

Neurological Manifestation of Spinal Metastasis of Malignant Melanoma : Clinical Analysis of 26 Patients

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Although malignant melanoma is one of the most common causes of central nervous system metastases, spinal metastases from it are relatively rare. Despite spinal metastases primarily are not fatal, they may be catastrophic because of ambulation loss and sphincter disturbances. The purpose of this study was to review the course of this illness after the development of neurological deficits and to assess the efficiency of radiation therapy on symptoms and signs of spinal metastasis. 26 patients with neurological manifestations from spinal metastasis of melanoma were analyzed retrospectively. Median age of the patients was 48 years (range 24-87). Fifteen patients had cord compression by epidural metastasis, 6 patients had intramedullary, and 5 patients had leptomeningeal metastasis. 17 of these patients suffered from pain. In 12 patients, first symptom was neurological disturbance, while in 14 patients it was pain. In patients who received radiotherapy for pain, in 5 patients pain improved, in 13 patients remained unchanged, in 2 patients worsened. In patients who received radiotherapy for neurological deficits, in 9 patients deficit improved, in 7 patients worsened, in 10 patients did not change. While radiotherapy had significant effect on neurological recovery ($p<0.03$), it did not have any effect on pain. [Journal of Turgut Özal Medical Center 1997;4(1):21-25]

Key Words: Spine, melanoma, neurological complication, metastasis

Spinal metastazlı malign melanomaların nörolojik bulguları

Merkezi sinir sistemine sıklıkla metastaz yapan tümörlerden biri olmasına rağmen, malign melanomaların spinal metastazları kısmen nadirdir. Primer olarak ölümcül olmayan spinal metastazlar, hastanın ambulasyonunda bozukluklara ve sfinkter kusurlarına neden olarak, oldukça sıkıntılı bir tablo oluşturabilirler. Bu çalışmanın amacı, bu hastalığın, nörolojik tablo geliştikten sonraki seyrini belirliyerek, radyoterapinin semptomlar ve nörolojik bozukluklar üzerine etkinliğini araştırmaktır. Malign melanoma'nın spinal metastazının, nörolojik bozukluk yaptığı 26 hasta retrospektif olarak analiz edildi. Median yaş 48'di (24-87 arası). 15 hastada epidural metastaza bağlı kord kompresyonu, 6 hastada intrameduller, 5 hastada leptomeningeal metastaz vardı. Bu hastaların 17'sinde ağrı şikayeti mevcuttu. 12 hastanın ilk şikayeti nörolojik bozukluklar iken, 14 hastada ilk şikayet ağrıydı. Ağrı şikayeti olup ta radyoterapi yapılan hastaların 5'inde ağrı kayboldu veya azaldı, 13'ünde değişmedi, 2'sinde arttı. Radyoterapi yapılan hastaların, 9'unda nörolojik defisitler düzelirken, 7'sinde arttı, 10'unda değişmedi. Radyoterapinin, nörolojik düzelmeye üzerine önemli derecede etkisi varken ($p<0.03$), ağrı üzerine herhangi bir etkisi olmadığı saptandı. [Turgut Özal Tıp Merkezi Dergisi 1997;4(1):21-25]

Anahtar Kelimeler: Vertebra, melanoma, nörolojik komplikasyonlar, metastaz

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The incidence of symptomatic spinal metastases has increased resulting from improvement of patient survival after the diagnosis of metastatic malignancy concomitant with advances in cancer therapy (1-4). Despite metastasis to spine from malignant melanoma is respectively rare, it is expected that it will increase because the incidence of malignant melanoma is rising rapidly (5-9).

Neurological complications from spinal metastases affect patient's life quality rather than being fatal (10,11). On the other hand many important questions have remained unanswered about spinal metastases (12-14). Whereas in the patients with cancer the goal of therapy is to increase the quality of life and to relief symptoms as well as to increase survive.

MATERIALS AND METHODS

In this study, our parameters included the interval from initial diagnosis of melanoma to diagnosis of spinal metastasis (latent interval), the levels of pain and neurological status in pre- and post-treatment, and survival time after spinal metastasis.

