

¹³¹I treatment for brain metastases from differentiated thyroid carcinoma

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Abstract To assess the clinical value of treatment with ¹³¹I for brain metastases from differentiated thyroid cancer (DTC), we have observed 8 cases of brain metastases from DTC who received follow-up after ¹³¹I therapy (2 male, 6 female, aged 12~65 years). The results of ¹³¹I therapy were evaluated with clinical presentation, imaging scan and survival analysis. The main results are as follows. (1) All cases had been survival for 2~35 years in follow-up. (2) A space-occupying lesion in right cerebellum was reduced after taking 20.65 GBq and disappeared after 23.61 GBq, demonstrated by computed tomography. (3) The sequences and doses of ¹³¹I therapy were clearly decreased for the cases with total thyroidectomy in comparison with those with semithyroidectomy ($p < 0.01$). (4) The brain metastases with lung and/or bone metastasis from DTC were 75% (6/8) and it was difficult to cure these metastases at the same time. It is concluded that the postoperative treatment of ¹³¹I for brain metastases from DTC after undergoing thyroidectomy may improve clinical symptoms and life quality, reduce lesions, and prolong survival.

Keywords Thyroid neoplasms, Iodine-131, Radiotherapy, Brain neoplasms

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1 Introduction

Differentiated thyroid carcinoma (DTC) typically has an excellent prognosis and a low incidence of distant metastasis. However, once metastasis has developed in a distant site, prognosis is markedly diminished. Brain metastases from differentiated thyroid carcinoma are extremely rare, with a frequency of 0.1%~5.4%.^[1-4] But such metastases behave more aggressively and become threatening, and almost always involve concomitant lung or bone metastases which may be the first metastatic sites. Currently, there are no provided therapeutic guidelines for treating brain metastases from thyroid carcinoma. Therapeutic protocols for brain metastases from differentiated thyroid carcinoma are not firmly established. The consensus regarding management has not been reached yet. It is generally treated with a combination of surgical, chemical, and radiological modalities.^[5-8] The postoperative adjuvant radioactive iodine (¹³¹I) therapy has resulted in an excellent outcome, but particular attention should be paid to the relevant side effects.

To assess the clinical value of ¹³¹I treatment of brain metastases from differentiated thyroid carcinoma, we describe and analyse here clinical details of 8 cases of brain metastases from 354 cases of differentiated thyroid carcinoma in follow-up.

2 Materials and methods

Data of patients are shown in Table 1. Of 8 cases of brain metastases from differentiated thyroid carcinoma (papillary in 4, follicular in 2, unknown in 2), six were female and two were male. The mean age at first diagnosis of brain metastases was (38.1±21.7) years (ranging 12~65 years). Only in two patients, brain was the unique site of metastatic spread; in others, lungs and bones were also involved. All patients received thyroidectomy, 3 cases for total-thyroidectomy, 3 cases for semi-thyroidectomy and 2 cases for part-thyroidectomy. Brain metastasis lesion of five patients were identified from primary thyroid carcinoma with brain postoperative pathology, three with brain computed tomography scan and magnetic resonance imaging. All patients received ¹³¹I treatment

Table 1 Data of patients

Case No.	Sex	Age	Thyroidectomy	Pathology	Brain metastasis	Diagnosis	Companying
1	F	39	Part-	Papillary	Right forehead	Patho./ ¹³¹ I/ CT/MRI	
2	F	17	Part-	Papillary	Left cerebellum	Patho./ ¹³¹ I/ CT/MRI	Lung/bone
3	F	12	Total	Papillary	Left forehead	¹³¹ I/CT	Lung
4	M	18	Total-	Papillary	Left temple	Patho./ ¹³¹ I	Lung
5	F	33	Semi-	Unknown	Right cerebellum	¹³¹ I/ CT	Lung
6	F	65	Total-	Unknown	Occiput	Patho./ ¹³¹ I/X-ray	Bone
7	M	60	Semi-	Follicular	Conarium	¹³¹ I /MRI	Bone
8	F	61	semi-	Follicular	Left foramina jugulare	Patho./ ¹³¹ I/ CT/MRI	

and all brain metastases were seen during the uptake of ¹³¹I.

