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Spinal Metastasis as Presenting Feature of Follicular Type Thyroid Carcinoma: A Case Report and Review of the Literature

Spinal Metastazla Belirti Veren Folliküler Tip Tiroid Karsinomu: Olgu Sunumu ve Literatür Taraması

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Abstract

Objective: Follicular type thyroid carcinoma (FTC) rarely presented with spinal metastasis. We aimed to report such a case and to review the literature.

Method: A 45 year old male with L2 metastasis of FTC was reported, and other 26 cases were found in literature. Characteristics of the patients and tumors were evaluated.

Results: Total 27 patients were 55.2±15 years of age, and male/female ratio was 12/15. Nineteen patients had paresis of extremities, 9 of them could not mobilize on admission. Total resection of the spinal tumor had been performed in 14 cases and subtotal resection in 5. Radioactive iodine treatment had been added in 20 cases with or without other adjuvant treatment. Twenty-three patients had been followed for 43.7±53.2 months. Only four of them died 214, 66, 36 and 7 months after their presentations. Out of other 19 cases, 13 had been neurologically normal. Type of surgery (total resection versus others) the only factor affecting outcome. In the patients treated with total resection, outcome had been statistically better.

Conclusion: Spinal metastasis as initial finding is very rare in the patients with FTC. However, prognosis is quite well with total tumor resection and adjuvant treatment. This cancer type must be kept in mind for differential diagnosis and must be screened in the patients with spinal tumors.

Keywords: Differentiated thyroid carcinoma, follicular type thyroid carcinoma, spinal metastasis, spinal tumor

Öz

Amaç: Folliküler tip tiroid karsinomu (FTK) nadiren spinal metastazla belirti verir. Böyle bir olgu sunmayı ve bu konuda literatür taramayı amaçladık.

Yöntem: Lomber 2 spinal metastazla belirti veren 45 yaşında erkek FTK olgusu sunuldu ve literatürde benzer 26 olgu bulundu. Tüm olguların özellikleri değerlendirildi.

Bulgular: Toplam 27 olgu 55,2±15 yaşındaydı (35-88 arasında, ortalama ± SS) ve erkek/kadın oranı 12/15 idi. Başvuruda 19 olguda kol ve/veya bacaklarda güçsüzlük vardı ve 9'u mobilize olamıyordu. Spinal tümör 14 olguda total, 5 olguda subtotal çıkarıldı. Yirmi olguya radyoaktif iyot tedavisi eklendi. Olguların 23'ü 3-214 ay (43,7±53,2, ortalama ± SS) süreyle izlenmişti, sadece 4 olgu başvurudan 214, 66, 36 ve 7 ay sonra ölmüştü. Halen sağ olan 19 olgunun 13'ü nörolojik olarak normaldi. Uygulanan cerrahi tipi (total çıkarmaya karşılık diğer cerrahi tipleri) son durumu etkileyen tek faktör olarak saptandı. Tümörü total çıkarılan hastalarda sondurum anlamlı olarak daha iyiydi.

Sonuç: Folliküler tip tiroid karsinomunun spinal metastazla belirti vermesi çok nadirdir. Ancak total tümör çıkarılması ve adjuvan tedaviyle prognoz iyidir. Spinal tümörlü hastalarda bu kanser tipi de ayrıcı tanıda akılda tutulmalı ve tarama testleri yapılmalıdır.

Anahtar kelimeler: Diferansiye tiroid karsinomu, folliküler tip tiroid karsinomu, spinal metastaz, spinal tümör

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Introduction

Differentiated thyroid cancers (DTC) contain papillary, follicular and Hurthle cell types. Follicular type thyroid cancer (FTC) is the second most frequent type of DTCs, and it is more inclined to metastasize to the bone than papillary type (1). This characteristic is probably due to that FTC usually spreads via blood, however, papillary type prefers lymphatic route for dissemination (2). There is bone involvement in 7-12% of the cases with FTC (3), and the most frequently involved region is spinal column (4). However, most of the spinal metastases occur in the late stage of the disease, and presentation of the disease with spinal metastasis is extremely rare during initial diagnosis.