All of these patients were thoroughly evaluated as the extent of their disease by complete examination and diagnostic studies. In all of patients, the diagnosis made sure histologically.

As a diagnostic study, at least one of, plain X-ray, of CT, or of MRI was performed in each patients. All of these patients were followed through of the course of their disease until expiration date. When we made this study 3 patients were alive.

Clinical informations and follow-up datas were collected from inpatients and outpatients records. As a statistical method, the likelihood ratio chi square test was used to measure the effectivity of treatment.

RESULTS

Between 1984 and 1994, a total of 5692 patients were registered at M.D. Anderson Cancer Center with a diagnosis of melanoma. Of them, 158

(2.8%) patients were found to have spinal metastatic disease. 144 patients' medical records were available for retrospective review. Thirty of 144 patients had neurological deficits. Four patients who underwent surgery excluded in study because the number of patients was not enough. In 26 patients who received radiotherapy, 15 had cord compression by epidural metastasis, 6 had intramedullary, and 5 had leptomeningeal metastasis. In 13 patients, epidural metastasis were associated with vertebral metastasis.

Eighteen of 26 patients were male (65%), 8 of them were female (35%). Male/female ratio was 2.2/1. Their age ranged from 24 years to 87 years (median age was 48). Most of the patients were between 40 and 60 years. The peak age ranged 40 to 50 years.

In most of the patients, the site of primary tumor was trunk (10 patients). This followed by eye (4 patients), head-neck, upper extremity, lower extremity (each of them 3 patients), unknown (2 patients), and rectum (1 patient). Survive and latent interval were not affected by localization of primary tumor.

Interval from initial diagnosis of melanoma to diagnosis of spinal metastasis from it (latent interval) ranged 0 to 138 weeks. The median of latent interval was 19 weeks. The peak of latent interval ranged 0-20 weeks. 7.6 % of patients first presented with the spinal metastasis from the malignant melanoma.

As list in Table 1, 17 patients (65% of patients) complained of pain. 14 patients (82% of patients with pain) complained of pain, while 12 patients (46% of patients) had neurological disturbance at presentation with spinal metastasis. In 14 patients (54% of patients), neurological deficits developed later.

As a diagnostic study, CT was performed in 11

Table 1. Symptoms and signs

Symptom	Presentation	%	Later	%	Total
Pain	14	82	3	18	17
• Localized	10	100	-	0	10
• Radicular	2	67	1	33	3
• Loc+ Rad.	2	50	2	50	4
Neurological deficit	12	46	14	54	26
• Weakness	2	12.5	14	87.5	16
• Sensorial change	5	50	5	50	10
• Reflex change	4	100	0	0	4
• Sphincter disturbance	2	25	6	75	8

patients, MRI were performed in 10 patients, plain X-ray and myelography were performed in 9 and 5 patients respectively.

As seen in Table 2, in most of the patients, the location of lesion was thoracic area. While, in most of the patients with epidural metastasis and in all of the patients with intramedullary metastasis, the lesion located thoracic region, in the patients with leptomeningeal metastasis, the lumbar and the sacral areas were involved mostly.

Eighteen patients had undergone excision, 4 patients had received radiotherapy to primary tumor before spinal metastasis. In 2 patients both treatment had been carried out together for primary tumor before spinal metastasis. 2 patients had not been known to be suffering from malignant melanoma at the time of their presentation with spinal metastasis. There was not any effect of these treatment on latent interval and survive after spinal metastasis.

All of patients received palliative radiotherapy to spinal area for spinal metastasis, and received systemic chemotherapy and/or immunotherapy. None of these treatments had any effect on survive.

As shown in Table 3, while radiotherapy did not have any effect on pain, it had significant effect on neurological recovery ($p < 0.03$).

Survival time after spinal metastasis, ranged 1 to 24 months (median 4 months). In most of the patients, survive was less than 9 months. Radiotherapy to spine and chemotherapy and/or immunotherapy did not have any effect on survival time.

