Neuroendocrinology Letters No.4 August Vol.26, 2005
 ISSN 0172–780X **www.nel.edu**

ORIGINAL ARTICLE

Selective embolization of thyroid arteries (SETA) as a palliative treatment of inoperable anaplastic thyroid carcinoma (ATC)

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Submitted: February 22, 2005 *Accepted: May 3, 2005*

Key words: **anaplastic thyroid carcinoma; selective embolization of thyroid arteries; palliative treatment**

Neuroendocrinol Lett 2005; **26**(4):401–406 **PMID:** 16136001 NEL260405A19

Abstract

OBJECTIVES: Anaplastic thyroid carcinoma (ATC) is one of the most aggressive solid tumors in humans. Despite intense application of multimodality of treatment with surgery and/or external beam radiotherapy and chemotherapy, the survival rates remain low – generally the mean survival is about six (6) months after diagnosis. Rapid development – particularly over the last decade – of interventional radiology, provides methodology that allows examining thyroid arterial embolization as an alternative approach to ablating thyroid tissue.
The aim of the present study was to evaluate selective embolization of the thyroid arteries (SETA) as a possible alternative for the palliative treatment of advanced, inoperable ATC.
PATIENTS AND METHODS: The study group comprised five (5) patients with advanced stage of inoperable ATC. All the patients underwent SETA of the superior and/or inferior thyroid arteries. SETA was performed using polyvinyl alcohol particles, ranging from 500–710 μm in diameter. After SETA, selective angiography of thyroid arteries was performed to ensure that the targeted arteries were completely occluded.
CONCLUSIONS: The results of the present study suggest that SETA is minimally invasive and save method of palliative treatment of ATC and, as such, may be recommended in cases of intractable hemorrhage and pain caused by ATC progression.

Abbreviations:
ATC Anaplastic Thyroid Carcinoma,
SETA Selective Embolization of Thyroid Arteries

Introduction

Thyroid cancer is a relatively rare neoplasm but it is the most common malignancy in the endocrine system. Anaplastic thyroid carcinomas (ATCs) are the least common but at the same time with the highest mortality rate out of all the thyroid cancers. ATC, accounting for 5% to 15% of primary malignant thyroid neoplasms, is one of the most aggressive solid tumors in humans [9].

ATC, typically, has a rapidly progressive course and, despite intense application of multimodality of treatment with surgery and/or external beam radiotherapy and chemotherapy, the survival rates remain low; generally, the mean survival period is about six months after diagnosis [1, 9].

The major clinical problem with ATC, is that it is usually inoperable when diagnosed. Therefore, only a small portion of patients can undergo surgical resection of the cancer in hopes of cure. Moreover, ATC is not responsive to I^{131} therapy and the treatment with individual anticancer drugs has been reported to produce partial remissions only in some patients [7, 22].

Although selected patients may benefit from aggressive multimodal therapy, in most of cases, it is important to provide an appropriate palliative care. Requirements for the palliative treatment include a minimal burden or risk for the patient and reasonable effectiveness.

In the present study, we decided to analyze the usefulness of minimally invasive procedure – selective embolization of thyroid arteries (SETA) – in the palliative treatment of patients with inoperable ATC. Because SETA is a minimally-invasive technique and offers immediate relief of symptoms, it may become an attractive option for ATC patients with intractable bleeding or signs of tracheal and esophageal compression.

Tumor embolization is defined as a blockage of the vascular supply to the tumor. Artificial embolization, as a therapeutic modality was introduced more than 30 years ago in the management of arterio-venous malformations [18]. In the following decades, the technique of selective embolization was extended from the treatment of vascular lesions, like arteriovenous malformations [4, 11, 18], hemangiomas [13, 14] and aneurysmal bone cysts [12] to severe hemorrhage [10, 20] and preoperative and therapeutic management of well vascularized benign and malignant tumors. Rapid development – particularly over the last decade – of interventional radiology, provides methodology that allows examining selective thyroid arterial embolization as an alternative approach to ablating thyroid tissue. The reports concerning SETA concentrate on the embolization of thyroid arteries in toxic goitres – particularly in Graves' disease [8,17, 27]. There are also some reports on the use of SETA in the treatment of vascular lesions of the thyroid arteries [15, 16, 19]. Although there are numerous studies on the embolization of the skeletal metastases of the differentiated thyroid carcinomas [3, 6, 23–25], the number of reports on the use of SETA in primary thyroid cancers is limited [2].

