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Case report

ANAPLASTIC THYROID CANCER: A CASE SERIES WITH A WIDE SPECTRUM OF TREATMENT IN EMERGENCY

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ABSTRACT

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive malignancies of the neck, and for the majority of these patients the cause of death is a compromised airway, metastatic disease, superior vena cava syndrome, asphyxiation, or exsanguination. In case of the airway being compromised, emergency treatment is mandatory but not well defined. We report 4 different kinds of acute presentation of complications. Anaplastic thyroid cancer; diagnostic, clinical and prognostic indication, evaluation of choice of treatment are discussed. The spectrum of treatment varies from observation and preservation of the airway from a tracheostomy to extensive surgery. When a potentially curative resection is not feasible, the major challenge for the surgeons is the management of airway due to tracheal compression, unilateral or bilateral vocal cord paralysis and direct infiltration of the tumor in the tracheal lumen. Tracheostomy is indicated only in cases of insufficient respiratory glottic space and has the possible purpose of avoiding urgent tracheostomy. In cases of respiratory failure, after urgent tracheostomy it is also useful to perform a thyroid biopsy to make a diagnosis. PEG positioning is always indicated for the purpose of better nutrition in dysphagia patients. Any further surgical therapy, in cases of non-urgency and with a confirmed diagnosis, is, in our opinion, contraindicated due to the poor prognosis of the neoplasm.

1. Introduction

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive malignancies; it makes up 1-3% of all thyroid cancer and few patients survive 6 months beyond initial presentation [1-2]. ATC affect patients 60 to 70 years old, while presentation before 50 years is extremely rare. Women are more commonly affected than men, with a ratio of 3:2, and 80% of these malignancies may occur with a coexisting carcinoma and may represent transformation of a well-differentiated thyroid cancer [3-4]. At the exordium, typically, patients have a long-standing neck mass that enlarges rapidly; often accompanied by pain, dysphonia, dysphagia, and dyspnea, in particular when the mass is fixed to the tracheolaryngeal framework, which results in vocal cord paralysis and tracheal compression [5].

For the majority of these patients, the cause of death is a compromised airway, metastatic disease, superior vena cava syndrome, asphyxiation, or exsanguination [6-7]. In the present report, we describe four patients with anaplastic thyroid cancer (ATC) presenting with acute compressive symptoms and cutaneous extensions.

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2. Cases presentation

The four cases are summarized in table 1.

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	Age	Sex	Signs&Symptoms	Imaging	Procedures
Patient 1	51	M	Neckswelling, dyspnea	CT: Underioidabscess	• Laryngoscopy • Abscess Drainage • Thyroid aspiration • ATC diagnosis • Oncology transfer for radio-chemo treatment
Patient 2	75	M	Front mass of the neck, dyspnoea	CT: Thyroid goitre Videolaryngoscopy: Hypopharyngeal mass	• Videolaryngoscopy • Trans-tracheostomy between 1st and 2nd tracheal ring • Drainage of the lateral and retro pharyngeal abscess, after dissection of the left thyroid lobe • Thyroid mass biopsy and liquid culture analysis • ATC diagnosis with lymph node metastasis • Oncology transfer for radio-chemo treatment
Patient 3	77	F	Pain and mass in the anterior region of the neck, dyspnoea, ulceration of the skin, pain in palpation	CT: Thyroid mass invading the laryngo-tracheal axis	• Videolaryngoscopy • Transfer to thoracic surgery for tracheostomy retro sternal approach
Patient 4	72	F	Pain and goiter anterior region of the neck, dyspnoea		• Tracheal gold intubation • Debulking surgery • Tracheostomy on the tracheal counter • Endoscopic placement of PEG 20 CH • Follow-up with death at 7 months by cardio-circulatory arrest in the absence of macroscopic signs of disease recovery

Table1. Presentation of the four cases treated in the case series analysis.

Case 1

A 51-year-old man was admitted to our emergency department with neck swelling and dyspnea. CT highlighted an abscess of the subhyoid region (red arrows in figure 1), so he was taken to consultation at our ENT unit. At the palpation of the neck, the mass appeared to be elastically stretched and with a crackle. At laryngoscopy, the respiratory space proved to be sufficient at rest, making laryngo-tracheal intubation possible. After intubation and general anaesthesia, we performed cutaneous incision and drainage of the yellowish and serous complexion abscess. In the following days, the cavity was medicated with iodoform gauze and washed with rifampicin.

