Metastatic Renal Cell Carcinoma Simulating Sarcoidosis*

Analysis of 12 patients with Bilateral Hilar Lymphadenopathy

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Case summaries of four patients with bilateral hilar lymphadenopathy (BHL) caused by metastatic renal cell carcinoma are presented, and these and eight similar cases from the literature are analyzed. In nine patients, sarcoidosis was the provisional clinical diagnosis, but four of these patients had a past history of renal cell carcinoma. In the remaining five patients, a distinction from sarcoidosis could not be made by history, physical examination, and chest roentgenogram. This underscores the need for tissue confirmation in the diagnosis of sarcoidosis and alerts the physician to consider metastatic renal cell carcinoma in the differential diagnosis of BHL.

Roentgenographically detectable intrathoracic lymphadenopathy is rarely caused by metastasis from extrathoracic malignant neoplasms. McLeod and associates found intrathoracic lymphadenopathy in 25 of 1,071 cases of extrathoracic malignant neoplasms reviewed. It is notable that in nearly one half of their cases with intrathoracic lymphadenopathy, the primary lesion was a genitourinary neoplasm. A type of intrathoracic lymphadenopathy—bilateral hilar lymphadenopathy (BHL)—is of particular importance to the clinician because it simulates the roentgenographic appearance of sarcoidosis. A number of case reports of renal cell carcinoma manifesting as BHL have appeared in the literature. In a recently completed review of 46 cases of renal cell carcinoma, we found six patients with BHL. In four of these patients, BHL was the sole roentgenographic manifestation of renal cell carcinoma. These four cases and eight similar cases from the literature were analyzed for features that may help distinguish them from sarcoidosis.

Case Reports

Case 1

A 53-year-old asymptomatic black man was seen in the chest clinic of Wood Veterans Administration Medical Center (VAMC) for evaluation of BHL, detected on a preemployment chest roentgenogram (Fig 1, left). A chest roentgenogram taken a year before was reported to be normal, but on review showed BHL in a less pronounced form (Fig 1, right). Physical examination was normal. Sarcoidosis was suspected, and he was scheduled for hospital admission and transbronchoscopic lung biopsy. However, the patient did not report on the scheduled date but was admitted three weeks later, acutely ill with staphylococcal pneumonia. He had cough, fever, rales in the right interscapular area, leukocytosis, and Gram-positive cocci seen in clusters in Gram stained sputum, the culture of which yielded Staphylococcus aureus. Microscopic hematuria was also noted but was attributed to previously documented sickle cell trait. Chest roentgenograms showed marked increase in BHL and a right lower lobe pneumonia. He continued to be febrile even after a week of intravenous nafcillin, and fiberoptic bronchoscopy was performed. Biopsy of a reddened and nodular area in the right intermediate bronchus showed adenocarcinoma. The patient's course was rapidly downhill, and he died a week later. Autopsy revealed renal adenocarcinoma with metastasis to the hilar nodes and multiple metastases to the lungs.

Case 2

A 57-year-old white man entered VAMC for an elective inguinal herniorrhaphy. He had no symptoms, and physical examination disclosed no abnormalities other than the inguinal hernia. Chest roentgenogram showed BHL (Fig 2). Tomographic studies revealed no additional findings. Results from laboratory examination including complete blood cell counts, urinalysis, liver function tests, and serum calcium were normal. A mediastinotomy was done and a right hilar node measuring 2 cm in diameter was resected. Histopathologic examination of the node revealed adenocarcinoma. While in the hospital, the patient developed an episode of frank hematuria. An intravenous pyelogram showed a mass in the right kidney which was resected and was found to be a renal adenocarcinoma. The patient died 26 months later with widespread metastases.

Case 3

A 55-year-old white man was sent to Wood VAMC by his private physician for evaluation of BHL without parenchymal abnormalities, found on chest roentgenogram during an annual checkup. Three years earlier, he had a renal cell carcinoma removed by left nephrectomy. He had no symptoms, and physical examination results, as well as complete blood cell count, urinalysis, and liver enzyme values were normal. Tomograms of the lung confirmed adenopathy, but no additional findings were evident. The examining physician at VAMC considered a provisional diagnosis of sarcoidosis and recommended hospital admission. However, the patient declined admission. Three years later, he was referred again by his private physician because of a marked change in roentgenographic findings. He still had no symptoms but chest roentgenogram showed pronounced BHL with multiple parenchymal and pleural nodules. Examination revealed an enlarged firm left supraclavicular lymph node.
node on which a biopsy was performed. This showed a carcinoma with mixed papillary and clear cell pattern similar to the histopathologic findings of the resected primary renal neoplasm. Although further progression of metastases including cerebral metastases has occurred, the patient is still alive 54 months after the initial appearance of BHL.

