

## Congenital Heart Disease in Patients with Primary Lymphedemas

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### Summary

An association is described between congenital heart disease and abnormality of the thoracic duct. Abnormality of the thoracic duct is associated with a distinctive pattern of lymphatic *hyperplasia*. Five of 31 patients with this lymphatic anomaly were found to have congenital heart disease.

Various forms of hypoplasia of lymph pathways are much more common anatomic anomalies in primary lymphoedemas but the incidence of congenital heart disease in these is low.

### Introduction and Methods

It has been recognized that patients with primary lymphedema may have abnormalities affecting other systems (1) and sometimes have congenital heart disease (2).

A retrospective review was performed of 475 patients who underwent lymphography for primary lymphedema of the lower limbs at St. Thomas's Hospital between 1965 and 1980. An increased incidence of congenital heart disease was noticed particularly in patients with lymphedema of the lower limbs and hyperplasia of the lymphatic pathways. These patients were studied in detail from the cardiac and lymphatic aspects.

Bipedal lymphography was performed as previously described (1). As a routine, radiographs of the chest including oblique views were taken at the end of the investigation. This was done to demonstrate the thoracic duct and if the duct was not shown further radiographs were taken at intervals after repeated massage of the lower limbs and abdomen to promote filling of the duct.

Congenital heart disease is interpreted as an abnormality of the heart or adjacent great vessels.

### Results and Comments

#### *The association of congenital heart disease and lymphatic hyperplasia*

Lymphatic hyperplasia is an uncommon finding in primary lymphedema being present in only 31 of 475 (6.5%) patients who underwent lymphography for primary lymphedema. Five of these 31 patients (16%) had a congenital cardiac lesion.

The typical radiographic features of lymphatic hyperplasia are outlined and then brief case histories are given of the 5 patients with lymphatic hyperplasia and congenital heart disease.

Lymphatic hyperplasia occurs when the thoracic duct is congenitally absent or deformed (1, 2). This causes an obstruction to the flow of lymph through the mediastinum. The characteristic findings on lymphography are abundant dilated lymphatics on the dorsum of the feet, numerous dilated channels in the lower limbs and often more than 15 afferent channels at the groin. The inguinal and pelvic lymph nodes are more numerous than usual and enlarged. There may be filling of many nodes in the root of the mesentery indicating obstruction at the level of the cisterna chyli or above. The thoracic duct may not be shown at all or only the lower part fills. In other patients the duct is deformed or breaks up into fragments. The opacification of inter-



**Fig. 1** Case 1. Lymphadenogram showing hyperplastic intra-abdominal lymph nodes in a patient with a deformed thoracic duct. In particular note the mass of nodes to the left of the midline, presumably in the root of the mesentery.