Patients and methods

The study group comprised five (5) patients with advanced stages of inoperable ATC (Table 1), enrolled in the study from June 2003 to February 2004. The study protocol had been approved by the Ethics Committee of the Medical University of Łódź. The patients were informed of the procedure, associated risks and potential side effects, afterwards, they signed a consent form as their approval to undergo arterial embolization.

Selective Embolization of Thyroid Arteries

All the patients underwent SETA of the superior and/or inferior thyroid arteries. The procedure was performed by a qualified team, using the Seldinger's technique [21].

A typical procedure required less than one hour. In brief, the patient was placed in a supine position. The inguinal pulsation point of either the left or right femoral artery was chosen as the puncture site. A small skin incision was made under local anesthesia (1% procaine, 2–3 ml). The puncture needle, along with a cannula, was inserted into the femoral artery through the incision. Next, the needle was removed while the cannula remained in the vessel lumen as an entry portal for a 4 or 5F-size angiographic catheter (Vertebral – Cordis, Europe NV, The Netherlands and Multipurpose, Balton, Poland). The catheter was advanced from the femoral artery *via* the abdominal aorta and sequentially to both superior and one of the inferior thyroid arteries. Migration of the catheter was visualized through use of a digital imaging x-ray device (Angiorey DFP–50A, Toshiba, Japan). Before embolization, contrast media (Ultravist 300; Schering AG, Germany) was injected into the vessels, thus allowing us to visualize the arteries and regions of the thyroid to which they supplied blood. Granules, consisted of polyvinyl alcohol (PVA, Cordis Neurovascular Inc., Miami, USA), ranging from 500–750 μm were injected slowly into the vessels. An added step for embolizing the superior arteries involved use of a non-magnetic wire coil with synthetic fibers (MReye® IMWCE 35–5–8, Cook, Denmark) of appropriate size, depending on the diameter of the lumen of the arteries in question. After SETA, selective angiography of the thyroid arteries – as DSA images – was performed to ensure complete occlusion of the targeted arteries.

Determination of concentrations of free triiodothyronine (FT_3), free thyroxine (FT_4), tyrothropin (TSH) and thyroglobulin (Tg)

The Tg, FT_3, FT_4, and TSH concentrations were measured using electrochemiluminescence (ECL) method with Modular E170 (Roche) analyser and appropriate kits (Roche–Diagnostics).

Table 1: Characteristics of the five patiens with ATC undergoing SETA.
Normal values: TSH – 0.27–4.2 mU/l; FT_3 – 3.95–6.8 pmol/ l; FT_4 – 12–22 pmol/l, Tg – 1.4 –78 ng/ml).
M: male; F: female

Patient	Age	Sex	Before SETA				One week after SETA				Survival period after SETA
			Tg [ng/ml]	**TSH** [mU/l]	**FT3** [pmol/l]	**FT4** [pmol/]l	**Tg** [ng/ml]	**TSH** [mU/l]	**FT3** [pmol/l]	**FT4** [pmol/]l	
1	45	M	45	2.7	5.5	17.4	–	–	–	–	3 days
2	78	F	24	3.6	4.6	14.5	40	4.8	3.6	11.8	3 weeks
3	81	F	68	1.4	6.2	20.4	80	3.9	4.4	12.4	8 weeks
4	72.5	F	15	1.2	6.4	19.6	60	3.2	3.2	14.8	2 weeks
5	80	F	46	3.8	4.2	14.8	76	5.2	3.2	8.6	13 weeks

Results

The data considering the age of the patients, the survival period after SETA and the concentrations of TSH, FT_3, FT_4 and Tg before and one week after SETA are presented in Table 1.

