ORIGINAL REPORT

Radiological findings in Currarino syndrome

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Abstract
Objective: To describe the clinical, radiological and genetic findings of a family affected by Currarino syndrome (CS) (agenesis of the sacrum, presacral mass, and anal-rectal anomalies), and to familiarize the radiologist with this condition that, although uncommon, could be suspected by its characteristic images.

Materials and methods: A study was made of 8 out of 9 family members (the parents, 7 siblings, 4 males and 3 females) suspected of having CS. The clinical and genetic findings are described. Using simple X-rays, ultrasound and magnetic resonance imaging, the presence of agenesis of the sacrum, a presacral mass and anal-rectal anomalies were investigated. Furthermore, a genetic analysis of the HLXB9 gene was performed. Permission by the Ethics Committee was not requested as all the family members gave their consent by signing a document.

Results: The mother with a scimitar-shaped sacrum confirmed that she was the transmitter of the genetic mutation. One of the seven siblings had complete CS (sacral agenesis, anorectal stenosis, and anterior meningocele). Four siblings had an incomplete CS: 3 with sacral agenesis and a presacral mass (two anterior meningoceles and one teratoma) and the fourth with sacral agenesis and anorectal stenosis. One sibling had no anomalies. The mother, as well as four siblings, did not have the HLXB9 gene mutation.

Conclusion: When there is sacral agenesis, the possibility of presacral masses and anorectal changes should be investigated. Likewise, if there is familial association, they should be investigated for a CS.

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KEYWORDS
Sacral agenesis; Presacral mass; Anterior meningocele; Currarino triad

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PALABRAS CLAVE
Agenesia sacra; Masa presacra; Meningocele anterior; Triada Currarino

Hallazgos radiológicos en el síndrome de Currarino

Resumen
Objetivo: Describir los hallazgos clínicos, radiológicos y genéticos de una familia afecta de síndrome de Currarino (SC) (agenesia del sacro, masa presacra y anomalías anorrectales) y familiarizar al radiólogo con esta entidad que, aunque infrecuente, podemos sospechar por sus imágenes características.

Material y métodos: Se estudiaron 8 de los 9 miembros de la familia con sospecha de SC: los padres y 7 hermanos (4 varones y tres mujeres). Se detallaron los hallazgos clínicos y genéticos; y mediante radiografía simple, ecografía y resonancia magnética se investigó la agenesia del sacro y la presencia de masas presacras y anomalías anorrectales. Además, se realizó un análisis del gen HLXB9. No se solicitó el permiso al comité de ética aunque todos los miembros de la familia dieron su consentimiento.

Resultados: La madre con un sacro en cimitarra confirmado era la transmisora de la mutación genética. Uno de los 7 hermanos era un SC completo (agenesia sacra, estenosis anorrectal y meningocèle anterior). Cuatro hermanos presentaron un SC incompleto, tres con agenesia del sacro y masa presacra (dos meningocéles anteriores y un teratoma) y el cuarto una agenesia sacra y estenosis anorrectal. Un hermano no tenía alteraciones. Tanto la madre como 4 hermanos presentaban la mutación en el gen HLXB9.

Conclusión: Ante una agenesia sacra se deberían investigar posibles masas presacras y alteraciones anorrectales. Así mismo, en caso de asociación familiar habría que descartar un SC.

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Introduction

The Currarino syndrome (CS) is a rare autosomal dominant disorder characterized by a triad of anorectal stenosis, sacral agenesis and presacral mass.1 It was first described by Kennedy in 1926, but in 1981 Currarino established the "scimitar sacrum" as the defect required for CS and recognized these disorders as a complex syndrome that can be ascribed to a common developmental anomaly.1 The prevalence of the CS is unknown.2 In the general population, the prevalence of total or partial sacral agenesis is estimated to be 0.09–0.43.3 The first case of CS was described in 1926 and up to 2005 less than 250 cases of complete or incomplete syndrome have been reported in the literature.2,4 In 2000, genetic studies revealed that the locus involved in normal anorectal and sacral development is located in chromosome 7 (7q36).5 Mutations within the locus of the HLXB9 gene,6-8 involved in the development of anterior motor neurons, is responsible for CS. The objective of this study is to describe the clinical, radiological and genetic findings in CS and familiarize the radiologist with this entity that, albeit uncommon, can be suspected by the characteristic imaging findings.

