



Multiple Extracranial Metastases from Secondary Glioblastoma: A Case Report and Review of the Literature

Sekonder Glioblastomaya Bağlı Gelişen Çoklu Ekstrakraniyal Metastazlar: Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

Mevlut Ozgur TASKAPILIOGLU¹, Ulas AKTAS¹, Pinar ESER¹, Sahsine TOLUNAY², Ahmet BEKAR¹

¹Uludag University, Faculty of Medicine, Department of Neurosurgery, Bursa, Turkey

²Uludag University, Faculty of Medicine, Department of Pathology, Bursa, Turkey

Corresponding Author: Mevlut Ozgur TASKAPILIOGLU / E-mail: ozgurt@uludag.edu.tr

ABSTRACT

Glioblastoma represents extreme anaplasia in astrocytic tumors. In spite of this aggressiveness, extracranial metastasis of glioblastoma is very rare and has been documented in only a few patients in the literature. In this article, a 30-year-old woman with secondary glioblastoma associated with extracranial distant metastasis was presented. In September 2008, an intracranial lesion in the left frontal region was diagnosed by magnetic resonance imaging (MRI) after admission to the hospital by headache and seizure and subsequently resected. The histology of the lesion revealed an anaplastic astrocytoma (grade III). Upon recurrence of the tumor 7 months later, the patient underwent a second craniotomy for recurrence tumor resection. The histological diagnosis was glioblastoma. After radiotherapy and chemotherapy, cranial computerized tomography (CT) and whole body scintigraphy revealed metastatic lesions in the right cervical lymph nodes and the left ischium. A neck dissection and parathyroidectomy on the right side was performed. The cytomorphological and histological features of the tumor supported the diagnosis of metastatic glioblastoma.

KEYWORDS: Glioblastoma, Extracranial metastasis, Secondary glioblastoma, Prognosis

ÖZ

Glioblastom astrositik tümörler içerisinde en fazla anaplaziyi gösterenidir. Bu agresif davranışı yanında ekstrakraniyal metastazları oldukça nadirdir ve literatürde çok az hastada bildirilmiştir. Bu makalede, 30 yaşında sekonder glioblastoma bağlı ekstrakraniyal uzak metastazları bulunan bir bayan hasta sunulmuştur. Eylül 2008 tarihinde baş ağrısı ve nöbet şikayeti ile hastaneye başvuran hastanın çekilen kraniyal manyetik rezonans görüntülemesinde sol frontal bölgede intrakraniyal kitle saptanmıştı. Hasta opere edildi. Patoloji tanısı anaplastik astrositom (grade III) olarak raporlandı. 7 ay sonra rekürrens nedeniyle hasta tekrar opere edildi. Histolojik tanısı glioblastom olarak raporlandı. Radyoterapi ve kemoterapiden sonra çekirtilen bilgisayarlı tomografi ve tüm vücut sintigrafisinde sağ servikal lenf nodları ve sol iskiümde metastatik lezyonlar saptandı. Sağ taraflı boyun diseksiyonu ve paratiroidektomi uygulandı. Sitomorfolojik ve histolojik çalışmalar metastatik glioblastomla uyumlu olarak bildirildi.

ANAHTAR SÖZCÜKLER: Glioblastom, Ekstrakraniyal metastaz, Sekonder glioblastom, Prognoz

INTRODUCTION

Glioblastoma, the most common and most aggressive primary brain tumor, constitutes 50-60% and 12-15% of primary brain tumors and intracranial tumors, respectively (5). Glioblastoma may constitute either primarily or secondary to progression of low grade or anaplastic astrocytoma. These subgroups have different genetic characteristics, prognoses and treatment responses and they affect different age groups. Secondary glioblastoma patients are younger and they progress at a lower rate and they have better prognoses.

Extracranial metastasis is seen in only 0.44% of all neuroepithelial tumors and two third of these metastasis is formed by glioblastoma. Especially they spread to lymph

nodes (51.4%), lungs and pleura (59.7%), bone (30.5%) and rarely to liver (22.2%). Other more rare extracranial metastatic places are spinal cord, skin, small bowel, parotid gland and other organ systems (6, 12).

Both extracranial metastasis and diagnosis of glioblastoma during pregnancy are rare entities. Here, a secondary glioblastoma pregnant patient with cervical lymph node and parotid gland metastasis is reported and discussed under the light of the literature.

CASE REPORT

A thirty-year-old female at the 22nd gestational week of her pregnancy was admitted to the neurosurgery outpatient department with the complaint of seizure and

frontal headache presented for a month. Her neurological examination was normal. Cranial MRI showed a 5x4 cm left frontal mass lesion (Figure 1A). The lesion was excised macroscopically totally in September 2008 (Figure 1B). The lesion was yellow-purple and elastic, and had hemorrhagic and necrotic areas in its center. Histopathological examination of the tissue revealed diffuse infiltration of atypical cells with ovoid, big and hyperchromatic nuclei and some of them with wide clear cytoplasm. There were mitosis, necrosis, diffuse S-100 and focal GFAP expression in the tumoral cells. The histopathological diagnosis was concordant with anaplastic oligodendroglioma grade III.

