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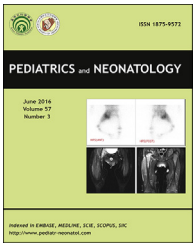

CASE REPORT

Complete Resolution of Retroperitoneal Lymphangioma with a Single Trial of OK-432 in an Infant

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Retroperitoneal lymphangioma is extremely rare. Although these neoplasms are benign, they can grow progressively with subsequent compression and infiltration of the adjacent structures. Surgical excision is demanding when the lesion surrounds vital structures and it is generally fraught with a high recurrence and morbidity rate. We report the case of a huge retroperitoneal lymphangioma in a newborn treated successfully with intracystic injection of OK-432.
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1. Introduction

Lymphangiomas are congenital anomalies of the lymphatic system. Cystic lymphangiomas can occur in any location in which lymphatics are normally found, but most are located in the head and neck (75%) and the axillary region (20%).[1] Retroperitoneal lymphangiomas account for nearly 1% of all lymphangiomas.

Large but localized lymphangiomas can be excised completely, although the surgical treatment of diffuse and multiple lesions is extremely difficult and is associated with a high morbidity and recurrence rate.[2,3] The intracystic injection of a sclerosing agent is considered appropriate for the treatment of surgically unresectable lesions and, according to the wide experience reported by Ogita et al,[3] OK-432 is the preferred sclerosing agent. To the best of our knowledge, only two cases of successful sclerosing (OK-432) treatment of retroperitoneal lymphangioma have been

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reported in the literature.[4,5] Herein, we report the case of an infant with prenatal diagnosis of a huge right retroperitoneal lymphangioma who was successfully treated with a single injection of OK-432.

2. Case Report

A 36-year-old woman, gravida 1, para 0, was referred to our hospital at 24 weeks' gestation for evaluation of a fetal intra-abdominal cystic mass. Ultrasound examination at 24 weeks' gestation showed a mass (37 × 26 mm) in the right side of the fetal abdomen, extending from the lower kidney pole down to the bladder. Magnetic resonance imaging (MRI), performed at 25 weeks' gestation, revealed a multilocular right retroperitoneal mass (53 × 47 × 37 mm) with medial displacement of the ipsilateral kidney (Figure 1). Neither fat nor calcifications in the tumor were evident at MRI. These findings were compatible with a lymphangioma.

At 38 weeks' gestation, a 4200 g boy was born by an elective cesarean section following an uneventful pregnancy. On physical examination the abdomen was soft and the documented mass was not easily palpated. No other abnormalities were detected. On Day 5, abdominal ultrasonography confirmed the presence, characteristics and limits of the large retroperitoneal multiseptated cystic mass. In order to better define its relationship with the renal vessels and the inferior vena cava, an MRI was performed on Day 8 (Figure 2).

The multiloculated lesion extended from the inferior surface of the liver down to the right iliac fossa, measuring 80 × 60 × 50 mm; the right kidney was encircled and displaced medially. Posteriorly the lesion infiltrated the posterolateral abdominal wall, involving the latissimus dorsi muscle.

At 8 weeks, the patient underwent sclerotherapy with OK-432. Using ultrasound guidance, we injected 0.1 mg of OK-432 diluted in 10 mL of saline after aspiration of the same volume of straw colored clear fluid from two superficial cysts on the right flank.

One and 4 months after the treatment abdominal ultrasound examination was performed: no mass was evident. At 12 months of follow-up, the patient is asymptomatic.

3. Discussion

Lymphangiomas are rare benign cystic tumors of the lymphatic system. Abdominal lymphangiomas account for less than 10% of all these congenital lesions. Retroperitoneal lymphangiomas are even less common: 50% of them are present at birth and 90% are diagnosed within the first 2 years.[6]

Surgical excision is the preferred treatment for lymphangiomas, to avoid rapid growth, superinfection, rupture, or bleeding that can require an emergent laparotomy.[7]

Although surgery is considered to be the treatment of choice, complete surgical removal may not be possible when lesions surrounding great vessels and vital nerves are present because of the inherent high risk of damaging the adjacent structures. The reported complication rates following operative intervention for lymphangiomas range from 12% to 33%.[8,9]

A subtotal excision, with preservation of vital structures, is reported to be unsatisfactory with a rate of recurrence of 12–53%.[10]

