

Congenital Pulmonary Lymphangiectasia, Associated with Total Anomalous Pulmonary Venous Return

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Congenital pulmonary lymphangiectasia (CPL) is very rare. It shows diffuse pulmonary lymphatic dilatation without lymphatic proliferation. CPL can occur as a primary disorder or arise secondarily from other diseases such as the obstruction of pulmonary veins or lymphatics. The prognosis of CPL is very poor. Approximately 50% of infants are stillborn and most others usually die within the first day of life. The present case showed diffuse lymphangiectasia in the subpleural, interlobular, and peribronchovascular areas. The flat lining cells were immunohistochemically positive for D2-40 and CD31. CPL is usually diagnosed by clinicoradiological or postmortem examinations. However, our case was diagnosed by an antemortem lung biopsy. We report a case of CPL with total anomalous pulmonary venous return.

Key Words: Congenital pulmonary lymphangiectasia; Pulmonary venous return anomaly

Congenital pulmonary lymphangiectasia (CPL) is a rare pathological diagnosis. It was first reported by Virchow¹ in 1856. CPL is histologically characterized by pulmonary lymphatic dilatation without lymphatic proliferation in the subpleural, peribronchovascular and interlobular areas. The prognosis of CPL is very poor where approximately 50% of all infants are stillborn and most others usually die within the first day of life.²

CPL can occur as a primary disorder or arise due to other diseases.³ CPL is often related to congenital heart diseases such as total anomalous pulmonary venous return (TAPVR), obstructed pulmonary venous return and hypoplastic left heart syndrome.⁴

Most cases of CPL are usually diagnosed by clinical and radiological exams, while some cases are confirmed by postmortem examinations.⁵ However, our patient was an extremely rare case, diagnosed by an antemortem lung biopsy. We report a case of CPL with TAPVR, confirmed by an antemortem lung biopsy.

CASE REPORT

A 1-day-old male was admitted to the department of thoracic

surgery of our hospital. He was born at 37 weeks of the gestational age by Caesarean section with a history of severe polyhydramnios and TAPVR, type 1 (supracardiac type). His mother was diagnosed with gestational diabetes mellitus at another hospital. The neonate weighed approximately 3,010 g, and the Apgar scores were 5 at 1 minute and 7 at 5 minutes. At birth, no crying was noted and the general appearance was poor. He presented with cyanosis, chest retraction and poor fetal movements. Blood laboratory data were unremarkable. A chest X-ray showed bilateral reticulogranular infiltration and a marked congestive pattern in the lungs. There was no evidence of cardiomegaly (Fig. 1A). A chest computed tomography scan revealed diffuse patchy ground-glass opacity in the subpleural and perihilar areas of the lungs (Fig. 1B).

An echocardiogram showed TAPVR, type 1 (supracardiac type) with a superior vena cava connection. An atrial septal defect (ASD; 6.84 mm in diameter, right to left shunt) and tubular patent ductus arteriosus (PDA; 4.61 mm in diameter, right to left shunt) were also detected. The level of oxygen saturation was <60% at birth and artificial ventilation with intubation was performed. He underwent an operation for TAPVR repair, PDA ligation and ASD closure, and was admitted to the inten-

