A Case of Pulmonary Adenocarcinoma Accompanied by Superior Vena Caval Thrombosis in a Patient with Peutz-Jeghers Syndrome

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A case of lung adenocarcinoma and extensive deep vein thrombosis in a patient with Peutz-Jeghers syndrome (PJS) is presented. A 31-year-old Chinese man complained of shoulder pain and swelling of the right arm. A series of diagnostic procedures revealed a primary adenocarcinoma in the left upper lobe with cervical and supraclavicular lymph node metastases accompanied by deep vein thrombosis in the superior vena cava and right jugular vein. In addition, typical pigmentation of the lips and oral mucosa and multiple hamartomas in the stomach, duodenum and colon led to the diagnosis of PJS. PJS is known to be associated with increased risk of malignancies, especially in the gastrointestinal tract, breast, genitals and pancreas. As bronchoscopic examination showed no hamartomatous lesions in the bronchi, the development of primary lung cancer in this young patient might be independent of any hamartomatous lesion and might be associated with some genetic factors relating to PJS.

Key words: Peutz-Jeghers syndrome – lung cancer – pulmonary adenocarcinoma – deep vein thrombosis

INTRODUCTION

Peutz-Jeghers syndrome (PJS) is an inherited disease state characterized by gastrointestinal hamartomatous polyposis and mucocutaneous melanin pigmentation. Recent studies revealed that the syndrome is associated with germline mutations of serine threonine kinase 11 (STK11) gene at chromosome 19p13.3. Patients with PJS are known to be at increased risk of both gastrointestinal and non-gastrointestinal malignancies (1–5). Here, a young patient with pulmonary adenocarcinoma concomitantly diagnosed with PJS is reported.

CASE REPORT

A 31-year-old Chinese male student was admitted to our hospital because of shoulder pain and right arm swelling. About 6 months earlier, his screening chest radiogram in a routine health care protocol at his school showed an infiltrative shadow in the left pulmonary field and subsequent bronchoscopic examination led to the positive PCR detection of M. tuberculosis in a bronchial lavage specimen. Thereafter, he had been treated with isoniazid, rifampicin and ethambutol hydrochloride for 6 months until his admission to our hospital. From 2 months earlier, however, bilateral shoulder pain, productive cough and dyspnea on effort developed. Because the left pulmonary infiltration was unimproved during the course of antituberculosis therapy, and the gradual development of shoulder pain and following the sudden development of right arm swelling about a week before admission, he was referred to our hospital. He was a non-smoker and there was no history of any malignant disease or PJS among his relatives to the fourth degree of relationship.

He looked pale but was in good general condition on admission. On physical examination, his body temperature was 37.2°C, pulse was regular at 108/min, conjunctivas were anemic, lips and oral mucosa had scattered black pigmentation (Fig. 1), right side of the neck and right arm were edematous and swollen and multiple cervical and supraclavicular lymph node swellings were observed. There was no other abnormal finding on physical examination. Laboratory data included elevated white blood cell count of 10 300/mm³, decreased hemoglobin of 7.3g/dl, increased platelet count of 87.2×10⁴/mm³

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and elevated C-reactive protein of 5.2mg/dl. Carcinoembryonic antigen and cytokeratin-19 fragment in serum were elevated to 52.4 ng/ml and 12.0 ng/ml, respectively. Prothrombin time was 13.6 s (84% of predicted), partial thromboplastin time was 34.5 s and fibrin/fibrinogen degradation product was 10.3 µg/ml. Other laboratory data for hepatic and renal function, including urinalysis, were all normal. A skin test with purified protein derivative was negative. A chest radiograph revealed a focal infiltrative shadow in his left middle lung field and widening of the upper mediastinum. A chest CT scan showed a nodular shadow in the left S3 of 17 mm diameter accompanied by pleural indentations (Fig. 2) and surrounding ground glass opacities. An extensive thrombus extending from the right jugular vein to the superior vena cava was also demonstrated by contrast medium-enhanced CT (Fig. 3).

As these findings together suggested PJS and primary lung carcinoma with lymph node metastases and superior vena cava involvement, a series of diagnostic procedures were performed. Cytological examination of a transbronchial biopsy specimen and histological examination of cervical lymph node biopsy material established a diagnosis of poorly differentiated adenocarcinoma of the lung (Fig. 4). In addition, gastroduodenoscopy and colonoscopy revealed multiple polyps in the stomach, duodenum and colon (Fig. 5) and their histological analysis revealed benign hamartoma (Fig. 6).

Thrombolytic therapy with heparin sodium followed by urokinase was started immediately after admission, but the arm...
swelling failed to improve, partly because of the delayed initiation of the therapy, i.e. approximately a week after the onset of the apparent right arm swelling. A course of chemotherapy consisting of carboplatin and paclitaxel was also ineffective. At his request, he was transferred to a hospital in China. He reportedly died from sudden cardiopulmonary arrest immediately after micturition, 5 weeks after admission to our hospital.

DISCUSSION

PJS is an inherited state, characterized by lip and mucosal melanin pigmentation and multiple gastrointestinal hamartomatous polyps. This syndrome is considered to be caused by mutational inactivation of LKB1 (STK11) gene at 19p13.3 encoding serine/threonine kinase. As there are some cases without the mutation of LKB1, another responsible gene at 19q13.4 has also been reported (6,7). In addition, a recent study suggested that a leucine-rich repeat containing protein, LIP1 (or LKB1 interacting protein), interacts with LKB1 and regulates its function by controlling its subcellular localization (8). Our case was diagnosed as PJS based on typical manifestations of the syndrome, i.e. mucosal pigmentation and multiple hamartomatous lesions in the gastrointestinal tract, although genetic analysis was not performed. He seemed to be a sporadic case of PJS, as there was no history of familial malignancy or PJS to the fourth degree of relationship; about half of the cases of PJS are reportedly sporadic (9). A high risk for malignancies in PJS was first reported in 1987 (10) and similar reports followed (1–5). Accordingly, the relative risk of all cancers is 15.2 and that of gastrointestinal tract cancer is as high as from 84 to 520, with mean age at first diagnosis of cancer being 42.9 ± 10.2 years (1). Although cancers of the gastrointestinal tract may arise in hamartomatous polyps, non-gastrointestinal carcinomas are seen mainly in the breast, genitals and pancreas. As for lung cancer, the relative risk is 17. Our case seemed to be an example of such cases.

In addition, our case also had extensive deep vein thrombosis in the superior vena cava and right jugular vein. The sudden cardiopulmonary arrest on his death immediately after micturition seems to suggest a condition of fatal acute pulmonary embolism. Although, to the best of our knowledge, there have been no reports about an increased risk of deep vein thrombosis in patients with PJS, the possibility of a relationship between deep vein thrombosis and PJS could not be ruled out. Further clinical observations of patients with lung cancer associated with PJS may cast some light on the carcinogenesis in the lung of such cases.

References