Seven months later, the patient was admitted to the hospital with the complaint of right hemiparesis. Her cranial CT showed 4x4 cm mass lesion in the prior operation site with heterogeneous contrast enhancement and peripheral edema (Figure 1C, D). She was again operated on. Soft tissue particles that were gray-yellow-brown macroscopically contained microscopically atypical tumoral cells with big, hyperchromatic, prominent nucleoli around the necrotic area. They were staining strongly with GFAP and p53. The final diagnosis after the pathological examination was glioblastoma. Following the surgical approach, radiotherapy (RT) and 7 cycles of Temozolomide treatment were performed.

Ten months later, a 7x5 cm mass lesion was detected in the right parotid gland. Her facial CT and whole body scintigraphy showed lymph nodes in the right cervical, preauricular, and retroauricular regions, and metastasis in the left ischium, respectively (Figure 2A, B). Plastic surgery department performed right parotidectomy and right radical neck dissection. The tumoral cells were round shaped with hyperchromatic nuclei, clear cytoplasm showing prominent nucleoli in places and prominent pleomorphism. Tumoral cells were stained with vimentin and S-100 focally and diffusely, respectively. Histological examination of the tumoral cells in the parotid gland and the dissected neck region revealed glioblastoma diagnosis (Figure 3). She died 6 months after the parotidectomy and radical neck dissection operation.

DISCUSSION

Glioblastomas, on the molecular basis, have two subtypes as primary and secondary. Secondary glioblastomas form 5% of all the glioblastomas. Secondary glioblastomas are seen in younger patients than primary glioblastomas (9, 10). Our patient was a 30-year-old woman.

Secondary glioblastomas form as a result of astrocytoma and anaplastic astrocytoma gaining more malign anaplasia. The mean time needed for a low-grade astrocytoma to