In 1987, Ogita reported good results in patients with unresectable lymphangiomas after intracystic injection of OK-432, a sclerosing agent derived from a strain of *Streptococcus pyogenes*.[11] In fact, the use of OK-432 has proved safe and effective for treatment of lymphangiomas in children yielding a complete resolution of the lesion in 92% of cystic lymphangiomas.[12] The injection of OK-432 causes the induction of neutrophils and macrophages, responsible for an increased production of tumor necrosis factor (TNF). The increased level of TNF is considered to play an important role in the regression of lymphangiomas.[13] The local inflammation does not damage the overlying skin and does not lead to scar formation, thus not impairing a possible surgical therapy whenever sclerotherapy has proved unsuccessful.

Although the sclerosing treatment with OK-432 has become a well-known approach for cystic lymphangiomas, its application is confined to superficial and accessible lesions, such as those in the limbs or head and neck region.

So far, four cases of retroperitoneal lymphangiomas treated with sclerotherapy have been reported (Table 1).[4–6,14] Of these, only two cases have been treated with OK-432;[4,5] in one case as a first line treatment and in the other as a rescue therapy after failure of a former marsupialization followed by a partial resection.

In our case, considering the huge size of the lesion and its close relationships with the right kidney and ureter, a complete resection was deemed difficult and risky, so ultrasound guided percutaneous intracystic injection of OK-432 was decided upon. This approach was possible due

Table 1 Cases of retroperitoneal lymphangiomas treated with sclerotherapy.

Case no.	Author	Sclerosing agent	Starting treatment	Associated treatments	No. of injections	Outcome
1	Rothenberg et al[14]	Doxycycline	13 y	Partial excision	1	Resolved
2	Shankar et al[6]	Tetracycline	4 y	Percutaneous catheter drainage	1	Resolved
3	Uchida et al[4]	OK-432	4 wks	No	2	Resolved
4	Güvenc et al[5]	OK-432	6 wks	Marsupialization, Limited surgical excision	1	Resolved
5	Present case	OK-432	8 wks	No	1	Resolved

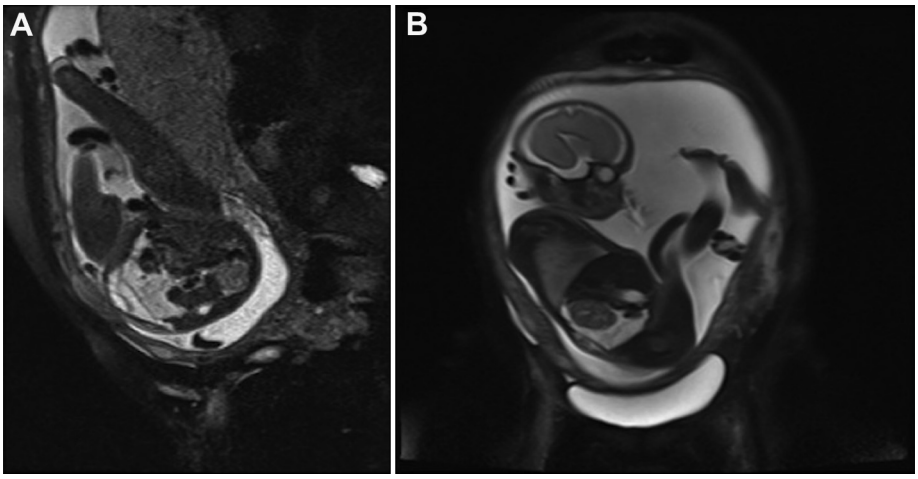

Figure 1 (A) Axial T2-weighted HASTE MR image shows a right retroperitoneal cystic mass with septations displacing the bowel loops and no sign of infiltration. (B) Sagittal T2-weighted MR image shows the lesion surrounds the right kidney without infiltrating it.

to the presence of two superficial cysts on the right flank, documented on ultrasound examination. OK-432 was injected at a dose of 0.1 mg, according to the method of Ogita et al: 0.1 mg of OK-432 in 10 mL of physiologic saline and the volume of aspirated fluid replaced with an equal volume of OK-432 solution.[12] One month after the sclerosing treatment, abdominal ultrasound examination showed a complete disappearance of the lymphangioma and no damage occurred to the overlying skin (Figure 3).

