Surviving campomelic dysplasia has the radiological features of the previously reported ischio-pubic-patella syndrome

A C Offiah, S Mansour, S McDowall, J Tolmie, P Sim, C M Hall

The radiological findings in five patients with features of the ischio-pubic-patella syndrome are presented. All of these patients have genetic/cytogenetic evidence of campomelic dysplasia. The ischio-pubic-patella syndrome appears to be a distinct entity from the small patella syndrome as first described by Scott and Taor. The findings in the five presented cases with radiological evidence of the more severe ischio-pubic-patella syndrome but genetic/cytogenetic evidence of campomelic dysplasia suggest that they are the same condition, that of surviving campomelic dysplasia. Campomelic dysplasia should be considered in patients with the clinical and radiological features of the “ischio-pubic-patella syndrome”.

Scott and Taor and Taò independently presented cases of defective ischio-pubic ossification and absent/hypoplastic patellae in 1979. In the former paper, 12 members of one family, all of whom had absent or hypoplastic patellae, were described and the authors coined the term the “small patella syndrome” for the condition. All seven in whom the information was available had abnormalities of the pelvis consisting of coxa vara or valga, buttressing of the femoral necks, hypoplastic lesser trochanters, and defective ischio-pubic junction ossification. In the single patient presented by Taò, there was bilateral agenesis of the ischia and patellae. Since then, 32 further patients have been described, and the term the “small patella syndrome” has been dropped in favour of the “ischio-pubic-patella syndrome”. A review of published reports shows much heterogeneity in the severity of the clinical and radiological features in the published cases, and raises the possibility that they may not represent a single entity.

CLINICAL FEATURES
In the majority of cases reported with the ischio-pubic-patella syndrome, the facial appearance has not been described. It may be that these patients had no facial abnormality. Table 1 summarises the facial features in the five patients presented and compares them with those of four other published cases where this information was available. The reader should refer to Mansour et al for more detailed clinical features of these five patients.

RADIOLOGICAL FEATURES
All five patients presented had defective ischio-pubic ossification and hypoplastic lesser trochanters, and in the three patients in whom radiographs of the knees were available hypoplastic patellae were seen. Four of the five patients had elongated femoral necks. These are the major diagnostic features of the ischio-pubic-patella syndrome. Figs 1 and 2 illustrate these findings and they are summarised in table 2, which provides a comparison with findings from other reported cases.

<table>
<thead>
<tr>
<th>Facial finding</th>
<th>This report (n=5)</th>
<th>Sandhaus et al (n=1)</th>
<th>Kasowski and Nelson (n=1)</th>
<th>Habboub and Thneibet (n=1)</th>
<th>Azouz and Kasowski (n=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broad/depressed nasal bridge</td>
<td>5</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Micrognathia/retrorhithia</td>
<td>5</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Epicanthic fields</td>
<td>5</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Relative macrocephaly</td>
<td>5</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Long/prominent philtrum</td>
<td>5</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Low set ears</td>
<td>3</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>High/cleft palate</td>
<td>3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Anteverted, flared nares</td>
<td>2</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Synophrys</td>
<td>1</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

+ present; – absent.

*Two patients were reported in this paper, but clinical findings were only available in one (patient 1) and it is the findings in this patient that are summarised here.

Key points
- There is much heterogeneity in the clinical and radiological phenotype of published cases of the small patella/ischio-pubic-patella syndrome.
- It is likely that the small patella and ischio-pubic-patella syndromes are distinct entities.
- Five patients with features of the ischio-pubic-patella syndrome are presented.
- In all of these patients there is genetic/cytogenetic evidence of campomelic dysplasia.
- Campomelic dysplasia is not uniformly lethal.
- Patients suspected of having ischio-pubic-patella syndrome should be investigated for campomelic dysplasia.
DISCUSSION

The small patella syndrome was first described by Scott and Tao1 and Tao and Tao2 in 1979. In neither paper was mention made of other associated clinical features, and radiology was limited to the pelvis and knees. The phenotype appears to have been relatively mild. Since these initial descriptions, the clinical and radiological phenotype has been expanded.

Vanek3 was the first to use the term ischio-patella dysplasia in a report on three members of one family. This author...
described an infra-acetabular “axe cut notch” consisting of a well-defined defect in the region of the ilioischial synchondrosis. This finding was also present in the 15 family members described by Morin et al., however, it has not been seen in any of the 27 remaining published cases, nor in any of the five cases presented in this paper.