In the 10th post-operative day, thyroid needle aspiration was performed with the consequent diagnosis of anaplastic thyroid carcinoma. Therefore, it was addressed to the oncology unit for radio-chemotherapy treatment.

Figure 1. Subhyoid abscess (red arrows)

Case 2

A 75-year-old man with a voluminous mass at the anterior region of the neck, coming from the emergency room of our hospital, arrives at our ENT unit for dyspnea. TC shows a voluminous thyroid goitre that dislocates the laryngotracheal axis towards the right and reduces the respiratory space (figure 2 a-b). A videolaryngoscopy displays the presence of a voluminous hypopharyngeal mass that compresses the epiglottis and impedes visualization of the glottic plane (figure 2 c) with restricted respiratory space (figure 2 d).

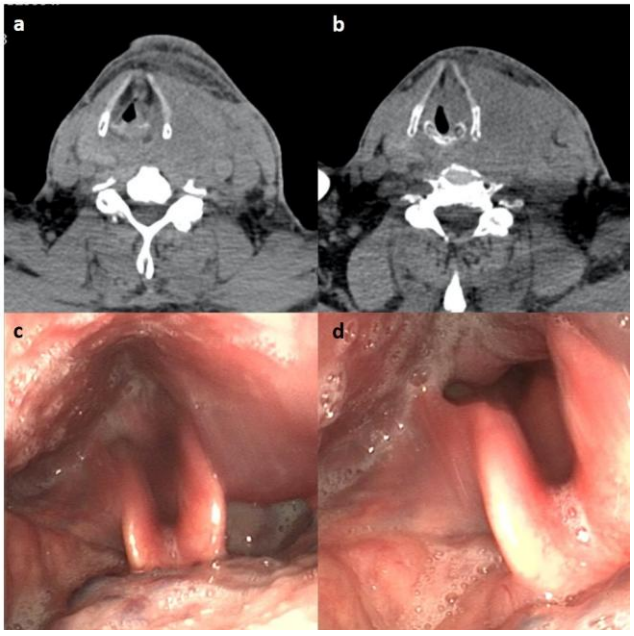

Figure 2. a-b) tracheal compression from huge goiter; c) hypopharyngeal mass; d) narrowing of respiratory space

Case 3

A 77-year-old woman with dyspnea and pain in the anterior neck region comes to our ENT unit. The examination of the anterior region of the neck shows a voluminous mass attached to the superficial and deep surfaces, with ulceration of the skin and painful palpation (figure 3 a). TC shows an extensive thyroid neoformation completely encompassing the laryngotracheal axis, making it impossible to access (figure 3 b-e). Laryngoscopy displays a narrowing of the hypopharyngeal compression space, a poorly visible glottic plane, bilateral cordial paralysis and insufficient respiratory space (figure 3 f-g). Therefore the patient was sent to thoracic surgery for a retrosternal tracheostomy surgical approach.

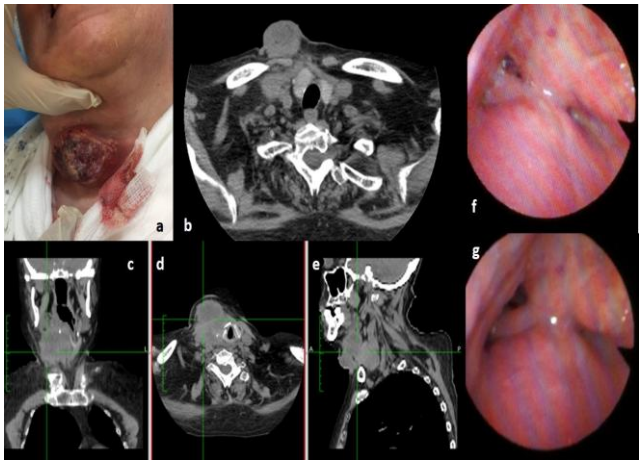

Figure 3. a) ulcerated mass of the neck; b-e) thyroid neoformation completely encompassing the laryngotracheal axis; f-g) hypopharyngeal compression and narrowing of respiratory space