Case reports

Patient 1

A 45-yrs-old male, admitted on emergency because of dyspnoea, dysphonia, dysphagia and solid, stiff, immovable large neck mass. Computerized tomography scan (CT–scan) of the neck and the thorax revealed the presence of a large thyroid tumor, infiltrating the esophagus, the trachea, the larynx, and the prevertebralis space on the level of C5–C7 [Fig. 1]. Moreover, the subclavicular veins, the branchiocephalic trunk and the superior caval vein were infiltrated and completely closed by the mass of the tumor. There were also solid lesions found in the lumen of the right atrium and the right ventricle of the heart. After two days of stay at the Department of Surgery the signs of dyspnoe intensified, the general status aggravated and tracheostomy and gastrostomy were subsequently performed. After the operations, small, but systematically growing bleeding from the tumor appeared. Despite blood transfusions and several interventions under local anesthesia the bleeding increased. Reoperation was performed but the positive effect was transitory and the bleeding relapsed. In order to stop bleeding, SETA was performed. After the embolization of the left superior thyroid artery, bleeding was stopped. Because of severe status of the patient, the embolization of other thyroid arteries was abandoned. The patients died on the third day after SETA, presenting symptoms of massive embolia of pulmonary arteries – in the autopsy examination massive pulmonary embolia was confirmed – without the presence of the PVA particles in the pulmonary arteries.

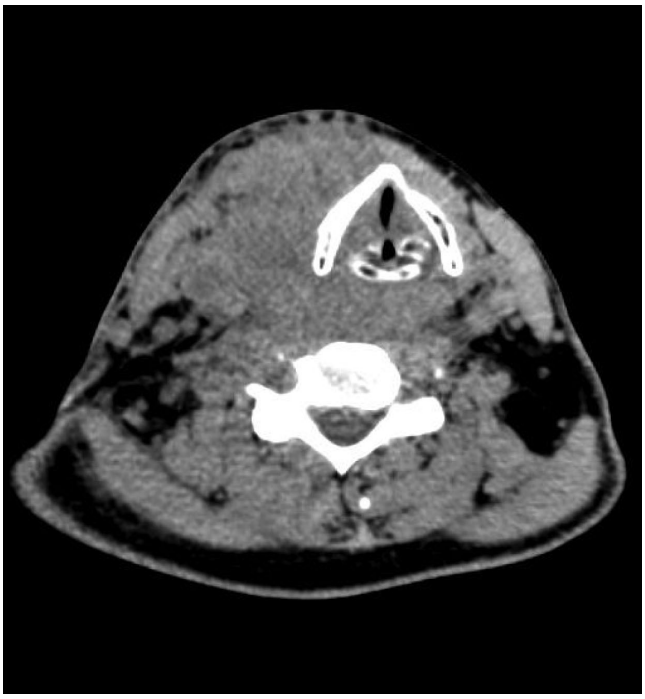

Figure 1: The CT–scan of the neck (Patient1) presenting large thyroid mass, compressing and moving trachea to the left. No visible blood flow in the veins of the neck. Signs of collateral circulation.

Patient 2

A 78-yrs-old female admitted with dyspnoe, dysphagia and large, immovable, fast growing (2 months) thyroid tumor. The patient consequently refused treatment till being almost asphyxiating. In anamnesis, non-toxic goitre untreated for 25 years, diabetes mellitus type 2, advanced ischeamic heart disease were present. Fine needle aspiration biopsy (FNAB) confirmed clinical diagnosis of ATC. In CT–scan large thyroid tumor, infiltrating esophagus, trachea, larynx, and the parapharyngeal space was found. The patient was disqualified from radical surgery because of the tumor size and character and of the general condition. The patient agreed and signed informed consent for SETA. Although patient reported improvement of swallowing and breathing after SETA, the tracheostomy and gastrostomy were performed two weeks after SETA. Tthe patient refused chemotherapy or radiotherapy and decided to leave the hospital.

