Management of a Superior Sulcus (Pancoast) Tumor

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The patient is a 74-year-old gentleman who presented with a visual disturbance and right shoulder pain. On routine chest x-ray, he was found to have a right apical lung mass.

History
This patient sought medical attention following an episode of transient visual loss. Upon further questioning, he admitted to a deep aching pain in his right shoulder but no arm pain or weakness. He also complained of a productive morning cough but denied hemoptysis. There was no accompanying history of dyspnea, weight loss, or fatigue. His review of systems was unremarkable. He had been previously well, except for a past medical history of hypertension treated with amlodipine besylate and multiple skin cancers, which had been removed. The visual disturbance resolved spontaneously and was attributed to a transient ischemic attack (TIA); he was prescribed aspirin therapy. He had a 60 pack-year history of cigarette smoking but stopped 2 years ago. There was no family history of cancer.

Physical Examination
The physical examination revealed a healthy-appearing gentleman who looked his stated age. His vital signs were normal. His Eastern Cooperative Oncology Group (ECOG) performance status was 1. Examination of his cranial nerves revealed a subtle miosis of his right pupil, but no definite ptosis or anhidrosis. No cervical or supraclavicular lymphadenopathy was evident. Dullness to percussion was noted in the apex of his right lung. His cardiac, abdominal, and musculoskeletal examinations were unremarkable. No additional neurologic findings were observed. Specifically, there was no evidence of weakness or muscle atrophy of the right arm.

The initial investigations performed at his local hospital included a chest x-ray, chest computed tomography (CT) and brain magnetic resonance imaging (MRI) scans. In addition, the patient had pulmonary function tests, which revealed a forced expiratory volume in 1 second (FEV1) of 1.92 L (58% of predicted value) and a diffusing capacity of the lung for carbon monoxide (DLCO) that was...
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62% of predicted.

Discussion

Initial Imaging

Dr. Karen Kelly: Dr. Garg, could you please review the outside imaging studies? FIGURE 1

CT, PET, and Fused CT/PET Imaging

Dr. Kavita Garg: The chest x-ray shows a right apical mass. This is better characterized on the subsequent chest CT, which confirms the large right upper lobe lung mass, measuring 7.5 x 6.5 x 8.0 cm and extending from the lung apex to the level of the carina (Figure 1). No enlarged hilar or mediastinal nodes are seen. Probable extension into adjacent thoracic wall is evident. No evidence of disease is appreciated in his liver, adrenal glands, or visualized bones. His brain MRI is negative for metastasis.

Further Assessment

Dr. Kelly: What do you think is the best approach for obtaining tissue—a CT-guided needle biopsy or a bronchoscopy?

Dr. Patrick Nana-Sinkam: The utility of fiberoptic bronchoscopy depends on both location and size of the lesion. In the case of peripheral lesions such as this one, bronchoscopy has only a modest diagnostic sensitivity of 33% in lesions < 2 cm and 62% in lesions > 2 cm.[1] However, bronchoscopy may be particularly useful for assessment of the central airways. Transthoracic needle aspiration (either CT- or ultrasound-guided) carries a much higher sensitivity (85%-95%) in larger peripheral lesions.[2]

Dr. Kelly: A CT-guided fine-needle aspiration (FNA) was performed. Dr. Franklin, please review the biopsy result.

Dr. Wilbur Franklin: The FNA shows a poorly differentiated non-small-cell lung cancer (NSCLC).

Dr. Kelly: Dr. Garg, would this patient benefit from a positron-emission tomography (PET) scan?

Dr. Garg: Yes. This patient appears to have a localized lesion and is an ideal candidate for a PET scan to confirm or refute the staging based on CT. A recent meta-analysis of 17 studies including 883 patients compared the sensitivity and specificity of [18F]-fluorodeoxyglucose (FDG)-PET with that of CT for detecting mediastinal lymph node metastases.[3] The sensitivity and specificity of CT for detecting mediastinal lymph node metastases was 59% and 78%, respectively. PET performed significantly better, with a sensitivity and specificity of 83% and 92%, respectively.[3] The performance of PET may be further improved by the use of integrated PET/CT.[4]

FDG-PET also is important for detecting extrathoracic disease. It appears to be superior to CT for detecting adrenal or liver metastases and to bone scans for detecting bone metastases. A prospective randomized study has shown that FDG-PET staging reduced the incidence of unnecessary surgery by 25%.[5] However, it is important to remember that inflammatory cells can also take up FDG, so PET false-positives can be seen in active inflammatory or infectious diseases.