**Case 4**

A 63-year-old white man was seen at the outpatient clinic, VAMC, for right shoulder pain. Examination showed restriction of right shoulder movements which were painful. The remainder of the examination was unremarkable. The chest roentgenogram was initially reported as within normal limits, but on review was found to show BHL. Four months later, he was admitted to the hospital with hematuria. Examination and roentgenographic studies revealed peripheral lymphadenopathy of the supraclavicular and inguinal areas, osteolytic lesions of the right humerus and thoracolumbar spine, and BHL with multiple pulmonary nodules. A biopsy was done on an enlarged, firm, left supraclavicular node, and this specimen showed clear cell carcinoma strongly suggestive of metastasis from a primary renal neoplasm. The patient declined further investigations and treatment. He died 12 months following the initial appearance of BHL.

**Discussion**

Renal cell carcinoma may metastasize to the hilar nodes in multiple ways. These include progressive extension from regional nodes in an ascending order, direct spread through the lymphatics of the inferior pulmonary ligament, retrograde flow into bronchomediatinal and peribronchial lymphatics presumably through incompetent valves and from possible extension of tumor emboli in the pulmonary artery to the adjacent peribronchial lymphatics. Metastasis to the mediastinal nodes (including hilar nodes) from renal cell carcinoma has been reported in roentgenographic studies to occur in 7.2 percent to 28.2 percent of patients. One autopsy study reported mediastinal nodal metastasis in 16 of 34 (47 percent) consecutive cases of renal cell carcinoma. We found BHL in 13 percent of 46 consecutive cases of renal cell carcinoma.

Sarcoidosis is the most important cause of BHL, and this finding has been noted in 75 percent of cases of sarcoidosis and in 50 percent of cases is the sole chest roentgenographic finding. Other causes of BHL include lymphoma, tuberculosis, fungal infections, silicosis, and metastatic neoplasms of thoracic and extrathoracic origin. Winterbauer and associates categorized 85 patients with BHL on the basis of symptoms and signs. All 34 of their asymptomatic
Table 1—Analysis of 12 Cases of BHL Due to Metastatic Renal Cell Carcinoma

