En nuestra paciente se constató un foco infeccioso extendido de forma hematógena sin origen aparente alguno tras el estudio de extensión.

Prácticamente cualquier bacteria puede infectar la tiroides[8]: Neumococo, Salmonella, Klebsiella, Bacteroides, Treponema pallidum, Pasteurella spp. y micobacterias. Existen organismos que pueden causar infección crónica o insidiosa, especialmente en pacientes con enfermedad por VIH, entre ellos el Mycobacterium tuberculosis, micobacterias atípicas, Aspergillus spp., Coccidioides immitis, Cryptococcus neoformans, Histoplasma capsulatum, Candida spp., Treponema pallidum, Equinococcus spp. y Pneumocystis carinii.

El síntoma clínico dominante es el dolor en la región de la glándula tiroides, que posteriormente aumenta de tamaño y temperatura. Nuestra paciente también refería disfagia, aunque otros síntomas como ronquera, dolor de garganta o disfonía[9], no estaban presentes. Tampoco presentaba linfadenopatías locales. Este tipo de presentación obliga a descartar la posibilidad de un proceso neoplásico. Como ocurrió en nuestro caso suele presentarse más comúnmente en otoño e invierno, por lo general después de las infecciones del tracto respiratorio superior.

El análisis de la función tiroidea no mostró alteración, como es habitual en los casos de tiroiditis piógena.

La realización de una ecografía de la glándula tiroides para la punción aspirado con aguja fina es la técnica de imagen de elección inicial para el diagnóstico.

Una tomografía computarizada puede ser útil en la identificación de la ubicación del absceso, pero esto es necesario solo en situaciones excepcionales.

El tratamiento debe iniciarse con antibioterapia de amplio espectro empírica por vía parenteral basada en la sospecha diagnóstica tras el radiodiagnóstico[10]. Se procederá a la exploración quirúrgica en todos aquellos casos en los que se objetive alteraciones anatómicas tales como fístulas del seno piriforme o presencia de un conducto tirogloso remanente. El drenaje quirúrgico se debe llevar a cabo siempre que las pruebas de imagen muestren la presencia de un absceso o formación de gas intraglandular. Si se desarrolla necrosis, o la infección persiste pese a una adecuada antibioterapia, será preciso una lobectomía tiroidea[3].

Aunque para el tratamiento de la tiroiditis piógena únicamente son necesarios 14 días de antibioterapia, se recomienda prolongar la misma hasta 4 semanas cuando hay bacteriemia.

En conclusión, la tiroiditis piógena es una patología muy infrecuente que suele aparecer sobre tiroides patológicos, fístulas del seno piriforme y, especialmente, en niños o pacientes inmunodeprimidos. Nuestro caso no cumplía ninguna de estas características lo que lo hace aún más inusual.

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Neurohypophyseal germinoma: hCG in cerebrospinal fluid as a key for a diagnostic challenge

Germinomas neurohipofisarios: hCG en líquido cefalorraquídeo como pieza clave para un reto diagnóstico

Neurohypophyseal germinomas are rare neoplasms, with slow growth and variable clinical presentation that occasionally complicate their diagnosis in the early stages of the disease. Although the determination of human chorionic gonadotropin (hCG) in serum and cerebrospinal fluid (CSF) may help, definitive diagnosis of these tumors is determined by the histopathological findings. We present two new cases of germinomas with special features that delayed their diagnosis for several years, and a review of the literature on this pathology.

A 14-year-old boy was referred to our department because he presented growth arrest for the previous two years. Seven years before he had been evaluated for an

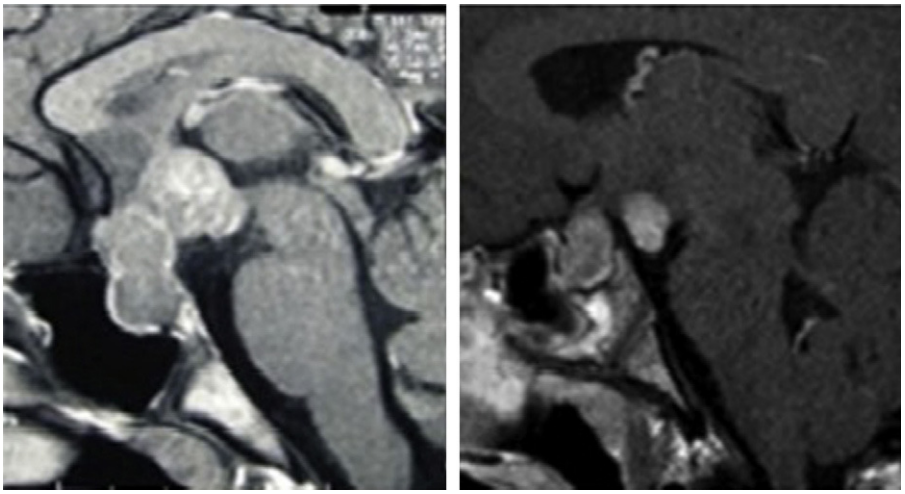

Figure 1 Hypophyseal MRI findings, Sagittal acquisitions, TI-sequencing after gadolinium contrast injection. Case 1. Hypothalamic-hypophyseal lesion affecting both cavernous sinuses, compression of the optic chiasm and deformation of the third ventricle. Case 2. Thickening of the hypophyseal stalk and enhanced uptake nodule in the *tuber cincrcum*, measuring 7 mm in size.