We presented such a rare case who was admitted with lumbar spinal metastasis, and thyroid cancer was diagnosed after pathological evaluation of the spinal tumor. Also we reviewed the literature for presentation with spinal metastasis of FTC, and we evaluated the characteristics of the cases that we found.

Case Report

A 45 year-old male was admitted to our outpatient clinic with complaints of low back and severe left leg pain and numbness of left leg for 5 months. There was hypoesthesia on left L1 and L2 dermatomes on his physical examination. Muscle strength was full. Radiological examinations revealed an L2 vertebral body tumor. On lumbar computerized tomography (CT) examination, an osteolytic heterogeneous tumor involving left half of the L2 vertebral body extending into the left paravertebral muscles and into the left L1-2 and L2-3 neural foramens was seen (Figure 1). On lumbar magnetic resonance imaging (MRI), it was hypointense on T1-weighted images, and heterogeneous hypo- and hyperintense on T2-weighted images (Figure 2). The lesion was hypermethabolic on positron emission tomography (PET) CT, and there were also a hypermethabolic enhancement in the left thyroid lobe and mildly hypermethabolic bilateral multiple cervical lymph nodes.

A lumbar biopsy was performed and a carcinoma consistent with FTC was diagnosed (Figure 3a). It was decided to perform tumor resection and stabilization for lumbar tumor first because there was severe leg pain of the patient and instability of the lumbar spine, and also the tumor was the sole metastasis on the PET-CT. Total tumor resection and stabilization with interbody cage insertion and pedicle screw fixation was performed via posterior approach (Figure 4). There was not residual tumor on postoperative MRI.

Immunohistochemical investigations revealed that the tumor cells were positive for thyroglobuline, thyroid transcription factor 1 (TTF-1), Hector Battifora mesothelial cells 1 (HBME-1) and cytokeratin-19 (CK-19), and negative for calcitonin (Figure 3b-f). These findings verified the diagnosis of DTC.

Total thyroidectomy was performed by endocrine surgery team 10 days after our lumbar operation, and pathological

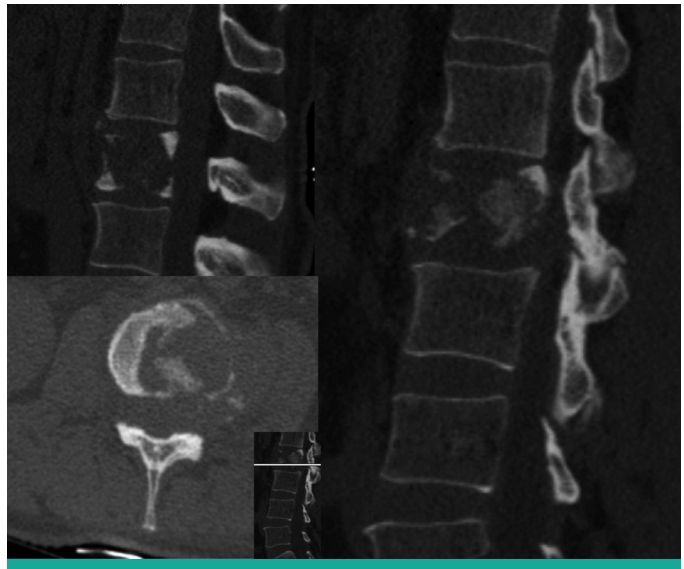


Figure 1. Sagittal and axial sections of the lumbar vertebral computerized tomography demonstrating lytic L2 vertebral tumor extending into the left paravertebral region and neural foramens

