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Clinical case

Intratesticular heterotopic adrenal tissue in a patient with Coffin-Siris syndrome

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RESUMEN

El hallazgo de tejido corticoadrenal heterotópico puede ocurrir en todo el trayecto del descenso testicular desde el celoma dorsal hasta su localización intraescrotal. La heterotopía adrenal es más frecuente cuando hay criptorquidia, cualquiera sea la ubicación de la misma. Se comunica el caso de un paciente con las manifestaciones clínicas del síndrome de Coffin-Siris con hernia inguinal y criptorquidia. El examen histológico del testículo resecado reveló nódulos de corteza adrenal dispuestos entre los conductos de la *rete testis* y los túbulos seminíferos. Las células fueron positivas para α-inhibina y vimentina. Esta peculiar localización de la heterotopía parece haber sido referida sólo una vez en la bibliografía.
Palabras clave: criptorquidia, heterotopía adrenal, síndrome de Coffin-Siris, testículo.

ABSTRACT

Heterotopic adrenal tissue can be found all the way in the migration of the male gonad from the dorsal coelom to its intrascrotal position. Any level of cryptorchidism increases this anomaly. In the present report we refer a patient with the clinical constellation of Coffin-Siris syndrome presenting inguinal hernia and cryptorchidism. The histological examination of the resected testis revealed nodules of adrenal cortex arranged between *rete testis* ducts and the seminiferous tubules, cells were positive for alpha-inhibin and vimentin. This peculiar adrenal cortex heterotopia seems to have been reported only once.
Key words: Adrenal heterotopia, Coffin-Siris syndrome, cryptorchydism, testis.

Coffin-Siris syndrome (CSS) (OMIN 135900) is a rare AR multimalformation condition first reported by two authors in 1970.[1] Patients present a combination of cranial-facial anomalies with coarse features, bushy eyebrows, broad nose, wide mouth, micrognathia, generalized hypertrichosis with scalp hypotrichosis, scoliosis, nail hypoplasia of fifth finger, and delayed mental and height-weight development.[2-6] There are less than 100 reported cases, the cariotype being usually normal[2-4] in two recent case reports[7,8] show that the 7q32-q34 region could contain the candidate gene for the CSS.

CSS patients frequently present suction and swallowing difficulties, and an increased frequency of respiratory and gastrointestinal infections. At the same time often there are heart (septal defects, tetralogy of Fallot), urogenital

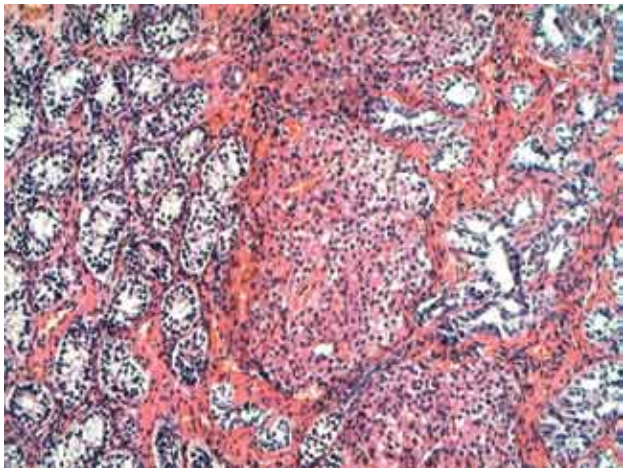

Figure 1. Low power view of the nests of adrenal cortex tissue arranged between the *rete testis* (right side of the figure) and the seminiferous tubules.