Case 4

A 72-year-old female hairdresser at home, already followed in the Department of Endocrinology for a large goiter, presents with acute dyspnea, pain in the anterior region of the neck and considerable increase in the size of the goiter (see figure 4 a-b), reaches our operative room. Immediately subjected to orotracheal intubation, a debulking surgery was decided with a simultaneous surgical tracheostomy and a percutaneous endoscopic gastrostomy (PEG). In the intraoperative phase, the mass appeared adherent and infiltrating all the surrounding structures, such as to make total thyroidectomy impossible. In consideration of the clinical picture and the impossibility to guarantee the oncological radicality, we opted for a debulking (keeping in situ thyroid parenchymal tablets close to the infiltrated vital structures), visualization and respect in situ of both recurrent nerves and at least 3 on 4 parathyroids (figure 4 c-e) and on tracheostomy packaging (figure 4 f) on tracheal shed and with endoscopic placement of PEG 20 Ch. The post-operative course was good, the patient was discharged on the fifth post-operative day and the histological examination confirmed the suspect of anaplastic thyroid carcinoma. The follow-up continued for 7 months, when, in terms of well-being, the patient died of cardio-circulatory arrest, in the absence of macroscopic signs of disease relapse.

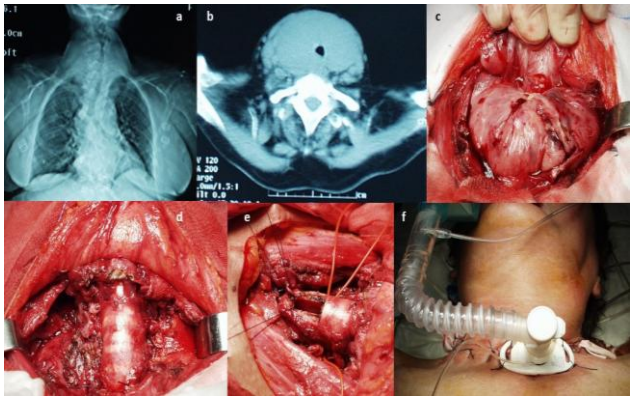

Figure 4. a-b) huge goiter; c-e) mass debulking and creation of tracheal window; f) tracheostomy

3. Discussion

Anaplastic thyroid carcinoma (ATC) is a very rare and extremely aggressive tumor of thyroid follicular cells. It amounts for less than 10% of all thyroid cancers (1.7% in the USA, 2% in Italy), with an age-adjusted incidence of 1 to 2 cases per million population per year [10-11]. Due to the rarity, in the past were published time cases series over several decades. In a study conducted among 1,771 patients between 1949 and 2007, was observed a slight prevalence of cases among women (64%), a median survival following diagnosis of 5 months, making it one of the most aggressive solid tumors to affect humans. Finally, the median age of onset is 71.3 years (±SD 12.7 years) [12].

ATC's is composed by undifferentiated cells. Usually 20% of patients diagnosed with anaplastic thyroid carcinoma will present with a previous history of differentiated thyroid cancer and 20-30% will have a co-existing differentiated cancer (papillary, follicular, Hürthle cell), that tipically tend to have a single mutation, instead of ATC that commonly has multiple gene mutations [10].

The clinical presentation of patients with ATC is frequently the sudden growth of a longstanding goiter, that could be accompanied by laryngeal, tracheal, and esophageal obstruction with dysphagia (40%), voice change (40%), and stridor (24%), noticeable lymph node mass (54%) and neck pain (26%) [11]. Other not common symptoms associated include chest pain, bone pain, headache, confusion, and abdominal pain from metastases. Metastases were found in 50% of patients, most commonly to the lungs (80%), bone (6-16%), and brain (5-13%) [12-13].

According to UICC, all ATC's are classified asstage IV, which is further divided into three categories; stage IVA (tumor confined to the thyroid), stage IVB (extra capsular invasion of adjacent structures), stage IVC (presence of distant metastases).

The high aggressiveness of ATC is associated to the direct invasion of the adjacent organs (in more than 90% of patients), the lymph node metastases (in half patients) and systemic metastases (50-70% of the patients) [14]; all of them are important prognostic factors.

The existing options for treatment of ATC include surgery, associated or not with chemotherapy and radiotherapy, however, a standardized treatment protocol still does not exist.

The role of surgery remains controversial and ranges from a simple palliative tracheostomy to a radical en-bloc resection aiming to a complete cure.