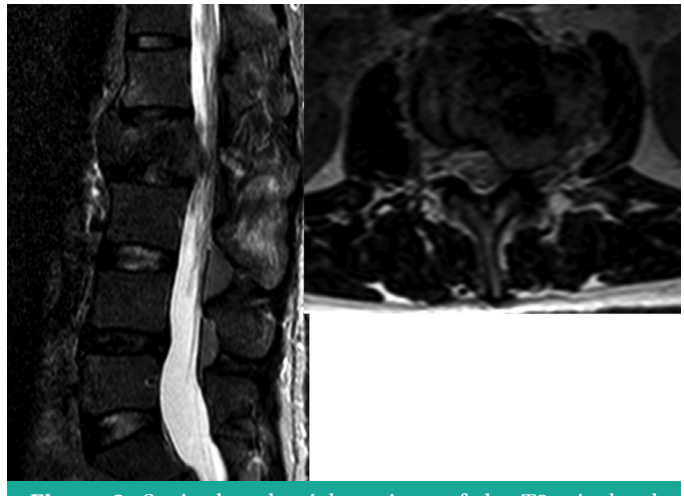


Figure 2. Sagittal and axial sections of the T2-wieghted lumbar spinal magnetic resonance imaging demonstrating heterogeneous hypo- and hyperintense tumor in the L2 vertebral body compressing the nerve roots

examination revealed follicular type carcinoma. He was treated with iodine 131 ablation. His follow-up examinations were uneventful, and there was not recurrence or new metastasis 2 years later.

Material and Methods

Review of the literature: we reviewed the literature for spinal metastasis as presenting feature of FTC from Medline and Google Scholar. We found 28 such cases. However 2 cases were not introduced into the study because there was not adequate data in the articles (5,6). The characteristics of total 27 cases including our one were evaluated (1,2,4,7-24) (Table 1). Demographic characteristics, levels and numbers of the spinal metastases, neurological conditions, other metastases, treatment modalities, follow-up time, and outcome of the cases were recorded.

Outcome was accepted as good if the patient was neurologically normal or could mobilize without external support, and it was accepted as poor if the patient could not mobilize without support or was dead.

Statistical Analysis

For statistical analysis, chi-square test, Fisher exact test, and Student's t-tests were used, and $p<0.05$ was accepted as significant.

Results

The patients were 55.2±15 years of age (mean ± SD, between 35 and 88), and male/female ratio was 12/15. The most involved levels were thoracic and thoracolumbar segments. The involved vertebral levels in the patients were shown in the Table 2.

The lesion was intradural extramedullary (IDEM) in one case (20), and vertebral and/or epidural in the others. The IDEM tumor extended beyond 2 lumbar levels. In the others, only one vertebra was involved in 11 patients, 2 adjacent vertebrae in 5, and 3 adjacent vertebrae in 7 were involved. Most of the patients had solitary vertebral metastases or multiple adjacent levels involvement. In

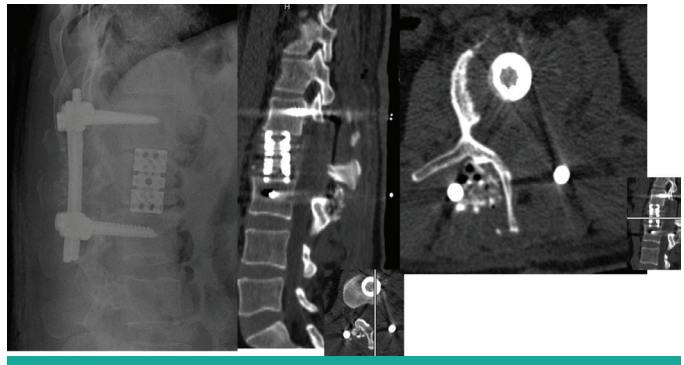


Figure 4. Lateral lumbar radiograph and sagittal and axial lumbar computerized tomography demonstrating total tumor resection and spinal stabilization with interbody cage and pedicle screws

