AFP-producing Squamous Cell Carcinoma of the Lung in an Adolescent

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We report a case of primary lung cancer in a 16-year-old boy. A histologic diagnosis of squamous cell carcinoma was made by bronchoscopic biopsy before surgery. The serum alpha-fetoprotein (AFP) level was markedly elevated at 193 ng/dl. Preoperative and postoperative evaluation revealed no evidence of scrotal mass. We performed right pneumonectomy with combined resection of the invaded portion of the left atrium under extracorporeal circulation. Despite the rapid improvement in the patient’s general condition after surgery, the AFP level continued to increase without a transient decrease and reached 3160 ng/ml on the 23rd postoperative day. When the patient was readmitted because of dyspnea and headache on the 36th postoperative day, hypercalcemia of 13.9 mg/dl was noted, and this was resistant to subsequent treatment. The patient died on the 46th postoperative day.

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Key words: Lung cancer—Adolescent—Alpha-fetoprotein—Surgery

Introduction

Primary lung cancer occurs primarily in the seventh or eighth decade of life, and is rarely encountered in childhood and adolescence. For a young patient with an abnormal mass shadow on a chest radiograph, primary lung cancer may not even be considered in the differential diagnosis. This report describes our experience in treating a 16-year-old boy with squamous cell carcinoma in the lower lobe of the right lung, and focuses on the clinical and pathological features.

Case Report

An abnormal shadow was noted on a chest radiograph of a 16-year-old boy taken on entrance to high school. When he was referred to our hospital, he complained of cough with a small amount of expectoration. A physical examination revealed a decreased intensity of breath sound in the right lower lung field. A thorough examination was performed to rule out the possibility of scrotal mass; the bilateral testes were of normal size, and no scrotal mass was detected by ultrasonography. Results of hematologic examination were normal. Blood chemistry showed elevated levels of alkaline phosphatase and LDH at 452 IU/l and 489 IU/l, respectively. The serum alpha-fetoprotein (AFP) level was also elevated at 193 ng/ml. Levels of other tumor markers such as CEA, CA19-9, NSE, and SCC were all within normal limits. A chest radiograph taken on admission showed a nodular mass in the right lower lung field (Fig. 1). Chest CT scan further demonstrated a solid mass around the basal bronchus in the lower lobe of the right lung (Fig. 2).

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Fig. 1. Chest radiograph taken on admission. A round tumor mass, about 5 cm in diameter, is located in the right lower lung field.

and right atrial wall were resected and reconstructed under complete cardioplegia. After cardiac resuscitation, right pneumonectomy and complete lymph node dissection were performed through another lateral incision. The postoperative recovery was uneventful and the patient was discharged. However, the serum AFP level began to increase rapidly: 457 and 3160 ng/ml on the 14th and 23rd postoperative days, respectively, and no transient decrease was observed. Because of dyspnea, headache, and general malaise, the patient was readmitted to another hospital, where marked elevation of the serum calcium level (13.9 mg/dl) was observed. Despite further treatment, the serum calcium level could not be normalized, and the patient died on the 46th postoperative day.

Pathological Findings

Macroscopically the resected tumor was located around the right basal bronchus and invaded the atrial wall directly. The peribronchial and subcarinal lymph nodes were swollen and involved by the tumor. The tumor was elastic-hard and measured 7.5 × 6.5 × 6.0 cm. On the maximal cut surface, it was yellowish-white and well circumscribed. About 60% of the tumor tissue was necrotic in the central portion. Microscopically, the majority of the tumor was composed of solid nests with undifferentiated tumor cells, but histologic features of squamous cell carcinoma such as keratinization, intercellular bridges and cancer pearls were found in parts (Fig. 2). Therefore, the tumor was diagnosed histologically as poorly differentiated squamous cell carcinoma. Immunohistochemically, approximately 5% of the tumor cells were positive for AFP (Fig. 2, inset). Involvement of the subcarinal lymph nodes was demonstrated microscopically. The postsurgical (pathological) staging was pT4N2M0 (stage IIIB).

Discussion

Over the past 30 years, 2956 pulmonary resections for primary lung cancer have been carried out at the National Cancer Center Hospital, Tokyo. Of these treated patients, only the present one was under 20 years of age, comprising only 0.03% of the total. Thus, primary lung cancer is an extremely rare condition in the early stage of life.

