Sildenafil in Cystic Hygroma

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ABSTRACT
Cystic hygroma is a benign congenital malformation of the lymphatic system. Most of the cystic hygromas are found in the neck; other rare locations include axilla, mediastinum, and limbs. Symptoms range from mere presence of lesions to gross morbidity secondary to compression of adjacent organs, infection, hemorrhage etc. Treatment is primarily aimed at complete surgical resection. Other treatment modalities include sclerotherapy, radiotherapy and laser ablation as well as medical therapy with sirolimus but recurrence rate is high. We present a neonate with right sided cystic hygroma whose lesion settled completely with sildenafil.

Key Words: Cystic hygroma. Sildenafil. Neonate.

INTRODUCTION
Cystic hygromas are composed of embryonic lymph sacs of different sizes separated by connective tissue stroma. Six lymphatic sacs appear in the developing embryo at eighth week of gestation, two jugulars and two iliac, one at the base of root of mesentery and one dorsal to the abdominal aorta (cysterna chyli). These lymphatic sacs of various regions get connected by a network of lymphatic vessels and at the ninth week of gestation, these sacs are invaded by connective tissue to form lymph nodes.1

Cystic hygroma clinically presents in neonatal age but may appear at any age. Commonly present as an enlarging visible painless mass leading to disfigurement with or without pressure effects on surrounding structures.2 Can also present with local infection, inflammation and hemorrhage.3

Treatment options include surgery, sclerotherapy, radiofrequency ablation and laser excision but recurrence rate is high.4 Sildenafil citrate, a drug commonly used to treat Pulmonary Arterial Hypertension (PAH), has recently been reported to be effective in treating lymphatic malformations too. A possible mechanism of action of sildenafil in cystic hygroma is opening of dormant lymphatic channels due to relaxation of surrounding smooth muscles.5

CASE REPORT
A full-term female infant weighing 3.5 kg was delivered by cesarean section due to failed progress of labour and fetal distress to a 26 years mother. APGARs were 8 and 9 at 1 and 5 minutes respectively. A mass was noted on right chest, back and axilla. It was not reported on prenatal ultrasound. The mass gradually increased in size and another swelling appeared on the right side of neck at the age of one week when she was brought to our unit. These lesions appeared soft, compressible, non-tender and without any bruit (Figure 1 and 2). No signs of respiratory distress were noted at the time of admission. Baby remained well and on breast feed during her stay in neonatal unit. Ultrasound of the lesion showed multicystic lesion with internal septations and no blood flow was detected on colour Doppler ultrasonographs. CT scan demonstrated a cystic lesion in rightside of neck which extended inferiorly into the right axilla. The mass continued to increase in size still causing no symptoms to baby. While planning for a treatment option, literature search revealed effectiveness of sildenafil in cystic hygroma.5 A trial of sildenafil...
with 1 mg per kg per dose thrice daily was started. The swelling started regressing and disappeared in 3 months (Figure 3 and 4). No specific side effects were seen during treatment course. Parents are still continuing the treatment and are on regular outpatient follow-up. No untoward effects have been noted so far.

**DISCUSSION**

Cystic Hygroma (CH) is a lymphatic malformation with an incidence of approximately 1/6000 live births.1 It predominantly affects head and neck (75%). Axilla is affected in about 20% of cases and other less common sites include mediastinum, groin, and retroperitoneum.2 Embryonic development of lymphatic system starts around 8th week of gestation and initially 6 lymphatic sacs can be identified. These lymphatic sacs are two jugular sacs in neck, two iliac in lumbar region, one at the base of root of mesentery and one dorsal to the abdominal aorta (cysterna chyli).3 Later on, a network of lymphatic vessels develops that communicates with lymphatic sacs of various regions. During the ninth week of gestation, these sacs are invaded by connective tissue to form lymph nodes. Later, the lymphatics develop connections with venous system. CH is supposed to originate as a sequestration of one of these lymphatic sacs which fail to continue its communication with rest of the normal system and later increases in size to get cystic morphology.4

There are a number of proposed mechanisms to explain the pathophysiology. It can be divided into three types based on the size of cysts as microcystic, macrocystic and mixed lymphangiomas.2 CH, a macrocystic lymphangioma, occurs more frequently than other types of lymphangiomas and may be composed of single or multiple macrocystic lesions having scarce communication with normal lymphatic channels.2 The term is usually used for congenital lymphatic malformations detected in utero or observed at birth.

Diagnosis is commonly made clinically with large size, location and translucence. Although it tends to enlarge progressively over months, a relatively rapid increase in size has also been described.3 The management of CH is preferably surgical. Indications for surgery in pediatric cases include significant cosmetic deformity, obstructive symptoms, bleeding and recurrent infections.3,6 Other treatment modalities include aspiration, radiation, and injection of sclerosing agents, like bleomycin and OK-432, derived from a strain of *Streptococcus pyogenes*.7 Lymphangiomas have also been successfully treated with rapamycin (sirolimus).8,9 Phosphodiesterase (PDE) enzymes are important due to their unique tissue distribution, structural properties, and functional properties. Inhibitors of PDE can prolong or enhance the effects of physiological processes mediated by cAMP or cGMP by inhibition of their degradation by PDE.10 Sildenafil (Viagra) is an inhibitor of cGMP-specific PDE type 5, which enhances the vasodilatory effects of cGMP in the corpus cavernosum and is used to treat erectile dysfunction. Inhibition of PDE-5 decreases the contractility of vascular smooth muscle, producing vasodilation.10 A potential explanation for the therapeutic effect seen in CH is the relaxation of smooth muscle followed by cystic decompression. Alternatively, relaxation may allow secondary lymphatic spaces to open, or sildenafil may normalize lymphatic endothelial dysfunction.5

Considering the effectiveness of sildenafil in this case, the drug may be added as another very effective agent in the list of treatment modalities for CH despite very limited data in the literature about this off-label indication of the drug.

**REFERENCES**