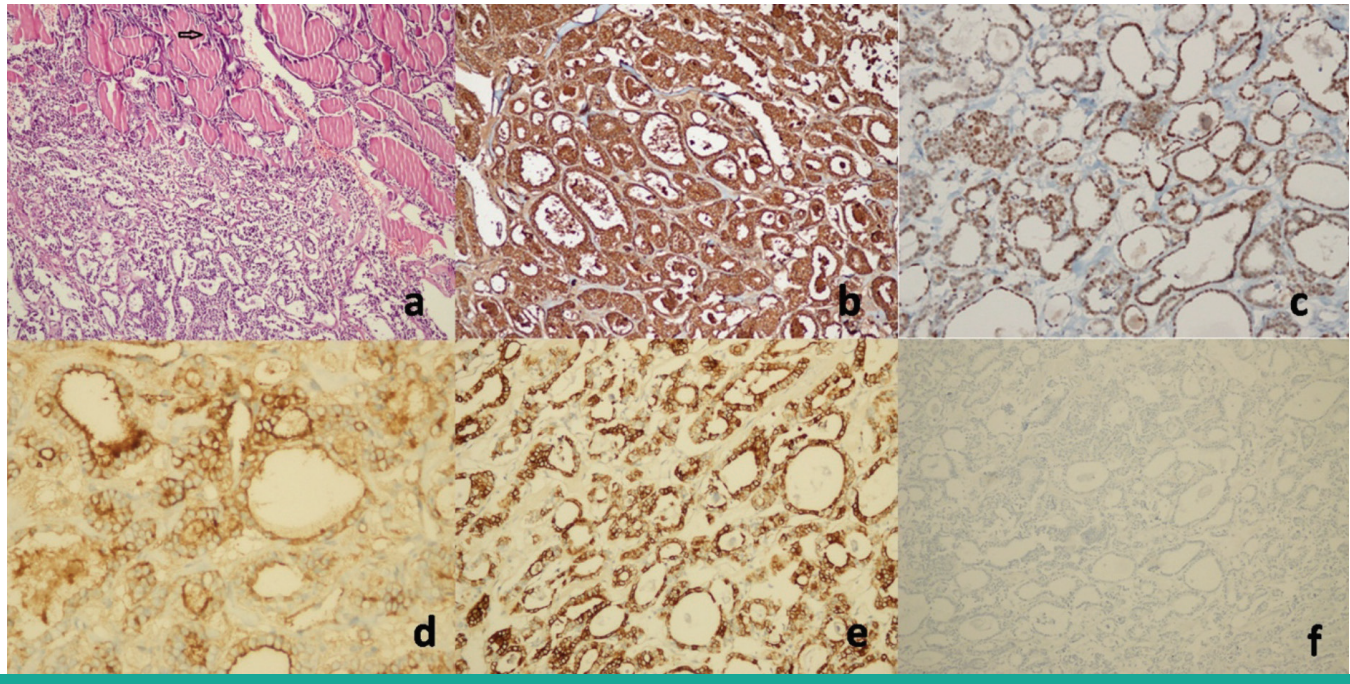


Figure 3. a) Spinal metastasis of the thyroid carcinoma, hematoxylin-eosin (HE) x10. The arrow indicated the tumor cells with colloidal appearance. b) Thyroglobuline (anti-Tg antibody, x10), c) TTF-1 (anti-TTF-1 antibody, x20), d) HBME-1 (anti-HBME-1 antibody, x40), and e) CK-19 (anti-CK-19 antibody, x20) positivity, and f) calcitonin negativity

