

Management of acute clinical presentation of anaplastic thyroid cancer.

A difficult choice



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Management of acute clinical presentation of anaplastic thyroid cancer. A difficult choice

AIM: evaluate emergency treatment of patients presenting with anaplastic thyroid cancer with acute compressive symptoms.

MATERIAL OF STUDY: In the present report, we describe three patients with anaplastic thyroid cancer who presented clinically with acute compressive symptoms.

All patients underwent debulking surgery in order to relieve the symptoms and perform a potentially curative resection.

RESULTS: The first two patients with diagnosis of ATC couldn't undergo to radiotherapy and chemotherapy for the presence of infection of the wound and for the earlier disease relapse in the mediastinum and died after 1 month and 3 months. The third patient (with papillary thyroid cancer with focal areas of anaplastic cancer) after surgical treatment underwent external radiotherapy and is alive over 2 years.

DISCUSSION: Compression, deviation, and infiltration of trachea have impeded the achievement of a safe respiratory access with tracheostomy and these three patients underwent debulking surgery to relieve compressive symptoms.

These three cases confirm the importance of acute local compressive symptoms of ATC and their difficult management.

CONCLUSIONS: In such cases a debulking surgery can be considered as a valid option in the emergency management. Nevertheless debulking surgery (and even radical excision of the tumor), when performed alone, offer a minimal improved survival.

KEY WORDS: Anaplastic thyroid cancer, Debulking surgery, Emergency treatment

Background

Thyroidectomy is usually the elective operation in thyroid neoplasm; however it is sometimes required in emergency, due to the presence of local compressive symptoms.

Airway obstruction is the most common finding often leading to acute respiratory arrest.

Moreover local nervous and vascular structures can also be involved by neoplasia, causing other symptoms as hemorrhage, syncope or pain.

The management of these important complications often needs a surgical approach.

In the present report, we describe three patients with anaplastic thyroid cancer (ATC) presenting with acute compressive symptoms.

Case report

CASE N. 1

A 31 years old Sri Lankan man was admitted in our general surgery department with a two weeks history of several syncope episodes associated to neck and left shoulder pain and dyspnoea.

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His medical history included thyroidectomy 5 months before for a rapid enlargement of thyroid mass. Histological examination revealed an undifferentiated thyroid cancer limpho-epitelioma like (thyroglobulin + pancitokeratina +) in the left lobe, incompletely resected (UICC 2009: pT2, pN1 M0 stage IVB).

After surgery the patient underwent 3 cycles of chemotherapy with cisplatin and epirubicine for 2 months; in the follow-up examination, realized with 18F-FDG PET-CT, disease recurrence on the left side of trachea was detected. One month before admission, the recurring neoplastic tissue enlarged rapidly, leading to the onset of the compressive symptomatology.

A computerized tomography (CT) after admission revealed an enlargement of neoplastic tissue (diameter 8cm) causing compression, displacement and infiltration of the upper airways, left jugular vein thrombosis, and left common carotid artery compression. There was no evidence of metastasis.

A flexible laryngoscopy revealed left vocal cord palsy with reduction of the laryngeal lumen.

Physical examination showed a hard and painful mass, trachea was not palpable. Left cervical lymphadenopathies were detectable. According to these evidences the patient was reoperated. Intra-operative examination revealed an extensive invasion to the surrounding tissues: skin, anterior neck muscles and adhesion to trachea. We performed completion of thyroidectomy with skin and minimal tracheal resection and left modified radical neck dissection. The left recurrent laryngeal nerve was not detectable.

Due to the invasion of the left jugular vein and common carotid artery, both blood vessels were resected and the common carotid was replaced by a goretex® prosthesis (7 mm in diameter).

Histological examination confirmed the recurrence of anaplastic thyroid cancer (UICC 2009: T4b N1b M0 stage IV B). Immunohistochemical study revealed the tumor cells were positive to cytokeratine MNF116, AE1/AE3 and CD45, and negative to thyroglobulin.

The patient had an uneventful postoperative course and was discharged after 8 days.

Three weeks after surgery the patient underwent a CT that revealed a mediastinal relapse of the neoplasm with large invasion of trachea that required a tracheal prosthesis. Two weeks later the patient died.

Adjuvant therapy was not performed due to the early relapse of the cancer.

CASE N. 2

A 80 year-old woman was admitted in our general surgery department with a one-month history of rapid growing neck mass, and reported progressively worsening dysphonia and dyspnoea within the last 10 days. Her medical history included a multinodular goitre in euthyroidism.

Physical examination revealed a large, firm and hard thyroid tumor, measuring 18 x 15cm extending from the sub-mandibular region to the supra-sternal notch with ill-defined borders; trachea was not palpable. There were cervical bilateral and supraclavicular right lymphadenopathies.

The patient was admitted for investigations and scheduled for early thyroidectomy on the surgeon's next elective list, which was to be three days later. Thyroid function tests (including calcitonin) were normal. The day after the admission the patient underwent a CT scan (head and thorax) that revealed a thyroid mass causing compression and infiltration of the upper airways, right jugular vein thrombosis (Fig. 1), multiple bilateral metastasis of lungs.

