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CASE REPORT

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Longterm survival after surgical removal of solitary brain metastasis from osteosarcoma

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Abstract The prognosis of osteosarcoma with brain metastasis is very poor. We report a 14-year-old girl with osteosarcoma of the right distal femur who is alive and free of disease 6 years after the craniotomy and irradiation for brain metastasis. This longterm survival is attributed to the absence of active pulmonary metastasis at the onset of brain metastasis and the complete removal of the brain metastasis by craniotomy. Patients without active pulmonary metastasis at the onset of brain metastasis may achieve longterm survival. In such patients, it would be worthwhile to perform craniotomy aggressively.

Key words Osteosarcoma · Brain metastasis · Craniotomy · Prognosis

Introduction

The most common primary lesions causing brain metastasis are cancers of the lung, breast, or kidney, followed by those of the gastrointestinal tract. Osteosarcoma is very rarely the primary source of brain metastasis.[1] The pattern of metastasis from osteosarcoma is usually hematogenous, with the lungs being the main target. Brain metastasis has been considered a rare event in osteosarcoma, but this may be changing with prolonged patient survival in the modern chemotherapy era.[2–5] We have observed the occurrence of brain metastases in several patients with osteosarcoma. Formation of brain metastasis is usually the final stage of the clinical history, and subsequent survival is, in general, several months.[2,3,5,6] There are only a few reports of osteosarcoma patients with longterm survival after the detection of brain metastasis.[3,7,8] We report here a girl with longterm survival after brain metastasis from osteosarcoma.

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Case report

A 14-year-old girl presented with right gonalgia. Plain roentgenogram at initial presentation demonstrated an ill-defined osteolytic change and destruction of the bone cortex at the right distal femur. Magnetic resonance imaging (MRI) demonstrated tumor infiltration outside the bone cortex (Fig. 1). She was diagnosed with conventional osteosarcoma by needle biopsy.

Before treatment, informed consent was obtained from the patient and her parents. Wide excision of the tumor and total knee arthroplasty were performed, after preoperative chemotherapy consisting of methotrexate, doxorubicin, and cisplatin. A histopathological examination of the excised specimen demonstrated 75% viable tumor cells. After surgery, chemotherapy, was performed mainly with etoposide and cyclophosphamide. The patient was discharged 10 months after her first admission.

Metastases to the left lung were found on pulmonary computed tomography (CT) 4 months after the first discharge, whereupon she was readmitted. After excision of three metastatic lesions by left thoracotomy, chemotherapy, mainly with carboplatin and doxorubicin, was administered for 6 months.

Metastasis to the right lung was found on pulmonary CT 8 months after the second discharge (Fig. 2), which led to her third admission. After the excision of one metastatic lesion by right thoracotomy, chemotherapy, mainly with ifosfamide and aclarubicin, was administered for 9 months.

Four months after the third discharge, the patient complained of contraction of the visual field and was admitted for the fourth time. Brain MRI demonstrated a solitary

Fig. 1. Magnetic resonance imaging of right distal femur (T1-weighted image). Infiltration of tumor was found outside the bone cortex

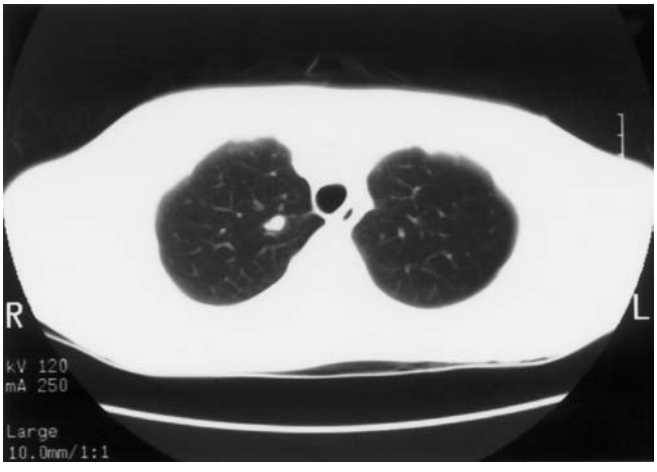

Fig. 2. Pulmonary computed tomography obtained before the third admission. A solitary metastatic lesion was found in the right lung

brain metastasis in the right occipital lobe (Fig. 3). However, no definite pulmonary metastasis was found on pulmonary CT. The metastatic lesion was excised (see Fig. 4 for histology) by craniotomy, and irradiation was performed subsequently, with 40 Gray for the whole brain and 20 Gray for the excised site for a total of 60 Gray. No chemotherapy was performed after the craniotomy. At present, 9 years and 6 months after the her initial presentation, 6 years after the craniotomy, the patient is alive and