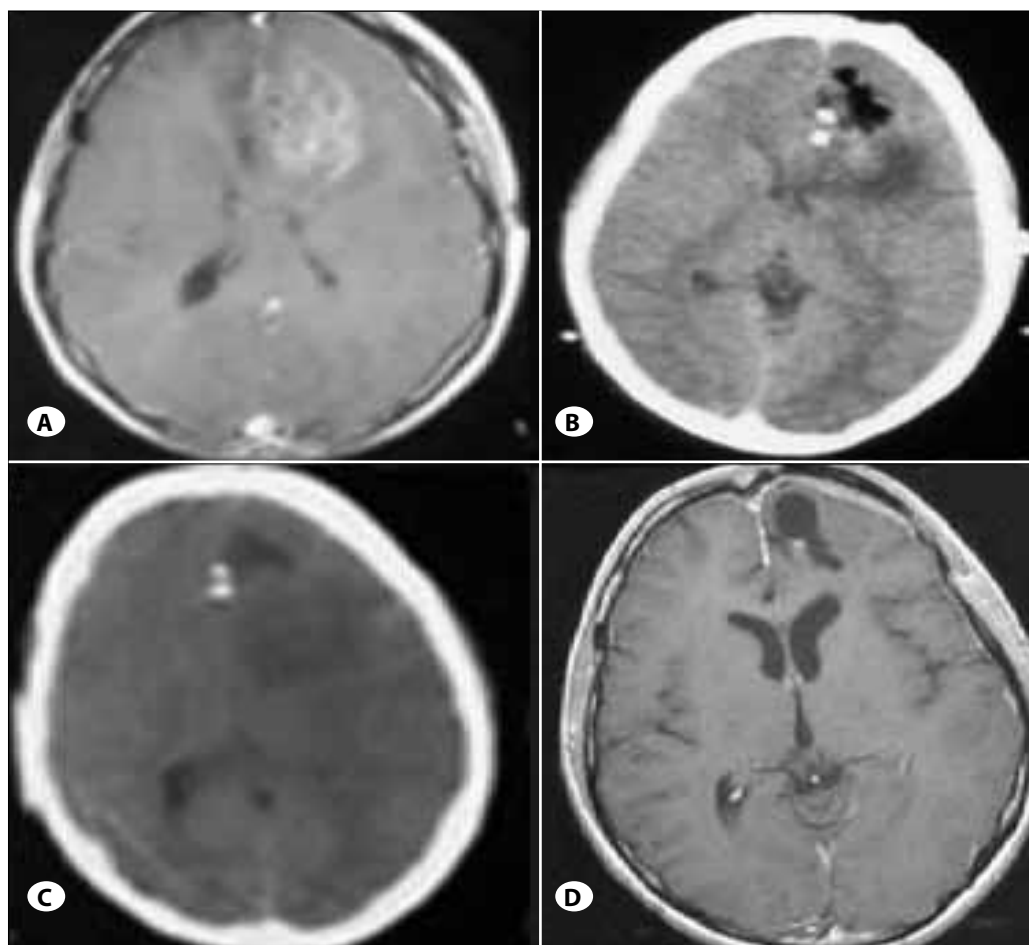


Figure 1: (A) Preoperative contrast enhanced cranial MRI revealed a left frontal mass; (B) Postoperative CT showed excision of the mass; (C) Second preoperative CT showed a recurrence mass at left frontal region; (D) Second postoperative contrast enhanced cranial MRI revealed total excision of the left frontal mass.

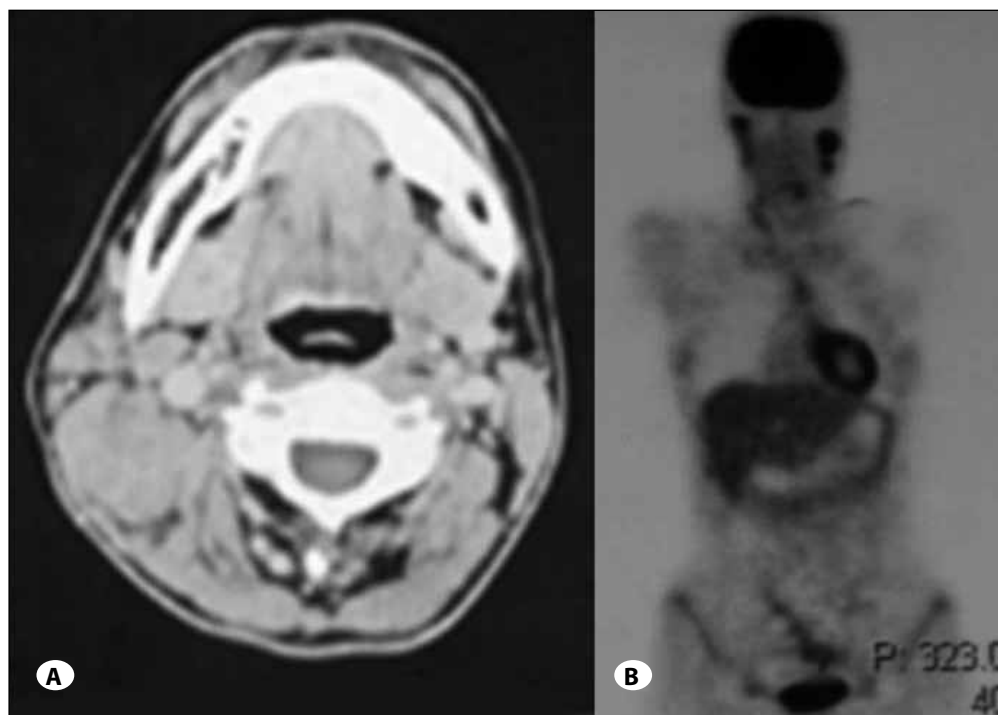


Figure 2: (A) Facial CT showed a mass lesion at the right parotid gland; (B) Whole body scintigraphy showed lymph nodes in the right cervical, preauricular, and retroauricular regions, and metastasis in the left ischium.

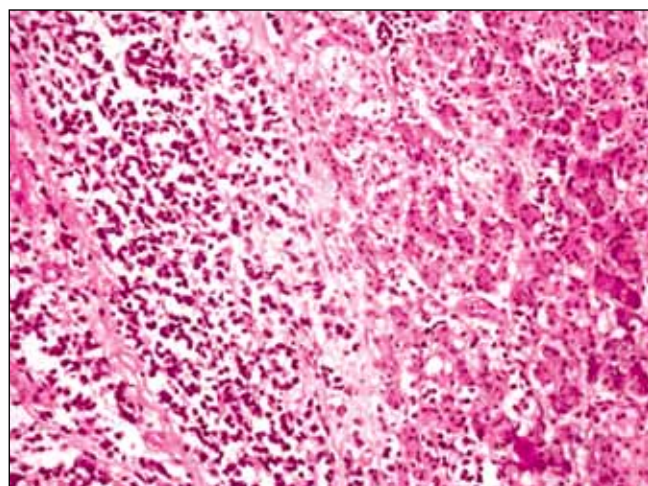


Figure 3: Normal parotid gland at right and tumor cells at left (HEx200).

transform into glioblastoma is 50–55 months (9). Although it must be shorter than low-grade gliomas, there is no exact data for the anaplastic astrocytomas. This time was 7 months in the presented case. The mean duration of survival in the secondary glioblastoma patients is 8.5 months and this is longer than the one in the primary glioblastoma patients (4.7 months) (5, 7). Fonkem et al. pointed that patients with metastasis to the liver had the longest and metastasis to the lung had the shortest time interval between diagnosis of the intracranial glioblastoma and detection of metastasis (2). In a recent natural history study the median overall survival time

was detected as 10.5 months and the duration of survival in this patient after the first operation was 18 months (7).

