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Telehealth allows for clinical trial participation and multimodality therapy in a rural patient with stage 4 non-small cell lung cancer

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ABSTRACT

Oligometastatic non-small cell lung cancer (NSCLC) has a poor prognosis for rural patients with traditional therapies. Implementation of multi-modality systemic therapy in conjunction with surgical resection can dramatically improve overall survival, leading to clinical complete remission. The currently accepted indications for resection in oligometastatic NSCLC include brain and adrenal metastases. Rural populations are known to have disparities in care of complex malignancies and the use of telehealth has been shown to improve outcomes. We present a case of a rural patient with stage IV NSCLC, who was able to participate in two clinical trials, undergo trimodality therapy, and remain disease-free for 18 months, whose care was facilitated via telehealth video conferencing with a tertiary care center.

1. Introduction

Non-small cell lung cancer (NSCLC) remains the highest mortality malignancy throughout the developed world, in large part because most patients have advanced stage disease at presentation [1]. Nearly 50% of NSCLC patients have distant metastases on presentation, with an associated 5 year survival less than 5% in stage IV patients [1,2]. Survival outcomes are reduced in patients from rural environments, often due to delays in diagnosis, treatment, and follow up as well as unavailability of advanced care including multi-modality treatment options and enrollment in clinical trials [3–6]. Systemic therapy is the primary method of treatment in these patients with local or distant metastatic disease, and when combined with appropriate surgical resection can lead to significantly improved survival rates [7].

Hellman and Weichselbaum described the term oligometastasis in 1995, which is now synonymous with 1–5 isolated distant metastases [8]. Outcomes in NSCLC patients with oligometastases are superior to widely metastatic disease but remain poor, and data is limited to retrospective single institution series [9]. The current National Comprehensive Cancer Network (NCCN) guidelines currently recommend surgical resection of lung primary tumors in oligometastatic disease only in those patients with either isolated brain or adrenal metastases [10]. There is a paucity of evidence for resection of primary lung tumors in patients with oligometastatic disease to other sites such as to the bones, vertebrae, liver, distant lung sites, and soft tissue, with variable success [11–14].

It is well known that cancer patients with limited access to high quality specialized medical care have worse outcomes compared to their counterparts near large medical centers with medical and surgical oncologic specialists [4,6,15]. In order to surmount the challenge of providing such rural patients with optimal multidisciplinary oncologic care, many centers have turned to telemedicine via videoconferencing [16–18]. Initial studies from multiple institutions have demonstrated that patient discussion in multidisciplinary video tumor boards improves patient satisfaction, provides more patients access to definitive surgical care, and does not significantly delay oncologic therapies [16,17,19,20]. However, these data are limited in an era where more and more institutions are using telemedicine to facilitate the care of these advanced stage cancer patients [21].

We present a report of a rural patient with T2N2M1b NSCLC with oligometastasis to the femur who participated in two therapeutic clinical trials, underwent multimodality treatment with chemoradiation at the local rural cancer center, and surgical intervention at the partnering tertiary care center through the successful coordination of telemedicine. The patient has been without evidence of disease for 18 months.

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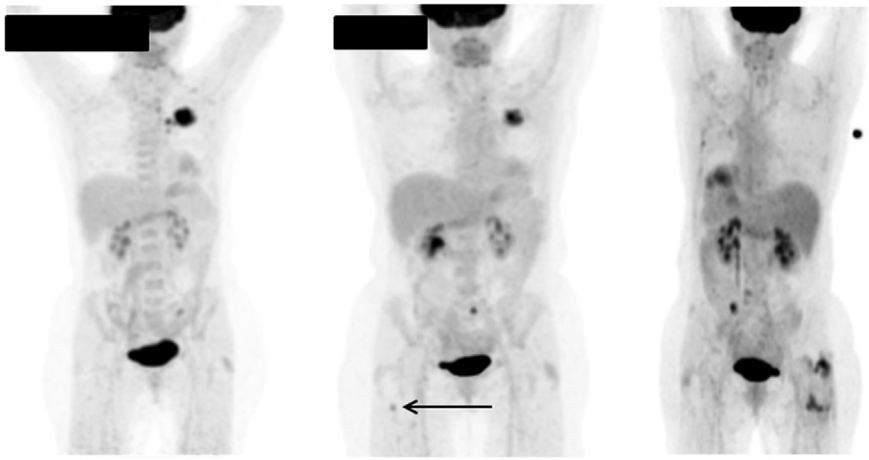

Fig. 1. a-c. (a) Initial positron emission tomography (PET) scan on 6/4/13 showing left upper lobe pulmonary mass and mediastinal/hilar lymph nodes. (b) Repeat PET scan on 9/12/13 after neoadjuvant chemoradiation showing an interval decrease in pulmonary mass size and lymphadenopathy as well as a new foci in the right femur (denoted by solid arrow). (c) Most recent PET scan on 3/17/16 showing no evidence of residual tumor or metastases.