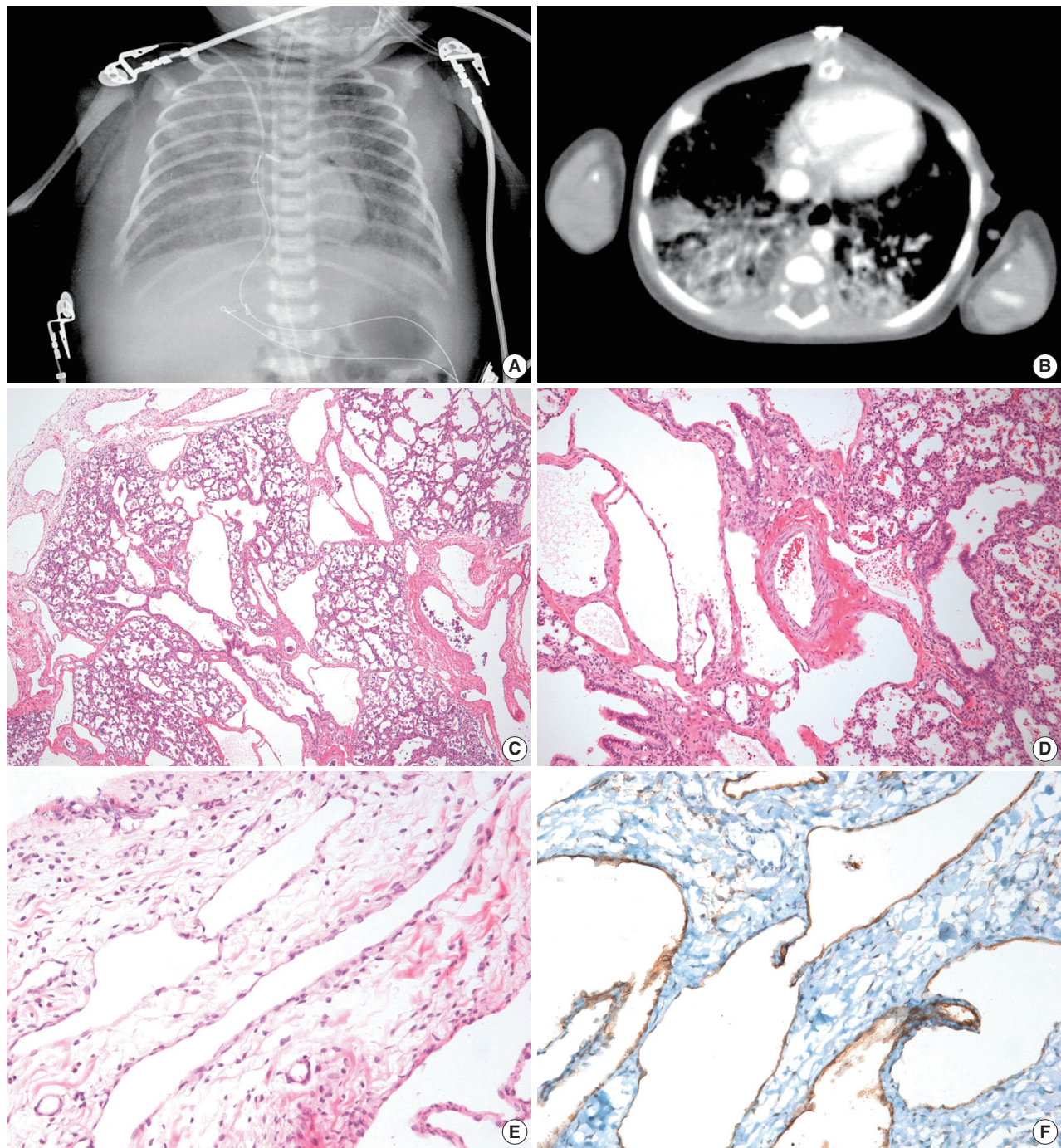


Fig. 1. (A) Chest X-ray shows bilateral reticulogranular infiltration and marked congestion in the lung. (B) Chest computed tomography reveals diffuse patchy ground-glass opacity in the subpleural and perihilar areas of the lung. (C) The microscopic examination of the lung biopsy specimen shows pulmonary lymphatic dilation without lymphatic proliferation in subpleural, interlobular, and peribronchovascular areas. (D) The microscopic examination of the lung biopsy specimen shows pulmonary lymphatic dilation in peribronchovascular areas. (E) The microscopic examination of the lung biopsy specimen shows pulmonary lymphatic dilation in subpleural areas. (F) The dilated pulmonary lymphatics are lined by flat endothelial cells, which are immunohistochemically positive for D2-40.

sive care unit (ICU) with extracorporeal membrane oxygenation (ECMO). In the ICU, ECMO weaning was performed 4 days after the operation. Persistent pleural effusion (daily effusion

drainage, 150 mL) and chylothorax were detected on a follow-up imaging study. He underwent a thoracic duct ligation and pleurodesis with a lung biopsy to treat severe pleural effusion.

Microscopic examination of the lung biopsy specimen showed widespread pulmonary lymphatic dilation without lymphatic proliferation in the subpleural, peribronchovascular and interlobular areas (Fig. 1C-E). The dilated pulmonary lymphatics were lined by flat endothelial cells, which were immunohistochemically positive for D2-40 (Fig. 1F) and CD31, but negative for cytokeratin. From these results and his clinicoradiological information, we diagnosed the lesion as CPL.

