Case Report: 84-Month Disease-Free Survival after Surgery for Anaplastic Thyroid Carcinoma

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We present a rare case of a patient with anaplastic thyroid carcinoma (ATC) who survived for 87 months after surgery. The patient was a 71-year-old man who presented with a painful enlarged mass in the right side of his neck that rapidly enlarged over 2 months. He was diagnosed with T4a, stage IVA ATC with no distant metastasis and underwent total thyroidectomy with modified neck dissection. Although only radiation and radioactive iodine therapy were administered after surgery, he remained disease-free for 84 months. Bone metastasis occurred after 84 months, and he was treated with Lenvatinib, but he died from a decline in his general condition 3 months later. We suggest that surgery is effective for stage IVA ATC, but adjuvant therapy is necessary for long-term disease-free survival in this patient population. (J Nippon Med Sch 2019; 86: 38–42)

Key words: anaplastic thyroid cancer (ATC), surgical treatment, relapse-free survival

Introduction

Anaplastic thyroid carcinoma (ATC) is a highly aggressive malignant thyroid tumor, and accounts for <2% of all thyroid malignancies

The prognosis is poor, with a mortality rate of >90% and a mean survival of 6 months after diagnosis. Although ATC has diverse histopathological features, to date, none have been found to have prognostic significance. Most existing knowledge about ATC is derived from single-institution studies with a limited number of patients and short-term follow-up. To obtain further insight into this disease, the ATC Research Consortium of Japan (ATCCJ) established a nationwide multi-institutional collaborative study group in January 2009.

Sugitani et al. devised a prognostic index (PI) for ATC based on four unfavorable prognostic factors: (1) acute symptoms (duration of severe complaints such as dysphonia, dysphagia, dyspnea, and rapid tumor growth of <1 month); (2) leukocytosis (leukocyte count ≥10,000/mm³); (3) tumor size >5 cm; and (4) distant metastasis. Patients were assigned a PI score of 1 to 4. In their study, patients with PI=1 experienced a 62% survival rate at 6 months, whereas no patients with PI=3 survived longer than 6 months and all patients with PI=4 died within 3 months. A study by Sugitani et al. confirmed the results of the ATCCJ and validated the ATC classification as a prognostic index. The authors recommended attempting multimodal treatment for patients with PI≤1, while avoiding aggressive treatment to maintain quality of life for patients with PI≥3.

Here we report a rare case of a patient with ATC pT4a, pN1b, M0, stage IVA, PI=1, who survived for 87 months after surgery.

Case Report

A 71-year-old man was referred to our hospital with a chief complaint of a rapid and painful right-sided neck enlargement. A palpable, hard, unmovable tumor was observed in the right side of his neck, along with a swollen, palpable, movable lymph node. Cervical enhanced computer tomography (CT) revealed a calcified tumor with internal heterogeneity, 4.6 × 3.6 cm in size, that was continuous with the upper pole of the right thyroid lobe, as well as enlargement (2.3 × 1.9 cm) of the right cervical lymph node; no obvious infiltration was seen (Fig. 1). No distant metastasis was observed. The leukocyte count was 5,400/mm³, with no other blood cell count abnormalities. The serum anti-thyroglobulin antibody (TgAb)
level was elevated to 500 ng/mL (normal range, <37.0 ng/mL), serum thyroglobulin (Tg) was not elevated (0.04 IU/mL), and thyroid hormone levels were within normal limits. His comorbidities included diabetes, hypertension, and supraventricular tachycardia. His medications included warfarin as a preventive measure against thrombus caused by supraventricular tachycardia. The thyroid tumor and lymph node nodule were investigated by fine-needle aspiration cytology (FNAC) under ultrasound guidance. The FNAC results were highly suggestive of ATC. Cervical enhanced CT performed one month later, the day before surgery, showed that the right thyroid lobe tumor and the right cervical lymph node had each increased in size by >30% to 6.2×3.2 cm and 3.4×2.3 cm, respectively (Fig. 2). The clinical diagnosis was ATC, cT4a, cN1b, M0, stage IVA, PI=0. However, these findings did not rule out surgery. Total thyroidectomy and central and right lateral cervical lymph node dissection were performed. Histopathological findings by hematoxylin & eosin (H&E) staining showed that the tumor consisted of 70% ATC components and 30% papillary thyroid carcinoma (PTC) components (Fig. 3, 4). The sarcoma components, which accounted for most of the tumor, were strongly positive for CD68 and vimentin, partially positive for S-100, and negative for Tg, α-SMA, desmin, CD20, CD79a, CD3, CD45RO, CD30, and CD5.
The sarcoma component stained strongly positive for CD68 and vimentin, partially positive for S-100, and negative for Tg, α-SMA, desmin, CD20, CD79a, CD3, CD45RO, CD30, and CD5. The MIB-1 labeling index showed a somewhat lower value of 30%. The tumor showed malignant fibrous histiocytoma-like features but was EMA-negative and was ultimately diagnosed as anaplastic thyroid carcinoma.

The Ki-67 labeling index was less than 30% in the ATC components. The tumor showed malignant fibrous histiocytoma-like features, but was EMA-negative (data not shown). The final diagnosis was ATC, pT4a (T3, EX 1), pN1b, M0, stage IVA.