incipient mammary button, and four years ago he had been diagnosed of primary polydipsia. Physical examination emphasized height and weight below the 3rd percentile, button left breast and testicular volume of 6 mL. The endocrine study that we performed, revealed anterior panhypopituitarism with hyperprolactinemia: T4L 6.4 pmol/L [normal values (nv), 10.3–25.7] TSH 2.44 mU/L (nv, 0.38–4.84), baseline cortisol 190 nmol/L (nv, 221–690), LH < 0.1 U/L (nv, 2–13.8), FSH 0.1 U/L (nv, 2–13.8), testosterone 8.1 nmol/L (nv, 10–35), PRL 28.4 μg/L (nv, 4.6–21), GH 1.6 μg/L (nv, 0–5), IGF-1 143 μg/L (nv, 112–450), and a GH peak after clonidine stimulation test of 1.3 μg/L (60 min). Given the presence of inappropriate undetectable LH concentrations for the testosterone levels, serum hCG was evaluated, yielding a concentration of 10.9 mIU/mL. Brain MRI identified a hypothalamic-hypophyseal mass (Fig. 1). The CSF showed an hCG concentration of 32.6 mIU/mL, with a CSF/serum hCG ratio of 2.9. A transsphenoidal biopsy of the lesion was obtained, with confirmation of the diagnosis of neurohypophyseal germinoma.

A 10-year-old boy presented with polyuria–polydipsia regarded as corresponding to primary polydipsia. Arrested growth was established after one year of follow-up, and the patient was referred to other hospital where somatotropic deficiency was detected (GH peak after clonidine stimulation test of 3.6 μg/L at 60 min), along with central diabetes insipidus (dehydration test suspended after 4 h due to hypernatremia (155 mmol/L) and 3% body weight loss). The brain MRI findings proved normal. Treatment was started with GH and inhalatory desmopressin. After 16 months the patient developed central hypothyroidism and replacement therapy was started. A new pituitary MRI revealed then a thickening of the hypophyseal stalk associated to a 7-mm nodule with enhanced contrast uptake in the hypothalamic *tuber cinereum* (Fig. 1). GH treatment was suspended. Transsphenoidal biopsy of the sellar component reported lymphocytic hypophysitis. GH treatment was resumed, with the introduction of corticoid therapy for four weeks and a new pituitary MRI was performed showing a progressive enlargement of the hypothalamic lesion and thickening of the hypophyseal stalk. GH treatment and corticoid therapy were suspended and serum hCG was measured proving low but detectable levels: 2 mIU/mL. So a second biopsy was performed which again confirmed the diagnosis of lymphocytic hypophysitis (Fig. 2). At this point the patient was referred to our department. We measured hCG levels in serum and CSF with the following results: 7.1 and 23 mIU/mL, respectively, so we asked our pathologist to review the pituitary biopsy performed in the referral center. The adenohypophyseal tissue showed a dense mononuclear inflammatory infiltrate with the occasional presence of small granulomas composed of epitheloid histiocytes compatible with lymphocytic hypophysitis. However, of note was the presence of large cells with a vesicular nucleus, a macronucleolus and clear cytoplasm, forming small nests delimited by lymphocytes (Fig. 2). The immunohistochemical study proved positive for c-Kit and placental lactogen, and negative for CD30, thus confirming the biochemical diagnosis of germinoma.

Intracranial germ cell tumors represent less than 1% of all intracranial neoplasms, but in children constitute up to 6.5% of such lesions.[1] These tumors include germinoma, embryonal cell carcinomas, and teratomas. After the pineal gland, the suprasellar region represents the second most common site of involvement. They are more common in the second decade of life, with a peak incidence between 10 and 14 years of age. The lesions originating in the pineal gland are more prevalent in males, while no gender difference in distribution is seen in the lesions appearing in the suprasellar region.[2]

Among the suprasellar germ cell tumors, the most common lesions are germinomas, followed by teratomas and pinealomas of an ectopic or metastatic nature.[2] Neurohypophyseal germinomas may be pure or contain syncytiotrophoblastic giant cells which secrete hCG. Measurement of hCG is an important adjunct method in the diagnostic of germ cell tumors. At high concentrations hCG can be detected in serum, but when the serum hCG levels are low, evaluation of the hormone in CSF may be of help