Table 1: Characteristics of the patients and tumors

No	Literature	Age/ gender	Level	Neurologic Finding	Other metastases	Surgery	Thyroid surgery	Other treatment	FU (mos)	Outcome
1	Akhtar (7)	52/M	L4-5	Paraparesis 4/5	Rib	TR/St	TT	RAI	12	Good (ASIA E)
2	Baiao (8)	84/F	T7-8-9	Paraparesis 0/5	No	B	TT	RAI	6	Poor (ASIA B)
3	Carhill (1)	49/F	S1	Pain	Ilium, multiple lung and liver	B	TT	RAI	43	Good (ASIA E)
4	Chafiki (9)	81/F	L4-5-S1	Paraparesis 0/5	No	B	TT	RAI	NM	NM
5	Chander (4)	57/F	L3	Right leg weakness	NM	TR/St	NM	RAI	61	Good (KPS 80)
6	Dong (10)	48/F	C2-3	Paresis of both arms	C5, L1, S1,	D	TT	RAI	52	Good (ASIA E)
7	Khan (11)	35/F	T11-12-L1	Paraparesis 1/5	NM	D	NTT	RAI	6	Good (ASIA E)
8	Kim (12)	72/M	L4	Right big toe DF weakness	No	TR	TT	RAI	15	Good (ASIA E)
9	McNeely (2)	88/F	T8-9-10	Paraparesis 3/5	Multiple lung nodules	B	No	RT/TSH	NM	Poor (could not walking)
10	Ogbodo (13)	79/F	L1-2 IDEM	Right leg weakness 3/5	Multiple lung nodules	TR	No	RT	6	Good (ASIA E)
11	Okutan (14)	33/F	L3	Paraparesis 4/5	No	TR/St	TT	RAI	NM	NM
12	Sandu (15)	50/F	T11	Pain	Multiple lung nodules, L3, ilium, femur	D/St	TT	RAI	45	Good (ASIA E)
13	Sharma (16)	39/M	S1-2-3	Urinary incontinence	No	B	TT	RT/RAI	12	Good
14	Sharma (16)	35/F	T2-3	Paraparesis NM	No	D	TT	RT/RAI	6	NM
15	Shibuya (17)	67/F	L4	Pain	No	B, D/St (2yrs), D/St (5 yrs)	TT	RT/RAI	66	Died/lung metastases
16	Toshkezi (18)	55/M	T4-5-6	Paraparesis 4/5	No	TR	NTT	RAI	36	Good (ASIA E)
17	Upreti (19)	55/F	C1-2	Tetraparesis 0-2/5	NM	D/St	TT	RAI	3	Poor (could not walking)
18	Hakeem (20)	58/M	L2	Paraparesis 4/5	No	TR/St	TT	RT/RAI	36	Good (ASIA E)
19	Hakeem (20)	50/M	T1-T2	Pain	No	TR/St	TT	RT/RAI	36	Died/systemic metastases
20	Matsumoto (21)	48/M	T8	Paraparesis 4/5	No	TR/St	NM	NM	156	Good (ASIA E)
21	Matsumoto (21)	42/M	T8-9-10	Paraparesis 3/5	No	TR/St	NM	NM	125	Good (ASIA D)
22	Scarrow (22)	50/M	C6	Pain	No	TR	TT	RAI	NM	NM
23	Goldberg (23)	65/F	C2	Paresthesia on one hand	No	TR	NTT	RAI	28	Good (ASIA E)
24	Goldberg (23)	43/F	T1	Paraparesis	No	Biopsy	STT	RT	7	Ex
25	Brodner (24)	57/M	T5-6	Paraparesis	No	TR	TT	RAI	12	Good (ASIA D)
26	Brodner (24)	56/M	L2, C6	Paraparesis	No	No	TT	RAI	214	Ex due to leukemia
27	Our patient	45/M	L2	Pain	No	TR/St	TT	RAI	24	Good (ASIA E)

ASIA: American spinal cord injury association, D: Decompression, IDEM: Intradural extramedullary, NM: Not mentioned, KPS: Karnofsky performance score, NTT: Near total thyroidectomy, RAI: Radioactive iodine, St: Stabilization, STT: Subtotal thyroidectomy, TR: Total resection, TT: Total thyroidectomy

Table 2: The involved vertebral levels of the patients. The presenting levels were shown as red boxes, and the associated involved levels were shown as green boxes

Level	Patient 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
C1																											
C2																											
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only 3 patients, there was multiple non-adjacent vertebral levels involvement. There were 5 patients with other bony metastases and/or systemic metastases such as lung or liver.

Nineteen patients were presented with paresis of arms and/or legs (9 of them could not mobilize without support), one with urinary incontinence and other 7 with back, neck, arm, or leg pain.

Various surgical modalities were performed in the patients. They could be classified as biopsy (in 7 cases), decompression with subtotal resection of the tumor (with or without stabilization, in 5 cases), and total resection of the tumor (with or without stabilization, in 14 cases). Any surgical procedure was not performed in one patient. Spinal stabilization was performed in total 10 patients during first surgery. In one patient in whom biopsy was performed first, subtotal resection and stabilization was performed in 2 times, 2 and 5 years after first biopsy.

