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Case Report

A Rare Case Report: Spinal Metastasis of Anaplastic Pleomorphic Xanthoastrocytoma

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Abstract

Anaplastic Pleomorphic Xanthoastrocytoma is a very rare tumor of the Central Nervous System (CNS). BRAFV600E mutation is a common mutation in pleomorphic xanthoastrocytoma. We present a 52-year-old male patient who underwent total resection due to a temporal lobe mass. The primary tumor in the temporal lobe was given postoperative radiotherapy. During follow-up, genetically and histologically proven metastasis was detected in the paraspinal region. The adjuvant RT was given to metastasis after surgery. The patient, who used the combination of dabrafenib and trametinib after recurrence, is being monitored in remission.

Introduction

Anaplastic Pleomorphic Xanthoastrocytoma is a very rare tumor of the CNS. According to the World Health Organization (WHO) Classification of Tumors of the CNS fifth edition, pleomorphic xanthoastrocytomas are classified under circumscribed astrocytic gliomas. The most common genetic alterations are BRAFV600E mutation and CDKN2A/B deletion. Although these mutations are typical, they are not essential for diagnosis. According to the CNS WHO classification, pleomorphic astrocytomas can be grade 2 and 3. Grade 3 tumors have increased mitotic activity and necrosis [1]. Diagnostic criteria are based on histopathology, astrocytic glioma with pleomorphic tumor cells, including large multinucleated cells, spindle cells, xanthomatous cells, and eosinophilic granular bodies and require increased mitotic activity (mitotic index ≥5 mitoses/10 HPF) [2,3].

BRAFV600E mutation is a common (approximately %65) mutation in pleomorphic xanthoastrocytoma [4]. BRAF mutation is generally seen in melanoma, colon cancer, and thyroid papillary carcinomas, but can also be seen in CNS tumors, causing and driving activation of the Mitogen-Activated Protein Kinase (MAPK) signaling pathway. In the presence of mutation, the tumor can be targeted for treatment with RAF and MEK inhibitors [5].

Case presentation

A 52-year-old male patient came to the hospital complaining of seizures. The patient underwent further examinations.

Brain MRI showed a mass lesion area of approximately 6 x 4.5 x 5 cm located in the right temporal region, with a distinct contrast-enhancing component and widespread vasogenic edema area around it. Subfalcine and uncal shift was present and an approximately 1.5 cm shift to the left of the midline is observed. Areas of diffusion restriction were also observed within the lesion. The first brain MRI image of the patient is shown in Figure 1a,1b.

The patient, who was radiologically thought to have a brain tumor, was operated on by a neurosurgeon, and the tumor was grossly removed. Postoperative brain MRI showed a surgical resection cavity in the posterior part of the middle and inferior temporal gyrus in the right brain. Its dimensions are 56 x 38 x 30 mm. It is seen that the hemorrhagic mass observed in the previous examination was removed grossly and completely. No obvious findings are suggestive of residue were detected.

Pathology results show a tumor that infiltrated the glial tissue and was rich in necrosis, with predominantly spindle