**Table 1** Summary of findings in 5 patients with congenital heart disease and lymphatic hyperplasia

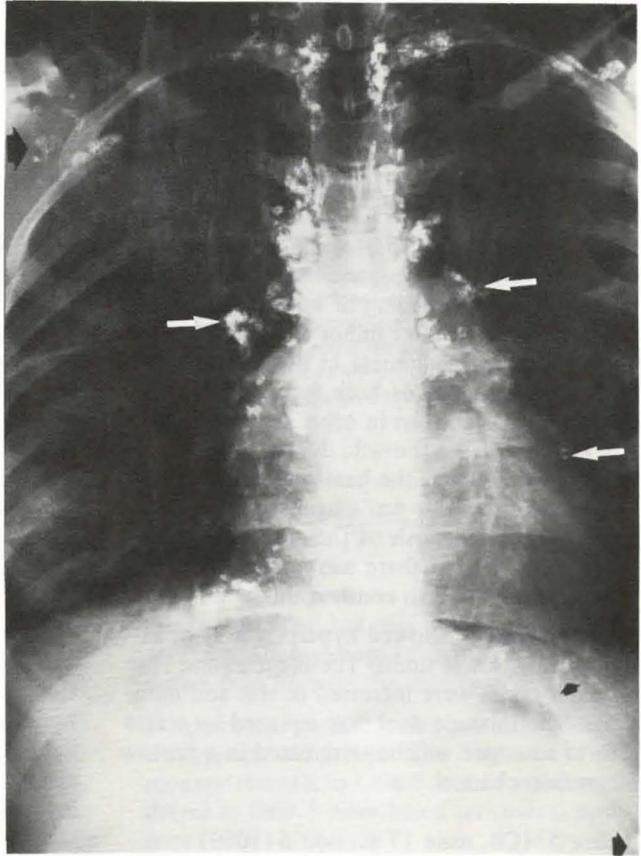
patient	lymphatic abnormalities		
	limbs and abdomen	thoracic duct	cardiovascular abnormalities
1. JL male 24 y, 796149	hyperplasia	deformed	pulmonary stenosis
2. ES female 16 y, 505869	hyperplasia	absent	pulmonary stenosis, ostium secundum ASD infundibular stenosis
3. PN male 12 y, 486463	hyperplasia	deformed	pulmonary stenosis ostium secundum ASD
4. SW male 15 y, 782741	hyperplasia	deformed	congenital stenosis of innominate or right carotid artery
5. CB mal 17 y, 541089	hyperplasia	absent	absent IVC bicuspid aortic valve

ASD, atrial septal defect. IVC, inferior vena cava

costal and axillary collateral pathways may also provide evidence of an obstructed thoracic duct.

Five case histories are described. The numbering corresponds to that in Table 1 which provides a summary of the abnormalities.

*Case 1* (JLL, male 24 y., no.: 796149)  
This patient was referred from Belgium for treatment of a severe protein losing enteropathy caused by intestinal lymphangiectasis. At the age of 12 congenital pulmonary stenosis had been corrected by valvotomy. There



**Fig. 2** Case 2. This radiograph illustrates the collateral lymphatic pathways in a patient whose thoracic duct was absent. The white arrows demonstrate filling of mediastinal and bronchial lymph nodes. Lymphatics are shown along the line of a lower left rib (black arrow) and there is filling of right axillary lymph nodes (black arrow) and supraclavicular nodes

was also a history of left chylothorax and chylous ascites together with swelling of both feet and legs.

On bipedal lymphography the only trace of his thoracic duct was some dilated fragments in the upper mediastinum. The striking abnormality was a great mass of hyperplastic nodes in the abdomen particularly in the root of the mesentery (Fig. 1).

*Case 2* (ES, female 16 y., no.: 505869) This girl underwent pulmonary valvotomy and closure of an ostium secundum atrial septal defect at the age of 14. At 16 she developed lymphedema of the left foot and leg. She was also found by chromosome studies to have a mosaic form of Turner's syndrome. Lymphography showed hyperplasia of the dis-

tal lymphatic tree with more than 15 afferent vessels in both groins. The intra-abdominal lymph nodes were normal but no thoracic duct could be outlined at all. Lipiodol was seen in mediastinal and bronchial lymph nodes and in intercostal, axillary and supraclavicular collateral channels (Fig. 2).

*Case 3* (PN, male 12 y., no.: 486463) Multiple congenital abnormalities were observed in this 12 year old boy who presented with a 2 year history of swelling of both lower limbs. At the age of 16 he required surgical correction of pulmonary stenosis and an ostium secundum atrial septal defect. He had bilateral undescended testicles and evidence of Marfanism with a high arched palate and long digits. Reflux of chyle resulted in

multiple chyle filled vesicles on his right lower limb.

Lymphography showed hyperplasia in the lower limbs and abdomen and late filling of the lower thoracic duct. The upper thoracic duct could not be opacified and instead there was filling of intercostal collateral lymphatics.

*Case 4* (SW, male 15 y, no: 782741)

This 15 year old boy presented with a one year history of swelling of both feet and legs which appeared after minor trauma. There were capillary angiomas in the skin along the lateral borders of both feet. This abnormality has been seen in other patients with deformity of the thoracic duct (1). A loud bruit was heard at the base of the neck on the right side. This was diagnosed clinically as congenital stenosis of the carotid or innominate artery but there was no indication for arteriography to confirm this.