Materials and methods

From the index case who gave rise to the suspicion of CS, all the first-degree relatives were invited for CS screening. They were the mother and seven siblings (3 women and 4 men) with ages ranging from 30 to 65 years. All the participants underwent an examination that involved a detailed clinical history, plain X-ray of the pelvis (AP projection) (Axiom Aristo FX plus Siemens), abdominal ultrasound (Acuson Antares Siemens), and an MRI (magnetic resonance imaging) scan of the pelvis and lumbosacral spine (Symphony Siemens 1.5) with the following sequence protocol: axial and sagittal T1-weighted sequences, with and without gadolinium with fat saturation, axial and sagittal T2-weighted sequences with fat saturation. Pelvic X-ray was selected as the screening method for sacral agenesis.6 Pelvis and lumbar spine MRI is the technique of choice for the detection and characterization of presacral masses.6,7 The different types of sacral agenesis have been described and classified into the following categories:6 (1) total sacral agenesis with normal or short transverse pelvic diameter and some lumbar vertebrae possibly missing; (2) total sacral agenesis without involvement of lumbar vertebrae; (3) partial sacral agenesis with intact S1; (4) hemisacrum; (5) coccyegeal agenesis. Anterior meningocèle is defined as the herniation of the dural sac through a defect in the sacrum, and sacrococcygeal teratoma is a germ cell tumor that contains tissue from all three germinal layers.8 Additionally, the index case underwent an abdominal computed tomography (CT) with IV contrast agent (Lightspeed General Electric) when diagnosed in the emergency department. Lastly, to evaluate the genotype–phenotype correlation of CS, given the variable phenotype expression described in the syndrome, molecular testing, involving bi-directional sequencing of the HLXB9 gene and 50 pb of the flanking region of the gene, was performed on an ABI3130x1 automatic sequencer.9 Ethics Committee approval was not sought, but all family members gave written consent to genetic testing and verbal consent to imaging examinations.

Results

Eight out of nine members of the family with suspected CS (the parents and 7 siblings, 4 males and 3 females) were
studied. Table 1 summarizes the demographic, clinical and radiological data as well as the genetic findings of the family members with Currarino syndrome. Fig. 1 shows the family tree and the tests performed. Cases 1, 3 and 4 correspond to Figs. 2–4, respectively. The ninth patient could not be examined, and the father showed no abnormalities, having no relevance for the study. The mother, with a confirmed scimitar sacrum, was the transmitter of the genetic mutation, but the study of this patient was not completed because she refused to undergo the MRI. The study was completed in five of the six siblings, and one sister refused to undergo the MRI. One brother showed no abnormalities and the remaining five siblings had CS with different degrees of phenotypic expression. One brother has complete CS, and the remaining siblings have incomplete CS, with three with sacral agenesis and presacral mass and one sister with sacral agenesis and anorectal stenosis. In this patient, the presence of an occult presacral mass could not be ruled out because she refused to undergo MRI examination. Therefore, the five affected siblings showed sacral agenesis, three had hemisacrum, one had partial hemisacrum, and one had partial agenesis with preservation of S1. Regarding the presacral masses, three were anterior meningoceles and one was a teratoma. Two siblings had anorectal stenosis and another had meningitis. In addition, two sisters had recurrent urinary tract infections. Genetic testing confirmed mutation of the HLXB9 gene in the mother and four siblings.

**Discussion**

CS should be suspected in the presence of sacral agenesis, with or without presacral mass and/or anorectal anomaly. In addition, all family members should undergo screening to rule out familial association. Few studies describe the typical radiological findings of the disease. Moreover, there are very few families with CS and they are usually small-sized families. In contrast, the family described here is large, with

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age/sex</th>
<th>Radiography</th>
<th>Ultrasound</th>
<th>Magnetic resonance</th>
<th>HLXB9 mutation</th>
<th>Clinical findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Fig. 2)</td>
<td>36 years male</td>
<td>Partial sacral agenesis with S1</td>
<td>Anechoic collection</td>
<td>Anterior meningocele</td>
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<td>2</td>
<td>31 years female</td>
<td>Partial sacral agenesis with S1</td>
<td>Hypoechoic collection</td>
<td>Anterior meningocele surgically treated</td>
<td>Yes</td>
<td>Lumbar pain urinary tract infections Meningitis</td>
</tr>
<tr>
<td>3 (Fig. 3)</td>
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<td>Hemisacrum</td>
<td>Normal</td>
<td>Anterior meningocele</td>
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<td></td>
</tr>
<tr>
<td>4 (Fig. 4)</td>
<td>39 years male</td>
<td>Hemisacrum</td>
<td>Normal</td>
<td>Cystic teratoma/hamartoma</td>
<td>Yes</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>5</td>
<td>35 years male</td>
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<td>Not performed</td>
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<tr>
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<td>Normal</td>
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<tr>
<td>7</td>
<td>63 years female</td>
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<td>Not performed</td>
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<td>Urinary tract infections</td>
</tr>
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<td>8</td>
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<td>Not performed</td>
<td>Not performed</td>
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<td></td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>Not performed</td>
<td>Not performed</td>
<td>Not performed</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1** Genealogical tree of a family with Currarino syndrome. The black square represents the patient who could not be examined. 0: no findings; 1: sacral agenesis; 2: sacral agenesis and presacral mass or sacral agenesis and anorectal malformation (incomplete CS); 3: sacral agenesis, presacral mass and anorectal malformation (complete CS). The age of each family member and the imaging tests performed are provided. X-ray, radiography; MRI, magnetic resonance imaging; CT, computed tomography.
Figure 2  Case 1: 36-year-old male with Currarino syndrome. (A) AP plain radiograph of the pelvis shows partial sacral agenesis with preservation of S1. (B) Ultrasound. Presacral hypoechoic collection (asterisk) that displaces the bladder. (C) Computerized tomography with intravenous contrast shows a large, presacral cystic mass with well-defined margins that connects with the spinal canal (asterisk). (D) Sagittal T1-weighted MR image shows hypointensity of the presacral mass. (E) Sagittal T2-weighted MR image with fat suppression shows hyperintensity of the mass. (F) Sagittal gadolinium-enhanced T1-weighted MR image shows that the lesion does not enhance after contrast administration. All the findings are suggestive of anterior meningocele (asterisk).