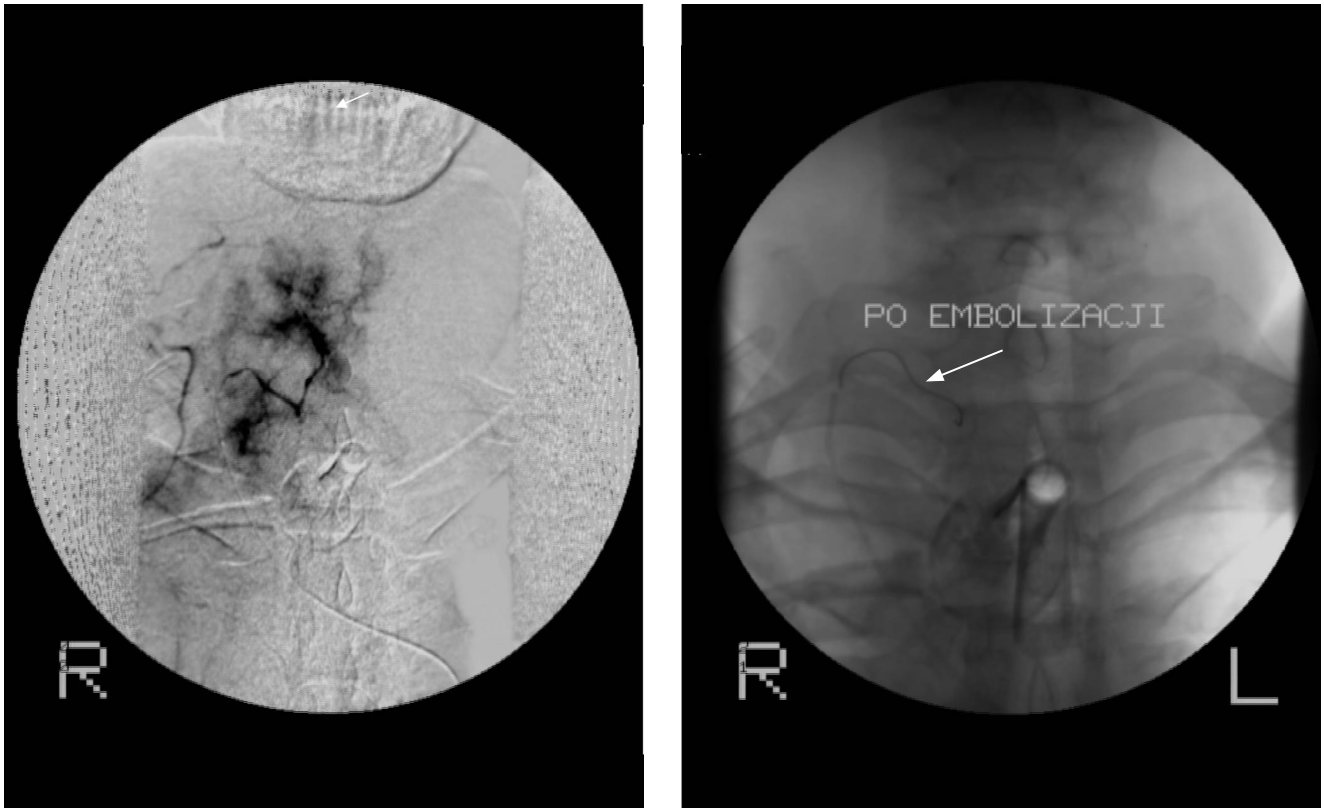

Figure 2: Embolization of the right superior thyroid artery using non-magnetic wire coil (Patient 1). On the left – status before embolization (pathological vascularization is visible), on the right – status after embolization of the artery. White arrow shows where the coil is placed.

Patient 3

A 72,5-yrs-old female was admitted asphyxiating on emergency. In CT–scan a large thyroid tumor, infiltrating the neighboring organs and the subcutaneous tissue and skin was found. According to the patient's report, the tumor had been growing very quickly for 3–4 months. The patient has presented dysphagia for two weeks and dyspnoe for 1 month. In anamnesis, an untreated nontoxic goitre was reported. Patient was intubated but disqualified from radical surgery. Furthermore, she refused tracheostomy or gastrostomy. She signed an informed consent for SETA. After SETA, although the patient reported improvement in breathing, general condition and the relief of the pain of the neck she was intubated because of the risk of the collapse of the trachea. After another 2 days the tracheostomy was performed after a written consent of the patient. She was transferred to radiotheraphy department.

