Clinical spectrum of infantile scimitar syndrome: A tertiary center experience

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ABSTRACT

Aim: Infantile scimitar syndrome is a rare condition, with most of the literature reports being limited to case reports and a few case series. The aim of this study was to review patients with infantile scimitar syndrome who presented to our hospital from July 2000 to January 2011.

Materials and Methods: In this retrospective study, we evaluated the medical records of patients aged 0–14 years who were symptomatic before the age of 1 year and were subsequently diagnosed with the syndrome. A total of 16 patients with the infantile form of scimitar syndrome were identified from the database.

Results: The median age at presentation was 14 days, with a median age at diagnosis of 55 days. Fifty-six percent of the patients were females. Tachypnea was the major presenting symptom and 13 out of 16 patients had pulmonary hypertension. Of the 13 patients with pulmonary hypertension, 7 had systemic collaterals, which were treated by coil occlusion together with medications, and 3 had corrective surgery. The mortality rate was 3/16 (18.8%) over the 10.5 years study period.

Conclusions: Infantile scimitar syndrome is a rare congenital anomaly that needs a high degree of suspicion for early referral and management. The association of the syndrome with pulmonary hypertension leads to recurrent and prolonged hospitalization.

Keywords: Cardiac, hypoplasia, pediatrics, pulmonary, scimitar

INTRODUCTION

Scimitar syndrome is a rare, but well-characterized constellation of anomalies that include hypoplasia of the right lung, total or partial anomalous pulmonary venous return of the right lung, dextroposition of the heart, right pulmonary artery hypoplasia, and systemic collaterals from the aorta. Intracardiac defects are the most common anomalies associated with this syndrome with a prevalence of 40%.[1]

Incidence ranges from 1 to 5 per 100,000,[2,3] and these data are primarily based on case presentations of tertiary medical centers.

In the early 90s, several publications started to classify scimitar into two distinct presentations, infantile and adult. The infantile form presents early in life with symptoms of tachypnea, chest infection, heart failure, and failure to thrive and, as a result, always requires intervention. The adult form, however, is asymptomatic, with findings that are incidental and rarely requiring intervention.[2-5] Although there is no clearly identified genetic cause, five familial cases have been reported in the literature.[6,7]

To date, few published studies have focused only on the infantile type of scimitar syndrome. Therefore, the aim of this review was to present the experiences with infantile scimitar cases encountered at our center and to review the clinical presentations, radiological findings, factors affecting the severity of the disease, unusual findings and associations, interventions, and related outcomes.

MATERIALS AND METHODS

A retrospective review of the medical records of patients who presented to our center with scimitar syndrome...
between July 2000 and January 2011 and who were symptomatic within the first year of life was done. Patient records were reviewed for both baseline and follow-up data. Baseline information included demographic data, i.e. age, gender, gestational age, birth weight, consanguinity, family history, age at diagnosis, and age at presentation. Other baseline information included chest radiography results, echocardiogram (ECHO) studies, chest computerized tomography angiography (CTA), and the modalities of intervention, either medical and/or surgical. The follow-up information that was obtained included ECHO findings, any details regarding subsequent hospitalizations, and mortality data. We considered pulmonary hypertension if the tricuspid regurgitation velocity was >3.4 m/s by Doppler or the estimated right ventricular pressure was more than 50% of the systemic pressure for neonates and infants, and in children, if the mean pulmonary pressure by cardiac catheterization was ≥25 mmHg and the systolic right ventricular pressure was more than 50% of the aortic pressure during catheterization. A pediatric cardiologist who is an expert in pulmonary hypertension (OT) reviewed all ECHO and cardiac catheterization procedures. Statistical analysis included summaries of frequencies, means, and median. Approval for the study was obtained from the committee for ethical research, and no consents were required as stated in the committee’s policy and the guidelines for retrospective chart reviews.