External beam radiation therapy (EBRT) of 40 Gy (2 Gy × 20 fraction) was performed on the neck after surgery. A marked rise in TgAb was observed 24 months later, and 1.85 GBq (50 mCi) of radioactive iodine (RAI) ablation therapy was performed, after which the TgAb gradually decreased. RAI therapy appeared to be effective, so 4.44 GBq (120 mCi) of RAI therapy was additionally administered. After RAI therapy, the Tg level did not change (average, 18.5 ng/mL), but the TgAb level decreased from 500 to 52 ng/mL (Fig. 5). After RAI ablation, ¹³¹I uptake was seen only in the thyroid bed on a whole body scan, and this disappeared after RAI therapy (data not shown). The patient experienced a disease-free survival period of 84 months. However, at 84 months, he developed lumbar pain. CT revealed a mass on the lumbosacral vertebrae (Fig. 6). The patient was taking warfarin and core needle biopsy (CNB) of the lumbosacral vertebrae was contraindicated because of the high risk of nerve palsy due to bleeding. CT examination did not reveal any primary lesions that could cause bone metastasis, thus the bone mass was diagnosed as a sacral ATC metastasis. Tyrosine kinase inhibitor (TKI) therapy with Lenvatinib 24 mg was started. No decrease in the size of the lesion was observed 6 weeks after the initiation of TKI therapy. Although no adverse effects of TKI administration were observed, the patient died 3 months after the diagnosis of recurrence due to a decrease in his general condition.

Discussion
It has been reported that 15–50% of patients have significant local infiltration and distant metastases at the time of ATC diagnosis. No effective treatment for ATC has been established, long-term survival is rare, and the prognosis is poor, with a mortality rate of >90% and a mean survival of 6 months after diagnosis.

Among the 677 registered ATC cases accumulated by ATCCJ, clinical varieties of ATC were classified into four types: common type (n=547), incidental type (n=29), anaplastic transformation at the neck (n=95), and anaplastic transformation at a distant site (n=6). The incidental type was associated with better outcomes than the other types, followed by anaplastic transformation at the neck. Anaplastic transformation at a distant site was associated with the worst outcomes. The 6-month and 1-year cause-specific survival (CSS) rates for common-type ATC were 36% and 18%, respectively. Among all cases, 84 (15%) achieved long-term (>1 year) survival. Multivariate analysis identified age ≥70 years, presence of acute symptoms, leukocytosis (leukocyte count ≥10,000/ mm³), large (>5 cm) tumors, T4b tumors, and distant metastasis as significant risk factors for lower survival. CSS rates also differed significantly depending on UICC stage, with 6-month CSS rates of 60% for stage IVA, 45% for stage IVB, and 19% for stage IVc. Among 36 of 69
External beam radiation therapy of 40 Gy was performed on the neck just after surgery. A marked rise in TgAb was observed 24 months after surgery, so an additional 50 mCi of radioactive iodine (RAI) was administered, and the TgAb subsequently decreased. The TgAb increased again 46 months after surgery, and 120 mCi of RAI was administered. After RAI therapy, the Tg level did not change (average, 18.5 ng/mL), but the TgAb level decreased from 500 to 52 ng/mL.

**Fig. 5** External beam radiation therapy of 40 Gy was performed on the neck just after surgery. A marked rise in TgAb was observed 24 months after surgery, so an additional 50 mCi of radioactive iodine (RAI) was administered, and the TgAb subsequently decreased. The TgAb increased again 46 months after surgery, and 120 mCi of RAI was administered. After RAI therapy, the Tg level did not change (average, 18.5 ng/mL), but the TgAb level decreased from 500 to 52 ng/mL.

Fig. 6 Plain computed tomography findings of sacral anaplastic thyroid carcinoma metastasis. An osteolytic bone metastasis of 8.1×4.7 cm was observed on the sacrum (arrow head), with no new primary lesions.
RAI therapy. This suggests that RAI therapy is an effective adjuvant therapy in ATC. It has been reported that outcomes are more favorable in patients who undergo curative resection, and their clinical course is slightly improved by the addition of EBRT and/or chemotherapy after curative resection, although this did not reach statistical significance in ATCCJ\(^4\). Our case occurred before the ATCCJ report was released, and adjuvant chemotherapy was not administered.

Although no currently established treatment strategies exist for ATC and it is associated with a very poor prognosis, some cases in which radical cure (i.e., surgical removal) leads to improvement in prognosis have been reported\(^9\), and surgical respectability has been indicated as an independent prognostic factor\(^5\). Furthermore, Onoda et al. reported the feasibility and objective outcomes of chemotherapy (weekly paclitaxel) for patients with ATC\(^5,10\).

In the present case, bone metastasis occurred after a disease-free survival period of 84 months. The patient received Lenvatinib but died from a decline in his general condition 3 months later. Although adjuvant chemotherapy was not administered, it was considered as an option. We suggest that surgical treatment is effective for stage IVA ATC, but an effective adjuvant therapy is necessary to achieve long-term disease-free survival.

Conflict of Interest: None declared.

References

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