ANAPLASTIC THYROID CARCINOMA WITH LONG TERM SURVIVAL AFTER COMBINED TREATMENT: CASE REPORT

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Anaplastic thyroid carcinoma (ATC) is associated with an almost uniformly rapid and lethal clinical course. ATC grows rapidly and invades surrounding tissues at an early stage. Despite surgery, chemotherapy and radiotherapy, few patients with ATC live more than 1 year follow-up diagnosis. The mean survival is reported to be only 7.2 months. Treatment of ATC is still controversial because of its rarity and advanced stage at the time of diagnosis.

We report herein an unusual case of ATC, 35 year old woman. She is alive without evidence of recurrence more than 36 months after combined therapy

Key words: Case report – Anaplastic thyroid carcinoma – Multimodal treatment – Surgery – Chemotherapy – Radiotherapy

Anaplastic thyroid carcinoma (ATC) is one of the most lethal primary malignant thyroid tumors, but fortunately it accounts for a small percentage of cases (HAIGH et al. 2001; SUGINO et al. 2002). Although less than 2 % of all thyroid carcinomas are anaplastic thyroid carcinoma, it accounts for 14-39 % of thyroid carcinoma deaths (AIN et al.1998; MITCHELL et al. 1999).

Most patients with ATC have local extensive and/or distant metastases at the time of presentation and their survival is dismal because there is still no standardized successful treatment protocol for ATC (HAIGH et al. 2001; MELVER et al. 2001). The most important treatment of choice for ATC is surgery, but chemotherapy and radiation theraphy are also being used with limited success. Aggressive treatment with the combination of surgery and chemoradiatherapy is usually preferred for these patients. ATC grows rapidly and invades adjacent tissues, so these treatment modalities are usually insufficient and the survival of ATC after diagnosis is very short.

We report a case of undifferentiated thyroid carcinoma (UTC) in a 35-year old woman with long term disease free survival. We diagnosed ATC incidentally and for treatment we used a combination of surgery, chemotherapy and radiation theraphy. There is no evidence of recurrence after 36 months.

Case Report

Thirty five years old woman was admitted with a rapidly growing thyroid nodule. Physical examination showed a nodular formation in the right thyroid lobe. She had no history of exposure to radiation or any remarkable family history. Serum levels of thyrotropin (TSH), free thyroxine (FT4), free triiodothyronine (FT3) and thyroglobulin (TG) were in normal range. Thyroid ultrasound examination revealed multiple nodules in the right thyroid lobe, the greatest nodule being 32 x 28mm. The left lobe of thyroid was found normal. FNAC performed from the dominant nodule did not reveal any signs of malignity. The scintigraphy showed a hypoactive nodule.

Because of the patient's age, nodule size of >3 cm and sudden onset, we decided to perform right lobectomy on January 2003. There was no evidence of malignancy on pathological examination.

After about 9 months the patient was admitted again because of a mass on the trachea. The ultrasound ex-