A flexible laryngoscopy demonstrated the presence of exophytic and ulcerated tumor filling more than 80% of the laryngeal lumen.

Two days after the admission the patient presented a critical airway obstruction and a hypoxemic cardiac arrest. The patient underwent cardiopulmonary resuscitation. An emergency endotracheal intubation was performed using an endotracheal tube of 5 mm in diameter, obtaining the stabilization of the vital signs (blood pressure 110/70 mmHg, spO2 96%, heart rate of 100 beats/min). Because of the size of the tumor and the presence of tracheal compression and deviation, both surgical team and anesthetists concurred on considering palliative tracheostomy too risky and technically complex; the final choice was to proceed with emergency debulking thyroidectomy.

Intra operative examination revealed extensive invasion of the surrounding tissues, including the anterior neck muscles, right jugular vein and larynx with exophytic growth. The patient underwent total thyroidectomy with partial laryngectomy plus modified radical neck dissection on the right side; including resection of the right jugular vein, ligation of lingual artery, resection of right half thyroid cartilage and hyoid bone.

The surgery was completed by a tracheostomy on the third tracheal ring, necessary for partial laryngectomy and for the evident area of tracheomalacia.

Histology: The thyroid gland was fully replaced by a hard multi-nodular mass of 13 x 8,5 x 6,5 cm (with necrotic and hemorrhagic areas), extending in both lobes with indistinct borders infiltrating perithyroid muscles, right jugular vein and trachea. The radical neck dissection of the right side showed the involvement of 6 lymph nodes. Histological examination confirmed the diagnosis of anaplastic thyroid cancer (UICC 2009: T4b N1b M1 stage IV C).

After debulking surgery and tracheostomy, the patient presented problems related to excessive secretions, wound bleeding and infection, requiring a prolonged hospitalization and nursing care. The patient was discharged home three weeks later in satisfactory general condition with tracheostomy. After the discharge the patient was

followed up in our outpatient's department with medications three times a week, relatives were instructed to the proper domiciliary management of the patient. After 25 days, during the dressing of the wound, an area of suspected local relapse of disease was identified near the tracheostomy. The biopsy of the lesion confirmed the presence of neoplastic tissue indeed. During the following dressing a progressive enlargement of the tumor associated to compression of trachea were observed, on the basis of which we decided to maintain the tracheostomy. The patient died 3 months after the surgery for metabolic complications due to the systemic disease progression.

CASE N. 3

A 76 years-old woman presenting progressively worsening dyspnea and an anterior neck mass was admitted in our department in emergency. The vital signs were spO₂ 87%, blood pressure 115/75, ph: 7,20. Physical examination showed the presence of a hard thyroid tumor of 10 x 12 cm, together with compression and deviation of trachea and larynx and right cervical lymphadenopathies. O₂ therapy was administrated obtaining the stabilization of vital signs. A CT scan revealed a thyroid mass causing compression and extensive infiltration of trachea and larynx. There was no evidence of distant metastasis and the patient was scheduled for thyroidectomy the following day. The patient underwent to total thyroidectomy with partial resection of trachea and total laryngectomy plus modified radical neck dissection on the right side; surgery was completed by definitive tracheostomy. The histological examination revealed the presence of a papillary thyroid cancer with small foci of anaplastic cancer. The cancer invaded both lobes with indistinct borders, infiltrated perithyroid muscles, trachea and larynx. The radical neck dissection of the right side showed the involvement of 9 lymph nodes (UICC 2009: pT4a N1b M0 stage IV A). The patient had an uneventful postoperative course and was discharged after 15 days. After 4 weeks the patient underwent external radiotherapy (40 Gy). The follow up realized with CT scan and ultrasound examination demonstrates no evidence of recurrence of disease or metastasis 24 months after surgery.

Discussion

ATC is a rare disease, accounting for less than 2% of all thyroid tumors and an annual incidence of two per million per year ²⁻⁴; nevertheless it is one of the most

aggressive malignancies known with median survival of 2 to 12 months from the time of diagnosis ^{1,5}.

The ATC has a peak of incidence in the sixth and seventh decades of life, with a F:M ratio of 1,5:1 and usually presents as a rapidly enlarging neck mass, often associated with dysphonia, dyspnea, dysphagia and neck pain ^{2,3}.

The diagnosis of ATC is usually made on clinical presentation and confirmed by fine-needle aspiration of the tumor or the lymph node metastases; CT scan and US are necessary for staging the disease and planning the correct surgical treatment.

According to UICC ATC is classified into Stage 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) ^{2,4}; all of them are important prognostic factors.

Most of the studies concerning ATC treatments are retrospective: case-report, case-series or cohort studies based on numerous different treatment protocols.

The existing options for treatment of ATC include surgery, associated or not with chemotherapy and radiotherapy, however a standardized treatment protocol still not exists. 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 as the extent of 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) ^{3,5,6}.

In Stage IVC the R0 and R1 resections are less decisive in the 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 ^{2,6,7}.

