Clinical-pathologic conference in general thoracic surgery: Disseminated nocardiosis presenting as Pancoast syndrome

Marco Larobina, MBBS (Hons)^a
Catriona McLean, MD, FRCPA^b
B. B. Davis, FRACS^c

Pancoast syndrome^{1,2} is a clinical constellation of an apical lung lesion and neurologic sequelae caused by compression of the adjacent lower trunk of the brachial plexus and sympathetic trunk in the superior pulmonary sulcus. The syndrome is usually associated with bronchogenic carcinoma, most commonly squamous cell carcinoma.

This article presents the first reported case of nocardiosis mimicking Pancoast syndrome in the immunocompetent individual. This highlights the importance of accurate histologic and microbiologic diagnosis before definitive resection of a presumed bronchogenic carcinoma.

Clinical Summary

A 61-year-old woman presented with a left upper lobe lung lesion and clinical evidence of T1 neuropraxia.

Her history included carcinoma of the ovary treated with surgical resection and adjuvant chemotherapy with paclitaxel (Taxol) 10 months before presentation. She had a 20 pack-year history of smoking, ceasing 10 years before, and was hospitalized as a child with pneumonia. She had taken only hormone replacement therapy before the diagnosis of the ovarian carcinoma.

She had become unwell in January 2001, with generalized lethargy, an intermittent cough, and a reduction in exercise tolerance from several kilometers to several hundred meters. Left shoulder pain extending down her arm preceded the development of some mild weakness of her left thenar eminence. She had had several upper respiratory illnesses in December but had no fevers or sweats, hemoptysis, change in voice, weight loss, or other neurologic symptoms.

Chest radiography revealed a mass in the superior pulmonary sulcus (Figure 1), which, on computed tomographic (CT) scanning, was shown to arise from the apex of the left lung and extend into the chest wall (Figure 2). This is highly suggestive of invasive carcinoma. Two percutaneous biopsy specimens were nondiagnostic, showing no malignant cells, occasional granulomata, and no organisms. Single photon emission computed tomography (SPECT) scanning showed soft tissue inflammation in the left supraclavicular fossa, with involvement of the first rib. The features were considered nonspecific. Anterior mediastinotomy failed to reveal any evidence of metastatic tumor, and the patient was transferred to our institution for definitive surgical intervention.

Registrar, Department of Cardiothoracic Surgery,^a the Department of Pathology,^b and the Cardiothoracic Unit,^c The Alfred, Melbourne, Australia.

Received for publication June 20, 2002; accepted for publication July 15, 2002.

Address for reprints: Marco Larobina, MBBS (Hons), The Alfred, Commercial Road Prahran, Melbourne, Victoria 3181, Australia (E-mail: marcolarobina@hotmail.com).

J Thorac Cardiovasc Surg 2004;127:568-71
0022-5223/\$30.00

Copyright © 2004 by The American Association for Thoracic Surgery

doi:10.1016/S0022-5223(03)01312-6

Figure 1. Plain chest radiograph showing a large apical lung mass.

Figure 2. Apical cut of CT chest scan showing soft tissue mass with no obvious rib involvement.

Posterolateral thoracotomy revealed a hard mass invading the first 3 ribs that enveloped the lower trunk of the brachial plexus. A frozen section of a mediastinal node showed no malignant cells, and a radical left upper lobectomy was performed, removing the mass en bloc with the involved ribs and lower brachial plexus trunk. The patient recovered well after the operation, with expected severe left-hand weakness and left Horner's syndrome.

Histologic examination showed a necrotizing granulomatous process, with no evidence of malignancy (Figure 3).

Figure 3. Histology slide showing a necrotizing granulomatous process with no evidence of malignancy. Giant cells are also visible.

Silver staining showed occasional fine-branching filaments within the central necrotic tissue, which is consistent with *Nocardia* species infection.

Nocardia asteroides was confirmed at culture. A diagnosis of pulmonary nocardiosis was made. Disseminated infection was evidenced by two 2 × 2-cm right frontal lobe lesions, which were highly suggestive of cerebral abscesses on CT scanning. HIV serology and antineutrophil cytoplasmic antibodies were negative.

Intravenous amikacin and ceftriaxone were commenced. After 6 weeks, repeat CT brain scanning revealed resolving cerebral abscesses, and oral therapy with trimethoprim/sulfamethoxazole (Bactrim) was commenced to be continued for 1 year.

Discussion

Pancoast syndrome is most commonly caused by bronchogenic carcinomas of the lung apex, most frequently squamous cell carcinoma, followed by adenocarcinoma and large cell carcinoma, and only rarely small cell lung carcinoma.³ Because of their peripheral location, the initial pre-

sensation of these tumors is dominated by features referable to invasion of local structures, principally nerves and the body wall.

Shoulder pain is the most common presenting symptom, related to the involvement of the lower trunk of the brachial plexus, the first 3 ribs, the vertebrae, or the parietal pleura. Horner's syndrome, recurrent laryngeal and phrenic nerve involvement are less common features. Pulmonary manifestations, such as cough, hemoptysis, and dyspnea, occur less often than with centrally located endobronchial lesions.¹

The differential diagnoses can be broadly classified into neoplastic and nonneoplastic causes, and evidence of tissue invasion, as seen in this case, is not *prima facie* evidence of malignancy. Apart from primary bronchogenic carcinoma, other intrathoracic neoplasms (including mesothelioma), hematologic conditions (eg, plasmacytomas and lymphomas), and metastatic deposits are all documented as mimicking the syndrome.

