Mycobacterium kansasii Infection Following Primary Pulmonary Malignancy*

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The purpose of this study was to determine whether any of the Mycobacterium kansasii cases were the consequences of primary lung malignancy. The records and chest x-ray films of 285 patients with M kansasii pulmonary infection were reviewed. The infection was found to complicate the primary lung neoplasm in four cases. Three patients had had treatment for malignancy: one patient with small cell carcinoma received chemotherapy, steroids and radiation; one with adenocarcinoma underwent a lobectomy and radiation; and the third patient had a lobectomy and radiation for malignant fibrohistiocytoma. The fourth patient developed the infection three years after lung malignancy manifested itself, which was only a few months before the clinical evidence of distant metastasis with adenocarcinoma was detected. We suggest that this infection be considered in patients from M kansasii endemic areas, especially after they have received radiation treatment for lung malignancy. This association has never been described before. (Chest 1992; 102:1460-63)

It has been generally accepted that pulmonary tuberculosis may be activated by malignancies, antineoplastic agents and radiation therapy. The development of nontuberculous mycobacterial infection following malignancy rarely has been reported. Mycobacterium kansasii pulmonary infection coexisting with acquired immunodeficiency syndrome and hairy cell leukemia is well known; however, a literature search fails to disclose a case of this infection developing following primary lung malignancy. The largest series from M. D. Anderson Hospital found M kansasii to be responsible for 12 of 30 atypical mycobacterial infections in patients with malignant diseases. It was reported that carcinoma of the lung was present in 5 of these 30 patients, and that cancer chemotherapy was considered the predisposing factor for the infection in some of these patients. The report, however, did not specify if any patient developed M kansasii pulmonary infection following lung cancer with or without cancer chemotherapy.

This report describes four patients with primary pulmonary malignancy who later developed pulmonary infection due to M kansasii. The infection followed local radiation therapy to the lung in three patients. Immunosuppressive drugs also were used in one of these patients.

Patients and Methods

Hines VA Hospital is a large tertiary medical center located in a western suburb of Chicago. For over 40 years, a separate Tuberculosis Section was devoted to the inpatient and outpatient management of tuberculosis and nontuberculous mycobacterial diseases. Between July 1982 and June 1990, 285 patients were found to have positive sputum cultures for M kansasii. All but four patients had at least two positive cultures in the absence of M tuberculosis or other pathogens. Medical records and x-ray films of these 285 patients were reviewed regarding the presence of the infection and its relationship with primary lung malignancy. Atypical mycobacteria are known to colonize in the upper respiratory tract without any evidence of tissue invasion. The diagnosis of M kansasii pulmonary infection in our patient population, therefore, was strictly based on the recommended criteria by the American Thoracic Society. Four cases of M kansasii pulmonary infection were found to occur after the establishment of primary lung malignancy. The following are their case summaries (Table 1).

Case Reports

Case 1

A 62-year-old man with chronic bronchitis had a workup for an occult malignancy in March of 1981 because of the findings of myasthenia syndrome. A chest x-ray film was interpreted as normal. A bronchoscopy on April 28, 1981 revealed an endobronchial lesion in the right upper lobe, with a biopsy specimen showing small cell carcinoma. He was placed on protocols including cyclophosphamide, vincristine, adriamycin, and procarbazine. He received radiotherapy to the chest and brain (June 24, 1981, to July 9, 1981) and therapy with prednisone was begun. The chest x-ray film on June 17, 1981 essentially was normal. A right upper lobe hazy linear infiltrate that spared the apex was noted on August 27, 1981, and was compatible with radiation pneumonitis. Therapy with a high dose of prednisone was initiated. Bronchoscopy in March 1982 was negative for tumor; two postbronchoscopy sputum cultures later grew M kansasii. A chest x-ray film on May 2, 1982 showed marked hilar fibrosis and a very small radiolucent lesion in the extreme apex with the "tail sign" of M kansasii infection. In retrospect, a small cavity had been present over the right apex since February 24, 1982. Isoniazid and rifampin were administered for 12 months. The patient is alive ten years after the diagnosis of lung carcinoma, with follow-up chest radiographs showing only apical pleural thickening and hilar fibrosis.

Case 2

A 60-year-old man with emphysema underwent a right lower lobectomy for adenocarcinoma in March 1982. There was no...