For the patients undergoing surgery as a primary treatment, postoperative chemoradiotherapy is recommended because of the high incidence of residual local disease: several studies have shown better results using hyperfractionated radiotherapy (dose >40 Gy) associated with doxorubicin to enhance radiosensitivity of tumor ^{9,10}. When a potentially curative resection is not feasible the major challenge of physicians 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 trachea impede the achievement of a safe respiratory access with tracheostomy, airway intubation is mandatory ⁷. Occasionally a partial tumoral resection or debulking surgery may be necessary in order to relieve compressive symptoms, due to the presence of an extensive tumor in front of the trachea.

Conclusions

The first two patients with diagnosis of ATC could not undergo to radiotherapy and chemotherapy respectively for wound infection and for the early disease relapse in the mediastinum.

The third patient underwent external radiotherapy after surgical treatment and he is at present alive, after over 2 years.

The positive course of the disease of the last patient is probably due to histology of the tumor that revealed the prevalence of papillary type neoplastic cells with focal areas of anaplastic cancer.

These three cases confirm the importance of acute local compressive symptoms of ATC and the difficulty in its management.

Performing tracheostomy is often technically difficult in ATC presenting acute airway obstruction, in these cases a debulking surgery can be considered a valid option in the emergency management. Nevertheless debulking surgery (and radical excision of the tumor) can offer a minimal improvement of survival.

Riassunto

Il tumore anaplastico della tiroide (anaplastic thyroid cancer, ATC) ha un'incidenza di 2 casi ogni 1.000.000 di abitanti, rappresentando il 2% di tutti i tumori tiroidei. Il picco di incidenza è nella sesta-settima decade di vita, con un rapporto F:M di 1,5:1.

La prognosi di questi tumori è infausta, con una sopravvivenza media inferiore ad 1 anno.

Nella maggior parte dei casi la neoplasia esordisce con un rapido aumento di volume della tiroide associata a sintomi da compressione locale: dispnea, disfonia, disfagia, dolore cervicale. Questi sintomi sono dovuti alla compressione ed infiltrazione dei tessuti limitrofi (trachea e laringe, muscoli pretiroidei, tronchi vascolo-nervosi del collo).

Il trattamento di questa neoplasia non risulta standardizzato a causa della sua elevata aggressività locale e della mancanza di casistiche statisticamente significative. La chirurgia riveste un ruolo fondamentale nella terapia di questi tumori, associata quando possibile a chemioterapia e radioterapia. Purtroppo però, anche in associazione, questi trattamenti non ottengono nella maggior parte dei pazienti risultati clinicamente rilevanti; ad ecce-

zione dei rari casi di tumore intratiroideo dove determinano un significativo allungamento della sopravvivenza media.

A causa della elevata invasività locale questi tumori causano spesso la comparsa di sintomi acuti (soprattutto dispnea) che mettono a rischio la vita dei pazienti.

In questi casi si hanno a disposizione limitate opzioni terapeutiche (tracheostomia, intubazione orotracheale, chirurgia demolitiva), la cui scelta è basata sull'estensione locoregionale e sistemica della patologia e sulle condizioni generali del paziente.

In questo articolo vengono presentati tre casi clinici caratterizzati da una improvvisa e grave sintomatologia dispnoica secondaria a tumore anaplastico della tiroide. In questi pazienti si è deciso di praticare una estesa chirurgia demolitiva (in regime di urgenza) con l'obiettivo di controllare la sintomatologia acuta; poiché l'esecuzione di una tracheostomia risultava tecnicamente difficile ed altamente rischiosa.

Con l'intervento chirurgico si poneva inoltre l'ulteriore obiettivo di intraprendere un valido percorso terapeutico. Successivamente al trattamento chirurgico, due pazienti (rispettivamente stage IVB e IVC)

non hanno potuto praticare alcuna terapia adiuvante, il primo per la comparsa di una precoce ripresa di malattia a livello mediastinico, il secondo per l'infezione della ferita chirurgica. Questi due pazienti sono deceduti rispettivamente 1 mese e 3 mesi dopo l'intervento.

Il terzo paziente (stage IVA) è stato sottoposto a radio-terapia postoperatoria ed a 24 mesi dall'intervento non presenta ripresa di malattia. La migliore prognosi di questo ultimo paziente è probabilmente dovuta all'istologia del tumore che risultava essere un carcinoma papillifero della tiroide con focali aree di anaplasia.

Questi tre casi confermano la difficoltà della gestione in emergenza dei sintomi locoregionali secondari a tumore anaplastico della tiroide.

In casi selezionati, quando l'ostruzione acuta delle vie aeree non può essere alleviata da una tracheostomia (per le difficoltà tecniche ed i rischi connessi alla procedura), la chirurgia demolitiva rappresenta una valida opzione terapeutica permettendo una buona gestione delle vie aeree. Essa tuttavia (anche se praticata con l'intento della radicalità) offre scarsi vantaggi in termini di sopravvivenza media per l'impossibilità di ottenere un effettivo controllo della malattia.

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