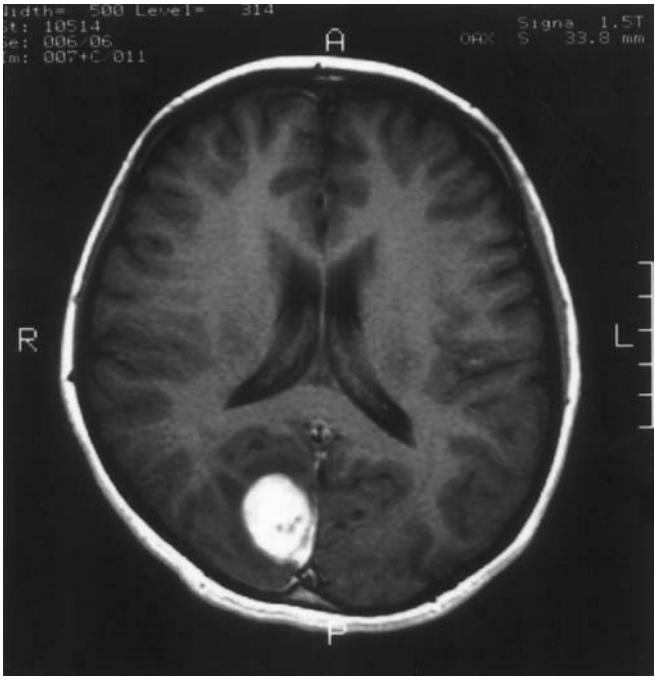

Fig. 3. Magnetic resonance imaging of brain on the fourth admission (gadolinium-enhanced T1-weighted image). A solitary brain metastasis was found in the right occipital lobe

free of disease without any difficulty in the activities of daily living.

Discussion

Brain metastasis is rare in osteosarcoma, and the incidence is reported to be 2%–6.5%.[2,3,6] At our hospital, the incidence was found to be 2.3% (3 of 128 patients). Brain metastasis is invariably found after lung metastasis. Presumably, brain metastasis develops via pulmonary metastasis. The possibility of brain metastasis should always be considered in patients in whom pulmonary metastasis has developed. It has been reported that systemic chemotherapy changed the pattern of metastasis, resulting in the incidence of extrapulmonary metastasis becoming higher.[4] It has also been reported that effective chemotherapy prolonged the survival time of patients with pulmonary metastasis, resulting in the incidence of brain metastasis becoming higher.[2,3,5] All patients with brain metastasis at our hospital in the series noted above were treated after 1987, when intensive dose chemotherapy was started. Of the 55 patients who developed conventional osteosarcoma after 1987, 24 patients were diagnosed with pulmonary metastasis. Brain metastasis was found in 12.5% (3 cases) of the patients with pulmonary metastasis treated after 1987. Therefore, performing brain CT or MRI periodically would be advisable in patients with pulmonary metastasis.

The prognosis of patients with brain metastasis of osteosarcoma is very poor, and most patients are reported to

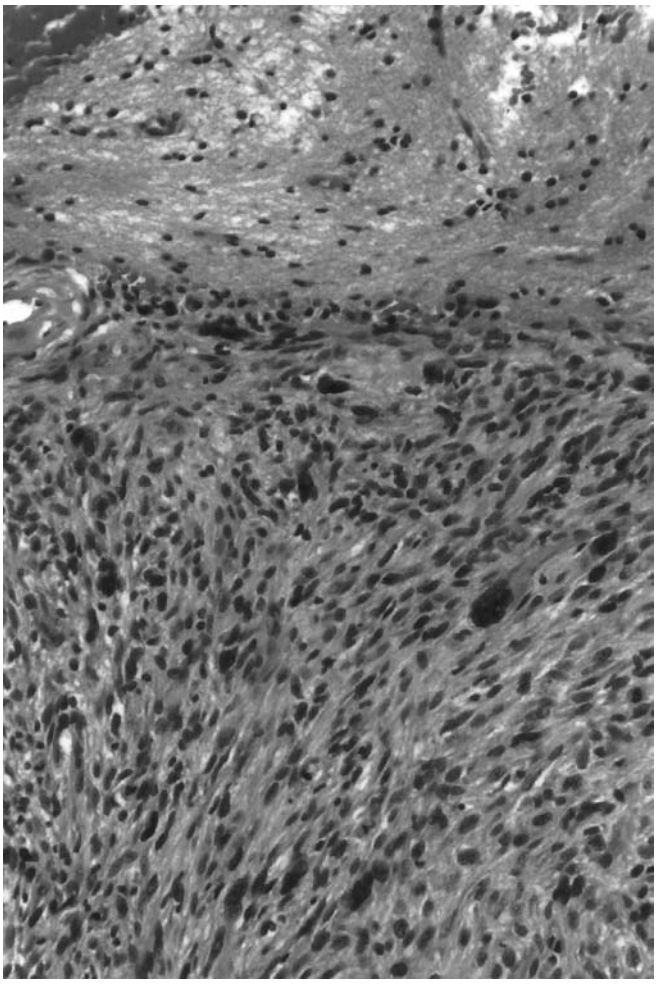

Fig. 4. Histopathological examination of brain metastasis. H&E, ×50

have died within several months.[2,3,5,6] As for longterm survivors of brain metastasis, only several such patients have been reported.[3,7,8] The absence of active pulmonary metastasis at the onset of brain metastasis and the complete removal of all brain metastases by craniotomy are common to the long-term survivors. In the present patient as well, no active pulmonary metastasis was found when the brain metastasis was detected. Those patients without active pulmonary metastasis at the onset of brain metastasis have the possibility of longterm survival. In such patients, therefore, it would be worthwhile to perform craniotomy aggressively.

Longterm survival was obtained in our patient despite the absence of chemotherapy after her craniotomy. Although chemotherapy is effective for pulmonary metastasis, it may be ineffective for brain metastasis in some patients because the blood-brain barrier prevents anticancer drugs from reaching the brain. In the present patient, pulmonary metastasis and brain metastasis might have occurred when chemotherapy was ineffective, while the modified chemotherapy administered later (ifosfamide and aclarubicin) was effective for metastases other than brain metastasis. Thus, it is possible that this effect explains why only the brain lesion remained.

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