

CASE STUDY

Successful treatment of hepatic oligometastases with stereotactic ablative radiotherapy and radiofrequency ablation in an anaplastic lymphoma kinase fusion-positive lung cancer patient

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Local ablative therapy with stereotactic ablative radiotherapy may improve survival in oncogene-addicted lung cancer patients with extracranial oligometastatic disease treated with targeted therapies. There is limited data on the use of radiofrequency ablation (RFA) in this same setting. We present a case of an anaplastic lymphoma kinase (ALK)-positive lung cancer patient with hepatic oligometastatic progression who was successfully treated with both stereotactic ablative radiation and RFA while continuing with an ALK inhibitor.

Introduction

The progression of non-small cell lung cancer (NSCLC) may be limited (oligometastatic) or more widespread. For

those patients with oligometastatic disease, local ablative therapies may help improve survival. Stereotactic ablative radiotherapy (SABR) is now one of the most frequently used modalities for local control of NSCLC hepatic

oligometastases.¹ While the use of radiofrequency ablation (RFA) in hepatocellular and metastatic colorectal cancer is well established, there is very little data on the use of RFA in NSCLC liver metastases. A PubMed literature search of RFA use in liver metastasis from NSCLC primaries yielded only a single retrospective study of a small number of patients.² The results suggested a benefit in overall survival in patients treated with RFA compared to those who did not receive RFA. We investigated the use of SABR and RFA to control limited progression of hepatic metastatic disease in a patient with an anaplastic lymphoma kinase (ALK)-positive lung cancer treated with ALK inhibitors.

Case Study

Written informed consent was obtained from the patient for the publication of this case study and any accompanying images.

A 51-year-old, never-smoker female, with no prior diagnosis of cancer, developed an acute onset of pleuritic chest pain and dyspnea in late 2012. A CT of the chest showed pulmonary emboli, a mass in the right middle lobe, an enlarged subcarinal lymph node, right pleural effusion and small pericardial effusion (Fig. 1a). CT scan of the abdomen and pelvis revealed a 4.5 cm mass in segment 6 of the liver (Fig. 1b). A bronchoscopic biopsy was sufficient to make a diagnosis of NSCLC, adenocarcinoma. Testing for epidermal growth factor receptor (EGFR) mutations was negative. The patient was treated with 4 cycles of carboplatin and pemetrexed, but failed to respond. ALK reverse transcription-quantitative polymerase chain reaction (RT-qPCR) analysis of the scant remaining lung biopsy sample yielded a positive result. The patient was started on crizotinib and responded well in all disease areas, but progressed after 9 months in the previously noted lesion in segment 6 of

the liver, which increased in size from 2.5 cm at maximum response to crizotinib to 4 cm at progression. The patient was started on the second-generation ALK inhibitor ceritinib resulting in a significant reduction in the liver lesion to 2.8 cm (Fig. 2a). To reduce the potential for future ALK inhibitor-resistant clones in the liver lesion, SABR was employed. Fiducial markers were placed to aid cone-beam online positioning verification. The gross tumour volume (GTV) was defined as the visible tumour mass on planning 4D-CT scan. An internal GTV (iGTV) was created that incorporated all movements of the GTV in 10 breathing phases. The iGTV was then expanded by 10 mm in all directions to create the planning target volume (PTV). Volumetric modulated arc therapy (VMAT), with two partial arcs and 6 MV photons was used to deliver a dose of 54 Gy in 3 fractions over 5 days. Dose prescription was defined such that 100% of the prescription dose covered 95% of the PTV. Ceritinib was held for 5 days before and 5 days after radiation therapy. Fluorine-18-fluorodeoxyglucose-positron emission tomography (¹⁸F-FDG-PET) performed 3 months after SABR revealed no FDG-avid disease in the ablated area of the liver (Fig. 2B). However, a new 2.5-cm liver metastasis in segment 8 of the liver, outside the previously irradiated field, was now detected (Fig. 3a). This lesion was treated with RFA of the liver, which involves the ultrasound or CT scan-guided percutaneous or intraoperative insertion of a needle electrode into a tumour. A high-frequency alternating current is then generated resulting in heating from ionic agitation leading to coagulation necrosis of the lesion.³ For our patient, a 4-cm electrode was introduced into the liver percutaneously with burns performed in two probe positions. The tract was then burned during withdrawal of the probe. There was an interruption of ceritinib for only 3 days before and 3 days after the procedure. A PET scan 3 months after RFA revealed no

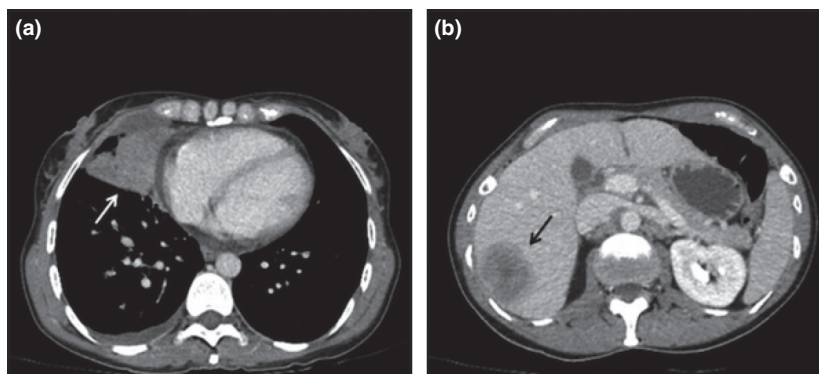


Figure 1. Computerized tomography scans of the chest (a) and abdomen (b) at diagnosis of stage IV NSCLC showing consolidation in the right middle lobe and a 4.5 cm mass in the liver.