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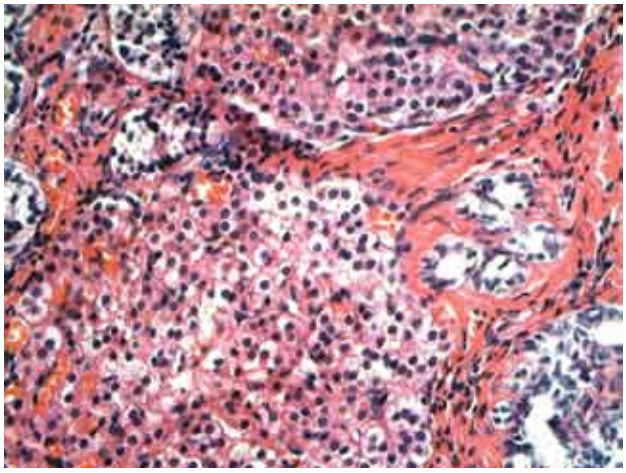

Figure 2. Higher power of figure 1 where two types of cortical cells can be recognized that of glomerular and fascicular layers.

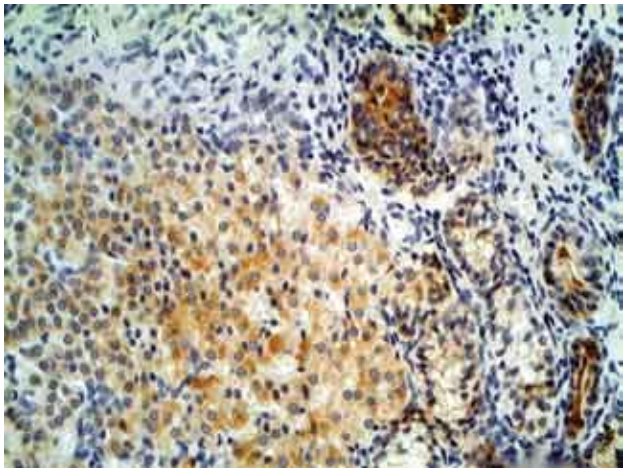

Figure 3. Alpha-inhibin positivity of the ectopic adrenocortical cells. The reactivity is less intense than that of Sertoli cells.

(chryptorchidia, hypospadias, uterus agenesis), and kidney (crossed ectopia, fused ectopia, hypoplasia) malformations.[9] The syndrome has also been reported in association with diaphragmatic hernia[10] biotinidase deficiency,[11] and hypoglycemia.[12] There seem to be no description of testicular lesions in the CSS.

We report the finding of adrenal cortex heterotopia in an undescended testis of a patient with CSS.

CASE REPORT

The patient had a long medical history with evidences of disease since the perinatal period moment at which several external and internal malformations were noticed. Cariotype, including G-banding, was normal. At age 28 months (04/92) an evaluation at the Genetic Clinic showed: weight, height and cephalic perimeter at P3, diffuse hypertrichosis, rounded head, flat occipital, scant scalp hair, small and narrow frontal region, flat supraorbital arch, triangular eyebrows, horizontal palpebral fissure, small malar bones, anteverted narines, triangular filtrum, coarse lips, the upper protruding over the lower, high-arched palate, micrognathia, low set and dorsaly-rotated ears, protruding antihelix, folded helix, short neck, wide thorax, widely-set mamillae, hipoplastic nails in 5th finger, transverse palmar crease, feets with nail hypoplasia in the 5th toe, psychomotor delay, difficulties in suction and swallowing, urinary malformations (paraurethral diverticulum, hypoplasia of left kidney associated with vesico-ureteral reflux grade 3-4), bilateral inguinal hernia, and dorso-lumbar kyphoscoliosis. The phenotype and the clinical data of the history were consistent with the diagnosis of CSS. At age 3.5 years (05/93) surgical correction of the inguinal hernias was done together with resection of the right testes that was found to be hypoplastic at the inguinal region. The left testis was absent.

PATHOLOGY FINDINGS

The testis size was 4x3x3 mm. Histological examination disclosed the presence of several small collections of epithelial cells readily identifiable as representing the glomerular and fascicular layers of adrenocortical tissue.