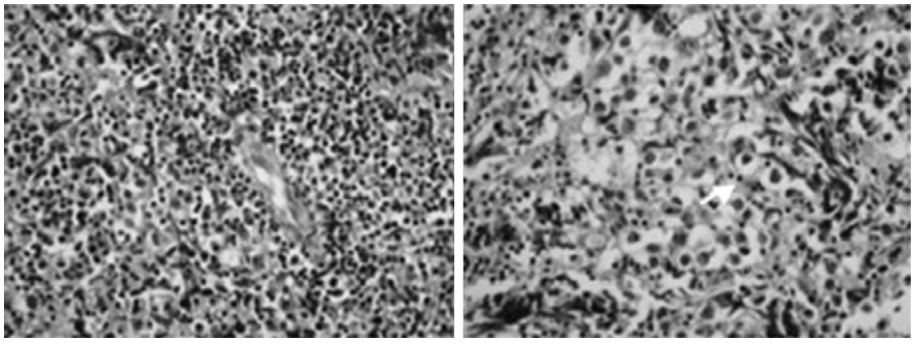

Figure 2 Histological specimen of transsphenoidal biopsy of case 2. Adenohypophyseal tissue showed a dense mononuclear inflammatory infiltrate (left image) with the occasional presence of small granulomas composed of epitheloid histiocytes compatible with lymphocytic hypophysitis. Of note was the presence of large cells with a vesicular nucleus, a macronucleolus and clear cytoplasm, forming small nests delimited by lymphocytes (right image).

in establishing the diagnosis, since this parameter is more sensitive as an indicator of tumor presence and even can precede to abnormalities on imagen techniques.[3–5]

The suprasellar germinomas often generate endocrine alterations. Over 90% of patients show clinical evidence of hypopituitarism that can manifest as gonadal dysfunction, secondary hypothyroidism and less frequently, alterations of the corticotropic axis. Children may present lack of sexual development and growth alterations as in our two patients. Neurohypophyseal and stalk dysfunction can manifest as hyperprolactinemia (symptomatic or otherwise), or as diabetes insipidus. The latter is observed in about 80% of all cases and may constitute an early finding. As an antecedent, our two cases were initially diagnosed with ''primary polydipsia''. Other potential symptoms are vision disturbances, including field defects or optic atrophy, hypothalamic manifestations, hydrocephalus, or symptoms of intracranial hypertension.[3]

In the MRI studies, thickening of the hypophyseal stalk is the most common finding, together with the loss of neurohypophyseal hyperintensity in T1-weighted sequences, in which the lesion appears isointense or slightly hypointense with respect to the normal hypophysis. After gadolinium contrast injection, uptake is less pronounced than in the normal hypophysis.[5]

The imaging findings are not specific and the differential diagnosis fundamentally must be established with tuberoinfundibular lymphocytic hypophysitis.[6] Since this disorder is infrequent in childhood, histological findings compatible with a lymphocytic inflammatory process can represent the first sign of a host reaction to occult germinoma, as illustrated in our second patient. This would justify the determination of hCG in CSF in all prepubertal patients with a presumed or histological diagnosis of lymphocytic hypophysitis, as well as the immunohistochemical study of the histological specimen with the determination of placental lactogen, c-Kit and CD30.[7]

As regards the treatment of intracranial germinomas, combined chemotherapy–radiotherapy has been the standard approach. However in non disseminated intracranial germinomas, the irradiation of the whole ventricular system without chemotherapy could be sufficient, as recent articles have shown that focal radiotherapy plus chemotherapy were associated with inferior control of these tumors, and a higher incidence of chemotherapy related toxicities.[8-10]

The prognosis of these tumors is dependent upon the histology, but also upon the size of the tumor and the extent of the disease at the time of diagnosis. An early diagnosis is key to treat such tumors before the hypothalamic-hypophyseal damage proves irreversible or adjacent structures suffer compression or metastatic disease became apparent.

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Síndrome de insensibilidad completa a andrógenos con persistencia de restos mullerianos. Descripción de un caso

Complete androgen insensitivity syndrome with persistent müllerian remnants. A case report

La diferenciación sexual es un proceso que se inicia precozmente durante la embriogénesis. En los varones, el gen SRY, ubicado en el brazo corto del cromosoma Y, codifica para el factor determinante testicular que determina la diferenciación de la gónada hacia testículo. La síntesis de andrógenos testiculares por las células de Leydig se inicia a partir de la octava semana del desarrollo, estimulada inicialmente por la gonadotrofina coriónica (HCG) placentaria y, posteriormente, por la hormona luteinizante (LH). Las gonadotrofinas fetales estimulan la producción a nivel testicular de hormona antimulleriana (AMH), que estimula la regresión de los conductos de Muller en los varones. La testosterona, cuya acción se inicia en la novena semana una vez que el receptor de andrógenos (RA) se encuentra presente, permite estabilizar los conductos de Wolff y su diferenciación hacia epidídimo, *vas deferens* y vesículas seminales. La conversión de la testosterona en su metabolito más activo, la dehidrotestosterona (DHT) permite el crecimiento del tubérculo genital dando origen al pene y el cierre del rafe ventral, originando la uretra peneana y el rafe escrotal (fig. 1).

