Syndrome of the month

Congenital contractural arachnodactyly (Beals syndrome)

Denis Viljoen

Abstract
Congenital contractural arachnodactyly (CCA) is an autosomal dominant disorder akin to, but usually less severe than, Marfan syndrome. The clinical features are marfanoid habitus, arachnodactyly, crumpled ears, camptodactyly of the fingers and adducted thumbs, mild contractures of the elbows, knees, and hips, and mild muscle hypoplasia especially of the calf muscles. Many patients have kyphoscoliosis and mitral valve prolapse and, very occasionally, aortic root dilatation and ectopia lentis have been described. Linkage to a gene coding for fibrillin on chromosome 5q23-31 has been shown in several kindreds. The prognosis for a normal lifespan is good and improvement in joint contractures is usual.

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Congenital contractural arachnodactyly (CCA) is an autosomal dominant disorder first delineated by Beals and Hecht in 1971. The eponymous designation “Beals syndrome” is now usually applied to patients with the condition. At least 40 families with more than 120 affected members have been reported to date. The classical clinical features of CCA are variable and tend to overlap with those of Marfan syndrome; interestingly, it is contended that the original patient described by Marfan actually had CCA. Distinct fibrillin defects in both disorders have recently been elucidated, thereby allowing differentiation of the two conditions on a molecular basis.  

Clinical features
The manifestations in CCA are summarised in the table.

HABITUS
Affected persons tend to have a distinctive Marfan-like appearance, being tall and thin with a span which exceeds their adult height measurement by more than 5 cm.

Review of the clinical manifestations of patients with CCA

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Review of 29 families by Ramos Arroyo et al</th>
<th>Review of 13 families reported after 1985</th>
<th>Total</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Craniofacial</td>
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<tr>
<td>Crumpled ear</td>
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<td>39/43</td>
<td>79/104</td>
<td>76.0</td>
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<td>Micronathia</td>
<td>11/47</td>
<td>10/32</td>
<td>21/79</td>
<td>26.6</td>
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<td>Highly arched palate</td>
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<td>10/35</td>
<td>25/88</td>
<td>28.4</td>
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<tr>
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<td>6/38</td>
<td>24/83</td>
<td>29.0</td>
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<tr>
<td>Limited extension of Elbows</td>
<td>54/64</td>
<td>40/45</td>
<td>94/109</td>
<td>86.2</td>
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<td>Knees</td>
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<td>38/45</td>
<td>78/107</td>
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<td>10/45</td>
<td>28/107</td>
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<td>Camptodactyly</td>
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<td>30/42</td>
<td>63/97</td>
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<td>32/40</td>
<td>77/88</td>
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<td>Other organ systems</td>
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<td>9/61</td>
<td>19/42</td>
<td>28/103</td>
<td>27.2</td>
</tr>
<tr>
<td>Eye</td>
<td>—</td>
<td>9/43</td>
<td>9/43</td>
<td>20.9</td>
</tr>
</tbody>
</table>

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CRANIOFACIAL FEATURES
A characteristic feature in CCA is a “crumpled” appearance of the external ears (fig 1) in which the upper helix is folded, the crura are prominent, and the concha is shallow. This sign, or variations thereof, was evident in 76% of published cases. Less frequent craniofacial features are mild micrognathia (26.6%), highly arched palate (28.4%), and cranial abnormalities including scaphocephaly, brachycephaly, doliachocephaly, and frontalbossing (28.9%).