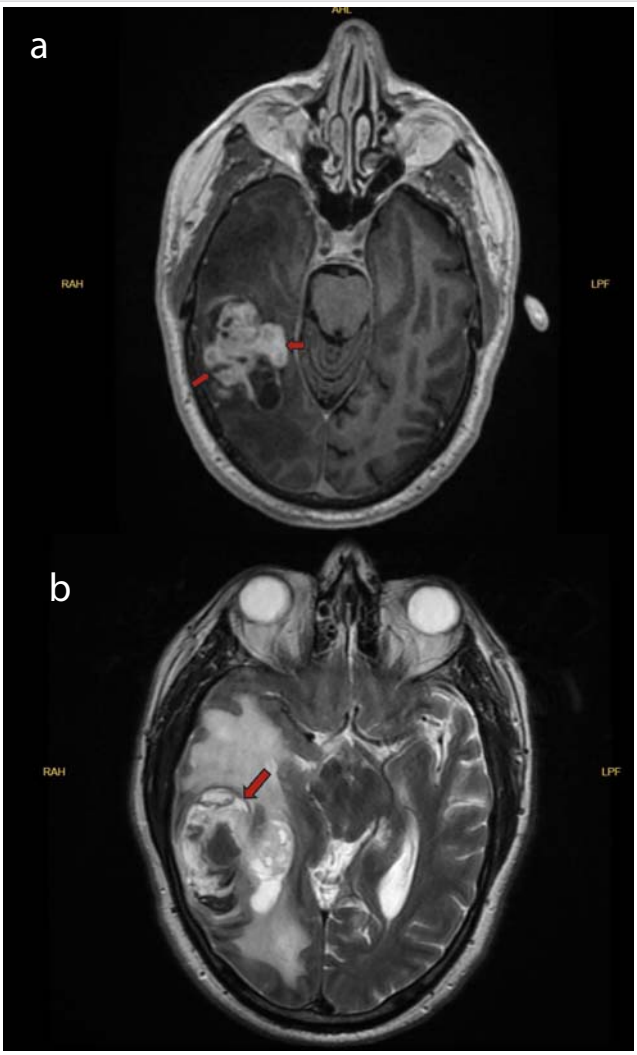

Figure 1: a: T1 with contrast. b: T2.

cells and occasionally vascular structures with epithelioid morphology. Pseudocyst structures are occasionally seen in the tumor and light blue accumulations within these cysts. The tumor cells have quite pleomorphic nuclei and contain abundant mitoses. The Ki67 index reaches approximately 70%. Pathological images showed findings in favor of high-grade glial neoplasia and the differential diagnosis included mesenchymal neoplasms such as astroblastoma, PXA, ATRT, gliosarcoma, glioblastoma, leptomeningeal melanomatosis, CIC-DUX4 sarcoma and other high-grade neuroectodermal tumors. However, Next-Generation Sequencing (NGS) and methylation profile studies were recommended for definitive typing.

When the patient was examined with NGS and methylation profiling, BRAFV600E mutation was detected. When the morphological findings were evaluated together with this mutation, the definitive diagnosis was made as Anaplastic Pleomorphic Xanthoastrocytoma grade 3.

The patient received a total of 60 Gy adjuvant radiotherapy with a daily dose of 2 Gy/day fractions accompanied by temozolomide (1-10 cc dose of the brainstem was 54-60 Gy, maximum dose of optic chiasm was 26 Gy). Adjuvant temozolomide was completed in two years and was given every 28 days, 400 mg/day between days 1 and 5. Dose color washes of the patient's radiotherapy plan are shown in Figure 2a,2b.

During the patient's routine follow-up, a spinal MRI was performed due to back pain that developed 2 years later. The MRI showed a mass lesion measuring 42 x 55 x 40 mm in size at the left costovertebral junction of the thoracic 7(T7) vertebra, destroying the left transverse process. MRI image of the patient is shown in Figure 3a,3b. Therefore, the patient underwent an 18-FDG-PET-CT examination for distant metastasis screening. The examination revealed a tumoral soft tissue structure measuring 34 x 53 mm in size, destroying the left 6th and 7th ribs and the left transverse process of the T7 vertebra in the left paravertebral region of the thorax, and intensely increased 18-FDG uptake (SUVmaks: 28.3).

