



Case report

Use of somatostatin analogues to treat chylothorax in a child with Generalised Lymphatic Dysplasia

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ABSTRACT

Generalised Lymphatic Dysplasia is a rare condition that may be associated with significant chylothoraces. The management of such effusions is often challenging. We present the case of a 15-year-old girl with bilateral chylothoraces and lymphoedema of her limbs. A clinical diagnosis of Generalised Lymphatic Dysplasia was made and long-term treatment with somatostatin analogues (somatostatin initially followed by monthly octreotide) was initiated. Over 12 months there was symptomatic benefit with some objective improvement in lung function and no adverse effects. After a year of treatment there was some reaccumulation of fluid, however this did not require any intervention. This is the first paediatric report of the use of somatostatin analogues to manage chylothorax in Generalised Lymphatic Dysplasia and we conclude that they represent a potentially useful treatment modality. Experience is only anecdotal however and further studies are required to establish an evidence base with regard to efficacy and safety.

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1. Introduction

Generalised Lymphatic Dysplasia is a rare condition affecting 1.15/100,000 people aged <20 years.¹ Historically patients have been divided according to age of onset, however an improved classification based on phenotype has recently been published.² Clinical presentation is variable and may include systemic involvement such as pleural effusions.^{2,3} In this context pleural effusions are recognised to be difficult to manage and are often refractory to conventional treatment approaches.⁴

2. Case report

A 15-year-old girl was referred to tertiary paediatric respiratory services following identification of bilateral pleural effusions during investigation of delayed puberty. She had initially presented with lymphoedema complicated by cellulitis in both lower limbs at 2 years of age and was managed with antibiotics and support stockings. Limb oedema then subsequently increased throughout childhood.

On examination there was significant bilateral lymphoedema of the legs and arms. Hypertrophied and discoloured nails (Fig. 1) were discovered after removal of nail varnish. A plain radiograph and computed tomogram of the chest demonstrated hyperinflation and bilateral pleural effusions, but no evidence of bronchiectasis or mediastinal abnormality. Echocardiography was normal apart from a small pericardial effusion. Thoracocentesis yielded milky fluid (protein 45 g/L, cholesterol 3.2 mmol/L, triglycerides 13.8 mmol/L, lactate dehydrogenase 120U/L, pH 7.75, white blood cells $0.79 \times 10^9/L$, 98% lymphocytes). A radionuclide lymphatic study demonstrated a symmetrical obstructive pattern proximally with extensive collateralisation in both legs and no pooling in the chest. Serum immunoglobulins, immunoglobulin G subsets and functional antibodies relating to vaccinations were all normal.

A clinical diagnosis of Generalised Lymphatic Dysplasia was made and therapeutic thoracocentesis was performed. The patient was then established on subcutaneous somatostatin followed by monthly long-acting octreotide. Prophylactic co-trimoxazole and a low-fat diet were also instituted. Review at 3 months showed improved lung function from presentation (FEV₁/FVC: 1.5/1.7 L vs. 1.07/1.16 L) with no reaccumulation of pleural fluid.

A year after initial assessment lung function had fallen slightly (FEV₁/FVC 1.25/1.8 L) and the left-sided effusion had reaccumulated to a degree. However the patient reported

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Fig. 1. Discoloured nails.

symptomatic improvement in terms of exercise tolerance and repeat thoracocentesis has not been required. In addition, there have been no adverse effects from somatostatin therapy and it has been well tolerated. Menarche has now occurred.

3. Discussion

In the Generalised Lymphatic Dysplasias abnormalities of lymphatic vessels result in impaired lymph drainage, but relatively little is known about the exact pathogenesis. Mutations in biologically plausible genes have been implicated in some cohorts and families with GLD.^{5,6} Lymphoedema is often associated with discoloured nails. It is important to note that Yellow Nail Syndrome is a specific clinical entity, which is often associated with autoimmunity, lymphoedema and respiratory tract involvement, and normally presents in later adulthood. The associated nail changes include slow growth, yellow or green discolouration, increased transverse and longitudinal curvature, onycholysis, shedding, cross-ridging and loss of lunulae and cuticles. Misdiagnosis of Yellow Nail Syndrome is relatively common and it was not the diagnosis in this case.⁶

Somatostatin analogues have been used to treat chylous pleural effusions of varying aetiology including congenital chylothoraces and trauma to the thoracic duct after cardiothoracic surgery.^{7,8} There are only limited reports in the adult literature of the use of somatostatin analogues to treat refractory pleural effusions in the specific context of Generalised Lymphatic Dysplasia however.^{9–11} To the best of our knowledge this is the first such paediatric case report. In our case there was symptomatic benefit with some objective improvement in lung function but ultimately reaccumulation of some pleural fluid a year in to therapy. Admittedly, there is also no way of knowing the relative contributions made by the institution of prophylactic co-trimoxazole or a low-fat diet.

Roehr et al. published a systematic review identifying 35 children in the medical literature treated with somatostatin or octreotide for chylothorax.¹² The cases identified were mainly postoperative with none associated with Generalised Lymphatic

Dysplasia. A positive treatment effect was reported in the majority. Importantly, a number of side effects were noted. Aside from minor effects such as transient hyperglycaemia and cutaneous flushing, particular care is advised in children who are vulnerable to vascular insults and cases of strangulation-ileus in a child with asplenia and necrotizing enterocolitis in a neonate with coarctation of the aorta were cited.¹²

In conclusion, somatostatin analogues represent a potentially useful treatment modality in children with chylothorax associated with GLD and warrant consideration in cases refractory to other management. Repeated thoracocentesis of chylothoraces may lead to problems with nutrition and presents major practical issues in children who may require general anaesthesia for the procedure.⁴ Further studies are required to establish an evidence base for the efficacy and safety of somatostatin analogues; although the rarity of this group of conditions makes it unlikely that a formal randomised controlled trial will be feasible.^{12,13}

Conflict of interest

All authors confirm that they have no relevant conflicts of interest relating to the above manuscript.

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