and multimodal treatment are crucial to patient survival.

Multimodal treatment combining surgery, chemotherapy and radiotherapy can provide better tumour control in patients in good general health who are able to benefit from it.

Targeted therapies and immunotherapy, which are not widely available in Morocco, represent a step forward in the management of this disease, but their place in the therapeutic arsenal has yet to be defined.

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