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Table 1—Findings of Four Patients with Mycobacterium kansasii Pulmonary Infection Following Malignancy

<table>
<thead>
<tr>
<th>Patient/Age (yr)</th>
<th>Malignancy</th>
<th>Therapy</th>
<th>Diagnosis of Infection</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/62</td>
<td>Small cell carcinoma, right upper lung (4/81)</td>
<td>Chemotherapy, steroids, radiation to brain and chest (4/81)</td>
<td>Right upper lung cavity (2/82); positive cultures (3/82)</td>
<td>Alive after 10 yr</td>
</tr>
<tr>
<td>2/60</td>
<td>Adenocarcinoma, right lower lobe (3/82)</td>
<td>Right lower lobectomy (3/82), chest radiation (12/86)</td>
<td>Right upper lung cavities (1/87); positive cultures (6/89)</td>
<td>Carcinoma recurred, metastasis to ribs and pleura (9/86); dead (9/89)</td>
</tr>
<tr>
<td>3/63</td>
<td>Malignant fibrohistiocytoma, right upper lobe and right middle lobe (12/84)</td>
<td>Right upper and middle lobectomy; rib resection; chest wall reconstruction; chest radiation</td>
<td>Right lung cavities and infiltrate (6/85); positive cultures (8/89)</td>
<td>Alive after 6 yr</td>
</tr>
<tr>
<td>4/48</td>
<td>No histology, left lower lung, coin-sized lesion (1/71)</td>
<td>Palliative radiation therapy to lobar metastasis (2/75)</td>
<td>Left hilar density extending to coin-sized lesion; positive cultures (2/74)</td>
<td>Neck node and left lumbar mass (2/75); biopsy: adenocarcinoma; dead (6/75)</td>
</tr>
</tbody>
</table>

Case 1

A 61-year-old man was admitted to the hospital at 1162 Small of lung infection. He was given isoniazid, ethambutol and rifampin on July 1, 1989. On September 30, 1989, he was admitted to a private hospital, had a cardiopulmonary arrest and died.

Case 2

A 63-year-old man with emphysema underwent a right upper lobectomy, right middle lobectomy and three-rib resection with anterior chest wall reconstruction for a malignant fibrohistiocytoma in December of 1984 (Fig 1). Histology showed no caseating necrotic lesion. There was no preoperative or immediately postoperative culture for mycobacteria. He completed a course of radiotherapy to the chest in April 1985, which was complicated by dysphagia due to radiation. Early follow-up chest x-ray films showed only postoperative fibrotic changes with marked tracheal retraction. The chest radiograph on September 30, 1985, revealed multiple cystic areas in the remaining right lower lobe that were thought to be due to radiation therapy (Fig 2). Serial chest x-ray films dated July 23, 1986, May 27, 1987, and September 8, 1988, showed progressive

FIGURE 1. Malignant mass on right. Bullous, emphysematous changes in left upper third.

FIGURE 2. Post-surgery and radiation with cysts in right upper third. Bullous formation on left.
increases in size and number of cystic infiltrates in the right upper thoracic cavity. By July 24, 1989, the infiltrate became dense and involved the remaining portion of the right lung (Fig 3). Sputum cultures of August, September and December 1989 grew M kansasii. Therapy with isoniazid, ethambutol and rifampin was begun in October 1989. The follow-up chest x-ray film of January 6, 1990 (Fig 4), showed significant improvement throughout the entire right lung. The patient remains alive to date.

CASE 4

A 48-year-old painter was admitted to the hospital in February 1974 with a history of night sweats and a 40-pound weight loss for six months. Past history included moderate cigarette smoking, alcohol drinking habits and a coin-sized lesion in the left lung since January 1971 for which he refused surgery. A physical examination was negative except for signs of emphysema. A chest x-ray film of February 1974 showed an irregular left hilar density extending to the noncalcified peripheral coin-sized lesion. The bronchoscopic and cytologic examinations on February 8, 1974, were negative. The sputum cultures grew M kansasii. The patient again refused thoracotomy, and therapy with isoniazid, rifampin and ethambutol was initiated in March 1974. He was readmitted in February 1975 with increasing shortness of breath, weight loss and a tender mass over the left lumbar region, which developed over a six-month period. Multiple enlarged cervical nodes also were detected. A chest radiograph revealed a patchy density with cavitation in the left upper and lower lung fields. Repeated cytology evaluations were negative. Biopsy of the left lumbar mass revealed adenocarcinoma. He completed a course of palliative cobalt therapy without improvement. Repeated sputum cultures grew M kansasii in spite of the antituberculosis medication. The patient continued to deteriorate, was readmitted and died on June 12, 1975.