Extracranial metastasis of glioblastomas is extremely rare. The lymph nodes and bone are common metastatic places while the parotid gland is a rare place for metastasis (8). There was metastasis both in the lymph node, bone, and the parotid gland. The lymph node metastasis has been reported especially in the cervical region on the same side with the previous craniotomy side (4). The patient's metastasis to the parotid gland and the cervical lymph node was contralateral to the previous craniotomy side.

The routes of extracranial metastasis in the glioblastomas are not clear. The hypoxic and proliferative zone of the glioblastoma has an angiogenesis-related breakdown of the blood-brain barrier and glioblastoma cells have direct communication with the systemic circulation (2). The metastases are seen commonly following surgery. This lead to the assumption that the tumoral cells gain may access to the lymphatics or veins during surgery. Another route is peritoneal metastasis via shunts (4). However, extracranial metastasis has been documented in patients who have not undergone any surgical procedure so metastasis via cerebrospinal fluid or blood is still possible (1, 3, 11). The presence of metastasis in the right cervical lymph node and bone makes lymphatic and hematogeneous routes most likely responsible for the metastasis.

The treatment of the glioblastomas includes generally surgery and adjuvant radiotherapy and chemotherapy. The survival may be lengthened significantly especially with

chemotherapy in the soft tissue metastasis and with the combination of three treatment modalities in the young patients. Even though several treatment approaches have been in clinical use, glioblastoma is still an aggressive tumor with unfavorable prognosis.

Despite of several theories to explain the mechanisms of distant metastasis of glioblastoma the issue has not been clarified yet. The diagnosis of extracranial glioblastoma metastasis has increased because of the modern diagnostic tools and prolonged survival of the patients.

REFERENCES

1. Brew BJ, Garrick R: Gliomas presenting outside the central nervous system. *Clin Exp Neurol* 23:111–117, 1987
2. Fonkem E, Lun M, Wong ET: Rare phenomenon of extracranial metastasis of glioblastoma. *J Clin Oncol* 29:4594-4595, 2011
3. Gams AS, Egelhoff J, Roloson G, Young J, Woods GM, Newman R, Freeman AI: Diffuse bony metastases at presentation in a child with glioblastoma multiforme. A case report. *Cancer* 66:180–184, 1990
4. González Cámpora R, Otal Salaverri C, Vázquez Ramirez F, Salguero Villadiego M, Galera Davidson H: Metastatic glioblastoma multiforme in cervical lymph nodes. Report of a case with diagnosis by fine needle aspiration. *Acta Cytol* 37: 938–942, 1993
5. Hess KR, Broglio KR, Bondy ML: Adult glioma incidence trends in the United States, 1977-2000. *Cancer* 101:2293-2299, 2004
6. Kraft M, Lang F, Braunschweig R, Janzer RC: Parotid gland metastasis from glioblastoma multiforme: A case report and review of the literature. *Eur Arch Otorhinolaryngol* 265: 709-711, 2008
7. Lun M, Lok E, Gautam S, Wu E, Wong ET: The natural history of extracranial metastasis from glioblastoma multiforme. *J Neurooncol* 105: 261-273, 2011
8. Ogungbo BI, Perry RH, Bozzino J, Mahadeva D: Report of GBM metastasis to the parotid gland. *J Neurooncol* 74: 337-338, 2005
9. Ohgaki H, Dessen P, Jourde B, Horstmann S, Nishikawa T, Di Patre PL, Burkhard C, Schuler D, Probst-Hensch NM, Maiorka PC, Baeza N, Pisani P, Yonekawa Y, Yasargil MG, Lutolf UM, Kleihues P: Genetic pathways to glioblastoma: A population-based study. *Cancer Res* 64:6892–6899, 2004
10. Ohgaki H, Kleihues P: Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendroglial gliomas. *J Neuropathol Exp Neurol* 64: 479–489, 2005
11. Wallace CJ, Forsyth PA, Edwards DR: Lymph node metastases from glioblastoma multiforme. *AJNR* 17:1929–1931, 1996
12. Yasuhara T, Tamiya T, Meguro T, Ichikawa T, Sato Y, Date I, Nakashima H, Ohmoto T: Glioblastoma with metastasis to the spleen--case report. *Neurol Med Chir (Tokyo)* 43:452-456, 2003