Additional radiological features in the patients of Morin et al. included pes planus and short fourth and fifth and sandal gap toes. Similar foot abnormalities associated with the condition were found in three family members reported by Dell."
hypoplastic patellae, defective ischio-pubic ossification, hypo-
plastic lesser trochanters, and elongated femoral necks with or
without a drumstick appearance to the proximal femora.

Figure 3 Chest (A) Case 1 aged 18 years. Long straight clavicles,
mild dorsal scoliosis, and small scapulae. (B) Case 4, neonate.
Spina bifida of lower cervical and mid thoracic spine, hypoplastic
scapular wings, long acromion processes, and scoliosis concave to
the left.

Figure 4 Thoracolumbar spine of case 4 aged 8 years. (A) AP, (B) lateral. Marked deterioration in degree of kyphoscoliosis (ref 38), lumbar
dysraphism, and exaggerated lumbar lordosis with horizontal sacrum.

Figure 5 DP L hand of case 2 aged 8 years. Short first metacarpal,
short middle phalanges, cone shaped epiphyses of middle
phalanges of middle and ring fingers, short terminal phalanges with
absent epiphyses, elongated capitate, absent distal ulna epiphysis,
and flat distal radial epiphysis.

There are marked similarities between the patients pre-
sented and the cases described by Koslowski and Nelson and
Azouz and Koslowski, particularly patient 1 in the former
publication. Although these five presented patients have the
diagnostic criteria of the ischio-pubic-patella syndrome, they
all have genetic/cytogenetic evidence of campomelic
dysplasia.
Clinically and radiologically, surviving campomelic dysplasia and patients at the severe end of the spectrum of the ischio-pubic-patella syndrome have the same findings: clinically, a depressed nasal bridge, high or cleft palate, long philtrum, micrognathia, relative macrocephaly, low set ears, and respiratory difficulties; and, radiologically, defective pelvic ossification, hypoplastic scapulae, talipes, and brachydactyly.

In some of the five presented patients, mild bowing of the tibia and fibula and relative shortening of the fibula compared to the tibia was seen. Two patients had vertical iliac wings and three had narrow iliac bones. Although not described in other cases of the ischio-pubic-patella syndrome, these are all features of classical, perinatally lethal campomelic dysplasia. Previously, it was thought that campomelic dysplasia was uniformly lethal with patients dying before the age of patella ossification (that is, 2 1/2 years in girls and 4 years in boys). Abnormalities of the patella and other radiological findings in this condition have therefore not been documented beyond early infancy, and comparison of the two conditions beyond this age is difficult.

In summary, there is much heterogeneity in the clinical and radiological phenotypes of the published cases of the ischio-pubic-patella syndrome; in some instances no clinical description is given (this may be because of a mild phenotype and the absence of clinical abnormalities). Furthermore, some skeletal surveys have been less extensive than others.

A few patients described as having the extended phenotype of the ischio-pubic-patella syndrome have marked clinical and radiological similarities to the five cases presented.

A review of published reports suggests the existence of more than one entity. (1) Small patella syndrome. A mild phenotype with no facial abnormalities and clinical abnormalities related to absent or small, recurrently dislocating patellae. Radiologically these patients have a hypoplastic patella, defective ischio-pubic ossification, elongated femoral necks, hypoplastic lesser trochanters, and may have coxa valga, and an infra-acetabular axis cut notch. Abnormalities of the foot may coexist. (2) Ischio-pubic-patella syndrome. These patients have a more severe phenotype, with facial and radiological features as summarised in tables 1-3. The patients whom we present fall into the second group.

It is proposed that the diagnosis of the ischio-pubic-patella syndrome be reconsidered; some cases at the mild end of the spectrum may represent a distinct entity, the small patella syndrome, and those at the severe end should be investigated for genetic or cytogenetic evidence of campomelic dysplasia. It is possible that the severe phenotype is the result of mosaic mutation in SOX9 or other milder mutations. It is also possible that the small patella syndrome, the ischio-pubic-patella syndrome, and campomelic dysplasia, form a spectrum of increasing phenotypic severity of a disorder caused by mutations at the same locus (SOX9). In either case, it would appear that the current nomenclature needs revision.

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References