Mediastinoscopy

Dr. Kelly: This patient did have a PET scan, which showed a maximal standardized uptake value (SUV) of 9.2 in the region corresponding to the lung mass. No metabolic activity was seen in the mediastinum or in extrathoracic sites. Dr. Mitchell, with a negative CT and PET scan, does the patient need a mediastinoscopy?

Dr. John Mitchell: Yes, a mediastinoscopy is appropriate. As Dr. Garg pointed out, false-negative results can occur with PET scans approximately 5% to 10% of the time.[3] Given the patient's age, pulmonary reserve, and comorbidities of hypertension with a recent TIA, I would be hesitant to perform a
resection without definitive staging to guide my decision. Of particular concern is the fact that several series of patients with superior sulcus NSCLC have shown poor survival despite surgery in the presence of mediastinal lymph node (N2) involvement.[6-8]

The long-term analysis of Intergroup trial 0319 did not show a survival benefit for the addition of surgery after neoadjuvant chemoradiation in patients with stage IIIA(pN2) NSCLC and concluded that concurrent chemoradiation is the standard of care in this situation.[9] For this reason, detailed evaluation of the mediastinum is particularly important in this patient population, and we elected to proceed to mediastinoscopy with this gentleman. Dr. Franklin, what did the mediastinoscopy show?

Dr. Franklin: We received multiple lymph node biopsies (2R, 4R, 4L, and level 7). There was no histologic evidence of malignancy in any of the sections examined.

Dr. Kelly: That’s good news. Dr. Weiss, what is the clinical stage of this patient’s disease?

Dr. Glenn Weiss: On the basis of a tumor with extension to the chest wall with no evidence of nodal involvement or extrathoracic disease, this patient’s tumor is clinical stage T3, N0, M0. While this had been previously classified as stage IIIA, in the new American Joint Committee on Cancer (AJCC) staging system, it has been reclassified as stage IIB with an expected 5-year survival rate of 22% following surgery.[10]

Pancoast Tumors

Dr. Kelly: Dr. Solomon, what can you tell us about Pancoast tumors?

Dr. Benjamin Solomon: Pancoast tumors or tumors of the superior sulcus of the lung have been defined as apical lung tumors that involve structures of the apical chest wall above the level of the second rib.[11] They derive their eponymous nomenclature after descriptions of their radiologic and clinical features by Dr. Henry Pancoast in 1924 and 1932.[12,13] NSCLC is the predominant cause of Pancoast tumors. However, only about 3% of all NSCLC cases involve the superior sulcus. Other primary tumors have rarely been reported as causes of Pancoast tumors, including small-cell lung cancer, carcinoid and metastatic tumor deposits, and nonmalignant conditions such as amyloidosis.

As a result of their anatomic position, these tumors cause a classic combination of symptoms that constitute Pancoast syndrome: shoulder or arm pain and Horner syndrome. Pain is the most common presenting syndrome. Typically this involves the shoulder region and radiates inferiorly down the medial (ulnar) aspect of the arm and is due to involvement of the inferior brachial plexus. In time, this can become associated with weakness of the arm and wasting of the small muscles of the hand. Pain can also occur as a result of invasion of the ribs or vertebrae. The nonspecific nature of this pain can lead to a delay in diagnosis. Horner syndrome—the triad of ptosis, miosis, and anhidrosis—arises due to involvement of sympathetic nerve fibers in the stellate ganglion.

As Dr. Mitchell pointed out, it is important to adequately stage patients with tumors of the superior sulcus. Most patients have T3 or T4 tumor. Survival has been shown to be better for T3 than T4 tumors, and mediastinal lymph node involvement is a strong, negative prognostic factor. The completeness of resection is another important prognostic factor.

