□ Case Report □

Pulmonary carcinoid tumor presented with recurrent pneumonia in adolescence

**Eun Sil Park, M.D., Ji Suk Park, M.D., Jae Young Lim, M.D.
Joung Hee Lee, M.D.* and Gyung Hyuck Ko, M.D.***

Departments of Pediatrics, Pathology, Gyeonsang National University College of Medicine, Jinju, Korea*

The incidence of endobronchial tumor in the pediatric period is very rare and the symptoms are very close to those of respiratory tract infection. Diagnosis can be delayed because of low clinical suspicion and the many ways in which these tumors can present. We report the first case, in Korea, of a pulmonary carcinoid tumor that presented with recurrent pneumonia at the same location in adolescence. Treatment is surgical and geared towards complete resection while sparing healthy lung parenchyma. Long-term and careful follow up is recommended to detect local and distant metastasis. **(Korean J Pediatr 2006;49:805-809)**

Key Words : Endobronchial tumor, Carcinoid

Introduction

Carcinoid tumor is neuroendocrine tumor that occurs mainly in young and middle aged adults with female predominance[1]. The appendix is the most common primary site, however intestine, bronchus, pancreas and ovary have also been reported as primary sites[2]. Histologically a carcinoid tumor can be divided into typical and atypical forms; typical carcinoids (TC) are generally more benign than atypical carcinoid (AC)[3]. Travis, et al[4] reported the 5- and 10-year survival as 87% and 87% for TC and 56% and 35% for AC. Complete excision is considered as the optimal treatment for TC; however there is a potential for regional and distant metastasis to liver, bone and brain. Many investigators have attempted to identify the prognostic factors for TC[5].

Bronchial carcinoid tumor is the most common endobronchial tumor in childhood; it commonly presents with obstructive bronchial disease and pneumonia[6, 7]. Endobronchial tumors, including carcinoids, are not considered as an initial presumptive diagnosis in the pediatric age group; this might result in diagnostic delay.

접수 : 2006년 2월 8일, 승인 : 2006년 4월 3일
책임저자 : 임재영, 경상대학교 의과대학 소아과학교실
Correspondence : Jae Young Lim, M.D.
Tel : 055)750-8697 Fax : 055)752-9339
E-mail : pedneu@gsnu.ac.kr

We here report a bronchial carcinoid tumor that presented with recurrent pneumonia in an adolescent.

Case Report

A 15-year-old girl was admitted to the clinic with intermittent cough for 3 days prior to admission. She complained of pleuritic chest pain during deep inspiration that radiated to the left shoulder. There was no prior history of fever, weight loss or night sweats. Three months prior to admission she was diagnosed with pneumonia and was treated medically at her primary hospital; there was no clinical improvement so she was referred to a university hospital where the pneumonia was controlled with antibiotics. On physical examination subcostal retraction was noted. Blood pressure was 120/70 mmHg, heart rate 120/minute, respiration rate 40/min, and the temperature 36.4℃. On auscultation, breathing sounds were decreased and coarse crackles were heard on the left lower lobe. On day one of admission the temperature increased to 39℃ and cefotaxime was administered. Chest radiography showed peribronchial consolidation and a small amount of pleural fluid. There was no difference in comparisons to X-rays from the prior admission three months previously (Fig. 1). Computed tomography of the chest showed multifocal consolidation at the left lower lobe basal segment, left upper lobe posterior segment, and left upper lobe lingular division

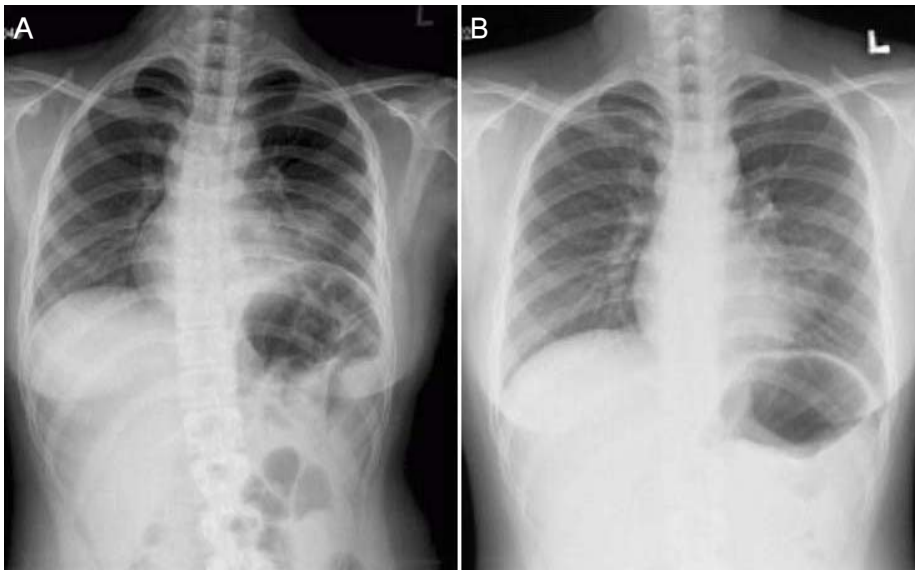

Fig. 1. Current Chest X-ray **(A)** showed the prominent infiltration along with left cardiac border, which was similar to that of previous 3 months **(B)**.