Lymphography showed hyperplastic lymphatics in the lower limbs. The inguinal and iliac lymph nodes were increased in size and number. The thoracic duct was replaced by a rete-form structure which terminated in a narrow common channel.

*Case 5* (CB, male 17 y., no.: 541089)

This was the only patient in the present series who had lymphedema present at birth. Both feet and legs were edematous and he also had a congenital left hydrocele and varicocele. By the age of 17 he had developed bilateral varicose veins and an ulcer on the lateral side of the left knee. The persistence of this ulcer led to his referral and the discovery of an unsuspected cardiovascular abnormality. Phlebography indicated absence of the inferior vena cava. Iliac phlebograms demonstrated normal femoral and iliac veins, devoid of any changes of recanalization to suggest past thrombosis and the venous return was via lumbar veins and the azygos system. A clinical diagnosis of congenital bicuspid aortic valve was also made on the basis of auscultatory signs and echocardiographic evidence.

Bipedal lymphography showed no thoracic duct. There were many small abnormal lumbar lymph

nodes with filling of axillary and supraclavicular lymph nodes via collateral pathways.

A further patient (SG, male 36y., no.: 509609) who has not been included among these 5 patients was found after full investigation including endomyocardial biopsy to have congestive cardiomyopathy. He had a history of lymphedema of both lower limbs since birth, hyperplastic lymphatics and a deformed thoracic duct. His cardiac lesion appeared to be acquired but it is conceivable that he might have had an abnormality of the lymphatic drainage from the heart causing stasis of cardiac lymph and tissue fluid.

*Cardiac abnormalities*

Cardiac lesions were single or multiple. Lymphatic hyperplasia was not associated with any particular congenital cardiac lesion. Pulmonary stenosis was the commonest lesion occurring in 3 of the 5 patients. These 3 patients are numbered 1-3 in Table 1 and their cardiac lesions were all confirmed at operation. The fourth patient in Table 1 was diagnosed as having congenital stenosis of the right carotid or innominate artery. This remained a clinical diagnosis as there was no indication for arteriography. The fifth patient in Table 1 was thought to have an absent inferior vena cava on clinical and radiological grounds, together with clinical and echocardiographic evidence of a bicuspid aortic valve but there was no operative confirmation of these findings.

*Family history*

There was no family history of congenital cardiac disease in these 5 patients but one had a family history of lymphedema.

*Numerical data*

The incidence of congenital heart disease in the general population is 8-10 cases per 1000 live births (3). Using the chi-squared test the incidence of congenital heart disease among the patients with lymphatic hyperplasia (5 in 31) was compared with the incidence of congenital heart disease in the general population. For performing the test the figure of 9

**Table 2** Summary of findings in 6 patients with congenital heart disease and lymphatic hypoplasias

patient	lymphatic abnormalities		
	limbs and abdomen	thoracic duct	cardiovascular abnormalities
1. DF male 24 y., 631407	proximal and distal hypoplasia	normal	coarctation of aorta
2. EB female 23 y., 685662	distal hypoplasia	normal	ostium primum ASD subvalvular aortic stenosis mitral leaflet prolapse
3. AW female 16 y., 782718	distal hypoplasia	normal	pulmonary stenosis
4. AC male 19 y., 662782	proximal and distal hypoplasia	not shown	patent ductus arteriosus ostium secundum ASD pulmonary regurgitation mitral leaflet prolapse dextro-rotation of heart agenesis left pulmonary artery
5. HR female 20 y., 647911	proximal and distal hypoplasia	not shown	ASD
6. MC male 23 y., 650781	proximal hypoplasia distal distension	not shown	patent ductus arteriosus

ASD, atrial septal defect

cases per 1000 live births was used. The value for chi-squared was 71 ( $P < 0.001$ ) which is highly significant.

