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Adult Turner syndrome associated with chylous ascites and vascular anomalies

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An adult female with Turner syndrome presented with severe lymphedema and chylous ascites. In addition, the patient was found to have a right-sided aortic arch and a left-sided inferior vena cava. Although lymphedema is common in infants with Turner syndrome, it usually resolves in childhood. Chylous ascites in association with Turner syndrome is previously unreported. In this patient, a peritoneo-venous shunt appeared to be beneficial.

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In 1938 Henry Turner described the association of sexual infantilism, webbed neck and cubitus valgus in adult women (Turner 1938). Subsequently, gonadal dysgenesis was defined as part of the syndrome and the characteristic chromosomal abnormality (45,X) was reported (Wilkins & Fleischmann 1944, Ford et al. 1959). A variety of congenital malformations have been described as Turner stigmata. Lymphedema occurs in 80% of newborns with Turner syndrome (Hall et al. 1982), but is usually transient. In this report we describe an adult with both lymphedema and chylous ascites. The latter has not previously been reported in association with Turner syndrome.

Material and Methods

Case Report

P. S., UMMC #1154–134-3, was a full term infant, smaller than her siblings at birth weight 3.2 kilograms. Edema was not noted at birth (in Mexico) but appeared in the right lower extremity at age three and subsequently in the left lower and left upper extremities. The edema was not associated with shortness of breath nor cyanosis, and edema of the right upper extremity never developed. At the age of eight, a diagnosis of pulmonary tuberculosis was made and she was treated with isoniazid and ethambutol for one year. Evaluation at age nine revealed no etiology for the edema, but hypertension was noted. Coarctation of the aorta was considered, but blood pressure was equal in all extremities. At age thirteen a karyotype showed 45,X and Turner syndrome was diagnosed. Premarin therapy was begun.

At age 25, P.S. experienced a gradual 5 kilogram weight gain and increasing abdominal girth. Examination revealed a 150 centimeter tall, 45 kilogram woman with blood pressure 150/120 (Figure 1). Hypoplastic nails and multiple pigmented nevi were present. She had mild micrognathia

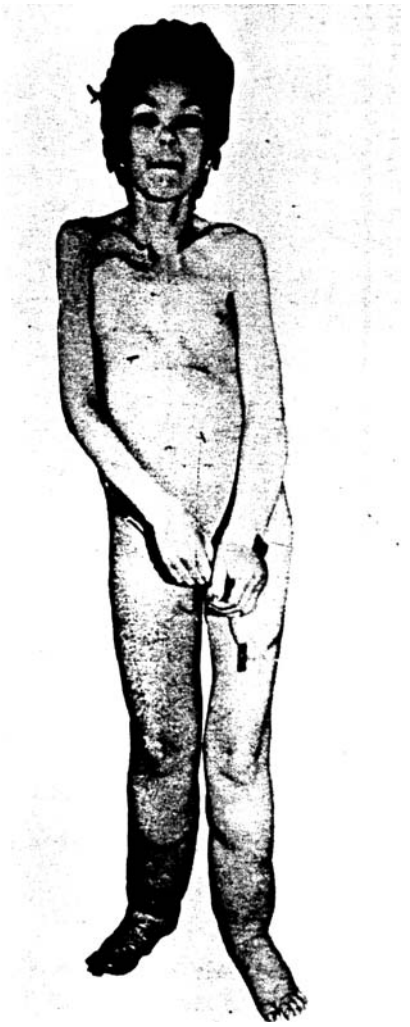

Fig. 1. The patient one week after the Denver shunt. Extreme lymphedema of the lower and right upper extremities is still present, but abdominal girth is substantially decreased. The figure illustrates the patient's widely spaced nipples, absent breast development, and pigmented nevi.

and low set ears, but a normal hairline and normal palate. No thyromegaly was present. A shield chest with broadly spaced nipples was apparent with no breast development. There was dextroscoliosis and an

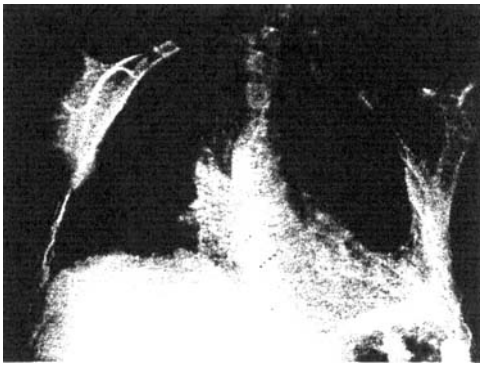

Fig. 2. Chest X-ray reveals elevated hemidiaphragms and right aortic arch. Chest wall deformity is evident.