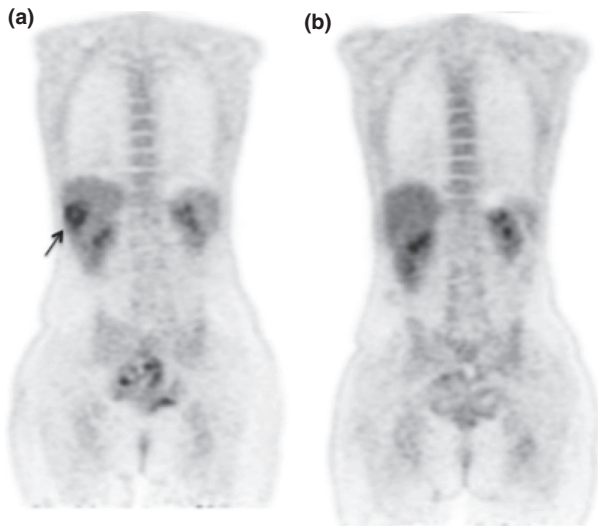


Figure 2. ^{18}F -FDG-PET scan coronal views of the abdomen before (a) and 3 months after (b) stereotactic ablative radiotherapy to an oligometastatic lesion in segment 6 of the liver. Normal FDG activity can be seen in the renal collecting system.

FDG-avid disease in the liver (Fig. 3b and c) or elsewhere in the body. The patient is now 28 months since her original diagnosis and 23 months since starting treatment with an ALK inhibitor.

Discussion

Treatment of ALK fusion-positive NSCLC with ALK inhibitors results in higher response rates and

progression-free survivals than observed with cytotoxic chemotherapy.^{4,5} However, most patients will eventually progress within 8–11 months, either in the brain and/or extra-cranial sites, as was the case with our patient.^{4,5} There is evidence suggesting that NSCLC patients with actionable mutations in the ALK or EGFR genes may have a longer progression-free survival if they are kept on targeted therapy while efforts to control oligometastases by other means are taken.⁶ In theory, resistant clones could be eradicated with local therapies, thus allowing for continued effectiveness of targeted therapy. The use of both SABR and RFA to treat oligoprogression of metastatic lesions in the liver allowed the continued use of ALK inhibitors in our patient for 23 months. It was recently demonstrated that SABR to oligoprogressive sites (1–4 sites) in ALK-positive NSCLC patients treated with crizotinib enabled continued administration of the ALK inhibitor for a median of 28 months compared with 10.8 months in those cases not treated with ablative therapy.⁷ Although our patient responded favourably to RFA, its role in metastatic NSCLC treatment needs to be further clarified in larger studies.

Conclusion

Our report provides support for the concept that subsets of NSCLC patients may have oligometastatic progression that can be controlled with local therapies. Although SABR is a frequently used modality for ablating NSCLC hepatic oligometastases, we have shown that RFA can also be effectively employed. Local ablative therapies should be

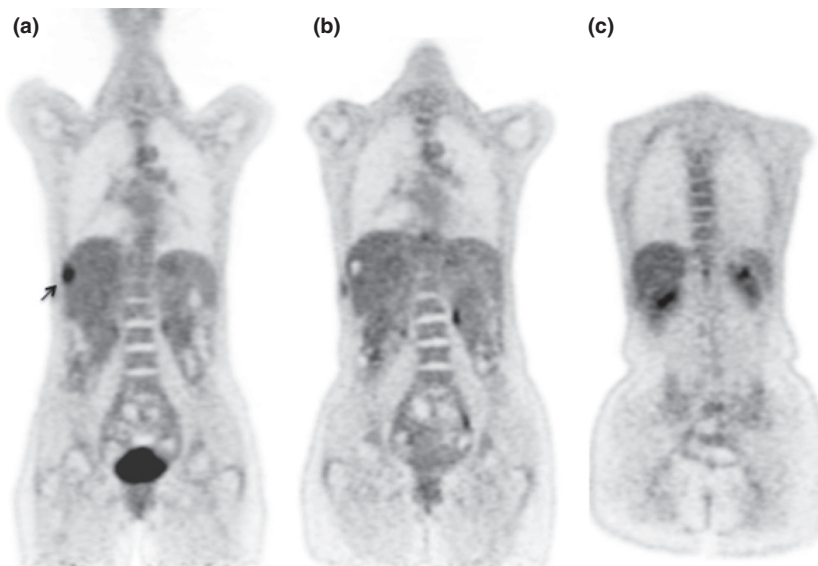


Figure 3. ^{18}F -FDG-PET scan coronal views of the abdomen before (a) and 3 months after (b) radiofrequency ablation to a metastatic lesion in segment 8 of the liver. There is no evidence of recurrent disease in segment 6 (c).

considered in oncogene-driven NSCLC oligometastatic progression, with the ultimate goal of improving survival.

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Conflict of Interest

D. Hout and S. W. Morris are employees and/or equity owners of Insight Genetics, Inc. The other authors have no conflicts of interest.

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