### Lymphatic hypoplasia

Various forms of hypoplasia are much commoner than hyperplasia in patients with primary lymphedemas. Hypoplasia was found in 425 of 475 patients (89.5%) investigated by lymphography. Congenital heart disease also occurs in these hypoplasias but it is much less common. There were 6 patients with congenital heart disease among the 425 with hypoplastic lymphatics, an incidence of 1.4%. This incidence is not much greater than among the general population and repetition of the chi-squared test gave a value of only 1.7 for chi-squared, which is not significant.

The characteristic lymphographic features of hypoplasia are slow transit of dye, fewer than 5 afferent channels at the groin and for those with a proximal defect, a paucity of intra-abdominal lymph nodes which are often small and misshapen.

The lymphatic and cardiac defects in these 6 patients with hypoplasia are summarized in Table 2. A normal thoracic duct was outlined in cases 1-3. In cases 4-6 the duct could

not be opacified but this was thought to result from slow passage of dye to the chest rather than because the duct was absent.

No particular cardiac lesion predominated in the hypoplastic groups. The diagnoses of pulmonary stenosis in Case 3 and of atrial septal defect in Case 5 were based on clinical evidence.

No further investigation was warranted in these 2 patients. The other 4 patients in the group required operation so their lesions were all confirmed.

Additional non-cardiac congenital defects were recorded in 2 patients with lymphatic hypoplasia. Case 3 had conjunctival edema of her left eye. Case 5 had hemi-atrophy of the right side of her body affecting the skeleton and soft tissues. Among these 6 patients there was no family history of congenital heart disease but one patient had a positive family history of lymphedema.

### Discussion

Patients with primary lymphedema are sometimes referred to a cardiologist because of suspected congestive cardiac failure. Usually the distinction between cardiac and lymphatic

tic edema can be made on clinical grounds. If the cardiologist finds no heart disease lymphography can be of great value in establishing a diagnosis of primary lymphedema. Occasionally the diagnosis of lymphedema may not be suspected because there are known cardiac anomalies which could account for peripheral edema and here it is important to recognize the association between congenital heart disease and an abnormal thoracic duct. Such patients should be referred for lymphography so that a diagnosis can be made and the appropriate advice given about the lymphedema.

It is not surprising that defects of the thoracic duct may co-exist with congenital cardiac anomalies as both sets of structures develop concurrently in the same anatomic region. Lymphatic spaces appear from the sixth week of intra-uterine life (4). Paired thoracic ducts form at the caudal ends of the jugular lymph sacs. At the same time septa are developing in the primitive cardiac tube to partition the heart into separate chambers. Development of the heart and thoracic duct could be compromised simultaneously by the same factor.

No cases of cyanotic congenital heart disease were found in this series. It is impossible to draw conclusions but as lymphedema is often not apparent until the second or third decade it may be that some infants with lymphatic abnormalities and a severe cardiac lesion die before lymphedema becomes manifest.

Some element of doubt surrounds the diagnosis of cardiac lesions made only on clinical grounds, or on radiological grounds in the patient with an absent inferior vena cava. If the analysis is confined to lesions confirmed at operation then 3/31 patients with lymphatic hyperplasia had congenital heart disease, an incidence of 9.7% which is still far in excess of the expected incidence of 0.9% of cases in the general population.

The association between congenital heart disease and this type of primary lymphedema appears not to have been described in detail before. Emanuel et al. (5) in a study of patients with congenital atrioventricular defects found that as many as 42% had associated non-cardiac congenital defects. These defects were mainly skeletal and there were no cases of lymphedema.

The association between congenital heart disease and congenital deformity of the thoracic duct may be even stronger than suggested. The thoracic duct was not shown on lymphography in 3 patients in the group with lymphatic hypoplasia despite special efforts to demonstrate it. This might have resulted from the slow upward passage of dye but it could have been due to absence of the duct itself, or at least to an obstructive lesion in the cisterna chyli or lower part of the duct. If the latter interpretation is correct then the link between deformity of the thoracic duct and congenital heart disease is stronger than has been suggested.

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