Despite intensive care, his respiratory distress and bradycardia were suddenly aggravated and cardiopulmonary resuscitation was performed. He died 3 months after the operation.

DISCUSSION

Lymphatic channels transport excess interstitial fluid from the body into the cardiovascular circulation. A defect in the lymphatic transport system can be related to the accumulation of interstitial fluid.⁶ The lymphatic channels of the lung are usually developed by 14 weeks of gestation. Lymphangiectasia usually arises from a secondary change in normal lymphatic channels. Pulmonary lymphatic channels start to regress after 20 weeks of gestation. CPL occurs if the regression of pulmonary lymphatics is prevented by various causes.⁷

The pathogenesis of CPL is not clearly understood. It can be a primary disorder or arise as a result of other diseases such as obstruction of pulmonary veins or lymphatics. CPL is sometimes found in isolation, and some cases are related to other congenital diseases.⁸

Patients with CPL show severe respiratory distress related to the poor prognosis, because the areas of CPL suppress normal alveolar tissue and decrease the alveolar space for pulmonary gas exchange.⁹ Severe respiratory symptoms often occur immediately at birth.¹⁰

Noonan *et al.*¹¹ classified this pathological entity into three groups. The first group is composed of cases with pulmonary lymphatic dilatation as part of systemic lymphangiectasis with pulmonary involvement. In these cases, the prognosis of CPL is good compared with cases in other categories.¹² The second group consists of patients with secondary lymphatic dilatation associated with primary diseases such as pulmonary venous obstruction *in utero*. Secondary pulmonary lymphangiectasia associated with congenital heart diseases such as TAPVR, obstructed pulmonary venous return and hypoplastic left heart syndrome are included in this group.¹³ The third group is composed of cases associated with developmental disorders of the pulmonary

lymphatic channels. Our case with both TAPVR and CPL was classified in Noonan classification group 2. Gestational diabetes mellitus has been known to be associated with congenital cardiac anomalies such as ASD, ventricular septal defect, hypoplastic left heart syndrome, pulmonary artery stenosis and TAPVR.¹⁴ In our case, maternal diabetes mellitus might be related to TAPVR, ASD and PDA of the neonate.

Radiological studies of CPL often demonstrate characteristic features.¹⁵ A chest X-ray reveals diffuse congestive patterns with prominent pulmonary vascular markings and reticulogranular patterns associated with cystic pulmonary lymphatics.¹⁶ Chest computed tomography reveals features of thickened pulmonary interstitium and fixed, patchy ground-glass opacity in the subpleural or perihilar areas of the lungs.¹⁷

On macroscopic examination, the lungs of patients with CPL appear incompressible and heavy. The pleural areas can show dilated small lymphatics or cystic lesions and the interlobular septum may be prominent in comparison with normal lung tissue. CPL is microscopically characterized by widespread pulmonary lymphatic dilatation without lymphatic proliferation in the subpleural, interlobular and peribronchovascular areas.¹⁸ The flat lining cells of the lymphatics are immunohistochemically positive for D2-40, CD34, and CD31 but negative for cytokeratin.

CPL should be distinguished from interstitial emphysema for an accurate diagnosis. Actually, many cases of interstitial emphysema have been misdiagnosed as CPL. Interstitial emphysema often appears with no lining cells on a microscopic examination and it can make the diagnosis more difficult. However, such areas of interstitial emphysema may be linked to other adjacent alveoli and the lining cells of the adjacent alveoli would be immunohistochemically positive for cytokeratin and negative for D2-40 or CD31. From these results, we distinguished CPL from interstitial emphysema.

CPL is usually diagnosed by clinicoradiological studies or postmortem examination. Our patient was an extremely uncommon case, diagnosed by an antemortem lung biopsy. He underwent lung biopsy during thoracic duct ligation and pleurodesis for the treatment of severe pleural effusion.

In summary, we report a very uncommon case of CPL with TAPVR, type 1 (supracardiac type), confirmed by an antemortem lung biopsy. Although CPL with TAPVR is extremely rare, we should not overlook that CPL with TAPVR could be one of the causes that induces severe respiratory distress or sudden death in neonates.

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