The choice of the appropriate surgical approach is made considering various characteristics such as the extent of the disease (local and systemic), the conditions of the patient, the lack of effective local and systemic therapy.

In stage IVA and some stage IVB patients have a significantly longer median survival when complete curative resection is performed (defined as either a R0 or R1 resection) [10].

In stage IVC the R0 and R1 resections are less decisive in long-term survival (due to the presence of metastasis), but the palliative local control of the disease (debulking surgery, R2) should be considered appropriate to avoid the acute airway obstruction and prevent death from local disease, as presented in our case.

When a potentially curative resection is not feasible, the major challenge is the airway management due to tracheal compression, unilateral or bilateral vocal cord paralysis and direct infiltration of the tumor in the tracheal lumen; in this context, different options are considerable. Elective tracheostomy is rarely performed - more frequently an episode of acute airway distress can make an emergency tracheostomy necessary. If compression, deviation, or infiltration of the trachea impede the achievement of safe respiratory access with tracheostomy, airway intubation is necessary.

Approximately 20-30% of patients may present with acute airway problems caused by extrinsic pressure on the central compartment of the neck from a large tumor, tracheal invasion by tumor, or paralyzed vocal cords on one or both sides (paralysis of one cord with impending paralysis of the other side, bilateral vocal cord paralysis, tracheal invasion by the tumor or bleeding inside the trachea). The airway problems may be accentuated by exertion or minor upper airway infection which may lead to a serious compromise of the airway [15].

Tracheostomy procedures can be quite difficult because there may be an extensive tumor in front of the trachea, making it practically impossible to identify the trachea or tracheal lumen; in these cases, as in ours, with a huge mass, the best approach would be a cricothyrotomy. Generally, a higher midline incision would be of help to expose the thyroid cartilage and search for the cricothyroid membrane.

Occasionally, a partial tumoral resection may be necessary for better exposure of the cricothyroid area. A long tracheostomy tube is generally recommended to bypass tracheal narrowing and some patients may require positive pressure ventilation to keep the airway open [15].

In our case, we performed a trans-isthmic tracheostomy for a better tracheal exposition and to perform a thyroid biopsy to make the diagnosis.

Occasionally, a partial tumoral resection or huge debulking surgery may be necessary in order to relieve compressive symptoms, due to the presence of an extensive tumor in front of the trachea [8]. In a retrospective study by Brignardello, 55 patients (median age 73.15 years), 31 with distant metastases (stage IV-C), R2 resection with minimal residual disease was obtained in 70.73% of operated patients as a first modality and resultedwith better survival than "partial R2" (6.57 months [CI 5.52–12.09] vs. 3.25 months [CI 0.66–4.80]), without any difference between stage IV-B and IV-C patients. Furthermore, 21% of patients submitted to "maximal debulking" died secondary to local progression of the tumor, whereas this was the case for 69% of patients treated with "partial debulking" or not operated on at all, demonstrating that early "maximal debulking" followed by adjuvant therapy, can improve the survival and meliorate the quality of residual life preventing the risk of suffocation [16].

Gaissert described tracheal resection and segmental laryngotracheal resection for invasive thyroid carcinoma [17]. Holting described his experience of tracheostomy for emergency respiratory management for ATC, reporting that survival was significantly lower in the group of patients requiring a tracheostomy, as related to the advanced nature of the disease in these patients [18].

4. Conclusions

The spectrum of presentation of anaplastic thyroid carcinoma is wide. This neoplasm, having a poor prognosis in all cases, does not have any possible radical surgical therapy.

In our opinion, tracheotomy is indicated only in cases of insufficient respiratory glottic space and has the possible purpose of avoiding urgent tracheotomy. In cases of respiratory failure, after urgent tracheotomy it is also useful to perform a thyroid biopsy to make a diagnosis. PEG positioning is always indicated for the purpose of better nutrition in dysphagia patients. Any further surgical therapy, in cases of non-urgency and with a confirmed diagnosis is, in our opinion, contraindicated due to the poor prognosis of the neoplasm.

Although very rare, ATC is a highly aggressive tumor that belongs to the family of killer tumors with a median survival time of no more than 6-8 months. Surgery, chemotherapy, and radiotherapy are the conventional therapeutic strategies implemented in an attempt to improve survival. Unfortunately, very often they do not produce relevant clinical effects, but only palliative results.

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