Nonneoplastic conditions include neurogenic thoracic outlet syndromes, inflammatory conditions (eg, Wegener granulomatosis⁴ and amyloidosis⁵) and a wide variety of infectious diseases, including tuberculosis, actinomycosis,⁶ cryptococcosis,⁷ aspergillosis,⁸ and pulmonary hydatid cysts.⁹

Nocardia species infections presenting as Pancoast syndrome have not been previously reported in the literature.

Nocardia species. The nocardiae belong to the actinomycetales group of bacteria, which are ubiquitous in the environment.

Impaired cell-mediated immunity, particularly HIV infection, corticosteroid use, chronic granulomatous disease, lymphoid and solid organ neoplasms, and use of cytotoxic agents,¹⁰ are common predispositions to infection, as are underlying chronic pulmonary diseases, such as chronic bronchitis and bronchiectasis.¹¹ Up to 40% of patients presenting with pulmonary *Nocardia* species infections have no predisposing risks for infection.¹²

Three dominant human pathogens are identified: *Nocardia asteroides*, the predominant human pathogen that causes pulmonary and disseminated disease⁹; *Nocardia brasiliensis*, manifests predominantly as cutaneous and subcutaneous abscesses; and *Nocardia otitidiscavarium*.

Infection is subdivided into localized disease with single-organ involvement or disseminated, with multiple organ involvement, and a predilection for central nervous system seeding. Cerebral abscesses are present in 45% of cases, but involvement of most body tissues has been reported.⁹

The presentation of *N asteroides* ranges from an acute suppurative pneumonia to a more chronic presentation mimicking carcinoma, and as in this case, diagnosis is difficult because of the nonspecific clinical and radiologic features. Early infection manifests as an acute inflammatory reaction dominated by neutrophils, whereas

lymphocytes dominate chronic disease. The granulomatous appearance, as reported here, is rare in the literature and probably resembles the more immunocompetent response to chronic infection.⁸

Diagnosis. This case highlights the management difficulty presented by solitary pulmonary masses in which a tissue diagnosis proves elusive. Diagnosis of pulmonary masses relies on cytologic, histologic, and microbiologic examination of tissue. For apical tumors, percutaneous biopsy is reported as the modality of choice, with a 95% sensitivity.¹³ The accuracy of this modality in the diagnosis of *Nocardia* species infection is unclear. In some case series of pulmonary nocardiosis, results of sputum cultures were positive in up to 90% of patients, making routine sputum microscopy and culture an important adjunct to sputum cytology.⁹

The cornerstone of diagnosis of *Nocardia* species remains identification of branching filaments in tissue section, Gram staining, and culture. Different species and subspecies show variable susceptibility to amikacin, third-generation cephalosporins, imipenem-meropenem, and sulfur-based antimicrobials. The optimal duration of therapy, the role for oral versus intravenous therapy, and the value of multiagent antimicrobial use are not well defined.

Conclusion

Although the initiation of treatment for apical lung lesions was once advocated without the acquisition of a precise histologic diagnosis,¹⁴ the recognition that Pancoast syndrome can be caused by a wide variety of conditions mandates that an accurate diagnosis is made in any pulmonary mass that appears clinically and radiologically to be a bronchogenic carcinoma. CT-guided percutaneous biopsy remains the modality of choice, but where the diagnosis remains elusive, open biopsy is required. In addition to histopathology, all lung biopsy specimens should routinely be sent for microscopy and culture if the wide variety of infectious diseases that can mimic lung carcinoma, such as nocardiosis, are to be diagnosed before surgical resection.

References

1. Hare ES. Tumor involving certain nerves. *London Medical Gazette*. 1838;1:16-8.
2. Pancoast HK. Importance of careful roentgen-ray investigations of apical chest tumours. *JAMA*. 1924;83:1407-11.
3. Arcasoy SM, Jett JR. Superior sulcus tumours and Pancoast syndrome. *N Engl J Med*. 1997;337:1370-6.
4. Reuss-Borst MA, Becker V, Sattler B, Grupp C, Muller GA. Wegener's granulomatosis presenting as Pancoast tumour. *Arthritis Rheum*. 2000;43:467.
5. Gibney RT, Connolly TP. Pulmonary amyloid nodule simulating Pancoast tumour. *J Can Assoc Radiol*. 1984;35:90-1.
6. Tolentino A, Ahkee S, Ramirez J. Pancoast's syndrome secondary to thoracic actinomycosis. *J Ky Med Assoc*. 1996;94:500-2.
7. Mitchell DH, Sorrell TC. Pancoast's syndrome due to pulmonary

- infection with *Cryptococcus neoformans* variety gatti. *Clin Infect Dis*. 1992;14:1142-4.
8. Simpson FG, Morgan M, Cooke NJ. Pancoast's syndrome associated with invasive aspergillosis. *Thorax*. 1986;41:156-7.
 9. Gotterer N, Lossos I, Breuer R. Pancoast's syndrome caused by primary pulmonary hydatid cyst. *Respir Med*. 1977;63:830-5.
 10. Lerner PI. Nocardiosis. *Clin Infect Dis*. 1996;22:891-903.
 11. Menendez R, Cordero PJ, Santos M, Goberado M, Marco V. Pulmonary infection with *Nocardia* species: a report of 10 cases and review. *Eur Respir J*. 1997;10:1542-6.
 12. Curry WA. Human Nocardiosis. A clinical review with selected case reports. *Arch Intern Med*. 1980;140:818-26.
 13. Walls WJ, Thornbury JR, Naylor B. Pulmonary needle aspiration in the diagnosis of Pancoast tumours. *Radiology*. 1974;111:99-102.
 14. Shaw RR, Paulson DL, Kee JL Jr. Treatment of the superior sulcus tumour by irradiation followed by resection. *Ann Surg*. 1961;154:29-40.