<table>
<thead>
<tr>
<th>Reference</th>
<th>Case No.</th>
<th>Age, Sex</th>
<th>Symptoms</th>
<th>Physical Findings</th>
<th>Time of Diagnosis of Renal Cell Carcinoma</th>
<th>Time of Follow-up Since BHL</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>57 White</td>
<td>None</td>
<td>Inguinal hernia</td>
<td>Concurrent; mediastinal nodal biopsy showed adenocarcinoma</td>
<td>26 Mo</td>
<td>Sarcoïdosis suspected. Supraclavicular lymph node biopsy showed neoplasm of the same histologic type.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>55 White</td>
<td>None</td>
<td>Normal</td>
<td>38 Months before BHL; nephrectomy showed carcinoma (mixed papillary and clear cell)</td>
<td>54 Mo</td>
<td>Sarcoïdosis suspected. Supraclavicular lymph node biopsy showed neoplasm of the same histologic type.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>63 White</td>
<td>Right shoulder pain</td>
<td>Restriction of right shoulder movement</td>
<td>4 Months after BHL</td>
<td>12 Mo</td>
<td>BHL missed in the first chest roentgenogram.</td>
</tr>
<tr>
<td>Khan &amp; Khan</td>
<td>5</td>
<td>52 White</td>
<td>Cough, fever</td>
<td>Respiratory rate-22/min</td>
<td>Concurrent</td>
<td>8 Mo</td>
<td>BHL alone; sarcoïdosis suspected. Later described parenchymal masses and infiltrate. BHL alone; sarcoïdosis suspected.</td>
</tr>
<tr>
<td>Ahmad &amp; Zevallos</td>
<td>6</td>
<td>53 White</td>
<td>Nonproductive cough</td>
<td>Normal</td>
<td>Concurrent</td>
<td>8 Mo</td>
<td>BHL alone; sarcoïdosis suspected.</td>
</tr>
<tr>
<td>Reinke et al</td>
<td>7</td>
<td>19 Oriental</td>
<td>Left groin mass, left leg edema, hematuria</td>
<td>Left subcostal mass, pelvic mass, inguinal adenopathy</td>
<td>Concurrent</td>
<td>Not given (NG)</td>
<td>BHL with symptoms and findings, lymphoma suspected.</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>61 White</td>
<td>None</td>
<td>NG</td>
<td>15 Months before BHL</td>
<td>NG</td>
<td>BHL alone. Bronchoscopic biopsy showed metastatic adenocarcinoma same as the renal neoplasm.</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>29 Black</td>
<td>Gross hematuria, right flank pain</td>
<td>NG</td>
<td>4 Months before BHL</td>
<td>NG</td>
<td>BHL alone. Mediastinal node and renal neoplasm both were adenocarcinoma. BHL with parenchymal lesions.</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>66 White</td>
<td>None</td>
<td>NG</td>
<td>42 Months before BHL</td>
<td>19 Mo</td>
<td>BHL alone; sarcoïdosis or lymphoma suspected. Autopsy showed metastatic renal carcinoma to the left lower lobe bronchus and bilateral hilar nodes.</td>
</tr>
<tr>
<td>Seaman</td>
<td>11</td>
<td>48 Race-NG</td>
<td>Mild cough</td>
<td>Normal</td>
<td>1 Month later dysuria and hematuria; scalene node biopsy showed carcinoma; mass in kidney found to be renal cell carcinoma</td>
<td>6 Mo</td>
<td>BHL alone; sarcoïdosis or lymphoma suspected. Autopsy showed metastatic renal carcinoma to the left lower lobe bronchus and bilateral hilar nodes.</td>
</tr>
<tr>
<td>King et al</td>
<td>12</td>
<td>49 Race-NG</td>
<td>None</td>
<td>Traumatic rib fracture</td>
<td>31 Months before BHL</td>
<td>NG</td>
<td>Biopsy of hilar node showed metastatic renal cell carcinoma.</td>
</tr>
</tbody>
</table>

patients had sarcoïdosis and only five of these patients had abnormal findings on physical examination. In contrast, all 11 patients with neoplastic hilar adenopathy were symptomatic and in nine of these, there were identifiable extrathoracic neoplasms on physical examination. They concluded that BHL in asymptomatic patients with negative physical examination is evidence of sarcoïdosis, and further biopsy confirmation is not necessary.

We analyzed data of 12 patients (Table 1) with BHL due to metastatic renal cell carcinoma for features that may separate them from sarcoïdosis. In three patients (cases 4, 7, 9), presenting symptoms or physical findings pointed to the presence of a neoplasm. In the other nine patients, sarcoïdosis was the provisional clinical diagnosis; six of these patients were asymptomatic, and four had no abnormal physical findings. However, an important and easily obtainable clue was present in the
past histories of four patients (cases 3, 8, 10, 12), ie, a renal cell carcinoma was diagnosed 15 to 42 months preceding the appearance of BHL. In the remaining five patients (cases 1, 2, 5, 6, 11), a distinction from sarcoidosis could not be made on the basis of history, examination, and chest roentgenogram. Though these patients were middle-aged (48 to 57), the possibility of sarcoidosis could not be discounted on the basis of age, sex, or race. Two were asymptomatic and three had cough of varying duration. Physical examination was normal in three; mild tachypnea was present in one, and the other had an unrelated finding of a hernia.

Two important conclusions can be drawn from our analysis. First, in a patient with BHL, a preceding history of renal cell carcinoma regardless of the elapsed time, provides a strong clue to the possibility of metastatic renal cell carcinoma. Secondly, BHL in asymptomatic patients with normal physical findings cannot be diagnosed as sarcoidosis without tissue confirmation since metastatic renal cell carcinoma may mimic sarcoidosis. In such patients, a transbronchoscopic lung biopsy, because of its low morbidity and high yield, is a reasonable first procedure. As part of the same procedure, biopsy specimens from areas of abnormal appearance in the bronchi can be taken. By this means, endobronchial metastasis was diagnosed in two patients (cases 1, 8). If diagnosis remains uncertain, biopsy of a mediastinal node may be needed.

References
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