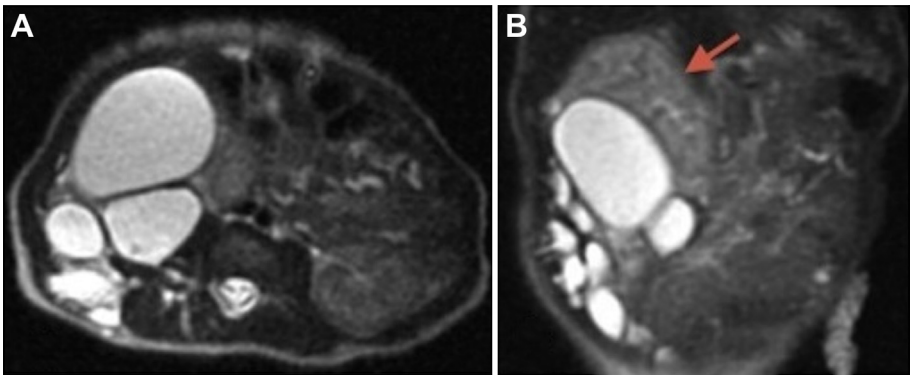

Figure 2 (A) Axial and (B) coronal T2-weighted MR images on Day 8 showing a retroperitoneal multiocular cystic mass. The lesion is hyperintense and shows multiple internal septae. The right kidney (arrow) is displaced anteriorly.

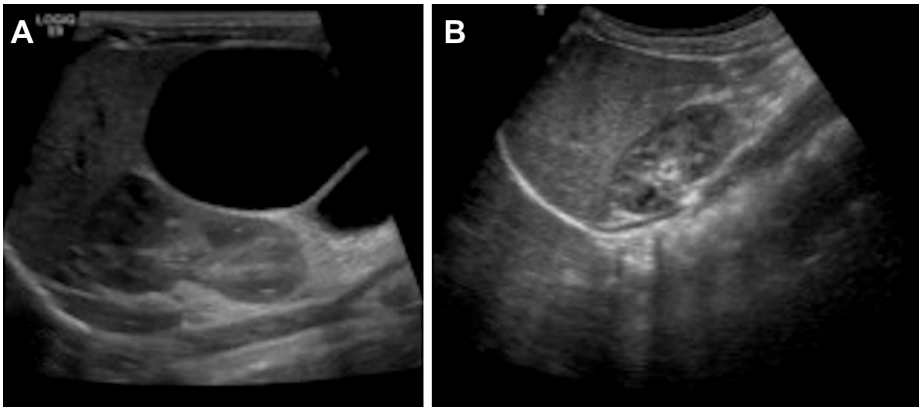

Figure 3 (A) Pre-treatment longitudinal US scan shows a cystic lesion with an internal septum, anteriorly to the right kidney. (B) Post-treatment longitudinal US scan shows no evidence of the cystic mass.

A case of retroperitoneal lymphangioma treated successfully with a single injection of OK-432 has not been previously reported in the literature. Actually, unlike to the two previous cases, the unique feature of our case is the rapid resolution of the lesion after the first sclerosing treatment, without resorting to a second intracystic injection of OK-432 or a surgical treatment to reduce the size of the lesion, as reported by Uchida et al[4] and Güvenc et al[5], respectively.

In all three cases the cystic mass was retroperitoneal and resolved with OK-432. Güvenc et al[5] performed an intralesional injection of OK-432 intraoperatively after a limited resection; whereas, in the case reported by Uchida et al[4] the site of injection was the flank, similar to our case, but two injections were necessary to obtain complete resolution of the lesion.

Laparoscopy can provide a less invasive approach than laparotomy in resection of abdominal lymphangiomas and its inherent magnification can certainly aid in facilitating dissection.[15] Moreover, in those cases in which the lesion is unresectable or when percutaneous approach is not feasible, laparoscopy could effectively enhance sclerotherapy aiding in localizing and injecting the lesions.

However, if the lesion is not reduced within 3—6 weeks after the first treatment, a second injection can be considered before performing a surgical approach.

The present case suggests that injection of OK-432 can be useful for the retroperitoneal lymphangiomas, avoiding surgery and the risks correlated with the surgical approach.

Conflicts of interest statement

Claudio Olivieri and co-authors have no conflict of interest to declare.

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