MUSCULOSKELETAL ANOMALIES
Symmetrical contractures of small and large joints are frequent in CCA. The fingers are usually long and narrow at birth with flexion contractures of the proximal interphalangeal joints (fig 2) and the toes are long and slender. The thumb tends to be adducted into the palm. Camptodactyly usually improves with age. Contractures of major joints are often present at birth with the elbows (86.2%), knees (81.3%), and hips (26.2%) predominantly involved. The ankles may be held in valgus and, peculiarly, have excessive dorsal flexion. Mild talipes equinovarus is evident in a proportion of patients at birth (31.7%) but responds rapidly to physiotherapy. Sternal deformities are frequent (fig 3). Spinal malalignment is present in more than 45% of affected persons (fig 4) and, unlike the joint contractures, tends to be progressive. Bowing of the long bones with radiological osteopenia is a feature in a few cases and is said also to worsen with age. Hypoplasia of the muscles, particularly those of the lower leg, is a frequent finding (fig 4).

CARDIOVASCULAR MANIFESTATIONS
Until the recent discovery of the separate gene defects in CCA and Marfan syndrome (MS), considerable debate has centred on differentiation of the two disorders on the basis of absence or presence of severe cardiovascular involvement. There remains considerable confusion as to whether aortic root dilatation and aneurysm formation in a tall, slender person with crumpled ears and joint contractures represents CCA or MS. Such diagnostic dilemmas will be resolved once the specific intragenic defects of each condition are fully elucidated. In the interim, it can be accepted that mitral valve prolapse with regurgitation is often a component of patients with CCA whereas patent ductus arteriosus, ventriculoseptal defect, and bicuspid aortic valve are occasionally present. Persons with joint contractures, eye manifestations, and
Differential diagnosis

The disorder most akin to CCA is Marfan syndrome. Differentiation is critical as the latter is potentially lethal, has considerable morbidity, and often requires life long medication with beta blockade. Although linkage to the respective fibrillin genes can be achieved through family studies, diagnosis of sporadic cases of CCA or MS remains clinical and problematical. Other conditions with which CCA can be confused are Stickler syndrome, Achard syndrome, homocystinuria, osteogenesis imperfecta, and distal arthrogryposis. The characteristic clinical manifestations in each of the latter disorders usually allow rapid differentiation.

Aetiology and genetics

CCA is an autosomal dominant disorder with variable expressivity within affected kindreds. The condition has been described mainly in white families of European extraction, but Japanese, persons of Indian descent, African Blacks, and Afro-Americans have also been documented.

Shortly after the finding of linkage of Marfan syndrome to the fibrillin gene on chromosome 15q15–21, Lee et al. and, later, Tsipouras et al. showed linkage of CCA families to a second fibrillin locus on 5q23–31. No intragenic mutations have so far been characterised in fibrillin 5. Nevertheless, Marfan syndrome and CCA have now finally been separated on a molecular basis as two distinct entities. Intragenic heterogeneity within the fibrillin 5 gene is likely to be responsible for the wide phenotypic differences in patients with CCA.

Management

In view of the normally benign prognosis of patients with CCA, management is usually confined to physiotherapy in early childhood to increase joint mobility and lessen the effects of muscle hypoplasia. Infrequent cardiovascular and ophthalmological appraisal (perhaps yearly) is recommended in all affected persons to exclude the rare development of aortic dilatation, complications associated with mitral valve prolapse, and progressive lens subluxation. Prenatal diagnosis is feasible in families that are large enough for linkage studies, but the demand for such investigations is likely to be small in view of the generally benign nature of the disorder.

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Figure 3  A young boy with CCA showing pectus carinatum (reproduced from Viljoen D, et al, Clin Genet 1991;31:181–8).

Figure 4  Severe kyphoscoliosis, joint contractures, and calf muscle hypoplasia in a boy with CCA (reproduced from Beighton P, Inherited disorders of the skeleton, 1988:407–8).

Aortic root dilatation may represent the severe end of the spectrum of CCA, MS, or a new, as yet undefined, genetic entity.

OPHTHALMOLOGICAL COMPLICATIONS

As with severe cardiovascular manifestations, the ophthalmological features of lens subluxation and myopia are also said to differentiate between MS and CCA. However, at least two patients with well documented, severe CCA have also been reported with ectopia lentis, keratoconus, and myopia.
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