Figure 3  Case 3: 41-year-old male with Currarino syndrome. (A) AP plain radiograph of the pelvis showing a hemisacrum. (B) Sagittal T1-weighted MR image demonstrates a hypointense cystic lesion that connects with the spinal canal (arrow). (C) Sagittal T2-weighted MR image with fat suppression shows hyperintensity of the lesion (arrow). Findings compatible with anterior meningocele.
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Figure 4  Case 4: 39-year-old female with Currarino syndrome. (A) AP plain radiograph of the pelvis showing a hemisacrum. (B)-(D) MR images show a multicystic lesion 2 cm in size and heterogeneous signal. Sagittal T1-weighted MR image (B) shows hypointensity of the lesion (arrow). Sagittal T2-weighted MR image with fat (C) shows hyperintensity of the mass (arrow) with no enhancement after gadolinium administration (arrow) (D). These findings are suggestive of sacrococcygeal teratoma or cystic hamartoma.

seven members with varying degrees of phenotypic expression. In previous studies, the syndrome is diagnosed during the first decade of life but the age range at presentation varies from birth to 64 years. However, in our series the age range was between 30 and 63 years, probably because of the triviality of symptoms. This means that the prevalence of the disease is probably higher than reported. Chronic constipation is the most commonly reported symptom. Other symptoms are related to recurrent urinary tract infections, nausea, headache and lumbar pain. One of our patients had meningitis when he was a child, two sisters had recurrent urinary tract infection and another had chronic lumbar pain. In addition, two siblings had anorectal stenosis.

The variability of the CS phenotype means that the manifestations and the severity of the syndrome do not depend solely on the HLXB9 gene mutation, but other unknown genes may also be involved in the penetrance of the mutation. In 50% of cases, the triad is familial; however, it may be incomplete when one or two features of the syndrome are missing. Our series shows a wide phenotypic variability. The presence of one asymptomatic patient with no abnormalities, one patient with the classic triad and four patients with at least two features suggested variable penetrance of the gene. Regarding the radiological findings, all the affected patients showed sacral agenesis, essential for defining the syndrome. In addition, an anterior
meningocele was seen in three patients and one teratoma in one patient, without histopathological confirmation. These findings are similar to those reported by other authors, for whom meningocele and teratoma were the most common presacral masses, even among members of the same family. Lastly, molecular testing will help to make a confident diagnosis by identifying the mutation in the HLXB9 gene. Genetic confirmation of the CS may be difficult. Nonetheless, the genetic mutation was confirmed in five patients of our series. When an index case is identified, the molecular analysis of the HLXB9 gene and the radiological examination of the family allow us to determine whether the CS is familial or sporadic. To sum up, the presence of sacral anomalies with presacral masses and/or anorectal anomalies are suggestive of possible familial CS.

Authorship

1. Responsible for the integrity of the study: CPVL, CSG, EUR, EDG, ADF and VRV.
2. Conception of the study: ADF, CPVL and CSG.
3. Design of the study: CPVL and CSG.
4. Acquisition of data: CPVL, CSG and EUR.
5. Analysis and interpretation of data: CPVL, CSG, EUR, EDG, ADF and VRV.
6. Statistical analysis: N/A.
7. Bibliographic search: CPVL, CSG, EUR and EDG.
8. Writing of the paper: CPVL, CSG, EUR, EDG, ADF and VRV.
9. Critical review with intellectually relevant contributions: CPVL, CSG, EUR, EDG, ADF and VRV.
10. Approval of the final version: CPVL, CSG, EUR, EDG, ADF and VRV.

Conflict of interest

The authors declare not having any conflict of interest.

References