The patient underwent surgery for this newly appeared

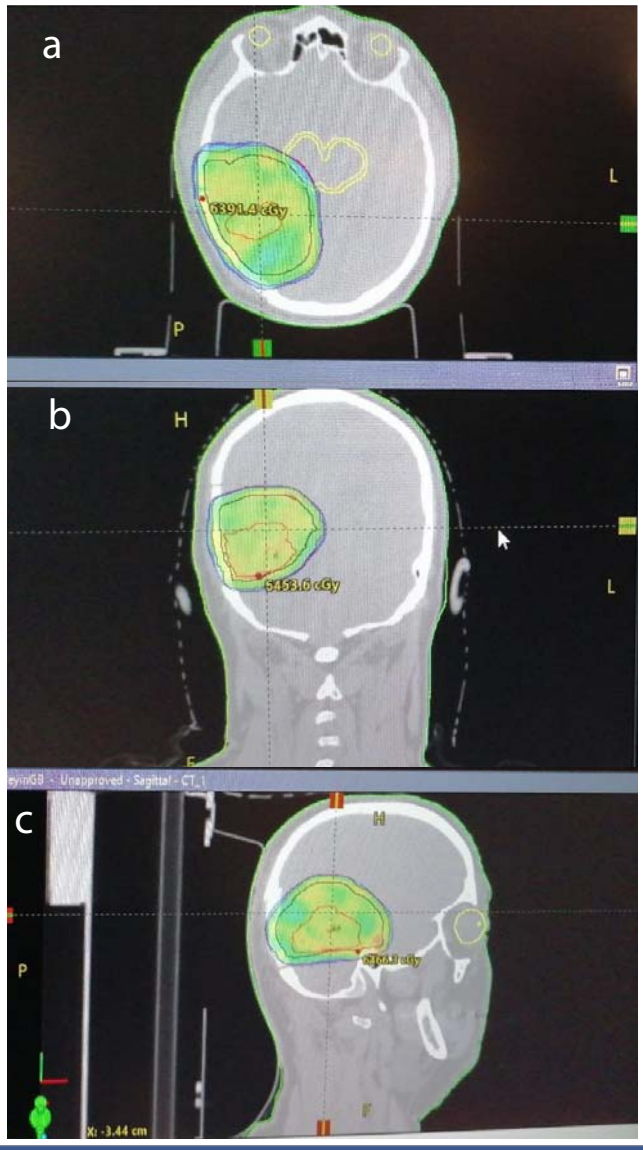

Figure 2: a: Dose color wash axial, primary tumor. b: Dose color wash coronal, primary tumor. c: Dose color wash sagittal, primary tumor.

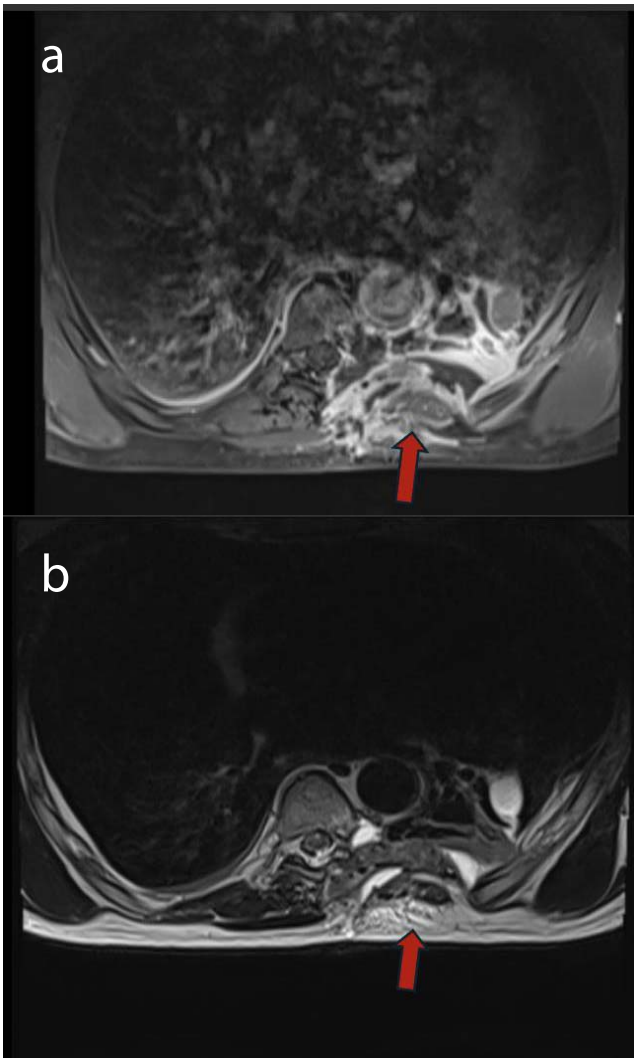

Figure 3: a(T1): The MRI showing a mass lesion. b(T2): The MRI showing a mass lesion.

lesion in the spinal region. The postoperative pathology was a high-grade malignant mesenchymal tumor with hemangiopericytomatous vascular structure characteristic with round-oval cell perivascular myxoid change showing neurogenic differentiation (compatible with recurrence/metastasis of the previous lesion). BRAFV600E mutation was also detected in this tumor. No clear interpretation could be made in terms of surgical margins, and it was accepted as positive.