Total or near total thyroidectomy was performed in 21 patients and subtotal thyroidectomy in one patient after spinal operation. Thyroid resection was not performed in 1 case and it was not mentioned in the article in 4. In 2 cases, adjuvant treatment modalities were not mentioned in the articles, only radioactive iodine treatment (RAI) was performed in 17 cases, only radiotherapy (RT) for spinal lesions in 3 cases, and RAI and RT in combination in 5 cases.

The follow-up time was not mentioned in the articles in 4 cases. Other 23 cases were followed during 3 to 214 months (43.7±53.2, mean ± SD). Outcome was not mentioned for 3 patients. Three cases died due to systemic metastases of the disease 66, 36 and 7 months after their spinal surgeries, and one case died due to leukemia 214 months after diagnosis of the thyroid cancer. This last case was neurologically normal without systemic disease until development of his second neoplastic disease. Out of other 19 cases, 15 had good outcome with good neurological condition and without systemic disease (12 of them were neurologically normal), 3 cases had severe neurological deficits, and one case alive with systemic disease, but neurologically normal. Some patients who were severe neurological deficits before operation were neurologically normal on last follow-up (11,13,21).

Presence of other distant metastases did not affect the last outcome (p=0.51). However, the type of the spinal surgery was found as an important factor on last outcome of the patient. The rate of good outcome was statistically higher in the patients performed total resection of the spinal metastasis than to be in the patients with only decompression or biopsy or without any surgical modality (p=0.027).

Discussion

Follicular type thyroid cancers constitute 15% of the DTCs (1). They are well-differentiated tumors and have good outcome when they are compared with other cancers. However, bony metastasis is not rare in the cases with FTC (2). Rate of bony metastasis of FTC was reported as 7 to 20% and the rate of spinal metastasis as 1 to 7% (7,25). This characteristic is probably due to spreading ability via blood of FTC in contrary to the lymphatic spreading tendency of the papillary thyroid cancer (1,2). FTC may synthesize some substrates providing attachment to bone matrix and promoting to bone reabsorbtion (1).

The FTC usually presents as tyhroid nodules. Presentation with distant metastases is quite rare, and it was reported in 1.9% to 11% of the cases with FTC (6,26). Presentation with spinal cord compression due to spinal metastases is extremely rare. Pomorski and Bartos (6) reported only one case out of 309 FTC cases. We could only find 26 cases in literature and we added our case. In the series reported by Marcocci et al. (25), there were 18 patients whose presenting symptoms were related to bony metastases, however, it was not mentioned that how much of them were spinal metastases.

Survival of the DTCs is very long. It was reported that 10 year survival rate was about 80-95%. However presence of bony distant metastases caused to decrease of this rate (12). Shaha et al. (26) reported that long-term survival in the cases with distant metastasis during initial presentation was quite high as 44%. On the other hand, in spite of this long survival trend, presence of spinal metastases causes to reduce quality of life due to severe pain and/or neurological deficits (27). Coleman (28) reported in a retrospective study that spinal metastases of the DTCs more frequently cause spinal cord compression than other spinal metastases. Most of the cases reviewed in our study had neurological deficits and 10 of them could not mobilize on their admissions, and the patients without deficits had severe pain due to spinal metastases.

Reeve et al. (29) reported in a series consisting 258 cases with DTCs that age and gender were the most important factors affecting long-term outcome, and older patients (<60 years) and males had significantly shorter survival. In our review, we could not perform survival analysis because most of the cases were still alive on their last follow-up.

However, both age and gender of the cases did not affect the rate of good outcome.