Patient 4

An 80-yrs-old female with cytologically diagnosed ATC was admitted to the department. Because of hopeless general condition, cancerous cachexia and advanced stage of ATC she was disqualified from radical surgery. In CT–scan large thyroid tumor infiltrating all the neighboring tissues was documented. SETA was performed. The patient reported relief of the neck pain and improvement in breathing and general condition. After tracheostomy she was transferred to radiotheraphy department.

Patient 5

An 81-yrs-old female with cytologically confirmed ATC was admitted to the department. She was disqualified from radical surgery because of severe general condition, cancerous cachexia and advanced stage of ATC. In CT, a large thyroid tumor infiltrating all the neighboring tissues was recognized. SETA was performed and the patient reported relief of the pain of the neck and improvement in swallowing and breathing. After tracheostomy and gastrostomy she was transferred to radiotheraphy department.

Discussion

Considering the very aggressive and invasive type of growth and the short mean survival period after diagnosis of ATC, there is a clinical need for a proper and effective treatment of ATC. Since that kind of treatment is not yest established, the quality of life in the last days of the patients with inoperable ATC is the most important goal in the management of that type of cancer.

In the present study, we evaluated the usefulness of SETA in the palliative treatment of ATC.

In the cases described, the most spectacular proof of the effectiveness of SETA was the antihemorrhage effect of embolization in case of intractable bleeding from ATC after tracheostomy. In the treatment of bleeding from malignant tumors, specially poorly differentiated, we face technical problems with the surgical management of hemorrhage. The problems are the effects of the delicate and fragile consistence of the tumor and its

