Dextrocardia in patients with Poland syndrome: Phenotypic characterization provides insight into the pathogenesis

Anwar Baban
Dipartimento Medico Chirurgico di Cardiologia Pediatrica.
Ospedale Pediatrico Bambino Gesú’, Roma.

Milano, 23-25 Settembre 2010
**POLAND SYNDROME** (OMIM N° 173800)

*Alternative Titles:*
Poland Syndactyly
Poland Anomaly
Poland Sequence
Pectoralis Muscle, Absence Of, Included

Characterized by **unilateral** hypoplasia or aplasia of the sternocostal head of the pectoralis major muscle and an ipsilateral hypoplastic hand with simple syndactyly and short fingers.

**Incidence** 1:30,000 live birth

Males > Females 2-3: 1
Right side > Left side
Mainly sporadic
Phenotype Analysis

Thoracic Anomalies

Upper Limb Anomalies

Other Associated Anomalies or Syndromes

Familial Cases

Symbrachydactyly
Etiopathogenetic Hypotheses

The aetiology of Poland syndrome is **UNKNOWN**.

Bavinck and Weaver suggested the term: “**Subclavian Artery Supply Disruption Sequence**”

Paradominant inheritance

- Poland
- Klippel-Feil
- Moebius
- Sprengel

subclavian

vertebral

and/or one of their branches

Autosomal lethal gene surviving by mosaicism

- Maurice and van Steensel, 2004

Remember branchial arches derived organs!

Lowry and Bouvet 1983; Happle 1999
Anatomo - Radiological Hints

Thoracic Anomalies

Clavicular Head
Sternocostal Head
Pectoralis Major Tendon
Abdominal Head

Pectoralis Minor
From 2003 till date more than 450 individuals had consulted AISP (Associazione Italiana Sindrome di Poland) and 210 of them had participated in our study.
Aims of the Study

- Describe the phenotype in a large series of patients.
- Verify the already present data in literature.
- Differentiate the severity according to clinical features, with definition of malformative risk factor according to gender, affected side and other phenotypic characteristics.
- Obtain a diagnostic standards.
- Obtain very useful information from prognostic and therapeutic points of view.
- Identify new etiopathogenetic hypotheses or validate the already present ones in literature.
Multidisciplinary Assessment of Patients

Geneticist
Psychologist
Statistician
Paediatric Surgeon
Orthopedic Surgeon
Radiologist
Plastic Surgeon

Heart position determination
Poland Syndrome and Dextrocardia

The association of Left sided PS and dextrocardia has been reported in 22 cases until now, accounting for 5.6% of reported PS cases.

Dextrocardia

Consequential vascular anomalies determine PS

Same causal factor

Considerations from literature on PS and Dextrocardia:
No reviews and only orphan case reports!
## Dextrocardia and Dextroposition

<table>
<thead>
<tr>
<th></th>
<th>Dextrocardia</th>
<th>Dextroposition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac mass</strong></td>
<td>Rt hemithorax</td>
<td>Rt hemithorax</td>
</tr>
<tr>
<td><strong>Apex deviated to</strong></td>
<td>right</td>
<td>left</td>
</tr>
<tr>
<td><strong>Underlying factor</strong></td>
<td>Anomalous rotation of primitive hrt tube</td>
<td>Left sided factor pushing the hrt to the Rt</td>
</tr>
<tr>
<td><strong>Viscera</strong></td>
<td>Situs solitus or inversus</td>
<td>Mainly solitus</td>
</tr>
<tr>
<td><strong>Intracardiac anomalies</strong></td>
<td>Higher frequency</td>
<td>Lower frequency</td>
</tr>
<tr>
<td><strong>Incidence / prevalence</strong></td>
<td>Livebirth 1/10 000- 30 000</td>
<td>Difficult to estimate</td>
</tr>
<tr>
<td></td>
<td>Adult pop 1/900 000 (!)</td>
<td></td>
</tr>
</tbody>
</table>
Materials and Methods

122 patients with PS were studied.

Heart position was determined in all individuals by means of:
- chest (103 patients),
- spine (25 patients),
- echocardiography (96 patients),
- CT or MRI in 21 patients for specific indications.

Informed consent, according to the guidelines approved by our ethics committee, was obtained from adult patients and from the parents or legal guardians of every child participating in the study.