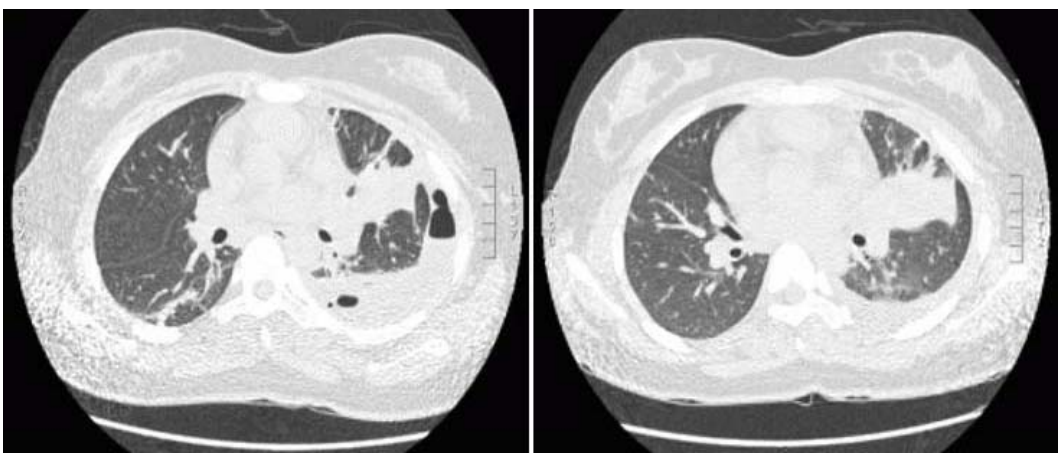

Fig. 2. CT showed multifocal consolidation at the LLL basal segment, LUL posterior segment, and LUL lingular division (Abbreviations : LLL, left lower lobe; LUL, left upper lobe).

(Fig. 2). The result of laboratory studies were as follows : hemoglobin level 11.2 g/dL, white blood cell count 20,157×$10^3/\mu L$, platelet 222×$10^3/\mu L$, and segmented neutrophils 91.2 %. Arterial blood gas analysis : pH 7.44, $PaCO_2$ 34, PaO_2 79, HCO_3 21, O_2 saturation 96.1%. Lactate dehydrogenase (LDH) was 237 mg/dL and C-reactive protein was 196 mg/L. The Mycoplasma antibody titer and cold agglutinin was 1 : 80 and 1 : 32, respectively. Pleural fluid : pH 7.0, RBC 1,800/mm^3, WBC >1,000/mm^3, neutrophil 77%, lymphocyte 19%, glucose 5 mg/dL, protein 38 mg/dL, LDH >2,700 mg/dL, adenosine deaminase (ADA) 57 U/L. The results of cultures obtained for bacteria, fungus, and tuberculosis were all negative. A Mantoux test was negative. The parapneumonic effusion was drained via a chest tube but the pneumonic consolidation was not improved and a septated effusion was observed. A pleural biopsy and bronchoscopic examination were performed on admission day 12, revealing a protruding mass into left upper main bronchus (Fig. 3). The mass was pinkish and oval shaped and measured 7 mm in diameter; it was obstructing the lumen of the bronchus. The patient underwent resection of the left upper lobe without complication. Pathological diagnosis was a typical carcinoid tumor with a clear surgical margin (Fig. 4). After the pathological diagnosis, immunostaining was performed of the paraffin blocked tissue with CD44, Ki 67, p53, bcl2, nm23 which is associated with metastasis and

