CLINICAL IMAGE

Lung adenocarcinoma metastasis to geographic skull

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A 71-year-old nonsmoking woman was admitted to our hospital for the diagnosis of metastatic lesions revealed by bone scintigraphy with ^{99}mTc-hydroxy-methylene-diphosphonate (HMDP). Accumulation of ^{99}mTc-HMDP in the cervical spine, thoracic spine, and occipital bone suggested bone metastases in these areas (FIGURE 1A). At the age of 68 years, the patient was diagnosed with lung adenocarcinoma on the basis of pathological and genetic examination of transbronchial biopsy specimens. Molecular analysis revealed a sensitizing exon 19 (delE746-A750) epidermal growth factor receptor (EGFR) gene mutation.

At the time of the initial diagnosis, distant metastasis was not detected except for pulmonary metastases in both lungs and Th6 vertebra. The patient received several lines of chemotherapy including platinum-containing chemotherapy and EGFR-tyrosine kinase inhibitors (EGFR-TKIs). Each time, the patient responded to the therapy, but then relapsed. On admission, apart from a painful, fixed, and hard skin lesion on palpation at the occipital area and a weight loss of 3 kg over the past year, the patient was asymptomatic. Laboratory test results revealed an elevated serum carcinoembryonic antigen level of 25.9 ng/ml. The patient underwent chest and abdominal computed tomography (CT) scan, and skull and brain magnetic resonance imaging (MRI). The chest CT scan revealed a well-circumscribed primary lesion in the left lower lobe of the lung, which was not increased in size (FIGURE 1B). No metastatic lesion was found on abdominal CT scan. Resection of the occipital skin lesion revealed adenocarcinoma (FIGURE 1C) with EGFR exon 19 deletion and positive thyroid transcription factor 1, but the acquired T790M mutation was not confirmed. The skull CT scan and brain MRI revealed that the

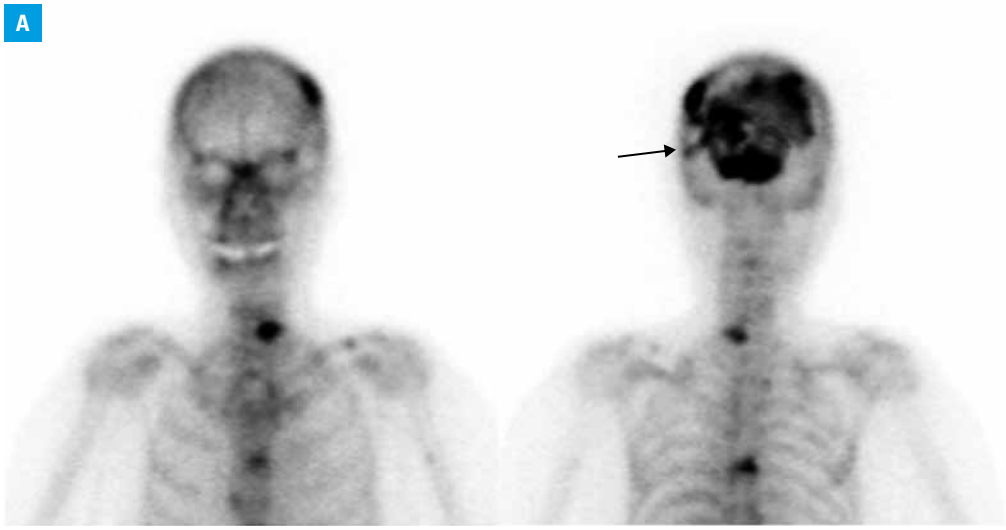

FIGURE 1 **A** – ^{99m}Tc-hydroxy-methylene-diphosphonate scan showing a radiotracer accumulated in the cervical spine, thoracic spine, and occipital bone (arrow), suggesting bone metastases in these areas. It should be noted that the uptake was observed in a geographic form on the occipital bone. In our case, the bone scan provided information indicating the site for biopsy where metastatic tissues would be obtained.