Schematic representation of rib defects in patients with Poland syndrome: partial rib agenesis (A) and rib hypoplasia (B).
Univariate analysis of clinical characteristics of patients with Poland syndrome

<table>
<thead>
<tr>
<th></th>
<th>Right side (n = 72), no. (%)</th>
<th>Left side (n = 50), no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22 (30.6)</td>
<td>17 (34)</td>
</tr>
<tr>
<td>Male</td>
<td>50 (69.4)</td>
<td>33 (66)</td>
</tr>
<tr>
<td><strong>Dextrocardia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>72 (100)</td>
<td>36 (72)</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td>14 (28)</td>
</tr>
</tbody>
</table>
Clinical features of patients with Poland syndrome with dextrocardia

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Affected side</th>
<th>Pectoralis major (ultrasound)</th>
<th>Pectoralis minor (ultrasound)</th>
<th>Affected ribs</th>
<th>Nipple</th>
<th>Upper limb</th>
<th>Cardiac defects</th>
<th>Other malformations</th>
<th>Sporadic/familial occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>L</td>
<td>H</td>
<td>A</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>BS+</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>L</td>
<td>NA</td>
<td>NA</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>L</td>
<td>H</td>
<td>A</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>NR</td>
<td>?</td>
<td>Right undesceded testis, splenomegaly</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>NA</td>
<td>PRA 2nd, 3rd</td>
<td>H</td>
<td>H</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>A</td>
<td>PRA 3rd, 4th</td>
<td>NR</td>
<td>NR</td>
<td>No</td>
<td>BHID and hyperelorium, Paternal grandiant with dextrocardia</td>
<td>S</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>A</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>H</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>L</td>
<td>NA</td>
<td>NA</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>A</td>
<td>PRA 4th, 5th, 6th</td>
<td>H</td>
<td>NR</td>
<td>ASD-SC</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>L</td>
<td>H</td>
<td>A</td>
<td>PRA 2nd, 3rd; H 1st, 4th</td>
<td>NR</td>
<td>NR</td>
<td>No</td>
<td>Convergent squint, astigmatism, hypermetropia</td>
<td>S</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>L</td>
<td>H</td>
<td>A</td>
<td>PRA 2-3-4</td>
<td>H</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>L</td>
<td>A</td>
<td>A</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>NR</td>
<td>No</td>
<td>Salivary IgA deficiency asymmetric mixed sternal abnormality</td>
<td>S</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>NR</td>
<td>PRA 3rd, 4th</td>
<td>H</td>
<td>AF+SA</td>
<td>No</td>
<td>No</td>
<td>S</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>L</td>
<td>A</td>
<td>NA</td>
<td>PRA 2nd, 3rd</td>
<td>H</td>
<td>BS+</td>
<td>ASD</td>
<td>Sylvian duct stenosis of malformative origin; Mother: postural scoliosis; Father: mild scalpeal asymmetry (higher left scapula)</td>
<td>S</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>L</td>
<td>A</td>
<td>A</td>
<td>PRA 4th, 5th</td>
<td>H</td>
<td>NR</td>
<td>VSD</td>
<td>Small congenital occipital vascular anomaly, vertebrobasilar insufficiency</td>
<td>S</td>
</tr>
</tbody>
</table>
High incidence of left-sided PS with rib defects presenting with dextrocardia (14/20 [70%]) and the correlation between the type of rib anomaly and dextrocardia.
Some considerations..

- This observation seems to suggest that dextrocardia in patients with PS can be caused by intrauterine mechanical factors pushing a normal heart toward the right side.
- CHD are not high enough as in dextrocardia
- If the mechanical hypothesis is correct, and the left rib agenesis associated with muscular defects is the causative factor. The displacement of the heart probably occurs during pregnancy*....

*Sepulveda W. Poland syndrome: a rare cause of cardiac dextroposition in the fetus. Prenat Diagn. 2009
Conclusions

1- left-sided PS can be associated with dextrocardia but more frequently than previously reported.
2- dextrocardia is a component of left-sided PS with PRA of 2 or more ribs.
3- dextrocardia might derive from a mechanical intrauterine displacement of a healthy heart toward the right side because of a lack of protection by the thoracic cage against external pressures.

Further studies are required to confirm this hypothesis.
Special Thanks to:

- Patients and their families,
- AISP: Associazione Italiana Sindrome di Poland,
- Clinicians for their precious collaboration.