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Case report-Olgu sunumu

Leptomeningeal carcinomatosis in a younger patient with signet-ring cell carcinoma

Taşlı yüzük hücreli karsinomlu genç hastada leptomeningeal karsinomatozis

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Abstract

Leptomeningeal metastasis (LMM) occurs in about 3-8% of patients with systemic cancer. It is very rare in patients with signet-ring cell carcinoma. But, the prognosis is also very poor. We report a case of a younger woman with signet-ring cell carcinoma of primary origin unknown who presented with meningeal carcinomatosis.

Keywords: Leptomeningeal metastasis; signet-ring cell carcinoma; prognosis.

Özet

Leptomenengeal metastazlar, sistemik kanserli hastaların yaklaşık %3-8'inde oluşur. Bu, signet-ring hücreli karsinomu olan hastalarda çok nadirdir. Ama prognoz da çok kötüdür. Meningeal karsinomatozisi olan ve birincil orjini bilinmeyen signet-ring hücreli karsinomu olan genç bir bayan olguyu bildiriyoruz.

Anahtar sözcükler: Leptomeningeal karsinomatozis; taşlı yüzük hücreli karsinom; prognoz.

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Introduction

Leptomeningeal metastasis (LMM), also named as carcinomatous meningitis, is the infiltration of the leptomeninges by malignant cells and occurs in about 3-8% of patients with systemic cancer [1, 2]. The presence of LMM associates with poor prognosis. It also decreases the score of the quality of life because of headache, nausea, vomiting, and neurological complications such as sensorial and motor nerve dysfunction, altered mental status, and seizures. The most common sources of LMM are breast cancer, small cell carcinoma of lung, malignant melanoma, and hematopoietic malignancies such as acute lymphoblastic leukemia and lymphoma [3, 4].

In English literature, there are several case reports developed LMM from signet-ring cell carcinoma. Primary origin of these cases is often gastric carcinoma. We report a case of a younger woman with signet-ring cell carcinoma of primary origin unknown who presented with meningeal carcinomatosis.

Case report

A 19-year-old woman without previously serious illness was admitted with abdominal

and back pain and discomfort in March 2006. On admission, there was also weight loss (10 kg for last 3 months). Her physical examination revealed a pelvic mass. The computed tomography (CT) of pelvis indicated bilateral ovarian mass. Because of suspicion of ovarian cancer, extensive surgery including total abdominal hysterectomy, bilateral salpingo oopherectomy, bilateral paraaortic and pelvic lymph node dissection, and omentectomy was performed. Pathological examination consisted with metastasis of mucinous type signet-ring cell adenocarcinoma. In immunohistochemical examination, neoplastic cells were positive for carcinoembrionic antigen, CK-20, CK-7, but negative for GCDFP-15. Because of the presence of signet-ring cells, her gastrointestinal tract was evaluated to detect the primary origin of the tumor. Endoscopy of upper gastrointestinal tract and double contrast colon imaging was performed, but revealed no abnormality. At 5 days after the admission, diplopia, nausea, and headache developed. She also complained with weakness, and disability. The neurological examination was unremarkable. Magnetic resonance imaging (MRI) of the brain and cervical spine demonstrated contrast enhancement nodular appearance of cerebellar fissures and leptomeningeal. Lomber punction was performed and the cytological examination of cerebrospinal fluid (CSF) revealed malignant epithelial cells with signet-ring morphology (Figure 1). CT of upper and lower abdomen showed peritoneal carcinomatosis and metastases of thoracal vertebreas. Spinal MRI demonstrated widespread metastasis in spinal column, compression fractures at T3, T10, and T11.