Total resection of the spinal metastases of the DTCs is usually recommended because of their resistance to radiotherapy. Furthermore, spinal metastases of the DTCs are usually isolated metastases (27). In our review, also, there were associated other bony or systemic metastases in only 5 cases. Demura et al. (5) reported in a study evaluating the results of total en bloc spondylectomy for spinal metastases of thyroid carcinoma that there was no significant difference between the rate of long survival after total spondylectomy and debulking surgery, however, the rate of local recurrence was significantly higher in the cases treated with debulking surgery than the cases treated with total spondylectomy. In our review, the rate of good outcome was significantly higher in the patients whose spinal metastases were totally resected. However, in our study, the term of "total resection" was not similar to "total en bloc spondylectomy" in the study by Demura et al. (5) We classified total tumor resection only without total spondylectomy also as total resection. Response to RAI of DTC is very well, and the guidelines recommended adding this treatment modality to high risk group patients such as the ones with distant metastases (30). To add RAI into the treatment protocol may provide to take away the mandatory of total en bloc resection of the vertebrae with metastases.

Embolization of the spinal metastasis of DTCs before operation may be a smart choice because of tendency of these tumors to profuse bleeding (4). Sellin et al. (31) reported in a study evaluating the factors affecting survival of the patients with spinal metastases of thyroid carcinoma that preoperative embolization was significantly associated with fewer complications. However, in the patients whose spinal metastases are the initial presentation, this choice can usually not be performed because the primary tumor is not known yet. In the patients presented with only pain without paresis, spinal biopsy may be performed and histological diagnosis can be provided before operation. However, emergency decompression may be required in some patients because of spinal cord or cauda compression, and there may not be adequate time for biopsy or embolization.

The Guideline of American Thyroid Association (ATA) reported in 2016 recommended resection of the lesion, stereotactic radiation treatment (RT) and RAI for treatment of central nervous system metastases of the DTCs (32). In our review, only 8 patients had received RT, therefore, we could not evaluate its efficacy on last outcome. Bernier et al. (33) recommended to perform total resection of bony metastases and RAI treatment instead of RT in the young patients (<45 years) with bony metastases of the FTC.

Biochemical thyroid functional tests are usually in normal levels in the patients with thyroid cancers (13), therefore, routine tests usually do not provide diagnosis of thyroid cancer in the cases with spinal tumors, and some imaging tests such as thyroid ultrasonography are required during primary site screening. In the cases with cervical spinal tumors, cervical MRI can provide diagnosis of the primary thyroid tumors however most of the spinal metastases of the DTCs are located in the thoracic and lumbar levels. Therefore, if the more possible sites such as breast, lung or prostate are negative in the screening tests, thyroid screening with imaging modalities must certainly be added to the screening protocol of the spinal tumors. PET is also a very valuable method to show both primary site of the cancer and metastases (34).

Survival of the patients with spinal metastases due to DTCs is quite long. Sellin et al. (31) reported median 15.4 months in 43 cases, and Bernier et al. (33) reported 4.1 years. We could not evaluate the survival time of the patients in our review because most of them was still alive on their reported last follow up time. However, their follow up times were quite long (43.7±53.2).

Conclusion

In conclusion, spinal metastasis as initial finding is very rare in the patients with FTC. However, this diagnosis must be kept in mind especially in the cases whose primary tumor site could not be found with routine cancer screening, and imaging modalities for thyroid must be added. Although survival of the patients with spinal metastases of FTC is significantly shorter than without spinal metastases, it is very longer than the patients with spinal metastases of other cancer types. Surgical resection of the spinal metastases especially in the patients with spinal cord or cauda equine compression, total/near total thyroidectomy and RAI treatment may provide a long term disease free survival to the patients.

Ethics

Ethics Committee Approval: N/A.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.T., B.E., A.T., N.B., Concept: A.T., B.E., A.T., N.B., Ö.Y.A., İ.G., M.S.V., M.K., G.V., F.K.G., Design: A.T., B.E., A.T., N.B., Ö.Y.A., İ.G., M.S.V., M.K., F.K.G., Data Collection or Processing: A.T., B.E., A.T., Ö.Y.A., İ.G., M.S.V., M.K., G.V., F.K.G., Analysis or Interpretation: A.T., B.E., A.T., N.B., Ö.Y.A., İ.G., M.S.V., M.K., G.V., F.K.G., Literature Search: A.T., B.E., A.T., G.V., F.K.G., Writing: A.T., B.E., A.T., N.B., Ö.Y.A., İ.G., M.S.V., M.K., G.V., F.K.G.

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