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Generalized Lymphatic Dysplasia Presenting As Cystic Hygroma – A Case Report

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Case Report

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Abstract: Cystic hygroma, though a benign lymphangioma seen in the pediatric age group is an isolated entity, its occurrence complemented with the incidence of Generalized Lymphatic Dysplasia is a rarity. Our baby was diagnosed prenatally with hydrops fetalis, however did not progress well after birth. The complications like respiratory failure and other biochemical comorbidities made the surgical management of cystic hygroma a challenge. There are very few studies which implicate the role of genetics in the pathogenesis of GLD. There is a dearth for exploratory research in this area, which will help in early diagnosis and prevention of such complications among the newborn.
Keywords: Cystic hygroma, lymphangioma, Lymphatic Dysplasia.

INTRODUCTION

Lymphatic dysplasia is a congential mal-development of lymphatic system resulting in effusion of chyle into visceral spaces and limbs [1]. The effusion of chyle may be restricted to specific areas like chylothorax or chyloperitoneum, or may be generalized, involving all the lymphatics of the body. Such a condition is termed as Generalized Lymphatic Dysplasia. GLD is broadly classified into two categories namely Multi-segment GLD (type 1) and Widespread GLD (type 2). While type 1 has segmental pattern of involvement, there is a low risk of recurrence compared to the type 2 variety, which causes in-utero facial features like edema. There is an autosomal dominant/ recessive link associated with type 2, however, in our patient, the karyotyping was normal.

GLD is said to be associated with other syndromes like Turner, Noonans, kippel- Trenaunay, Proteus Syndrome, etc. In this case report, we present a case of GLD, with normal karyotyping, presenting as cystic hygroma in a newborn.

CASE PRESENTATION

During the intrauterine period, the fetus was diagnosed with bilateral cystic hygroma and bilateral pleural effusion. In view of fetal hydrops, LSCS was planned and the baby was delivered with a weight of 2.14 kg and a height of 30.5 cm. In view of cystic hygroma (diffuse swelling of the neck), baby had poor respiratory effort, and was intubated at birth. Baby had respiratory acidosis on the 9th day of life and was given High Flow Oxygen. Chest X Ray showed right side lung collapse.

Baby underwent aspiration and sclerotherapy with Bleomycin injection on 2nd day of life and pressure bandage was kept in situ. MRI brain showed simplified gyral pattern. Ultrasound abdomen done was normal. Ultrasound neck was done, which showed a large cystic lesion with MRI neck done showing a huge cervical thoracic hygroma, extending up to T8 level. Neurosonogram was normal. Baby was taken up for neck dissection with thoracotomy on 21st day of life. Postoperatively, baby persistenly required high pressure and high FiO_2, but was not tolerated well. Repeat X-ray done showed right side collapse. Baby had repeated episodes metabolic acidosis, baby was started on inotropic support.

There were several comorbidities in this patient. With severe respiratory distress, sepsis was suspected and the patient was started on Piperacillin and Tazobactam combination, alongwith Amikacin. Blood counts showed the presence of High Sensitivity C-Reactive Protein (HSCRP) following which the antibiotic cover was changed to Vancomycin, Amikacin and Meropenam. Post surgery, HSCRP was persistently high and therefore Meropenam was substituted with Amphotercin B. Serum Bilirubin(SBR) levels done on day 1 was above cut off, hence the patient was started

on phototherapy. For pleural effusion, Intercostal drain was inserted on the right side in view of increasing pleural effusion. Pleural fluid analysis was suggestive of chyle. The baby was also diagnosed with anaemia, and was transfused with packed cells prior to surgery and also post surgery. The patient was also diagnosed with hyponatremia and was started on 3% saline supplements at 5mEq/kg/day. On day 20 of life again electrolytes done showed hyponatremia and therefore, sodium supplements were increased to 12meq/kg/day. Preoperative echocardiogram showed Patent Ductus Arteriosis with left to right shunt.

Despite all interventions, the patient developed bradycardia for which adrenaline was given. Bag and tube ventilation and Cardio Pulmonary Resuscitation was given, as per NRP protocol. The patient did not recover from bradycardia and was declared dead on 24th day after birth.

At Autopsy, edematous area on right side of neck showed skin with underlying fibroadipose tissue showing dilated lymphatic channels of varying calibre. Adjacent lymphoid infiltrate also noted, consistent with lymphangioma. The thoracic cavity was found to be filled with chyle. Right lung weighed 26 gm and measured 4*3*2 cm with 2 fissures, 3 lobes. Left lung weighed 26 gm and measured 3*2*2 cm, 1 fissure, 2 lobes. A grey white area measuring 0.2*0.2cm was seen in lower part of upper lobe.

