Adjuvant Radiation Therapy For Wedge-Resected Non-Small Cell Lung Cancer Adjacent To A Large Thoracic Aortic Aneurysm: A Case Report And Review Of The Literature

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Abstract

Lung cancer is the leading cause of cancer death in the United States, with an estimated 222,500 new cases diagnosed in 2010; non-small cell lung cancer (NSCLC) accounted for approximately 85% of these malignancies. Treatment for early stage NSCLC in an operable patient involves lobar resection. Thoracic aortic aneurysms form as a result of exposure to smoking, hypertension, atherosclerosis, and genetic connective tissue disorders. The literature is silent on the optimum course of action when the anatomic lobar resection for NSCLC is limited by a thoracic aortic aneurysm, particularly when a close surgical margin indicates consideration of adjuvant radiation therapy. Although there is some literature documenting the radiation injury pattern to intact great blood vessels, the literature is silent on the potential for further injury to the wall of the great vessels in the presence of an existing aneurysm. With the increase in the use of definitive stereotactic body radiotherapy for early stage NSCLC in medically inoperable patients, there is a potential for an increased risk of vascular injury secondary to radiation in patients whose vessels already have baseline atherosclerotic damage.
Herein, we report a case of a patient diagnosed with wedge-resected early stage NSCLC with close margin in the immediate vicinity of a pre-existing large thoracic aortic aneurysm.

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INTRODUCTION

Lung cancer is the leading cause of cancer death in the United States, with an estimated 222,500 new cases diagnosed in 2010;[1] non-small cell lung cancer (NSCLC) accounted for approximately 85% of these pulmonary malignancies.[2] The primary risk factor for lung cancer occurrence and mortality is tobacco smoking, which accounts for 85-90% of lung cancer deaths.[3] Treatment for early stage NSCLC in an operable patient involves anatomic (lobar) resection if possible. Segmentectomy or wedge resection with a 2 cm margin is appropriate in a patient with poor pulmonary reserve or a major co-morbidity that precludes lobar resection.[4]

Conversely, aortic aneurysms involving the thoracic aorta occur with an incidence between 5 and 10 per 100,000, of which only 31% affect the descending thoracic aorta.[5, 6] Risk factors leading to aneurysm formation include smoking, hypertension, atherosclerosis, and genetic connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome. Ultimately, it is cystic medial degeneration that is the common pathway of response to these risk factors. Treatment of descending thoracic aortic aneurysms is

evolving as the technology for endovascular repair improves. Current recommendations are for surgical intervention of the descending thoracic aorta when it approaches 6.5 cm in diameter and 6.0 cm in diameter in patients with connective tissue disorders. Symptomatic patients and those with a rapid growth rate in excess of one cm per year should receive acute intervention. Obviously, those with an acute rupture or complication-specific Stanford B dissection need emergent intervention.

Unfortunately, the literature is silent on the optimum course of action when the ability to achieve an anatomic lobar resection for NSCLC is limited by the presence of a synchronous thoracic aortic aneurysm, and in particular when the presence of a close surgical margin at wedge resection indicates consideration of adjuvant radiation therapy. The literature is also silent on the potential for further, radiation therapy-induced injury to the wall of the great vessels in the presence of an existing aneurysm.

Herein, we report a case of a patient diagnosed with wedge-resected early stage NSCLC with close margin in the immediate vicinity of a pre-existing large thoracic aortic aneurysm.

CASE REPORT

The patient was a 63-year-old Caucasion male with a medical history significant for an 80 pack-year smoking history, hyperlipidemia, and hypertension and a known history of a Stanford Type B type dissection and persistent descending thoracic aneurysm (DTA) of 5.0 cm diameter. A follow-up computed tomography (CT) scan of the chest demonstrated a stable DTA, but unfortunately the scan also demonstrated a new left upper lobe pulmonary nodule. After a CT-guided biopsy failed to reveal a specific diagnosis of this nodule, it was resected via wedge resection using video-assisted thorascopic surgery (VATS). Surgical pathology findings revealed a 1.2 cm adenocarcinoma with a 4 mm margin. Further staging failed to demonstrate evidence of nodal or metastatic disease. The case was discussed at a multidisciplinary tumor board conference and further input was provided by a second thoracic surgeon at an outside institution. Although completion lobectomy was felt to be technically possible, the risk of injury to the aorta was felt to be prohibitively high without planning for a concominant descending aorta repair or pre-operative endovascular repair. Unfortunately, multidisciplinary review of his CT aortogram found his proximal landing zone unsuitable for endovascular repair secondary to a very acute aortic arch and close proximity of this aortic arch branching which would require a debranching procedure. The patient was adamant that he did not want to incur the risk of paralysis associated with open repair of his aneurysm. Therefore, no additional therapy was recommended. He was followed with serial re-imaging and clinical exams for the next 18 months at which time a positron emission tomography (PET)/CT scan showed two additional lesions with increased metabolic activity adjacent to the wedge resection scar line in the left upper lobe. Both of the new lesions were amenable for wedge resection and one of them demonstrated adenocarcinoma. His case was again discussed at a multidisciplinary tumor board and the decision was made to consider adjuvant radiation therapy. A subsequent PET/CT scan prior to the initiation of radiation therapy indicated that although there was no new sign of distant metastases, an area in the left hilum demonstrated and increase in metabolic activity that was suspicious for a metastatic process. This area had been previously noted on PET/CT scans, but had been thought to be due to inflammation associated with his aortic aneurysm. Due to the possibility of residual gross disease, his radiation therapy was planned to encompass this area as well as the wedge resection staple line with margin and concurrent chemotherapy was administered. His gross tumor volume (GTV) consisted of the areas of PET-avidity with a 1 cm expansion of the GTV to arrive at a clinical target volume (CTV). The CTV was expanded by 0.5 cm radially to arrive at a planning target volume.

