A 67-year-old woman with no history of smoking presented with a 1-month complaint of headache and left hemiparesis. She also complained of a nonproductive cough and a weight loss of 15 pounds during the previous 3 months. She had a good performance status (PS 1) and no comorbidities. Magnetic resonance imaging of the brain revealed multiple ring-enhancing nodular lesions at the gray-white matter junction with marked surrounding edema, suggestive of metastases (Fig. 1). The edema was causing sulcal effacement and midline deviation to the left. The patient was immediately started on a steroid (dexamethasone, 4 mg orally every 6 hours), a proton-pump inhibitor (omeprazole, 40 mg daily), and a prophylactic anticonvulsant (phenytoine, 100 mg every 8 hours). After 24 hours, she had achieved partial recovery from the left paresis and her headache had been alleviated. Thoracic computed tomography (CT) scans revealed an irregular, heterogeneous, contrast-enhancing lung mass in the left upper lobe and left hilar, and mediastinal lymph node enlargements (Fig. 2). Abdominal and pelvic CT revealed no other abnormalities. A CT-guided lung biopsy was performed, and lung adenocarcinoma was confirmed. The adenocarcinoma harbored an epidermal growth factor receptor (EGFR) exon 19 deletion (del E746-A750).

Despite the presence of symptoms and the large number of brain lesions (seven in total), we decided to start the patient on oral erlotinib (150 mg/day) instead of whole-brain radiation therapy. There is evidence that omeprazole and phenytoine may reduce erlotinib absorption and activation, respectively. Nevertheless, these drugs were initially maintained, given the high risk of complications associated with the use of steroids and the possibility of seizures. The patient progressively recovered from her central nervous system-related symptoms; a remarkable response in all metastatic lesions, including resolution of the associated edema, sulcal effacement, and midline deviation, was demonstrated by brain magnetic resonance imaging 6 weeks later (Fig. 1). A major response was also observed in the thorax (Fig. 2). The patient is currently at PS 0, with great tolerability and quality of life, and visits our clinic every 4 weeks.

**DISCUSSION**

The EGFR tyrosine kinase inhibitors erlotinib and gefitinib are valid options before radiotherapy among patients with asymptomatic brain metastases that have arisen from non–small-cell lung cancers harboring sensitizing EGFR mutations. In such circumstances, the response rate is over 70%, median progression-free survival varies from 6.6 to 23.2 months, and overall survival ranges from 12.9 to 19.8 months. Furthermore, disease control tends to be superior among patients with classic exon 19 deletions, as compared to those with point mutations in exon 21. It should be noted, however, that use of this approach for patients with symptomatic central nervous system metastases has only been rarely described in the literature. As illustrated by the reported case, selected patients with sensitizing EGFR mutations may also be primarily treated with targeted therapy. Considering that whole-brain radiation therapy may delay systemic treatment and lead to significant medium-term cognitive deficits, the favorable and rapid response to EGFR inhibitors makes them a feasible and attractive alternative, providing strict neurologic vigilance is exercised.

**REFERENCES**

FIGURE 1. Axial contrast-enhanced fat-suppressed T1-weighted images before (left column) and after treatment (right column), showing remarkable reductions in both volumes of the multiple ring-enhancing nodular lesions at the gray-white matter junction and surrounding edema.