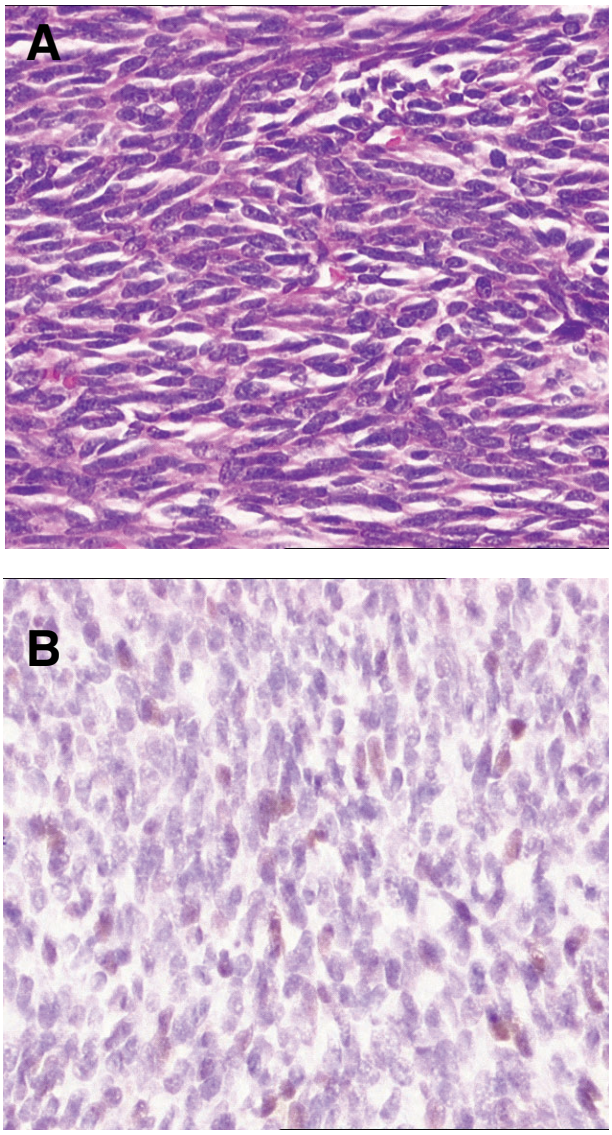

Figure 1: A: The tumor showed spindle cell growth pattern (H&EX200), B: P53 immunostaining was positive in the cell nuclei. (SAB-DABX200)

amination revealed 21 x 15 mm hypoechogenic nodule which was hypoechogenic. The FNAC of the nodule showed suspicious malignity and the patient was subjected to reoperation. Frozen section performed during the operation from the mass and adjacent soft tissue. The result of frozen section of the mass revealed undifferentiated carcinoma of thyroid. Mass on the trachea and strap muscles which were invaded by tumor, were excised totally and left lobectomy was performed. Histological examination revealed spindle cell tumor with prominent mitotic figures. No epithelioid areas

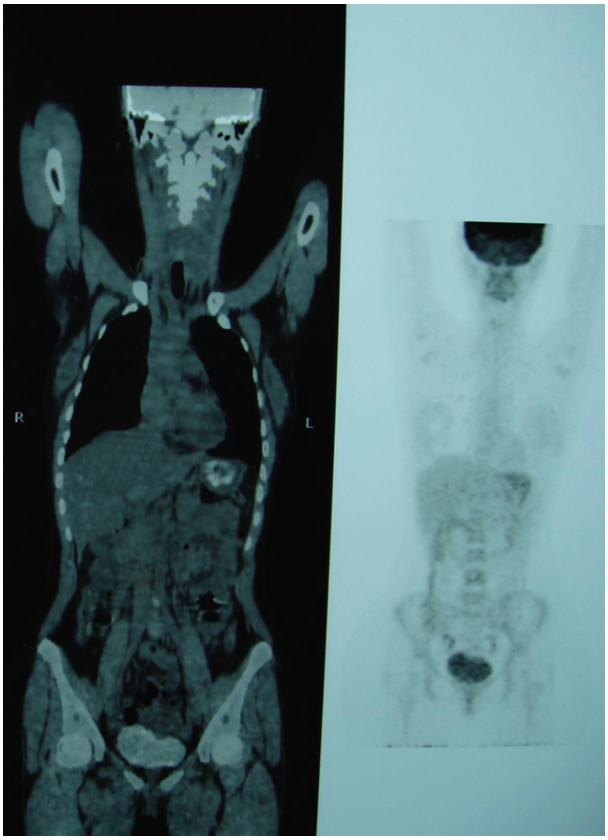

Figure 2: Control 18F-FDG in the PET-CT, 36 months after second operation. There is no recurrence or metastasis

were seen. Immunohistochemical staining results were positive for p53, Ki 67 and negative for SMA, calcitonin, CD34, desmin, chromogranin and S-100 (Figure 1A and 1B). Three lymph nodes were found metastatic. She had an adjuvant treatment of chemotherapy (docetaxel) and radiotherapy (6000 cG) combination after the operation.