Protocol and doses of ¹³¹I treatment are shown in Table 2. Before ¹³¹I treatment, all patients broke off taking thyroxin and rich-iodine food over 4 weeks. All patients received routinely examinations of peripheral blood, cervical ultrasonic, lungs X-ray, and whole-body bone scan with ^{99m}Tc-MDP. Whole-body ¹³¹I scan was performed one week after ¹³¹I treatment. Interval time of ¹³¹I treatment was 3~6 months.

The mean doses of ¹³¹I for the first ablating remainder of postoperative thyroid were (3.68±2.18) GBq (ranging 1.37~7.40 GBq), and the complete ablating mean doses were (16.78±12.55) GBq (ranging 1.85~37.00 GBq). The mean ablating frequency was (3.4±2.8) times (ranging 1~8 times). The mean total frequency of ¹³¹I treatment

was (6.9±3.8) times (ranging 2~13 times), and the mean accumulating doses were (39.45±21.60) GBq (ranging 8.14~65.64 GBq). The mean length of survival period was (10.9±11.7) years (ranging 2~35 years) after ¹³¹I treatment.

Statistical data were evaluated with analysis of variance and survival.

3 Results and discussions

Differentiated thyroid carcinoma is a common malignancy with a relatively good prognosis. However, distant metastases may develop and become threatening, particularly to older patients, in a more aggressive manner. Brain metastatic lesions can be life threatening. According to the literatures, surgery is the best therapeutic choice in the management of brain metas-

Table 2 ¹³¹I treatment and follow-up

Case No.	Initial doses (GBq)	Ablating frequency	Ablating doses (GBq)	Therapy frequency	Therapy doses (GBq)	Follow-up (years)
1	5.18	6	37.00	9	65.64	35
2	1.37	8	28.90	13	57.02	8
3	1.85	1	1.85	2	8.14	3
4	7.40	1	7.40	2	12.95	2
5	3.26	4	15.47	8	30.12	12
6	1.48	3	16.28	9	56.98	21
7	3.33	1	3.33	5	28.48	3
8	5.55	3	24.05	7	51.80	3

tasis. Alternative strategies, such as ^{131}I therapy, are recommended, but paying particular attention to the relevant side effects.

This article indicates that an early diagnosis with the appropriate surgical management of a brain metastasis followed by ^{131}I therapy could be valuable for achieving a prolonged disease-free period. The mean survival of 8 cases was (10.9 ± 11.7) years (ranging 2~35 years) with no death. All patients had marked uptake in the metastases (^{131}I positive, Figs.1~2) and had no symptoms from neurological system, except for accidental headache and insomnia for Case 1. For Case 5, a space-occupying lesion in right cerebellum was reduced after taking 20.65 GBq of ^{131}I treatment for 5 times and disappeared after 23.61 GBq of ^{131}I treatment for 6 times, demonstrated by computed tomography (Fig.3). ^{131}I scan showed that lesions of brain, lung and/or bone metastases did not advance in all cases. The results of Tg test had no distinct variation during ^{131}I treatment. Misaki *et al.*^[4] indicated that 9 cases with brain metastases from DTC (3 of them received removal of their brain tumors, 5 received conventional external beam irradiation, and 2 had stereotactic radiosurgery with supervoltage X-ray. None of the brain lesions showed significant uptake of ^{131}I), died 4~23 (mean 9.4) months after the first diagnosis. Salvati *et al.*^[2] indicated that the survival average was 19.8 months in 12 cases whose brain metastases had no uptake of ^{131}I . These data showed that the treatment of ^{131}I for postoperative brain metastases with having uptake of ^{131}I may improve patients' clinical symptoms and life quality, reduce lesions, and prolong survival.