El síndrome de insensibilidad completa a andrógenos (SICA) es un desorden del desarrollo sexual XY en que existe una pérdida de función del RA. Se presenta en individuos con cariotipo 46 XY con genitales externos de fenotipo femenino.

Presentamos el caso de un recién nacido a término producto de un embarazo fisiológico, primera hija de padres sanos no consanguíneos. El peso de nacimiento fue 3.420 g y la longitud de nacimiento 50 cm, con Apgar 9-10. Al examen físico presentaba genitales externos femeninos normales y 2 masas de 1 cm en ambos conductos inguinales, por lo que se sospechó una hernia inguinal. La ecografía abdominal demostró la presencia de un proceso peritoneo-vaginal persistente en ambas regiones inguinales con herniación del contenido abdominal y 2 formaciones ovoídeas homogéneas de un centímetro de diámetro con flujo al doppler en su interior, sin folículos sugerentes de gónadas. A los 2 días de vida presentaba LH y hormona folículo estimulante (FSH) menores a 0,1 IU/L (valores de referencia (VR): 0,02−7,0 mIU/l), testosterona de 1,45 nmol/L (VR: 0,42−0,72 nmol/L) y estradiol <73,4 pmol/L (esperable niveles marcadamente elevados).

Frente a la sospecha de gónadas en canal inguinal, la paciente fue sometida a cirugía al tercer día de vida. Una vaginoscopia intraoperatoria no mostró cuello uterino. La biopsia gonadal mostró un fragmento de parénquima testicular constituido por cordones sólidos con células de Sertoli y gonias, sin identificar células de Leydig. La biopsia de gónada izquierda mostraba un elevado número de gonias, hidátide quística y numerosas estructuras tubulares compatibles con epidídimo. En la vecindad, presentaba un conducto compatible con resto mulleriano (fig. 2). Se restituyeron ambos testículos en el abdomen.

El estudio del cariotipo fue 46 XY. El estudio molecular del gen del RA halló un cambio de base en el exón 5, que sustituía una arginina por glutamina en el codón 752 (R752X), mutación comunicada previamente en la literatura en un paciente con SICA[1], lo que confirmó el diagnóstico. El

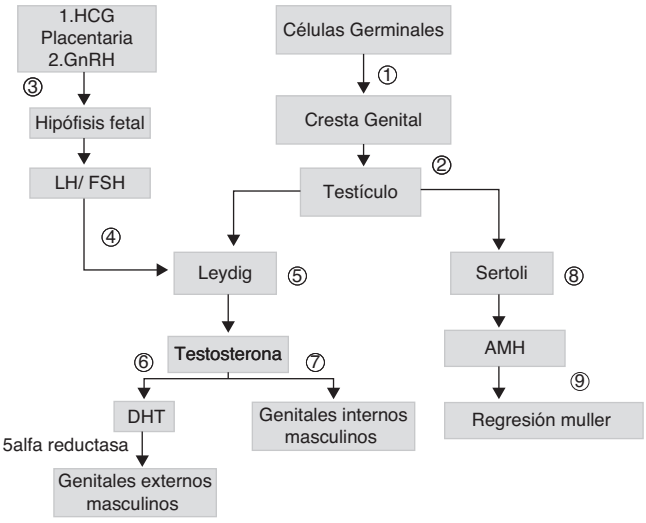

Figura 1 Esquema de desarrollo sexual embrionario: las células germinales migran hacia las crestas genitales (1), forman los cordones sexuales primitivos dando origen a los testículos (2). Las células de Leydig, son estimuladas por la gonadotrofina coriónica (HCG) placentaria y, posteriormente, por hormona luteinizante (LH) (4), que depende de la hormona liberadora de gonadotrofinas (GnHRH) secretada por el hipotálamo fetal (3), que estimula la producción de gonadotrofinas. Estas estimulan la producción de andrógenos (7) y de hormona antimulleriana (AMH) (8), que permite la regresión de los conductos de Muller (9). La testosterona secretada inicialmente (7), permite el desarrollo de genitales internos masculinos. La conversión de testosterona a dehidrotestosterona (DHT) permite la formación de los genitales externos masculinos (6).