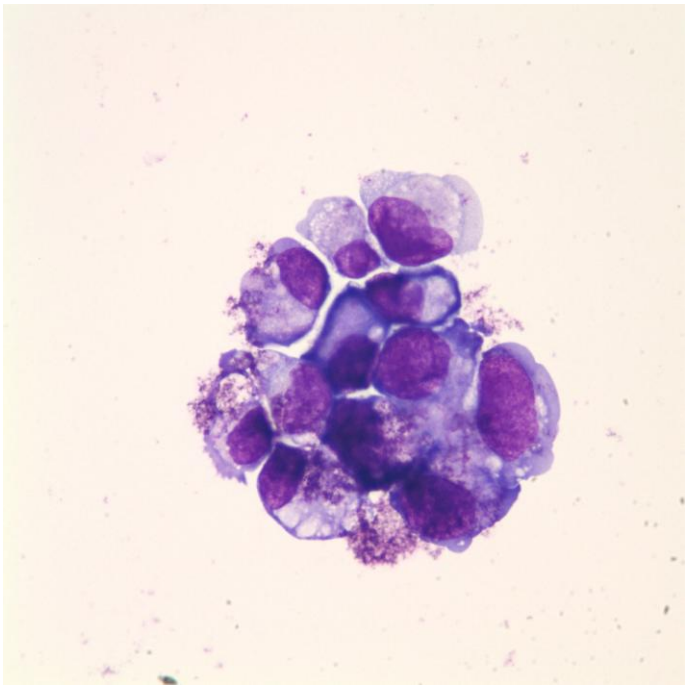

Figure 1: Malignant epithelial cells with pleomorphic nuclei. The nuclei are located eccentrically due to cytoplasmic mucin, giving the tumor cells signet ring appearance. MGG x1000.

The patient was initially treated with intrathecal methotrexate at doses of 15 mg/day. Treatment sessions were repeated twice a week for 3 weeks. The response was assessed by CSF cytology. After 6 cycles, CSF was cleared from malignant cells. The patient also received craniospinal radiotherapy for 10 days after intrathecal methotrexate therapy was completed. Because of signet-cell carcinoma of primary origin unknown, she also received the combined chemotherapy including docetaxel (60 mg/m2, day 1), cisplatin (60 mg/m2, day 1), and fluorouracil (600 mg/m2, 1-5 days) with concomitant granulocyte-stimulating factor prophylaxis for every 3 weeks. After 2 cycles, febril neutropenia developed. Despite of antibacterial therapy, her general condition was

unimproved. The patient died because of febril neutropenia and sepsis.

Discussion

Although LMM from solid cancers is uncommon, the prognosis is very poor. Median survival after LMM diagnosis is about 4-6 months [2, 5]. The clinical manifestations of LMM are very variable and include lower motor neuron weakness, headache, radicular pain, and diplopia. The neurological signs are characterized by reflex asymmetry, mental status changes, ocular muscle paresis, and motor neuropathy as well as sensorial loss [2, 6]. Quality of life deteriorates after the diagnosis because of neurological complications. The diagnosis is usually based on cytological examination of the CSF and/or MRI of brain and spinal tract. The detection of malignant cells in the CSF is the gold standard for the diagnosis. But, a positive cytology is demonstrated in only about 50% of cases [4]. Another diagnosis procedure of LMM is MRI. The enhanced contrast involvement of leptomeningeal surface on craniospinal MRI may be useful for diagnosis of LMM. Tumor metastasis to leptomeningeal surface occurs by a few mechanisms. Hematogenous spread is the most common source of LMM [6]. The others include direct extension of extradural tumors and meningeal seeding from brain metastasis. However, Batson's plexus can take a role in the tumor spread to CNS [6]. Treatment options for patients with LMM include radiotherapy and/or chemotherapy. Intrathecal chemotherapy is usually used for patients with LMM because most chemotherapeutic agents do not penetrate the blood-brain barrier. As intrathecal chemotherapy, methotrexate alone or combination with cytarabine and steroids is the most common used chemotherapeutic agents. In a study compared the efficacy of intrathecal methotrexate alone with combination therapy including methotrexate, cytosine arabinoside and hydrocortisone, combination therapy was superior to methotrexate alone. Both cytological response and the median survival were significantly higher in the combination therapy [7]. Radiotherapy is often used for symptomatic patients or bulky disease. Rarely, palliative surgery such as drainage of CSF may be useful for to be improved of neurologic symptoms. In English literature, 19 cases with LMM of signet-ring cell carcinoma have been reported [8-15]. Of 19 patients, 17 (11 male and 6 female) were evaluable. The characteristics of these patients were indicated at Table 1. The median age was 49 years. Of these patients, primary origin was stomach in 16 cases. Esophagus was primary origin in only one case and 1 patient was primary unknown origin as our case [14]. Median time from initial diagnosis to LMM was 6 months (minimum and maximum; at initial - 3 years). The longest survival after the diagnosis was 9.2 months. The best response was obtained in a patient treated with combination of intrathecal methotrexate, radiotherapy, and systemic chemotherapy. In this paper, we reported a younger patient who was diagnosed as signet-ring cell carcinoma with an unknown primary origin who developed LMM. Compared with the cases with LMM in the literature, the patient was very younger (19-year-old). In the published articles, while the stomach was the most common primary origin of signet-ring cell, primary origin of our case was unknown. The patient was treated with radiotherapy and intrathecal methotrexate and symptomatic improvement was obtained after the therapy. Because of metastatic disease, systemic chemotherapy including combination of docetaxel, cisplatin, and 5-fluorouracil was given, but she died after 2 cycles because of febril neutropenia.