It is important to give treatment as early as possible since the brain is the third most common distant

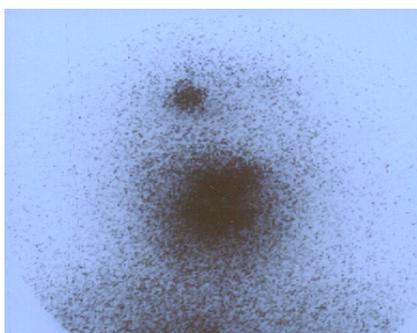


Fig.1 Case 1: ^{131}I positive lesion at right forehead.

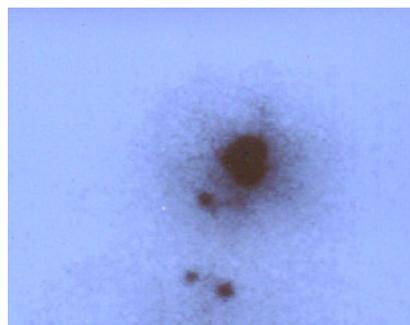


Fig.2 Case 4: ^{131}I positive lesion at left temple.

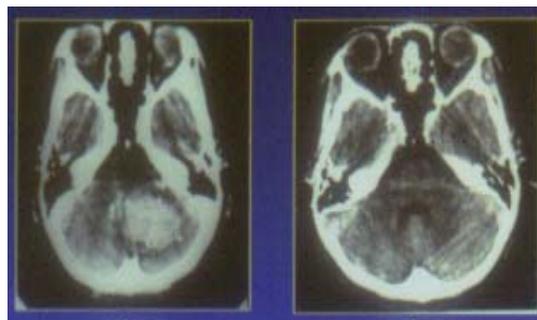


Fig.3 Case 5: a space-occupying lesion in right cerebellum (left, 1991) was reduced after taking ^{131}I 20.65 GBq and disappeared after 23.61 GBq (right, 1992), demonstrated by computed tomography.

metastatic site and the prognosis is poor. The postoperative remnant thyroid gland affects the uptake of ^{131}I in metastatic lesions, even in the cases from differentiated thyroid carcinoma, suggesting absence of differentiation between primary and metastatic disease. Therefore, the operative manners could affect the ablating for remnant thyroid and following ^{131}I therapy of brain metastases. According to statistical analysis with this article, the sequences and doses of ^{131}I therapy were clearly decreased for the cases with total-thyroidectomy in comparison with those with semi-thyroidectomy ($p < 0.01$).

The brain metastases with lung and/or bone metastasis from DTC were 75% (6/8). It was difficult to cure these metastases at the same time. The lung and/or bone metastatic lesions of Cases 3~7, including Case 5 whose brain metastatic lesions disappeared after ^{131}I treatment, still had uptake of ^{131}I in follow-up. The X-ray of Case 2 became negative after ^{131}I treatment for 2 times (9.29 GBq), and the ^{131}I scan of lungs became negative after ^{131}I treatment for 7 times (25.20 GBq), but the brain and bone metastatic lesions still had uptake of ^{131}I in follow-up.

The older patients (>60 years old) and the

younger one (<20 years old) were more than the patients with 21~60 years old (3:3:2); female was more than male (6:2); papillary was more than other types (4:2:2). It is similar to the information of current literatures.^[6-8]

Case 8 had temporal leukopenia and recovered after 3 months. It may be a result of administration of ¹³¹I with numerous doses in a short-term. All patients had functional damage of salivary glands, presenting saliva reduction and dry mouth.

4 Conclusions

The postoperative treatment of ¹³¹I for brain metastases from DTC may improve patients' clinical symptoms and life quality, reduce lesions, and prolong survival. Brain lesions should be identified and operated as early as possible. Removal of primary thyroid tumor should be treated as completely as possible (i.e. total-thyroidectomy). The brain metastases gone with lung and/or bone metastasis from DTC were difficult

to cure at the same time. The side effects resulted from ¹³¹I treatment were singularly seen.

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