2. Presentation of case

A previously healthy 59 year old Caucasian woman with a distant 2 pack-year smoking history was diagnosed with clinical stage IIIA (T2aN2M0) adenocarcinoma primary lung cancer in May 2013 after presenting with shoulder pain (Fig. 1). A computed tomography (CT) scan of the chest revealed a 4.8 cm pulmonary mass in the left upper lobe encasing the left upper lobe bronchus, as well as a suspicious 1.8 cm lymph node within the left aortopulmonary window. Core needle biopsy confirmed well-differentiated adenocarcinoma in-situ. Positron emission tomography (PET) imaging was concerning for metastases in mediastinal and left hilar nodes (Fig. 1a). Brain metastases were excluded with magnetic resonance imaging (MRI). Her case was discussed during the scheduled weekly multidisciplinary telehealth tumor board with the National Cancer Institute Comprehensive Cancer Center (NCI-CCC) partner. The consensus recommendation was invasive mediastinal staging, which was subsequently performed at the partnering NCI-CCC. Her mediastinum was staged with video cervical mediastinoscopy in June 2013; ten lymph nodes were negative for malignancy. At this time she began neoadjuvant chemoradiation at her local rural cancer center as part of planned trimodality therapy for stage IIIA disease. Her chemotherapy regimen consisted of two cycles of cisplatin and etoposide concurrently with 50.4 Gy given in 28 fractions of radiation to the involved lung and mediastinum.

A restaging PET scan was completed in September 2013, which showed a decrease in primary tumor size to 4.5 cm and resolution of fludeoxyglucose (FDG) avid nodal disease. However a new 1.0 cm focus of activity in the right femur was identified and CT-guided biopsy demonstrated bone metastasis (Fig. 1b). She subsequently completed 2 cycles of carboplatin, paclitaxel, and bevacizumab induction prior to 36 Gy given in 12 fractions of radiation to the right femur. At this point, an EGFR mutation was identified in the primary tumor and after multidisciplinary discussion via telehealth, she was enrolled in therapeutic clinical trials for both zoledronic acid and erlotinib in April 2014 at her local cancer center. For the remainder of 2014, imaging revealed resolution of her femur lesion and intrathoracic disease stability and her case was represented at multidisciplinary tumor board via telehealth for consideration of resection of her primary tumor.

In February 2015, she underwent left upper lobe lobectomy via thoracotomy secondary to central tumor location at the NCI-CCC partner. Her surgical pathology revealed a 0.6 cm mass with $< 10\%$ viable residual tumor, negative margins, and 13 lymph nodes negative for tumor (ypT1aN0M0). As of August 2016, she is without evidence of disease and she remains on the zoledronic acid and erlotinib protocols. Her only complication was a right hip fracture sustained after a ground level fall while hiking that required open reduction and internal fixation. She otherwise has been in excellent health with the functional capacity to continue her hiking.

3. Discussion

There are a significant number of surgical case series describing the treatment of oligometastatic NSCLC with isolated brain or adrenal metastases. These studies have shown a median overall survival of 7 to 27 months [7,9,11–14,22]. However, there is insufficient evidence on the surgical outcomes of oligometastatic NSCLC patients with other metastatic sites, likely driven by the lack of NCCN guideline support for surgical resection in these patients. Recently there have been increasing reports on the treatment of patients with oligometastases to the bones, vertebra, liver, intrapulmonary sites, and other soft tissue sites. (Table 1) Median overall survival in these patients ranges from 13 to 21 months, with between 15 to 30% of patients achieving complete remission such as was seen in our patient. The largest case series reported by Griffioen et al. had only 18% of patients with bony oligometastases, and 62% of their patients ultimately died of their cancer with a median overall survival of 13 months [7]. Up to 59% of their patients had brain oligometastases which significantly worsens the overall prognosis in these NSCLC patients [23–25]. As such, the survival seen in case series with a significant proportion of patients with brain oligometastases may not generalize well to patients such as our own with an isolated extracranial oligometastasis.

A prospective case series by De Ruysscher et al. described 18% of patients having bony oligometastases and a median overall survival of 13 months [14]. Only 23% of their patients underwent resection of the primary tumor, limiting the applicability of this data to patients like our own who had successful downstaging of her disease with neoadjuvant therapy to nodal and metastatic negative disease prior to surgery. However, this growing body of literature has influenced the recent European Society for Medical Oncology (ESMO) 2014 guidelines which emphasizes a potential role for radical resection in NSCLC patients with extracranial oligometastatic sites [26]. The ESMO guidelines stress the need to enroll these patients in prospective treatment trials to better guide treatment protocols.

Our case report describes the successful treatment of a patient with stage 4 NSCLC with oligometastasis to the femur with neoadjuvant chemoradiation and surgical resection. Her case is novel in that her nodal and bony metastases responded completely to induction therapy,