Treatment Evolution

Dr. Kelly: What treatment should a patient with this type of tumor receive, Dr. Bunn?

Dr. Paul A. Bunn, Jr: The treatment of tumors of the superior sulcus has evolved substantially in recent times. These tumors were considered incurable until Chardack and MacCallum reported good long-term survival in a patient who was managed with surgical resection followed by postoperative radiation.[14] Shaw, Paulson, and colleagues then introduced the use of radiotherapy followed by resection.[15] This approach became the standard approach used for most of the next 40 years and was associated with 5-year survival rates of about 30%.

In the largest reported series of patients with tumors of the superior sulcus, managed predominantly with preoperative radiotherapy followed by surgery, the complete resection rate was 56%, and 5-year survival was 46% for stage IIB, 0% for stage IIIA, and 13% for stage IIIB disease.[7] These modest figures highlighted the need to explore alternative strategies to increase complete resection rates and overall survival.

Trimodality Therapy

The feasibility of trimodality therapy—concurrent chemoradiation followed by surgery—in stage IIIA and selected IIIB NSCLC was demonstrated by the Southwest Oncology Group (SWOG) 8805 trial.[16] Martinez-Monge et al reported a small series of 18 patients with superior sulcus tumors treated with
chemoradiation prior to surgery, with a 76% complete resection rate and 56% 4-year survival.[17] This led to a phase II study, SWOG 9416 (intergroup trial 0160), which again evaluated this approach in the setting of superior sulcus tumors.[18] In this trial, 111 patients with mediastinoscopy-negative T3-4, N0-1 superior sulcus NSCLC were treated with preoperative chemotherapy (two cycles of cisplatin, 50 mg/m2 on days 1, 8, 29, and 36, and etoposide, 50 mg/m2 on days 1, 8, 29, and 36) given concurrently with thoracic radiotherapy to 45 Gy, followed by surgery and then two further cycles of chemotherapy with cisplatin and etoposide. Eighty-three patients (75%) underwent thoracotomies, of which 76 (92%) had complete (R0) resections and 28 (34%) had a complete pathologic response. The 2-year survival was 55% for all patients and 70% for patients who had an R0 resection.

Similar results have subsequently been reported in a Japan Clinical Oncology Group study (JCOG-9806) utilizing a different chemoradiation regimen (mitomycin, vindesine, and cisplatin).[19] As a result of the improved complete resection rate and survival observed in these trials, induction chemoradiation followed by surgical resection is the current standard of care for patients with superior sulcus NSCLC.

FIGURE 2

Schema of SWOG 0220 Trial

A current SWOG study (0220) is evaluating whether postoperative chemotherapy with docetaxel (Taxotere) improves outcomes after induction PE (cisplatin [Platinol], etoposide) and radiotherapy followed by surgery (Figure 2). The rationale for this design is based on the results of SWOG 9504, a phase II trial of three cycles of consolidation docetaxel after concurrent chemoradiation in patients with stage IIIB NSCLC that resulted in a median survival of 26 months and a 5-year survival of 26%.[20] If this patient is a surgical candidate, I would recommend enrollment on SWOG 0220.

Dr. Kelly: Dr. Weyant, do you think this patient is a surgical candidate?

Dr. Michael Weyant: Age alone is not a contraindication to surgery in this 74-year-old gentleman with a good performance status. His pulmonary function is of more concern. Although it is likely on the basis of the current imaging that a lobectomy is the operation of choice, in some circumstances, such as extension of the tumor through the fissure or involvement of the proximal bronchial stump, we may need to perform a pneumonectomy.

We generally would like to see a preoperative FEV1 of 2 L in patients for whom a pneumonectomy is considered. But perhaps more important is assessment of his predicted postoperative pulmonary function, which we could establish by split perfusion scan using intravenous technetium-99m. Patients with a predicted postoperative FEV1 Pound Sterling 1 L have a high incidence of postoperative pulmonary and cardiac complications and operative mortality.[21] In any case, as I'm sure Dr. Nana-Sinkam would agree, we should optimize his pulmonary function. I would also think it important for this patient to have a cardiology assessment given his hypertension and recent TIA.