In the follow-up examination, we revealed suspicious right cervical lymph nodes showed 18F-FDG in the PET–CT five months later. According to this result, she was reoperated and we performed right modified radical neck dissection. There was no metastasis in the lymph nodes.

In the follow-up examination, there is no evidence of recurrence or metastasis on 18F-FDG PET–CT examination 36 months after second operation and adjuvant treatments (Figure 2).

Discussion

Anaplastic thyroid carcinoma is twice as common in areas with endemic goiters (Demeter et al. 1991; Ain et al.1998), the peak incidence being in the six to seventh decade of life and 55 to 77 % of the patients being females (Venkatesh et al. 1990; Tan et al. 1995; Ain et al. 1998).

ATC grows rapidly and invades adjacent tissues at an early stage. Treatment of each patient is different because of the various clinical stages at the time of diagnosis. There is still controversy about the appropriate treatment for ATC and combined multimodal therapy seems to be the most common and accepted management strategy for this aggressive disease (Sugino et al. 2002). Surgery with combined chemotherapy and radiation therapy is the treatment of choice. ATC is one of the most aggressive malignant disease and its prognosis is very poor (Haigh et al. 2001; Sugino et al. 2002).

The optimal treatment modalities are not known. ATC is a rare but aggressive tumor and treatment is mostly ineffective. There are insufficient data in the literature about the optimal treatment choices. Most of ATC patients are old and have poor general condition who cannot tolerate aggressive cancer treatment (Haigh et al. 2001; Sugino et al. 2002). The overall survival is limited to months. Complete surgical resection is among most suggested treatments, but unfortunately in most of the patient, it is not possible. However, a few patients with resectable disease have been reported in the literature. With aggressive combination therapy consisting of surgery, radiation and chemotherapy the survival of patients may be prolonged (Pasieka 2003).

It is claimed that surgery is the most effective treatment for ATC and complete resection of thyroid and surrounding tissues is suggested, if possible. Thus, Kihara et al. (2004) found synchronous distant metastases at diagnosis in 47.3 % of their patients who underwent surgery and these had a significantly better survival than the patients who did not. When the 6 months, 1 year and 2 year survival of complete resection and incomplete resection was compared, the survival rates were 100 % vs. 17 % (complete vs. incomplete), 75 % vs. 17 % and 50 % vs. 0%, respectively. Some authors have also reported that complete resection was associated with longer survival than incomplete resection or biopsy (Melver et al. 2001; Pierie et al. 2002; Sugino et al. 2002). According to Kihara et al. (2004) the second independent prognostic factor is the size of the nodule. Patients with a tumor size smaller than 5 cm in diameter had a significantly better outcome than those with greater than 5 cm in diameter. Thus, this study revealed that the only prognostic factors were complete resection and tumor size <5 cm, while there was no association between survival and extrathyroidal invasion, distant metastases, extended resection, acute symptoms, gender, multimodality treatment, lymph node metastasis, leukocytosis or age..

Radical surgical resection of the tumor and surrounding tissues has been thought to have no effect on survival and result in the production of many sequelae (Nel et al. 1985; Venkatesh et al. 1990). Also, complete surgical resection of anaplastic carcinoma is difficult to perform in most of the cases. Although palliative debulking of these tumors shows a beneficial effect, there is no effective treatment for distant metastasis of ATC.

The sequence of the treatment was also studied and there no statistical difference between primary surgery and primary chemotherapy and/or radiation was found (Besic et al. 2001). The latter authors recommended that in very small or focal anaplastic carcinoma primary surgery followed by chemotherapy and radiotherapy may be the treatment of choice. Two of their patients were treated with primary surgery and the other one was treated by primary chemotherapy and radiotherapy with surgery.

Venkatesh et al. (1990) report the data on 121 patients with anaplastic carcinoma obtained by M.D. Anderson, among which 12 patients with complete macroscopic resection of tumor survived longer than 24 months, and 10 of these patients received combined radiation and chemotherapy postoperatively.