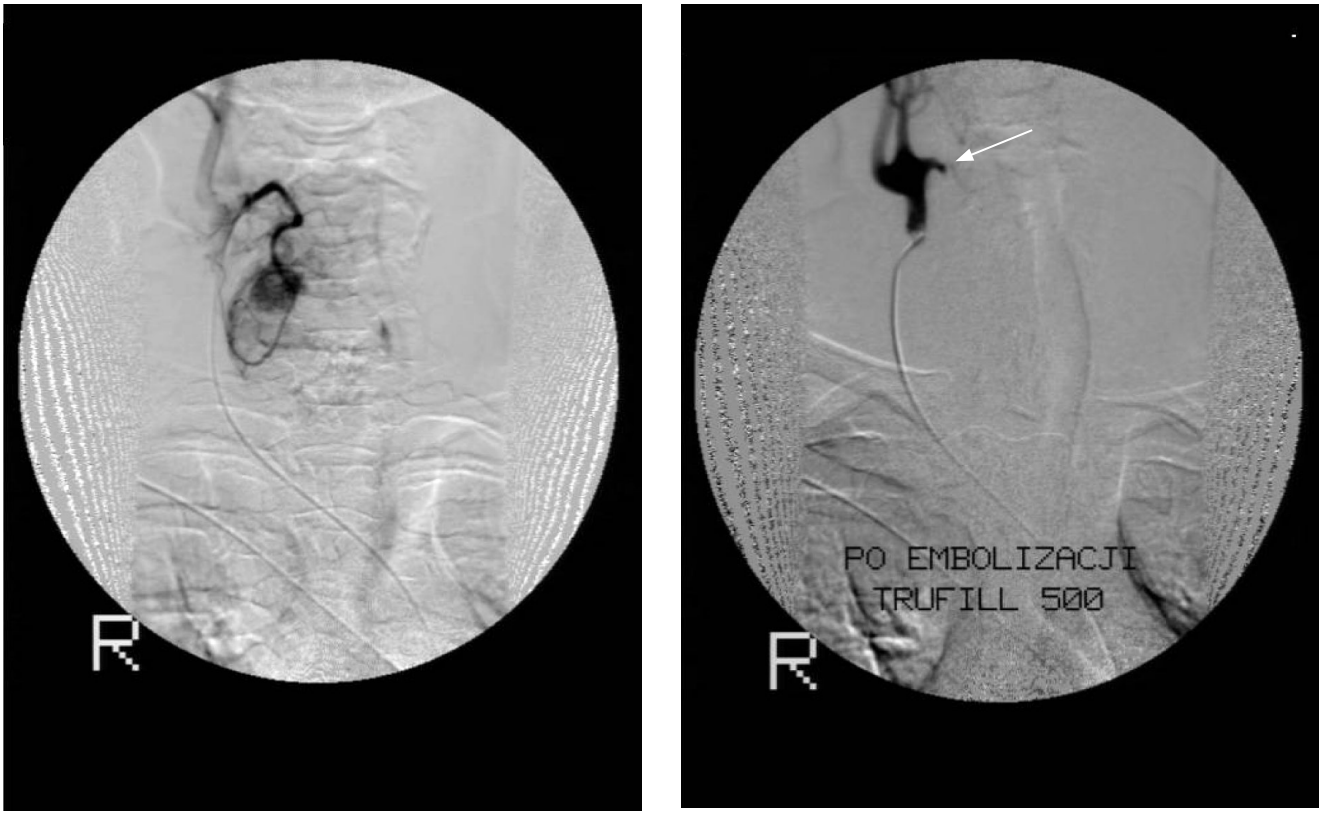

Figure 3: Embolization of the right superior thyroid artery (Patient 2). On the left - status before embolization (pathological vascularization is visible), on the right - status after embolization of the artery. White arrow shows where the artery is amputated.

pathological vascularization. It was mainly because of pathological vascularization that we decided to use the PVA molecules of the bigger diameter that those suggested by Xiao at al. (2002). In their work they estimated the diameter of the smallest thyroid arterioles in toxic goitre (0.04–0.11 mm) and suggested PVA granules of the 150 μm to be optimal for SETA [27]. However, considering some serious side effects of SETA, described in other reports [5, 26], in order to avoid passing the granules through the arterioles directly into veins of the pathological vascularization of the ATC, we decided to use the granules of much bigger diameter (500–750 μm). In the present study, we did not observe any embolic side effects of the SETA. Although one patient died from pulmonary embolia in the short period after the procedure, the accident had nothing to do with SETA. In CT–scan performed before SETA in the lumen of the right ventricle and the right atrium of the patient's heart the solid mass were discovered. In the autopsy examination massive pulmonary embolia was confirmed – without the presence of the PVA particles in the pulmonary arteries.

Another, direct proof of the effectiveness of SETA was the decrease of concentrations of FT_3 and FT_4 and increase of TSH concentration in blood of all the patients. This result was expected and consistent with the results of other studies [14]. However, the changes in the concentrations of these parameters, although evident, were rather slight, because of the short-period between the measures (one week). Surprisingly, although we observed increased Tg level after SETA; that increase was rather moderate. Elshafie et al. (2000) described massive rise in Tg after embolization of skeletal metastases from papillary thyroid cancer. In our study only slight increase of Tg resulted – most probably – from the fact that the embolized tissue was mainly the tissue of the tumor. Moreover ATC is an undifferentiated carcinoma that does not express Tg.

In favour of SETA use as palliative treatment in ATC, we observed improvement of swallowing in two (2) patients, decrease of the pain of the neck in three (3) patients and improvement of the general condition in two (2) patients. Similar and even more spectacular observations, considering pain relief and improvement of general condition, were made in the studies on the employment of embolization in the therapy of the skeletal metastases from differentiated thyroid cancer [3, 6, 23–25]. Although we had less spectacular results, one has to remember that the main goal of the palliative therapy is the improvement of quality of life of the patients, even if it has transitory character.

In conclusion, the results of this preliminary study suggest, that embolization of the large inoperable ATCs may be regarded as a treatment for intractable hemorrhage, and pain caused by ATC progression. We believe that SETA as an effective, minimally invasive, and save method of palliative treatment may become a valuable addition to the therapeutic strategies, particularly for inoperable ATC.

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