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OK-432 therapy for chylous pleural effusion or ascites associated with lymphatic malformations

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Abstract OK-432 therapy is effective for the treatment of macrocystic lymphatic malformations (LMs), but the optimal management of patients with microcystic LMs associated with large chylous pleural effusions or chylous ascites is not resolved. We performed thoracoscopic- or laparoscopic-guided injection of OK-432 for 2 patients with diffuse microcystic LMs accompanied by refractory chylous pleural effusion or chylous ascites. Both cases responded well to OK-432 therapy with improvement/resolution of fluid collections and associated symptoms. We recommend the use of OK-432 therapy as a promising treatment for microcystic LMs with functionally significant lymphatic fluid collections.

The clinical manifestations of lymphatic malformations (LMs) include both mass effects on surrounding tissue and the accumulation of large amounts of lymphatic fluid in the pleural or abdominal cavity. Diffuse microcystic LMs, in particular, can lead to large chylous pleural effusions or chylous ascites that are often refractory to treatment. Conventional conservative management of patients with LM is observation and feeding with medium-chain triglyceride–supplemented milk (MCT milk) [1], but MCT milk has only minimal effects on pleural effusion or ascites.

OK-432 is an inactivated preparation of *Streptococcus* pyogenes that is an effective sclerosing agent, and we have injected OK-432 into both macrocystic and microcystic LMs since 1987 [2]. However, the role of OK-432 in the treatment of LM-related pleural effusion or chylous ascites is unclear. Here, we report the successful treatment of two patients with microcystic LMs and pleural effusion or ascites with OK-432.

1. Protocol of OK-432 therapy for LMs

For neonates and infants as well as patients with LMs involving the tongue or face, OK-432 was injected under general anesthesia. For all other cases, it was injected under local anesthesia. OK-432 was prepared by diluting 0.1 mg of OK-432 stock solution in 10 ml of normal saline. Cystic fluid was aspirated, and an equal volume of diluted OK-432 was then injected. The maximum volume of OK-432 solution injected at one time was 20 mL (this means 0.2 mg of OK-432), regardless of the amount of fluid aspirated from the lesion. For patients in which aspiration of intralesional fluid was difficult (eg, microcystic LMs) the OK-432 solution was injected into the lesion at several sites. Repeat injections were performed every 6 to 8 weeks when there was evidence of clinical improvement and, more frequently, in the absence of a clinical response [3].

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2. Case reports

2.1. Case 1

A full-term female neonate was diagnosed with giant cystic meconium peritonitis in utero by prenatal magnetic resonance imaging (MRI). However, on physical examination after delivery, her abdomen was soft and distended with normal bowel sounds and without ascites. Postnatal MRI showed a high intensity mass within the abdomen, and large microcystic LMs were seen occupying the abdominal cavity (Fig. 1). The LMs surrounded the portal vein and extended into the retroperitoneum leading to significant abdominal distension. Laboratory findings were unremarkable, and we elected to observe the patient with careful monitoring of respiratory status without any other interventions. However, at 2 months of age, abdominal distension with ascites developed, and improved following administration of diuretics and MCT milk.

At 5 months of age, the patient developed tachypnea and anorexia secondary to a large chylous pleural effusion and chylous ascites, confirmed by chest and abdominal radiographs. (Fig. 2) These collections proved refractory to treatment with diuretics and MCT milk. We drained the pleural effusion and ascites with chest and abdominal tubes respectively. After stabilization of the patient, we injected 0.1 mg of OK-432 (10 mL) through the abdominal drainage tube into the abdominal cavity. In the pleural cavity, ultrasonography also demonstrated a thickened diaphragm with microcystic LMs, and a thoracoscope was used to guide the injection of OK-432 into the LMs of the diaphragm (0.03 mg, 3 mL) and the mediastinum (0.07 mg, 7 mL) (Fig. 3). The patient was followed up, and the ascites and pleural effusion decreased gradually over the following

Fig. 1 MRI (T2WI) showing a mass with high intensity occupying the entire abdominal cavity (arrows) (case 1).

Fig. 2 Thoracoabdominal X-ray showing right pleural effusion and ascites (case 1).

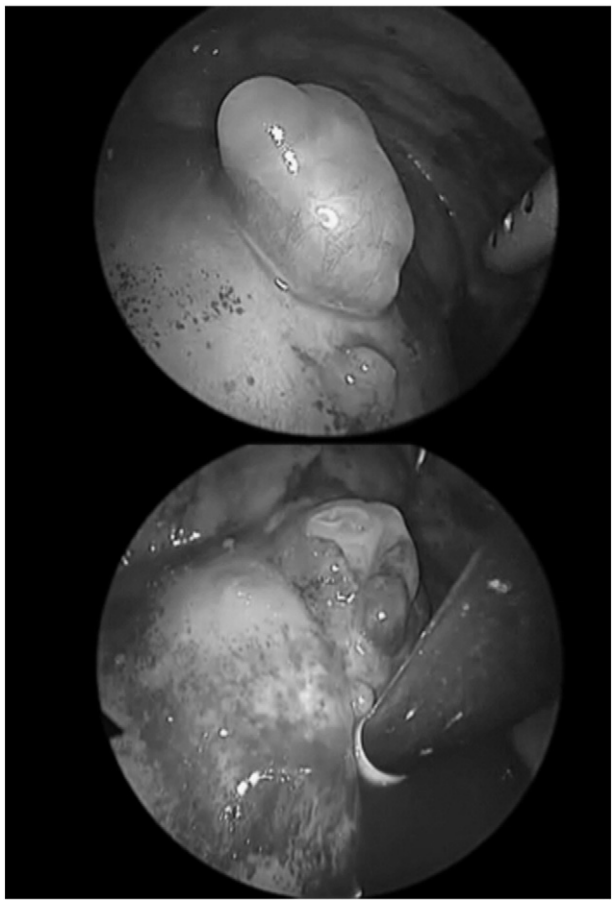

Fig. 3 Thoracoscopic injection of OK-432 into lymphangioma of the right diaphragm (case 1).