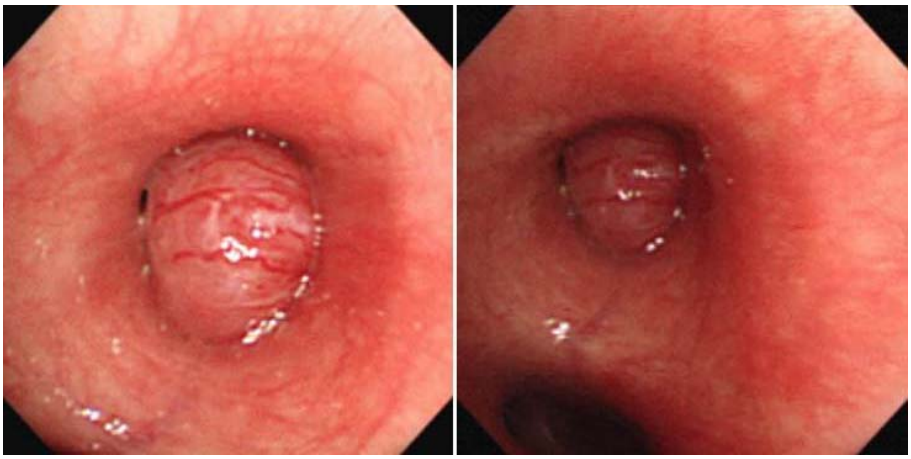

Fig. 3. Protruding mass into the left upper main bronchus was observed. The mass was pinkish and oval shaped and measured as 7 mm diameter; obstructing the lumen of the left bronchus.

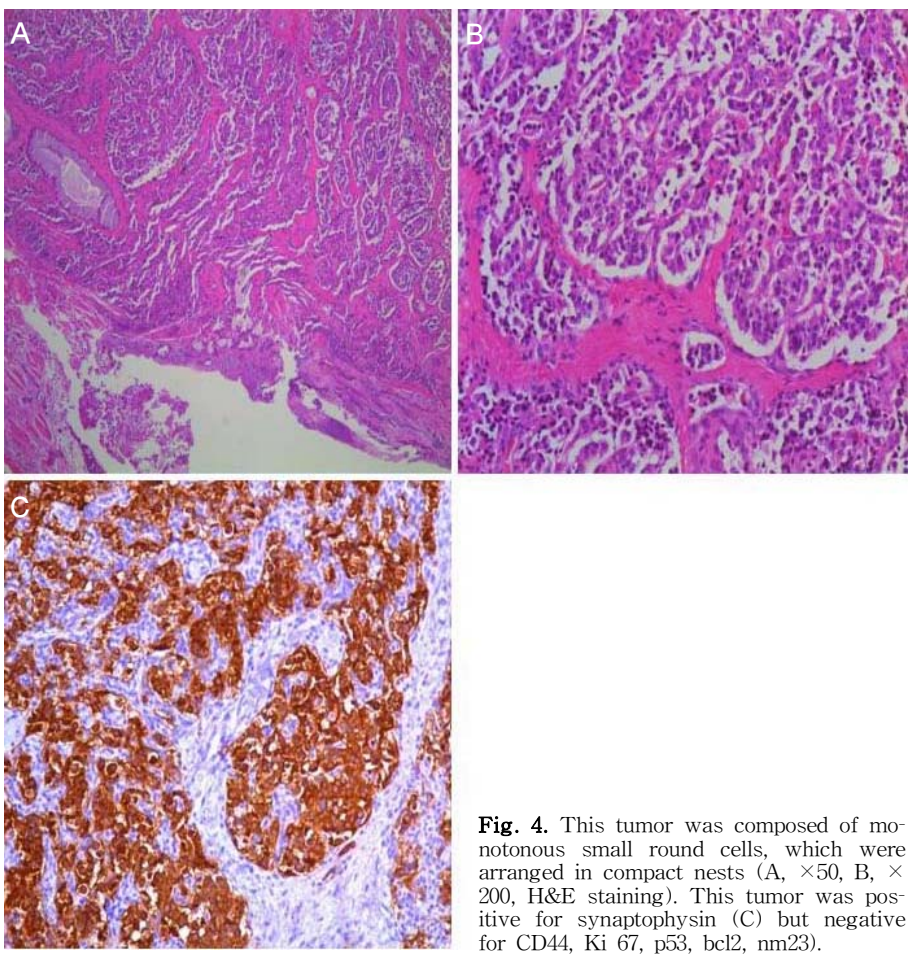

Fig. 4. This tumor was composed of monotonous small round cells, which were arranged in compact nests (A, ×50, B, × 200, H&E staining). This tumor was positive for synaptophysin (C) but negative for CD44, Ki 67, p53, bcl2, nm23).

survival, however the result was negative. The level of serum and urine 5-hydroxyindolacetic acid (5-HIAA) was evaluated and was within normal limits. A bone scan had no evidence of metastasis. Without further management the patient remains clinically well 5 months after diagnosis.

Discussion

Endobronchial tumors are very rare in the pediatric population, and for this reason they are often misdiagnosed as benign conditions. In our patient bronchial tumor was not considered at the time of the initial presentation, resulting in diagnostic delay. Recurrent pneumonia at the same location which dose not respond to standard medical therapy (including antibiotics) was considered to be an endobronchial lesion. This case is the first report in Korea, of a bronchial carcinoid tumor in an adolescent.

The most common endobronchial malignant tumor in children and adolescence is carcinoid tumor; but carcinoid tumors are very rare in the pediatric population.