DISCUSSION

The incidence of melanoma tends to increase (6,7). Between 1984 to 1994 a total of 5692 patients were registered at M.D. Anderson Cancer Center

Table 2. The location of lesions

Region	Epidural	Intramedullary	Leptomeningeal	Total
Cervical	-	-	2	2
Thoracic	5	6	3	14
Lumbar	4	-	4	8
Sacral	2	-	4	6

Table 3. The effect of treatments on pain and neurological recovery

	Unchanged	Improved	Worsened	Total	p<
Pain	13	5	2	20	0.4
Neurological deficits	10	9	7	26	0.03

with a diagnosis of melanoma, 144 of these patients (2.5%) were found to have spinal metastasis.

Although there are many reports about spinal metastasis, we could not find any reports about metastatic spinal melanoma, therefore we compared our series with the series of spinal metastasis of mix tumor.

In spinal metastases, all ages may be affected, but the age distribution corresponds predominantly to the relatively high cancer risk period of 40 to 65 years of age as well as the peak range of it that it is 50 to 60 years (15). The median age of our series was 48 years. This was lesser than that of other spinal metastasis series which their average ages ranged 52 to 57 years. Our results were similar to the results of the reports of malignant melanoma rather than the that of spinal metastases (11,12,16,17).

Either spinal metastases of melanoma have slight preponderance of males. In same studies, male to female ratio ranges from 1.5/1 to 7/1 (16-19). In our series, this rate was 2.2/1.

Pain especially localized pain is the earliest and the most common symptom in spinal metastases, and it usually precedes motor, sensory, and reflex changes. Sphincter disturbances commonly are seen as latest symptom or sign (1,9,11,19-22). In Constants' series, 60% of patients had pain, 61% of patients had weakness, 2.3% of patients had isolated sphincter disturbances presented with these ones at diagnosis of spinal metastases (19). In our series these rates were respectively 82%, 12.5%, and 25%. Also in 87.5% of patients with weakness, and in 75% of patients had sphincter disturbances, these signs developed after presentation.

Although spinal metastases usually occur in patients with advanced disease, Stark reported that in 47% of patients, Rodichock reported that in 8% of patients had not been known to be suffering from primary tumor at the diagnosis time of spinal metastases (20,23). In our series 7.6% of patients had not been known to be suffering from malignant melanoma at the time of their presentation with spinal metastasis.

In the spinal metastases, the neurological deficits are the consequence of the compression of

spinal cord by epidural metastasis or direct invasion of spinal cord parenchyma and/or leptomeningeal invasion. While the epidural spinal cord compression is more common, the others are rare (1,11,20,24-26). In our series, 15 patients had epidural, 6 patients had intramedullary, and 5 patients had leptomeningeal metastasis.

There are no clinical features by which an intradural lesion could be distinguished from an extradural lesion (1,9,11,19,20-22). In our series we could not find any clinical feature to distinguish the extradural lesion from intradural lesion. Clinical feature resembled each other.

While the goal of treatment of the patients with spinal metastasis to preserve motor functions and to decrease pain as well as to increase survive, the keystones of the treatment of spinal metastases are radiotherapy and surgery. Although the best form of treatment is still controversial, general tendency about the treatment of extradural spinal metastasis, as a first step to perform radiotherapy to spine, and in selected cases into the patients who do not respond to radiotherapy to perform spinal surgery (9,12,20,21). On the other hand, radiation therapy is the only treatment available for leptomeningeal and intramedullary metastases (26).

We could not find any series about treatments of intramedullary and spinal leptomeningeal metastases because they are rare. To the contrary there are many studies about the treatment of cord compression by epidural metastasis that had successful outcomes either by surgery or by radiotherapy to spine (2,12,22,27). In our study, radiotherapy had a significant effect on neurological recovery.

Both advanced melanoma and spinal metastases have short survival time and most of patients with spinal metastasis live less than one year (3,16,22,28). In our series, in most of the patients, the survive after spinal metastases were less than 9 months.

The effectiveness of radiotherapy, chemotherapy, and immunotherapy on malignant melanoma is controversial (27,29,30). In our series, palliative radiotherapy to spine and systemical chemotherapy and immunotherapy were not effective on survival.

In conclusion, although most of the patients with metastatic spinal melanoma have a limited life expectancy, radiotherapy seems to provide a better chance for neurological recovery. Thus early diagnosis and management of these patients increase quality of life in spite of short survival.

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