After the operation, 50Gy was applied to the surgical bed at the T6-T8 vertebral level with a dose of 2Gy/fraction, followed by an additional dose of 10 Gy in 5 fractions to the tumor bed. Radiotherapy fields are shown in Figure 4a-4c.

After progression, the patient was given dabrafenib (BRAF inhibitor) and trametinib (MEK inhibitor). In the patient's last follow-up MRI, there is no residual recurrence evidence except for soft tissue appearances due to postoperative and post-RT changes between T6-T8. The patient is still being followed up as disease-free with no signs of recurrence.

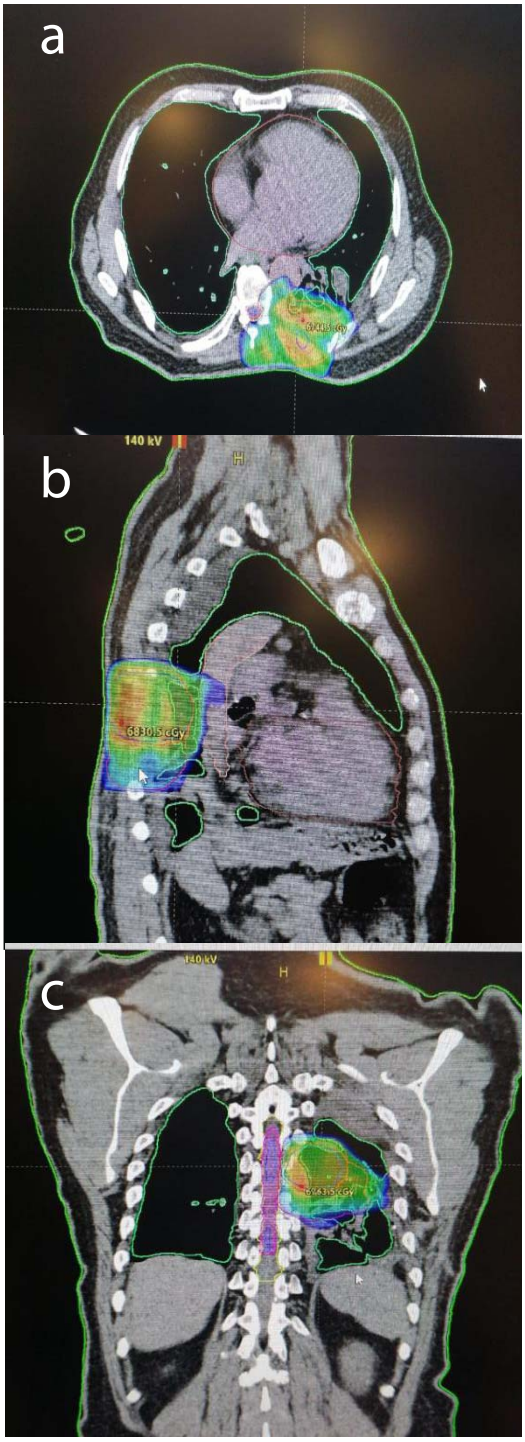

Figure 4: a: Radiotherapy fields are shown in the figure (Dose color wash axial, metastasis). A dose of 2Gy/fraction, followed by an additional dose of 10 Gy in 5 fractions to the tumor bed. b: Radiotherapy fields are shown in the figure (Dose color wash sagittal, metastasis). A dose of 2Gy/fraction, followed by an additional dose of 10 Gy in 5 fractions to the tumor bed. c: (Dose color wash coronal, metastasis).