Carcinoid tumor accounted for only 8 of 10,318 cancer patients (0.08%) over a 22-year period at St Jude Children's Research Hospital[8]. Their primary sites reported have been : appendix in 5, small intestine 1, bronchus 1, and liver and ovary with unknown primary site 1, respectively.

Endobronchial tumor to be differentiated from carcinoid tumor includes benign conditions such as hamartomas, hemangiomas, papillomas, inflammatory pseudotumors, leiomyoma, and mucus gland tumors as well as malignant diseases such as bronchial adenoma, carcinoid, mucoepidermoid carcinoma, adenoid cystic carcinoma and bronchogenic carcinoma.

Carcinoid tumors contain many neurosecretory granules. These granules can synthesize, store, and release substances such as serotonin (5-hydroxytryptamine; 5-HT), histamine, prostaglandin, kallikrein, and dopamine. Among these substances serotonin is the most frequently detected peptide which is degraded into 5-HIAA by monoamine oxidase and excreted in urine. These substances are thought to have endocrine functions.

The carcinoid syndrome presents with symptoms of periodic flushing, diarrhea, bronchoconstriction and peripheral vasoconstrictive symptoms. Clinical manifestations of bronchial carcinoid include: hemoptysis, cough, recurrent pulmonary infection, fever, chest discomfort, unilateral wheezing and shortness of breath. However, paraneoplastic syndromes are very rare in patients with pulmonary carcinoid tumor[9]. The patient in this report had normal level of 5-HIAA, so he had no serotonin related symptoms.

According to histologic criteria carcinoid tumors can be divided into typical and atypical forms with the latter exhibiting malignant features and aggressive clinical behavior [3]. Typical carcinoid (TC) is defined by <2 mitoses per 2 mm^2 with no necrosis, whereas atypical carcinoid (AC) is defined by ≥2 mitoses but <10 mitoses per 2 mm^2, coagulative necrosis, or both[1]. Both types can metastasize to regional lymph nodes and distantly. In previous reports[11, 12], 20% of bronchial carcinoid tumors (5 out of 25) had local and distant recurrence. Granberg, et al[5] reported that 12 out of 43 adult patients (28%) with typical bronchial carcinoid displayed metatstatic disease. Ten patients (23%) had lymph node involvement at diagnosis and 5 patients (12%) had distant metastasis. Five-year survival was 95%, and 10-yr survival was 91%; the investigators immunostained tumor tissue to identify prognostic markers. Positive staining of CD44 correlated with decreased risk for distant metastases and mortality (P<0.001). As the result of hormone staining using adrenocorticotrophic hormone (ACTH), gastrin-releasing peptide (GRP) and human chorionic gonadotrophin-α (hCGα), positive staining for GRP correlated with an increased risk for metastasis (P=0.04). Bcl-2 and p53 were associated with an increased risk for distant metastasis (P=0.01 vs <0.01) as well as decreased survival time (P<0.05 vs <0.001). Nuclear nm23 staining correlated with an increased risk for distant metastasis (P<0.001) but does not correlate with survival time[5]. We had done immunohistochemistry of prognosis related proteins, however, the result was all negative.

In cases of endobronchial localization of a TC, bronchoplastic parenchyma-sparing surgery is the standard surgical procedure. However, TC has potential for local and distant recurrence, and therefore close follow-up is essential; this should include clinical examination, chest X-ray, chest CT scan, urine and serum 5-HIAA and abdominal ultrasound scan to rule out hepatic metastases for a long time.

In conclusion, rare airway pathology in children may present diagnostic difficulty. Bronchial carcinoid tumor should be considered in the differential diagnosis in the presence of recurrent pneumonia. Survival is generally good, but physicians must be vigilant in monitoring for recurrence and associated tumors.

한 글 요 약

반복되는 폐렴으로 내원한 청소년기 폐 칼시노이드 종양

경상대학교 의과대학 소아과학교실, 병리학교실*

박은실 · 박지숙 · 서지현 · 임재영 · 이정희* · 고경혁*

소아의 기관 내 종양은 발생 빈도가 매우 낮고 그 증상이 소아에서 흔한 양성 호흡기 질환의 증상과 유사하여 진단 지연의 원인이 되기도 한다. 저자들은 동일 부위의 반복되는 폐렴으로 내원한 15세 여아에서 기관지 내시경을 통하여 기관 내 종양을 발견하고 병리 조직 검사를 통하여 전형적인 칼시노이드 종양을 진단하였기에 보고하는 바이다. 병리조직학적으로 전형적인 칼시노이드 종양은 수술적 절제만으로 완치를 기대할 수 있으나 원격 전이가 가능하기 때문에 장기간에 걸친 세심한 추적 검사가 필요하다.

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