RESULTS

Between July 2000 and January 2011, a total of 16 patients with a diagnosis of infantile scimitar syndrome were identified from a review of the medical records database. Of the 16 patients, 11 were referred from peripheral hospitals. Of note, the case reports of three of the patients included in this cohort have been previously published: two siblings with scimitar syndrome, one of them with meandering pulmonary vein, and another patient who was reported to have bilateral scimitar syndrome. All 16 patients received both an initial and multiple follow-up chest X-ray and ECHO studies, 14 patients had an initial CTA scan, and 13 underwent diagnostic and/or therapeutic cardiac catheterization. The follow-up ranged from 2 months to 4 years, depending on the time of referral during the 10.5-year period of this retrospective review.

Demographic data and clinical presentation

The detailed demographic and clinical data of the patients are presented in Table 1.

Two other patients had no recorded abnormal facial descriptions, but one had scoliosis, an imperforate anus, and hydronephrosis, and the other was diagnosed with Arnold–Chiari malformation.

Radiological and echocardiographic data

Table 2 illustrates the percentage of cardiac and pulmonary anomalies associated with the syndrome.

### Table 1: Demographic and clinical data of the study population

| Number (%) |
|----------------|
| Sex |
| Female | 9 (56) |
| Geschational age |
| Term | 11 (69) |
| Prematurity (35-36 weeks) | 4 (25) |
| Birth weight ≥ 2.5 | 8 (50) |
| Age of symptomatoloy |
| Median (range) | 14 days (0-210) |
| Age of diagnosis |
| Median (range) | 55 days (1-730) |
| Family history |
| Consanguinity | 8 (50) |
| CHD | 3 (18.75) |
| Scimitar | 1 (6.25) |
| Dysmorphic facial features | 2 (12.5) |
| Associated congenital anomalies | 2 (12.5) |
| Symptoms |
| Tachypnea | 9 (56.25) |
| Heart failure | 4 (25) |
| Failure to thrive | 2 (12.5) |
| Cyanosis | 1 (6.25) |
| Diagnosis |
| CHD | 8 (50) |
| Chest infection | 4 (25) |
| Scimitar syndrome | 2 (12.5) |
| Nonspecific | 2 (12.5) |

CHD: Congenital heart disease

### Table 2: Radiographic and echocardiographic data

| Number (%) |
|----------------|
| Chest X-ray |
| 16 (100) |
| Dextroposition of the heart | 10 (62.5) |
| Right lung hypoplasia | 10 (62.5) |
| Right lung opacity | 6 (37.5) |
| Echocardiography |
| Situs solitus | 16 (100) |
| ASDII | 9 (56.25) |
| VSD | 4 (25) |
| PDA | 5 (31.25) |
| PH | 13 (81.25) |
| Chest CT angiographic |
| Right lung hypoplasia | 12 (85.71) |
| Right lower lobe sequestration | 7 (50) |
| Horseshoe lung | 2 (14.3) |
| Bronchogenic cyst | 1 (7.14) |
| Tracheomalacia | 2 (14.28) |
| TAPVID | 2 (14.28) |
| PAPVD | 11 (78.57) |
| Systemic aortic collaterals | 12 (85.71) |
| Right pulmonary artery hypoplasia | 9 (64.28) |
| Scimitar vein stenosis | 1 (7.14) |

ASDII: Atrial septal defect secundum, PAPVD: Partial anomalous of pulmonary venous drainage, DA: Patent ductus arteriosus, PH: Pulmonary hypertension, TAPVID: Total anomalous of pulmonary venous drainage, VSD: Ventricular septal defect

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in our studied population. Chest X-ray was the initial diagnostic imaging that showed dextroposition of the heart with right-sided lung haziness in the majority of patients. Echocardiography was used to identify the intracardiac lesions and the Doppler measures the pulmonary pressure. CTA was used to identify pulmonary anomalies and the presence of systemic collaterals.

**Pulmonary hypertension**

The initial hemodynamic, medical, and interventional treatment and data at the time of death or normalization of hemodynamic parameters in patients with pulmonary hypertension are listed in Table 3. Advanced pulmonary hypertension therapy in the form of sildenafil with or without iloprost was started in seven patients, but stopped in one after the patient developed pulmonary vein stenosis and died later [Table 3].