He received 200 centigray (cGy) daily fractions to the PTV delivered in an anterior-posterior/posterior-anterior field arrangement with a subsequent off-cord boost to a final dose of 6,600 cGy with six weekly cycles of carboplatin and paclitaxel. He experienced mild intermittent odynophagia and a single episode of neutropenia that delayed one cycle of chemotherapy but he did not require hospitalization. His most recent PET/CT scan, completed eleven months after radiation therapy showed no evidence of distant or local recurrence with only residual inflammatory type pulmonary changes within the radiated lung parenchyma and no change in his TAA. His most recent pulmonary function tests indicate essentially no change in his pulmonary status since completing his surgery.

DISCUSSION

As was indicated above, the treatment of choice for early stage node negative NSCLC is surgical resection, preferably with an anatomic lobar procedure. In cases where lobar

resection is not possible due to poor lung function or other major co-morbidity, a segmentectomy or wedge resection can be accomplished.[4] An earlier prospectively randomized trial demonstrated a tripling of the local recurrence rate in this setting from 6% to 18%,[7] while a more recent, albeit, single institution, retrospective review, found no difference in locoregional recurrence or disease-free survival between the two resection strategies when the tumor was less than 2 cm in size.[8] Post-operative radiation therapy is indicated in the setting of a close or positive margin, but in the absence of these criteria, the PORT meta-analysis indicated a fairly clear potential for harm in early stage NSCLC patients.[9] In this patient with an oncologically sub-optimal resection, a margin less than 2 cm, and a proven history of recurrence after prior wedge resection, adjuvant radiation therapy was offered to limit the risk of local recurrence. Due to the subsequent findings on pre-radiation therapy re-staging PET/CT of a left hilar area that had increased in activity, the portals were increased to cover this new area, the planned dose was increased to a definitive therapy level, and concurrent chemotherapy was offered.

There is very little information in the recent literature discussing the direct resultant injury to the great vessels from radiation therapy. There are several small collected series dealing specifically with arterial injury[10, 11] (neither of which discuss thoracic aorta injury), but the largest collected series that discusses aortic injury specifically (three cases) appears to be by Fajardo et al from 1975.[12] These authors note that although chronic injury patterns are noted in the great vessels after irradiation, “the most important causes of spontaneous rupture of irradiated elastic arteries are local conditions independent of radiation.” These conditions include surgical manipulation which disrupts the adventia and its vessel nurturing vaso vasorum, as well as local chronic infection.

Regarding late injury to normal, intact vessels, Mesurolle et al indicate that radiation-induced vasculopathy has a latency of approximately 10 years and results in calcification, stenosis, and occlusion rather than perforation or pseudoaneurysm[13]. Benson notes a similar time course for arterial injury with intimal damage and thrombosis within 5 years, fibrotic occlusion within 10 years and the development of atheromatous plaque and periarterial fibrosis within 20 years.[10]

As noted above, the scant case literature regarding direct radiation injury to the aorta from radiation and/or concurrent chemotherapy deals primarily with those injuries to an otherwise “healthy” aorta; albeit in older patients that most likely have some degree of atheromatous plaque formation. These injuries are reported in the literature as they are the few that have resulted in catastrophic fistula formation or aortic rupture with variable latency periods from weeks to 30 years post therapy.[14-18] The primary malignancy involved is esophageal cancer, but two of these reports dealt with a lung cancer primary and subsequent stenting of the esophagus secondary to radiation-induced stricture. At the time of their aortoesophageal fistulas there was no evidence of malignancy in the vicinity of the communication. Regarding the injury latency noted above, an autopsy specimen of a patient that had undergone definitive chemoradiotherapy for esophageal cancer to a dose 5,940 cGy was noted to have fibrinoid necrosis in the esophageal wall with the lethal perforation center of this area, with no evidence of malignancy nearby.

The only manuscript discussing radiation therapy delivered to the mediastinum in the presence of a known thoracic aortic aneurysm is a case of preoperative therapy for a thymic carcinoma. These authors delivered 4,500 cGy to the carcinoma which was adherent to but not invasive of, a TAA. At surgery, presumably four to six weeks after radiation therapy, the carcinoma was “firmly adherent” to the TAA, and a combination of sharp and blunt dissection was used to separate the mass from the aortic wall. The authors note that they did not deliver postoperative radiation therapy as they felt additional radiation would cause further fibrosis, ischemia, and calcification of the aortic wall and the patient was doing well at last follow-up ten months after surgery.[19]

CONCLUSION

In conclusion, without adjuvant/definitive therapy, this patient would almost certainly have died of his primary lung malignancy. With aggressive treatment, he could also die from treatment-related side effects, both from the lung parenchymal injury or further weakening and subsequent rupture of his TAA. Although the plural of anecdotes is not data, in unique clinical situations, there are times when anecdotes and clinical judgment are all the guidance that is available. Careful evaluation and management of patients in multidisciplinary clinical setting, as well as a very thorough informed consent process are essential to ensuring the best possible treatment and outcome.

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