Optimizing Pulmonary Function

Dr. Kelly: Dr. Nana-Sinkam, what suggestions do you have to optimize his pulmonary function?

Dr. Nana-Sinkam: The approach to preoperative pulmonary assessment should include assessment for adequate oxygenation, exercise tolerance, intrinsic lung disease, and concomitant illnesses that may impede pulmonary function such as cardiac diseases, pulmonary hypertension, obesity, hypoventilatory states, and neuromuscular disease. In this case, it would be important to determine if the patient does, in fact, have underlying lung disease that may respond to therapy. Spirometry may be used to determine if there is an obstructive or restrictive defect. This could then be confirmed with full pulmonary function tests and possible further imaging (eg, high-resolution CT
The patient's pulmonary function suggests significant airflow limitation, which is likely secondary to smoking-related lung disease. In this case, I would evaluate the patient for adequate oxygenation (6-minute walk) and supplement as necessary. I would also institute inhaler therapy to determine if there is response to bronchodilators and evaluate for adequate nutritional status. Lastly, I agree with Dr. Weyant that a cardiology evaluation is in order, as this may directly affect the patient's pulmonary function.

**Radiotherapy Considerations**

Dr. Kavanagh, do you have concerns about radiation in this patient with borderline pulmonary function?

Dr. Brian Kavanagh: Certainly, a potential consequence of chemoradiation is a reduction in DLCO—changes in FEV are more variable. The most important predictor of this is radiation dose delivered to normal lung, but this risk is minimized with current three-dimensional conformal techniques. Nonetheless, I would agree that chemoradiation followed by surgery, either on or off study, should be our treatment recommendation. If the patient is found to be unsuitable for surgery after his induction chemoradiation dose (4,500 cGy), I would continue radiation therapy to a total of 6,100 cGy, preferably with concomitant chemotherapy. Hopefully, the decision to operate or not can be made early so there is not a long break in definitive chemoradiation.

Dr. Kavanagh: The SWOG 9416 study found a high incidence of brain relapse in patients treated with trimodality therapy. Dr. Gaspar, what are your thoughts about prophylactic cranial irradiation?

Dr. Gaspar: It is interesting to note that the new treatments appear to have changed the pattern of failure in this disease. Historically, about 60% to 70% of patients developed recurrent disease, and for the majority of these, the first site of failure was predominantly locoregional. However, in the SWOG 9416 study, the brain was the most common single site of relapse (in 16 of 39 patients, or 41%).[18] A similar finding was noted in a recent retrospective study from the University of Maryland, where brain metastases occurred in 9 (50%) of 18 patients who relapsed after trimodality treatment.[22] This pattern of relapse is very reminiscent of that seen in other chemoradiation studies for stage III NSCLC[23] and, as you point out, raises the issue of whether prophylactic cranial irradiation should be offered to these patients. Obviously, there are too few patients with Pancoast tumors to perform a randomized study in this population alone. However, an ongoing prospective randomized study by the Radiation Therapy Oncology Group (RTOG 0214) compares prophylactic cranial irradiation to observation in patients with treated stage IIIA or IIIB NSCLC.

As for this patient, there is insufficient evidence at this point to support the use of prophylactic cranial irradiation outside the context of a clinical trial, but I would recommend yearly brain MRI given the concerning data.

**Subsequent Management**

The patient was enrolled on SWOG 0220. He tolerated platinum/etoposide chemotherapy and concurrent radiotherapy with minimal toxicity consisting of nausea. He did not develop esophagitis. A restaging CT showed a partial response, and he proceeded to surgical resection. A lobectomy was performed via an anterior (Dartevelle) approach with an R0 resection of an AJCC pathologic stage IIB (T3, N0, M0) adenocarcinoma. Subsequently, the patient completed the planned three cycles of consolidation docetaxel without sequelae. He is disease-free 1 year later.

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