asymmetric pectus carinatum with the sternum displaced to the right. The abdomen was tense and distended with a fluid wave present, and the liver was palpable 3 centimeters below the costal margin with no tenderness, masses, or nodularity. Blood pressure was equal in all four extremities, and marked edema was present in all but the right upper extremity. Laboratory exams included a hematocrit 42.8%, white cell count 6100, sodium 135 mmol, potassium 3.8 mmol, urea nitrogen 19 mg/dL, calcium 7.9 mg/dL, SGOT 11 U/mL, alkaline phosphatase 128 IU/liter, serum protein 4.3 g/dL, and albumin 2.2 g/dL. Thyroid function tests were normal. A chest X-ray revealed a right-sided aortic arch (Figure 2) and abdominal X-ray was consistent with ascites, also revealing a hemivertebra of L-4 and lumbarization of S-1 (Figure 3a).

Paracentesis provided milky fluid with protein content <0.1 g/dL, glucose 107 mg/dL, 270 leukocytes per mm with 16% lymphocytes and 82% histiocytes, triglycerides markedly elevated at 2496 mg/dL, and negative cultures, negative cytology, and no acid-fast bacilli by smear or culture. Computed tomography of the abdomen and chest showed marked ascites, atrophic uterus, a right aortic arch, and bony deformity

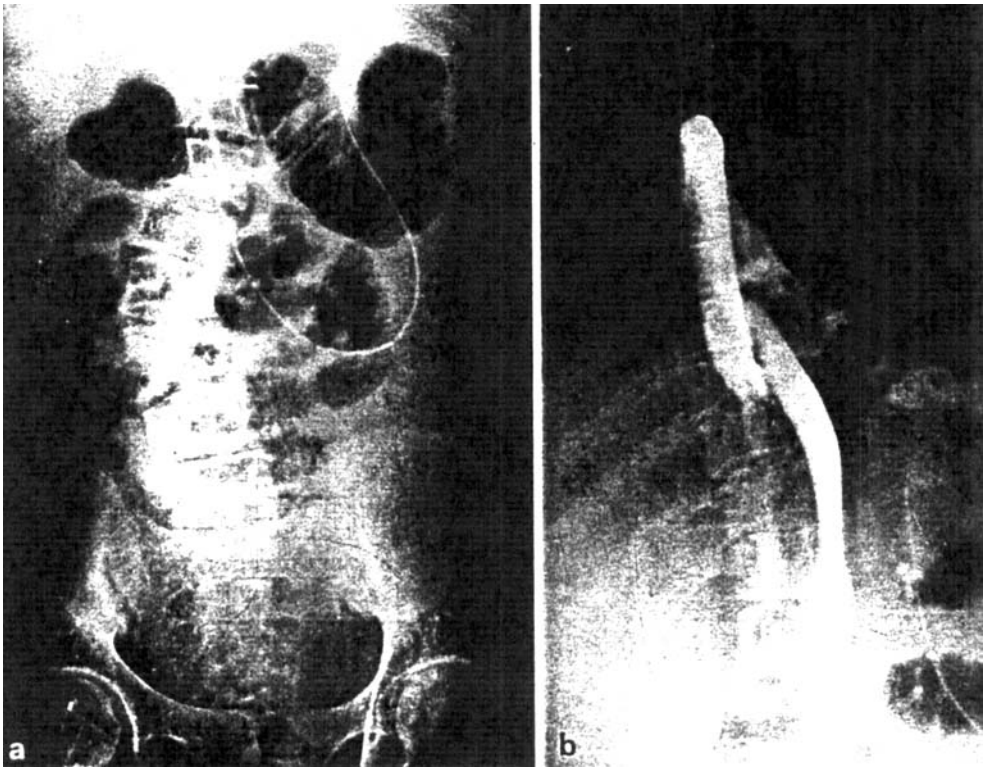

Fig. 3a. Abdominal X-ray is consistent with ascites and reveals dextroscoliosis with a hemivertebra at L-4 and lumbarization of S-1.
Fig. 3b. Venogram shows the left sided inferior vena cava crossing over into the azygous vein via the hemiazygous vein which arches into the superior vena cava.

of the chest wall. Upper endoscopy was performed with duodenal biopsies showing normal mucosa. Intravenous pyelogram was normal. Venogram was done showing left-sided inferior vena cava with crossover to the right side via the azygous vein (Figure 3b). A repeat G-banded karyotype showed 45,X in 15 cells, with no other rearrangements present.

A short course of low fat diet with supplementary medium chain triglycerides provided no relief and the patient remained dyspneic from her tense ascites. She underwent a Denver peritoneo-venous shunt. Post-operatively a left chylothorax appeared but slowly resolved as abdominal girth decreased and the patient became more ambulatory (Figure 1). Nine months post-operatively the patient continues to have marked peripheral lymphedema but abdominal girth is dramatically decreased from that before surgery.