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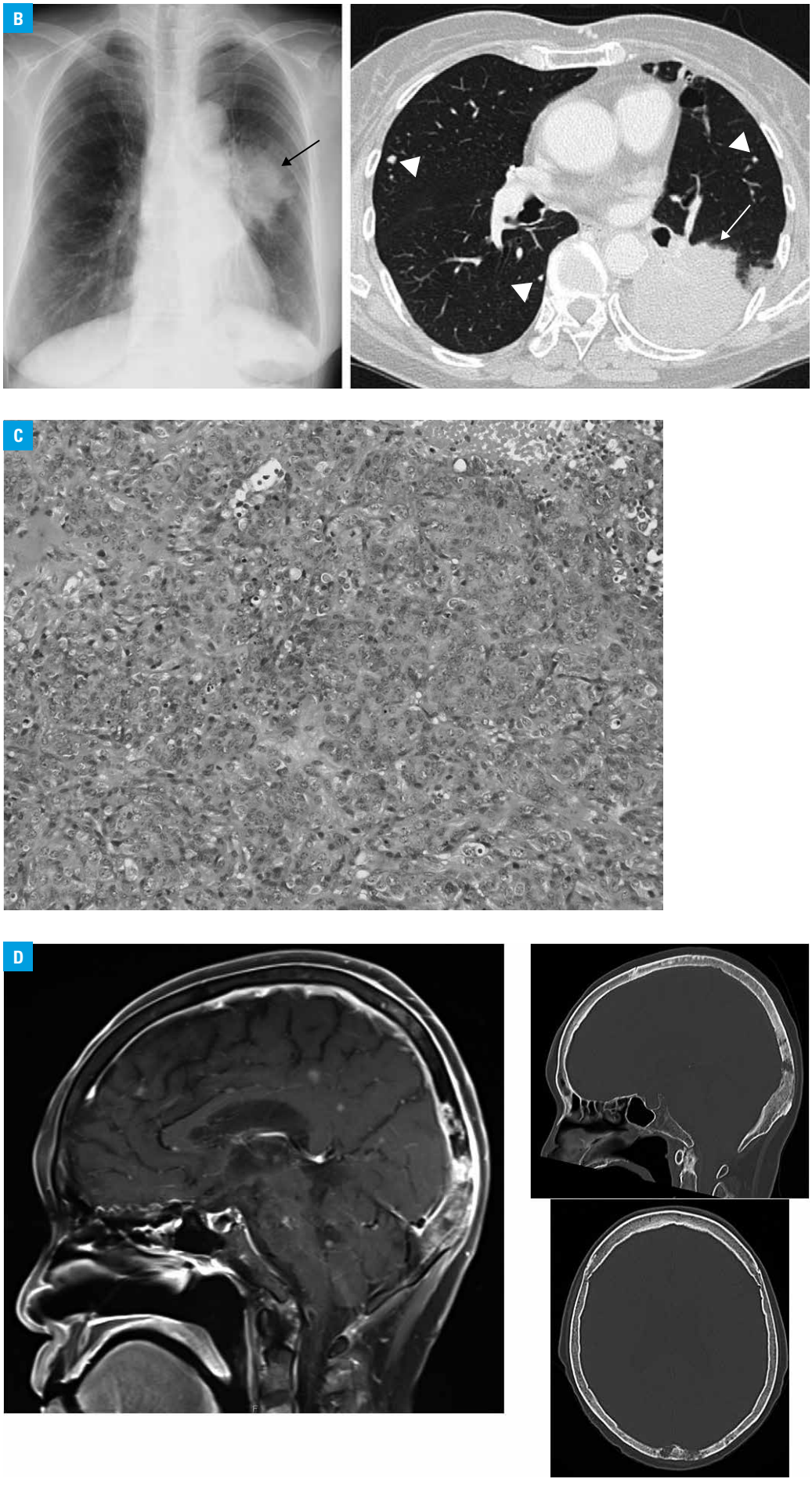

FIGURE 1 **B** – chest computed tomography (CT) scan revealed a well-circumscribed primary lesion in the left lower lobe of the lung (arrow) and pulmonary metastases in both lungs (arrow heads); **C** – resection of the occipital skin lesion revealing adenocarcinoma; hematoxylin–eosin staining; **D** – on T_1--weighted magnetic resonance imaging scan (left), the inner and outer laminas of the skull were relatively kept; however, the destruction of the interlaminal layer, diploe, was stronger than these laminas. A number of metastatic lesions were found in the brain, but no brain metastatic lesions adjacent to the occipital bone metastatic lesion. The destruction of the diploe was most notable in the sagittal (right upper) and coronal views (right lower) of the skull CT scan.

main metastatic lesion was the interlaminal layer, diploe, rather than the inner and outer laminas of the occipital bone. Since there was no evidence of brain metastasis in the occipital lobe or carcinomatous meningitis in skull and brain MRI (FIGURE 1D), we assumed that the tumor metastasized to the site via the blood stream.

Skull bone metastasis is not necessarily rare. There have been some reports of skull bone metastasis from thyroid cancer, pancreatic cancer, liver cancer, uterine sarcoma, soft tissue sarcoma, and lung cancer.[1,2] One of those reports was a recent case of lung adenocarcinoma with turban-like cranial metastasis.[2] Interestingly, that patient also had a sensitizing exon 19 (delE746-A750) EGFR gene mutation.[2] Because she was EGFR-TKI--naive, she was treated with erlotinib.[2] Therapy with EGFR-TKIs can be an important choice for patients with lung cancer with EGFR mutation.[3] After a long-term cancer control, however, recurrence in rare sites, such as the meninges, is a well--known fact.[4] Although metastasis to the occipital bone from lung cancer is rare, it should be noted that metastases to such a rare site may occur after a long-term control with TKIs in EGFR-mutated patients, as observed in our case.

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