To sum, the prognosis of patients presenting with LMM is very poor. For these patients, standard therapy is unclear. But, intrathecal methotrexate and/or craniospinal radiotherapy may improve clinical symptoms. Systemic chemotherapy might be useful, but severe complication may occur. In conclusion, clinicians should exclude LMM in signet-ring cell carcinoma patients presenting with neurological symptoms.

Table 1: Signet-ring cell carcinoma with leptomeningeal metastasis: summary of cases in the English literature

Author	Age	Gender	Origin of Primary tumor	CSF	MRI	Treatment	Interval	Overall Survival
Fuchizaki[8] et al. 2005	42	M	Stomach	+	+	NA	At initial	7 weeks
Lisenko[9] et al 2003	27	M	Stomach	+	+	RT	58 ms	?
	33	M	Stomach	+	-	ITMtx	8 ms	?
	49	F	Stomach	+	+	None	1 ms	?
	49	F	Stomach	ND	+	RT	6 ms	?
	52	F	Stomach	+	+	ITMtx	9 ms	?
Lee[10] et al 2004	38	F	Stomach	NA	NA	Supportive	0.7 ms	0.3 ms
	52	M	Stomach	NA	NA	ITMtx; RT; Sys Che	1.4	9.2
	52	M	Stomach	NA	NA	ITMtx; RT	1.8	2.7
	31	M	Stomach	NA	NA	ITMtx; RT	5.0	4.3
	46	M	Stomach	NA	NA	ITMtx; RT	10.5	2.5
	59	M	Stomach	NA	NA	Supportive	7.4	0.7
	39	M	Stomach	NA	NA	Supportive	6.7	1.2
	40	F	Stomach	NA	NA	ITMtx; Sys Che	28.2	1.6
Lee[11] et al 2007	49	F	Stomach	+	-	Supportive	At initial	UNK
Suto[12] et al 2007	70	M	Stomach	+	+	Supportive	At initial	1.0
Wagemakers[13] et al 2005	52	M	Oesophagus	+	+	RT	3 years	16 weeks
Nakatsuji[14] et al 2001	NA	NA	UNK	+	NA	-	At initial	UNK
Kakar[15] et al 1998	NA	NA	Stomach	NA	NA	UNK	NA	UNK

RT: Radiotherapy; ITMtx: intratechal methotrexate; Sys Che: systemic chemotherapy; UNK: unknown; NA: not applicable; ND: not done.

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