Although several reports in the English literature over the past 20 years have addressed lung cancer in relatively young patients, such as those under 40 years of age, very few adolescent patients have been described (Table I). For example, the series reported by DeCaro and Benifield and Pemberton et al. did not include patients in adolescence: the youngest patients were 22 and 25 years old, respectively. In the report by Kyriakos et al., which described 102 patients under 45 years of age, only three were adolescents: a 12-year-old with large cell carcinoma, a 13-year-old with carcinoid tumor, and an 18-year-old with small cell carcinoma (sexes unknown). The 82 patients less than 40 years of age collected by Icard et al. included a 17-year-old patient, but detailed information was not available. Case reports by several authors have included various histologic types; squamous cell carcinomas in 10 and 15-year-old boys, small cell carcinoma in a 12-year-old boy, bronchioloal-
Table I. Summary of Cases of Primary Lung Cancer in Adolescents in the Reported Literature

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Patients Age</th>
<th>Sex</th>
<th>Histology</th>
<th>Treatment</th>
<th>Prognosis</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyriakos(b) (1974)</td>
<td>12</td>
<td>ND</td>
<td>large cell</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>ND</td>
<td>carcinoid</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>ND</td>
<td>small cell</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Icard(d) (1992)</td>
<td>17</td>
<td>ND</td>
<td>ND</td>
<td>radiation</td>
<td>dead</td>
<td>6 months</td>
</tr>
<tr>
<td>La Salle(b) (1977)</td>
<td>10</td>
<td>male</td>
<td>squamous cell</td>
<td>surgery</td>
<td>alive</td>
<td>3.5 years</td>
</tr>
<tr>
<td>Niit(u) (1974)</td>
<td>15</td>
<td>male</td>
<td>squamous cell</td>
<td>chemotherapy</td>
<td>dead</td>
<td>8 months</td>
</tr>
<tr>
<td>Oka(b) (1984)</td>
<td>12</td>
<td>male</td>
<td>small cell</td>
<td>none</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Dosanjh(b) (1992)</td>
<td>15</td>
<td>female</td>
<td>bronchioalveolar cell</td>
<td>surgery</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Epstein(b) (1989)</td>
<td>16</td>
<td>male</td>
<td>adenocarcinoma</td>
<td>chemotherapy</td>
<td>dead</td>
<td>6 months</td>
</tr>
<tr>
<td>Fukuda(b) (1990)</td>
<td>18</td>
<td>male</td>
<td>adenocarcinoma</td>
<td>chemotherapy</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND, not described.

veolar cell carcinoma in a 15-year-old girl,\(^8\) and adenocarcinomas in 16-\(^9\) and 18-year-old boys.\(^{10}\) These case reports indicated no particular tendency for histology, sex, or clinical behavior, although other reports have demonstrated a higher incidence of adenocarcinoma and undifferentiated or small cell carcinoma than that of squamous cell carcinoma in childhood.\(^9\)

Although the tumor in this patient was diagnosed histologically as poorly differentiated squamous cell carcinoma, its major component was undifferentiated carcinoma, and its production of AFP was a very unusual feature for squamous cell carcinoma of the lung. Therefore, it is possible that an unknown primary germ cell tumor had metastasized to the lung in this case. However, the tumor was finally diagnosed as a primary lung carcinoma because it was solitary located in the lung and there were no tumorous lesions in either the mediastinum or sexual organs.

One of the unique features of the present tumor was its production of AFP, as demonstrated immunohistochemically, and subsequent elevation of the patient's serum AFP level. Among the case reports listed in Table I, only one patient (an 18-year-old with adenocarcinoma) showed an increased level of serum CA-125.\(^{10}\) No other particular tumor marker has been detected in the reported adolescent patients. The first sign of systemic relapse in the present patient was a rapid increase in the serum AFP level, despite the absence of clinical symptoms.

In the latter part of the clinical course, treatment resistant hypercalcemia developed. At present, the mechanism of hypercalcemia is not understood in detail. Mundy and Martin\(^{11}\) divided hypercalcemia into three categories: humoral hypercalcemia associated with solid tumors with bony metastasis, and hypercalcemia of hematologic neoplasms. Special histologic types and possible bone-resorbing agents were also recognized in relation to each type of hypercalcemia. Although both humoral and metastatic types of hypercalcemia might occur in lung carcinoma, squamous cell carcinoma is known to be strongly related to the former. Since this patient had no clinically detectable bony metastasis and the histology of the lung tumor was squamous cell carcinoma, unknown humoral factors might have been responsible for the hypercalcemia in this case. Such humoral factors could include epidermal growth factor, prostaglandins, osteoclast activating factor, and parathyroid hormone (or parathyroid hormone-related protein).\(^{12}\)

The early systemic dissemination of the disease after surgery, accompanied by hypercalcemia, might have been attributable to the use of extracorporeal circulation for atrial resection, in addition to the aggressive nature of this tumor. Tumor cells that had exfoliated during atrial resection may have been admixed in the recirculated blood and spread by systemic blood flow. Therefore, the blood in the operative field should not be recirculated during resection for malignant disease involving the heart and great vessels under extracorporeal circulation.

References

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