**Course, treatment, and outcome**

The median number of hospitalization was two admissions during the 10.5 years review period. The main reason given for hospitalization was respiratory

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**Table 3: Catheterization and follow-up data of patients with pulmonary hypertension**

| Age at 1st echo | TR | Cath data | Systemic Collaterals | Medical management | Intervention | Age of normalization of pulmonary pressure/death |
|----------------|----|-----------|----------------------|-------------------|-------------|-----------------------------------------------|
| 6 months       | 80 | PA 40/13/22 BP 70/35 | Present | Sildenafil, Budesonide, Salbutamol, Montelukast | Intra-atrial baffle, IVC patch enlargement | 22 months |
| 4 days         | 40 | PA 62/22/22 BP 64/35 | Present | Furosemide, Captopril | Coiling | Died at 7 months |
| 3 weeks        | 85 | PA 53/13/26 BP 77/41 | Present | Furosemide, Captopril, Iloprost, Salbutamol, Budesonide | Coiling ×2 | 1 year |
| 3 weeks        | 55 | PA 88/33/51 BP 101/55 | Present | Furosemide, spironolactone, Sildenafil, Iloprost, Salbutamol | Coiling | 19 months |
| 2 weeks        |    | PA 42/8/22 BP 70/40 | Present | Sildenafil, Furosemide | Coiling | Referred back to original hospital with no data |
| 4 months       | 55 | PA 42/10/22 BP 70/40 | Present | None | Coiling | 2 years |
| 2 months       | 70 | PA 46/15/27 BP 80/39 | Absent | Furosemide, spironolactone, Sildenafil, Salbutamol, Budesonide | None | Died at 2 years |
| 6 months       | 75 | PA 45/20/32 BP 85/48 | Present | Furosemide, spironolactone, Digoxin, Captopril | Coiling | 30 months |
| 3 weeks        | 75 | PA 41/13/26 BP 80/40 | Present | Salbutamol, Budesonide | Coiling | 1 year |
| 3 years        | 30 | PA 60/14/29 BP 81/38 | Present | Salbutamol | Intra-atrial baffle, Reconstruction of LPA, RPA | 5 years |
| At birth       | 55 | No cath performed | Present | Furosemide, Sildenafil, Salbutamol, Budesonide | None | Died at 4 months |
| 2 months       | 90 | No cath performed | Present | Furosemide, Sildenafil, Salbutamol, Budesonide | PDA ligation, VSD closure, Intra-atrial baffle | 3 months |
| 1st week       | 110 | No cath performed | Present | Sildenafil | Family refused | 8 months |

Cath: Catheterization, LPA: Left pulmonary artery, RPA: Right pulmonary artery, PDA: Patent ductus arteriosus, VSD: Ventricular septal defect, IVC: Inferior vena cava, PA: Pulmonary artery, TR: Tricuspid regurgitation, MPA: Main pulmonary artery
distress, and the median duration of each hospital stay was 22 days. Five patients (31.25%) had an immediate respiratory distress after birth, and three of them required intubation following delivery. Eight patients (50%) required pediatric intensive care unit (PICU) admission and intubation during the review period. Intubation duration ranged from 4 days to 1 month, and intubation was required due to respiratory failure in six patients (75%) and heart failure in two patients.

Of the 11 patients who had pulmonary hypertension and systemic collaterals, 7 underwent a procedure for collateral closure between the ages of 14 days and 2 years, and 5 of them had a significant drop in pulmonary pressure following a median period of 20 months [Table 3 and Figure 1].

Of note, severe gastro-esophageal reflux was diagnosed in three patients who continued to have recurrent pulmonary exacerbations and hospital admissions despite the occlusion of collaterals and the normalization of pulmonary pressure. All of these patients were started on anti-reflux medications, and one required fundoplication, after which the exacerbations were controlled and no further hospital admissions were recorded during the chart review period.

Only one of the patients in the cohort underwent a lobectomy, and this patient was referred to our hospital after lobectomy. The indication for lobectomy was not clear from past records.