Microscopically, Thymus showed early involuntary changes and neck structures showed dilated lymphatic spaces. Bilateral lung showed saccular stage of maturation with features of extensive Bilateral Bronchopneumonia. Many dilated lymphatics were also seen in the pleura, while the heart appeared unremarkable. Liver showed extramedullary hematopoiesis with congested sinusoids and many dilated lymphatics in the capsule Intestine and stomach showed dilated lymphatics in the serosa. Pancreas showed dilated peri pancreatic lymphatics and spleen showed congestion. Bilateral kidneys showed peri renal dilated lymphatics. Bilateral adrenals showed dilated lymphatics in peri adrenal tissue. Uterus and bilateral ovaries showed dilated lymphatics in peri adnexal tissue

Histologically dilated lymphatics were also seen in the neck structures. In view of extensive lymphatic dilatation in all the visceral structures and serous spaces, diagnosis of Generalized Lymphatic Dysplasia was made at post mortem.

DISCUSSION

Generalized Lymphatic Dysplasia (GLD) often presents as one of the varieties of primary lymphatic dysplasia. Primary Lymphatic Dysplasia is seen exclusively in infants and children, manifesting as chylothorax, chylous ascites or both, and rarely as GLD. The condition is a very rare entity, with very high mortality (almost 100%) and very low cure rates. GLD has a huge spectrum of clinical manifestation involving multiple organ systems. The predisposing factors for GLD have been under question for many years. Though it has been proposed that congential malformation is the key etiology for GLD, the influence of hormonal factors requiring longer growth period has also been proposed in the development of GLD, especially among adults [2].

There is an autosomal dominant/ recessive link associated with type 2, however, in our patient, the karyotyping was normal. GLD is said to be associated with other syndromes like Turner, Noonans, kippel-Trenaunay, Proteus Syndrome, etc. Based on the section of lymphatics involved, GLD is classified as Lymphangiodysplasia (LAD 1)- which is the dysplasia of the lymphatics, LAD 2 which is the dysplasia of the lymph nodes, and LAD 3 which is dysplasia of both the lymphatics and the lymph nodes.

The presentation of GLD is often seen in infancy and childhood, with thorax being the most commonly affected system. Bones are also involved in >75% of the cases with GLD. Within the thorax, single or multiple lymphangiomas may be present in mediastinum, pleura, lungs, heart and chest wall. The symptoms are often non specific, ranging from mild wheezing, non productive cough, chest pain, chest tightness, and dyspnea [3]. In severe cases, massive pleural effusion ensues, which are chylous, due to the spontaneous rupture of diseased lymph vessels within the lymphangioma. In some cases, patients develop chyloptysis, hemoptysis and chylopericardium, and the progressive pulmonary infiltration results in respiratory distress, failure and death [4-7].

The diagnosis of GLD is often delayed because of the rarity of the disease. While chest radiographs indicate diffuse interstitial infiltrates and pleural effusions, higher investigations like High Resolution Computer Tomography (HRCT) and MRI only provide suggestive information, but not a definitive diagnosis. Histopathological diagnosis by biopsy of the pleura may provide the conclusive diagnosis of GLD. The histopathology of GLD resembles a lymphangioma showing increased number of dilated anastamosing lymphatic channels lined by endothelial cells [8, 9]. The anastamosing spaces are often filled with chyle or eosinophilic material. Although these lesions infiltrate into adjacent tissues, they appear benign, composed of mature cells. The lymphatic endothelium is characterized by diffuse and strong expression of D2-40 [10]. There are few studies which have explored the genetic role in the pathogenesis of generalized lymphatic dysplasia (GLD). A study done by Fotiou E et al showed that mutations in PIEZO1 results in autosomal recessive form of GLD and presents as non immune hydrops [11].

The management of GLD is challenging, owing to its unknown/ genetic etiology and widespread involvement. The treatment is mostly palliative, and aims at slowing down the progression of the disease and alleviating the symptoms related to the compression caused on adjacent structures due to the chyle accumulation. Conservative management like dietary restriction of protein have not proven conclusive. Surgical methods like parietal pleurectomy, pleurodesis, and ligation of thoracic duct can be done to minimize the pleural effusion. Sclerotherapy with local injection of agents like Streptococcus antigen OK-432 helps in sclerosing the dilated lymphatic vessels [12, 13]. Radiation and systemic chemotherapy have also been tried, but without much success. Drugs aimed at reducing the Vascular Endothelial Growth Factor (VEGF) like propranolol, and bevacizumab, a monoclonal antibody have also been tried in some case reports [14, 15].

CONCLUSION

Generalized lymphatic dysplasia, a congenital maldevelopment of the lymphatic system is a rare entity and had presented with respiratory distress, in the newborn of our case report. With an overt presentation of cystic hygroma, the management of this patient had been challenging, owing to several systemic complications like sepsis and respiratory acidosis. The histopathological diagnosis has proven to be definitive, with the presentation of increased number of dilated anastamosing lymphatic channels lined by endothelial cells. There is an increasing need for research directed towards early diagnosis, in the antenatal period, in order to prevent morbidity, mortality and complications due to GLD.

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