Discussion

This patient illustrates many of the characteristic stigmata of Turner syndrome (Table 1) as well as some unusual findings. Congenital transient lymphedema which usually

Table 1

Clinical findings in Turner syndrome*

Short stature	100%
Sexual infantilism	99%
Multiple pigmented nevi	63%
Shield chest	55%
Cubitus valgus	55%
Low hairline	54%
Short fourth metacarpal	48%
Abnormal ears	48%
Hypoplastic nails	43%
Webbed Neck	41%
Lymphedema	36%
Arched palate	36%
Epicanthal folds	27%
Renal abnormalities	27%
Coarctation of aorta	10%
Hypothyroidism	8%

*Modified from Hall et al. (1982) with additional features from Palmer & Reichmann (1976).

resolves in childhood is seen in 80% of newborns with Turner syndrome (Hall et al. 1982). Recurrent lymphedema of the extremities is seen in some patients and may be exacerbated by estrogen therapy (Hall 1987). Lymphedema in Turner syndrome is almost always secondary to congenital hypoplasia of the lymphatic channels, although there may be similar lymphatic defects with and without lymphedema (Hall et al. 1982, Vittay et al. 1980). It is unclear why this patient's lymphedema spared her right upper extremity, but the lymph drainage of the right upper extremity is via the right lymphatic duct, whereas the other three extremities and the mesenteric lymphatics drain via the thoracic duct. Aplasia or hypoplasia of the thoracic duct at its junction with the left subclavian vein is, therefore, a possible explanation for her clinical findings. The development of chylous ascites at age twenty-five might have been due to rupture of dilated lymphatics on the serosal surface of the intestine.

A variety of arteriovenous vascular anomalies have been described in Turner syndrome. The most common malformation is coarctation of the aorta, which may occur in as many as 15% of patients with Turner syndrome, and as many as 50% of patients with a pure 45,X karyotype. The coarctation is, however, not always hemodynamically significant (Nora et al. 1974, Ferguson-Smith 1965). Less common malformations include aortic valve disease, pulmonic stenosis, ventricular septal defects, atrial septal defects, dextrocardia, hypoplastic left heart and anomalous pulmonary venous return (Lebecque et al. 1984, Price & Willey 1980). There is an increased incidence of multiple renal arteries over the general population (Hall et al. 1982). Right aortic arch, as noted in this patient, has been described in association with Turner syndrome (Price & Schicken 1974). In addition, this patient had unusual venous anatomy; although venous insufficiency could have contributed to her lower extremity edema or even to her ascites, a venogram demonstrated free flow of the contrast dye, without evidence of obstruction.

Vascular malformations including intestinal telangiectasia, varicosities, and hemangiomas may be present in patients with Turner syndrome and may result in gastrointestinal bleeding (Reinhart et al. 1983). Lymphagiectasia has also been described with associated protein-losing enteropathy, but these cases have not been associated with chylous ascites, presumably because the lymphatic leakage occurs into the intestinal lumen rather than the peritoneum (Rutlin et al. 1981). Other etiologies for chylous ascites include tuberculous, parasitic, neoplastic, or traumatic obstruction of the lymphatics, intestinal obstruction, portal vein obstruction, and mesenteric adenitis (Press et al. 1982, Kelley & Butt 1960). There was no evidence for any of these conditions in this patient; though she had a previous history of tuberculosis, the low protein of the fluid and the negative cultures mitigate against a diagnosis of tuberculous peritonitis.

There have been numerous reports of the use of peritoneo-venous shunts in the treatment of chylous ascites, particularly in children. In 1934, Wegner reported the successful treatment of congenital chylous ascites using a sapheno-peritoneal shunt, termed Routte's operation (Wegner 1934). LeVeen described the use of a prosthetic peritoneo-venous shunt for the treatment of ascites associated with cirrhosis in 1974 (LeVeen et al. 1974). Since the introduction of the LeVeen and Denver shunts, there have been numerous reports of their use in the treatment of chylous ascites with variable success. Chang in 1980 described the successful use of a Denver shunt in treatment of chylous ascites due to lymphangiomatosis, and others have reported its use in the treatment of iatrogenic and neoplastic chylous ascites (Chang et al. 1980, Guttman et al. 1982). The complications of these shunts include obstruction, disseminated intravascular coagulation, and infection, and the etiology of the chylous ascites probably influences their success (Press et al. 1982). The use of these shunts in the treatment of chylous ascites remains controversial because of complications and limited long term effectiveness.

Acknowledgments

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