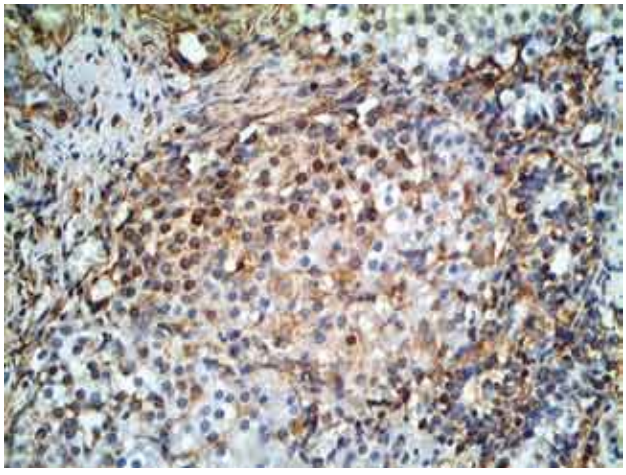

Figure 4. Ectopic adrenocortical cells with focal positivity for vimentin.

These groups of adrenal cortex cells were arranged deep inside the testis between the *rete testis* and the seminiferous tubules (figures 1 and 2). The latter contained rare spermatogonia and no Leydig cells were found at the interstitial tissue. The epididymis and *vas deferens* were normal. Restricted immunohistochemical study proved the cells to be positive for alpha-inhibin (less intensity than adjacent Sertoli cells) (figure 3), vimentin (50% of the cells) (figure 4) and keratin (AE1/AE3) (less than 10% of the cells), as well as negative for low-molecular weight keratin (CAM 5.2) (figure 5).

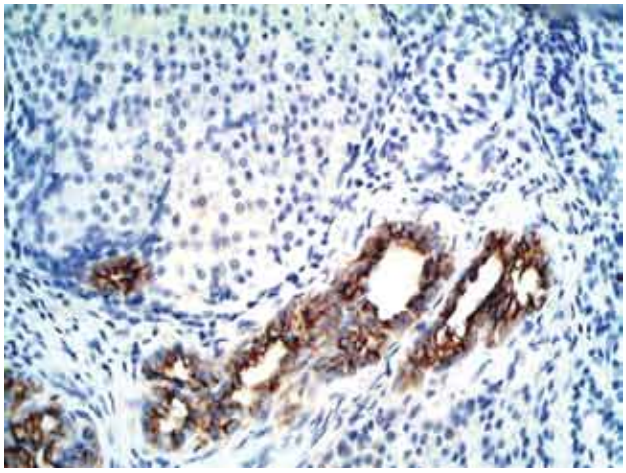

Figure 5. Low-molecular weight keratin immunoreactivity appears restricted to the *rete testis* cells.

DISCUSSION

Ectopic adrenal cortex tissue has been referred repeatedly as being found adjacent to the *vas deferens*, epididymis and testis, particularly in patients with cryptorchidism.[13-15] However, it has rarely been described as to be present within the gonad. One report mentions the same peculiar spot as the one recognized in present patient that is between the *rete testis* and the rest of the organ. This patient was an adult with undescended testis but no evidences of CSS.[16] So, the adrenal cortex heterotopia in our patient may have resulted an epiphenomenon related to the inguinal hernir-cryptorchidism or, being so extremely unusual, a peculiar developmental abnormality related to CSS. Recent papers favoring the existence of a common primordium for the adrenal gland and gonad[17-19] help to explain the occurrence of adrenal cortex ectopia all the way from the dorsal coelom to the gonadal tissue itself.

The immunohistochemical findings in present case are on line with the reported immunoreactivity of adrenal cortex cells.[20-22]

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Virus del papiloma humano. Una versión para todos

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El VPH es el principal virus oncógeno para nuestra especie, según la OMS ocurren cerca de 500 mil muertes por cáncer del cuello uterino y otros sitios, relacionados con este virus (6% de todos los cánceres, ¡uno de cada 20 casos!). En México mueren cerca de 4,000 mujeres al año por cáncer cervicouterino relacionado con la infección de este virus (la segunda causa de muerte por cáncer en mexicanas). El propósito de esta publicación es informar de la manera más amplia y sencilla posible sobre el VPH.