Incidentally discovered anaplastic carcinoma in a rapidly enlarging thyroid nodule has been reported in some series (Sugino et al. 2002). Although the survival rate of these patients with incidental anaplastic carcinoma was found in two studies to be significantly better than the typical anaplastic tumor, some patients with incidental anaplastic carcinoma had poor prognosis (Sugino et al. 2002; Pacheco-Ojeda et al. 2001). In that study all incidental ATCs were treated with surgery and 73 % of them survived more than 1 year, while 46 % survived more than 2 years. The implication of small foci of anaplastic carcinoma has not been thoroughly evaluated and a small focus of anaplastic carcinoma is often regarded as a life-threatening malignancy. The survival rate of patients with small focus of anaplastic carcinoma was significantly better than that for patients with ordinary anaplastic carcinoma (Sugino et al. 2002).

Most authors agree that early diagnosis and complete surgery are the most important predictors for survival of ATC. There can be a longer survival hope for these patients.

References

Ain KB: Anaplastic thyroid carcinoma: behavior, biology and therapeutic approaches. Thyroid **8,** 715-726, 1998

Besic N, Auersperg M, Us-Krasovec M, Golouh R, Frkovic-Grazio S, Vodnik A: Effect of primary treatment on survival in anaplastic thyroid carcinoma. Eur J Surg Oncol **27,** 260-264, 2001

Demeter JG, De Jong SA, Lawrence AM, Paloyan E. Anaplastic thyroid carcinoma: risk factors and outcome. Surgery **110,** 956-963, 1991

Haigh PI, Ituarte PH, Wu HS, Treseler PA, Posner MD, Quivey JM, et al.: Completely resected anaplastic thyroid carcinoma combined with adjuvant chemotherapy and irradiation is associated with prolonged survival. Cancer **91,** 2335-2342, 2001

Kihara M, Miyauchi A, Yamauchi A, Yokomise H: Prognostic factors of anaplastic thyroid carcinoma. Surgery Today **34,** 394-398, 2004

Melver B, Hay ID, Giuffrida DF, Dvorak CE, Grant CS, Thompson GB, et al.: Anaplastic thyroid carcinoma: a 50- year experience at a single institution. Surgery **130,** 1028-1034, 2001

Mitchell G, Huddart R, Harmer C: Phase II evaluation of high dose accelerated radiotherapy for anaplastic thyroid carcinoma. Radioth and Oncol **50,** 33-38, 1999

Nel CJ, van Heerden JA, Goellner JR, Gharib H, McConahey WM, Taylor WF, Grant CS: Anaplastic carcinoma of the thyroid: a clinicopathologic study of 82 cases. Mayo Clin Proc **60,** 51-58, 1985

Pacheco-Ojeda L, Martinez A, Alvarez M: Anaplastic thyroid carcinoma in Ecuador: analysis of prognostic factors. Int Surg. **86,** 117-121, 2001

Pasieka JL: Anaplastic thyroid carcinoma. Curr Opin Oncol **15,** 78-83, 2003

Pierie JP, Muzikansky A, Gaz RD, Faquin WC, Ott MJ: The effect of surgery and radiotherapy on outcome of anaplastic thyroid carcinoma. Ann Surg Oncol **9,** 57-64, 2002

Sugino K, Ito K, Mimura T, Nagahama M, Fukunari N, Kubo A, et al. : The important role of operations in the management of anaplastic thyroid carcinoma. Surgery **131,** 245-249, 2002

Tan RK, Finley RK 3rd, Driscoll D, Bakamjian V, Hicks WL Jr, Shedd DP: Anaplastic carcinoma of the thyroid: a 24 year experience. Head Neck **17,** 41-47, 1995

Venkatesh YS, Ordonez NG, Schultz PN, Hickey RC, Goepfert H, Samaan NA. Anaplastic carcinoma of the thyroid. Cancer **66,** 321-330, 1990

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