Discussion

Pleomorphic xanthoastrocytomas are rare tumors of the CNS classified under circumscribed astrocytic gliomas. It is more frequently seen in children and young adults, regardless of gender. They usually originate from the temporal lobe and present with seizures [2]. In our case, the patient presented with seizures, consistent with the literature, and the tumor

was first detected in the temporal lobe. However, it differs from the data in the literature because the patient was 52 years old. In a study published in 1999 with 71 patients, the median age was determined as 26 years, and it was shown that %98 of the cases originated from the supratentorial region and %49 originated from the temporal lobe [6].

In a study conducted in 2014, 74 patients were included in the study retrospectively, and the median age was found to be 21.5 years. Anaplasia, defined as a high mitotic index (≥ 5/10HPF) and the presence of necrosis, was detected in 33 cases, and BRAFV600E mutation was detected in 39 cases. It has been shown that anaplasia is associated with lower overall survival, while BRAFV600E mutation is associated with higher overall survival. Tumor recurrence was reported in 33 of 74 patients, and distant spread of the tumor was not mentioned [3]. There are rare cases of extracranial spread of pleomorphic xanthoastrocytomas in the literature. In a case published in 2022, extracranial bone metastases were detected in a 15-year-old patient after 12 years of disease-free survival [7]. Leptomeningeal spread was detected in a 27-year-old female patient with a diagnosis of anaplastic pleomorphic xanthoastrocytoma, and clinical stability was achieved with radiotherapy [8]. Another reported 27-year-old male patient had scalp metastases 3 years after diagnosis [9]. A 45-year-old male patient was reported with pleomorphic xanthoastrocytoma with intraventricular localization [10]. In our case, distant metastasis was detected, which was shown pathologically and genetically, and there are a few data or cases in the literature indicating distant metastasis of pleomorphic xanthoastrocytomas.

Cases originating from the spinal cord have been reported in the literature [11-13]. The reported cases of spinal cord pleomorphic xanthoastrocytoma appear to originate primarily from the cord, and metastasis is not mentioned. In a published case report, a 15-year-old male patient who presented with neck pain was found to have a cervical intramedullary mass with solid contrast enhancement on MRI, and his pathology was reported as grade 2 pleomorphic xanthoastrocytoma according to the WHO classification [14]. In the present case, during the patient's follow-up, the metastases were detected in the processes of the thoracic vertebrae and paraspinal tissue and differ from the cases in the literature.

Pleomorphic xanthoastrocytoma is a tumor composed of pleomorphic tumor cells that can appear in different morphologies and histologies, including large multinucleated, spindle, xanthomatous cells and eosinophilic granular bodies [2]. In this case, the first surgical pathology revealed cells rich in vascular structures and necrosis, predominantly spindle cells, showing pseudocystic structure, pleomorphic nuclei, and containing abundant mitosis. BRAFv600e mutation was also detected. Although pleomophyric xanthastrocytomas can be seen in different morphologies, this case is consistent with the literature in terms of histopathological features.

The primary treatment for pleomorphic xanthoastrocytomas is maximal resection. Especially grade 3 tumors should be evaluated for postoperative radiotherapy [2]. There are also patients in the literature who were treated with proton beam therapy, especially in complex diseases. A case has been reported in which proton beam therapy was used after incomplete surgical resection in a 9-year-old pediatric patient, with no recurrence detected in the 1-year follow-up, and no radiotherapy-related complications were observed [15]. In recurrent and refractory tumors, the combination of dabrafenib and trametinib may be beneficial [16,17]. In our case, the primary tumor in the temporal lobe was given postoperative radiotherapy, and the adjuvant RT was given to metastases after surgery. The patient, who used the combination of dabrafenib and trametinib after recurrence, is being monitored in remission. Radiotherapy to primary tumors and metastases was given in curative doses, and no grade 3 or 4 side effects related to radiotherapy and medical treatment were observed.

Conclusion

Pleomorphic xanthoastrocytomas are rare central nervous system tumors with limited data in the literature. Our case adds important information to the literature in order to understand the disease because it progresses with extracranial metastasis, a rare feature of a rare tumor.

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