RESULTS AND DISCUSSION

The central portion of the United States is endemic for M kansasii. In earlier reports, Lester et al. and Pfuette and colleagues found 18 percent of 929 consecutive admissions to hospitals in suburban Cook County, Illinois, to have mycobacterial pulmonary disease due to this organism. A more recent survey found Illinois to rank fourth in the nation in the number of M kansasii isolates of clinical significance, following California, Texas and Louisiana in that order. The disease has a predilection for middle-aged men with preexisting lung diseases, particularly chronic bronchitis and emphysema. Impairment of the clearance mechanism and the macrophage function has been considered to play a role in its pathogenesis.

Corticosteroid drugs are well known inhibitors of T cell function and may lower resistance to mycobacterial infections. Patients on long-term corticosteroid drug therapy are advised to have their chest x-ray films monitored regularly so that tuberculosis can be recognized and treated promptly.

Immunosuppressive agents also predispose patients to M kansasii infection. We found three substantiating case reports. Two reports described one renal transplant recipient each who developed M kansasii skin abscesses on the legs (one also with pulmonary nodules) while being maintained on immunosuppressive therapy. The third report was on a patient with
rheumatoid arthritis who developed a *M. kansasii* pulmonary cavitary lesion following long-term treatment with gold and penicillamine.\textsuperscript{13}

Besides its well known effects on immunity, radiation also impairs the clearance mechanism. Increased susceptibility to infection from radiation could result from a transient reduction in the number of macrophages. Radiation therapy for primary lung carcinoma was reported to precede pulmonary infection due to rapidly growing mycobacteria in one patient,\textsuperscript{14} and local radiation for breast carcinoma was believed to have activated *M. avium intracellulare* complex pulmonary infection in another patient.\textsuperscript{15} Many cytotoxic and other chemotherapeutic agents also have been shown to intensify the undesirable effects of radiation to the lung.\textsuperscript{16-18} Radiation therapy for pulmonary malignancy can create another diagnostic problem, namely, radiation pneumonitis, due to its protein clinical and roentgenographic manifestation.\textsuperscript{16}

It appears that in three of our patients the immune defense mechanisms were compromised not only as a result of lung malignancies but also as a result of their treatment which included radiotherapy with or without cancer chemotherapy and steroids. The early effects of radiation include engorgement and thrombosis of capillaries and arterioles, desquamation of alveolar epithelial cells and focal necrosis of the bronchial mucosa. These are followed by fibrosis.\textsuperscript{18} It is likely that in cases 1, 2 and 3, the local radiation to the lung malignancy significantly contributed to the overall immunosuppression. In case 4, in which there was no treatment for the pulmonary malignancy, invasion of *M. kansasii* organisms colonizing the area previously damaged by carcinoma could have led to active infection, since local tumor peptides or antigens may lay the groundwork for invasion and allow mycobacteria to proliferate.\textsuperscript{19} Further, the patient was a heavy smoker with emphysema, both of which are well known predisposing conditions for *M. kansasii* pulmonary infection.

Clinically it is difficult to differentiate *M. kansasii* complicating lung malignancy from radiation reaction, recurrence or spread of tumor. Radiographic changes in our patients fell into two groups: (a) isolated cavitary lesion adjacent to the area of radiation fibrosis in one patient and (b) progressive minute cystic changes over many months in three patients, two of which were incorrectly interpreted as radiation changes.

Since *M. kansasii* infections are not common in patients with malignant disease, its presence easily may be overlooked. From the experience with these patients, we suggest that sputum studies for mycobacterial organisms be performed at intervals on patients with lung malignancies who develop any adverse radiographic changes following treatment for malignancy, especially with radiation. Cultures should also be made before surgery and before irradiation or chemotherapy in unquestionable cases of carcinoma. This is especially important when they live in an area endemic for *M. kansasii* organisms.

**REFERENCES**