**Mortality**

Three patients with scimitar syndrome died during the chart review period, of which two deaths were due to scimitar vein stenosis and/or pulmonary veins stenosis.

**DISCUSSION**

To our knowledge, this is one of the largest reviews that describe the medical aspect of the infantile type of scimitar syndrome in a single tertiary center. In the present series, 13 patients (81.25%) had pulmonary hypertension, which is consistent with previous reports of the infantile form of scimitar syndrome. Dupuis et al. [2] recorded 23 patients with pulmonary hypertension of a total of 25 infantile scimitar patients, while Najm et al. [5] reported 11/19 and Uthaman et al. [9] reported 15/16.

Classic and unique forms of scimitar variants have been reported in the literature. [7,8,10-12] The forms of infantile scimitar found in our population are similar to the previous publications and include the classic scimitar, a scimitar variant with a meandering pulmonary vein that drains in the left atrium, bilateral scimitar in which all pulmonary veins drain into the right atrium with the presence of a bronchogenic cyst in the right middle lobe, [8] scimitar syndrome with scimitar vein stenosis and contralateral left upper pulmonary vein stenosis, [13] and scimitar syndrome with right and left pulmonary arterial stenosis at multiple levels.

The presentation of the syndrome could be as early as immediately after birth, and the diagnosis should be suspected when the signs of respiratory distress and/or other signs of heart failure are present in association with X-ray findings that include dextroposition of the heart along with right lung haziness. In our series, the radiologist had never reported scimitar shadow.

Ruggieri et al. and Kahraman et al. [14,15] reported the association of dysmorphic features, craniofacial and central nervous system anomalies, and renal agenesis with scimitar syndrome, in addition to the associations with Turner syndrome and VATER that were reported in the infantile group in the study by Najm et al. [9] In our study, one patient was diagnosed with Down’s syndrome, and three other patients had facial dysmorphic features and multiple system malformations that did not fit with any known syndrome. In addition, 50% of the patients were products of consanguineous marriage. These observations may indicate a complex genetic cause behind it.

Pulmonary arterial hypertension with infantile-type scimitar syndrome has been recognized as a cause of severe symptoms and poor outcome. [2,5] It is attributed to the following factors: 1) stenosis of the anomalous pulmonary veins, 2) the presence of systemic arterial supply to the right lung, 3) reduction of the pulmonary vascular bed on the right side, and 4) increased pulmonary blood flow from anomalous drainage or the presence of intracardiac lesion. [2]

In our population, those who had pulmonary hypertension required admission to PICU and had hospital admission frequency three times more than those without pulmonary hypertension.
A two-staged approach for the interventional management of scimitar patients has been recommended. Occlusion of the systemic collaterals as the first stage showed clinical improvement and reduction of left to right shunt and pulmonary artery pressure.[2,9,16] Yet, there is no clear consensus on the management guidelines for this syndrome. In our sample, the approach was individualized and we started using the advanced pulmonary hypertension medications since 2008. Coiling with diuretics produced a drop in pulmonary blood pressure in a period of 20 months compared to 14 months in those who received advanced pulmonary hypertension medications (sildenafil and or iloprost) with or without coiling. Although the review is retrospective and the sample is small to make a conclusion, we observed that advanced pulmonary hypertension medications are useful when used as the first-line treatment. Gastroesophageal reflux disease was another risk-factor for hospital admission. This co-morbidity should be addressed to enable better control of symptoms and reduce hospital admissions in a select subset of infants with scimitar syndrome.

The patients who died in our cohort were in the pulmonary hypertension group, two with pulmonary vein and/or scimitar vein stenosis and one with severe pulmonary hypertension during the course of the disease, with no postmortem study. Venous obstruction seemed to play a major rule in the death of two out of three patients.

In conclusion, infantile scimitar syndrome is a rare congenital anomaly that needs a high degree of suspicion for early referral and management. The association of the syndrome with pulmonary hypertension leads to recurrent and prolonged hospitalization. Further studies are required to clarify the efficacy of advanced pulmonary hypertension medications on a prospective basis.

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