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Congenital adrenal hyperplasia and Leydig cell tumor. Case report and review of literature

Adrenogenital Syndrome, more properly defined as Congenital Adrenal Hyperplasia (CAH), is related to the enzyme 21-beta-hydroxylase deficiency, with impaired glucocorticoids and aldosterone syntheses and increased ACTH synthesis. This report describes a case of a monorchid patient suffering from Adrenogenital Syndrome and Leydig cell tumor of his testis. A right orchidectomy with implantation of testis prosthesis was performed, after informing the patient on the consequences of his castration and obtaining his consent. Histology showed a testis measuring 4x3x2.5 cm with a 6 cm long spermatic cord; there was a yellowish, well-defined nodule measuring 3.5x1.5 cm, surrounded by normal parenchyma. This nodule had morphologic and immunohistochemical characteristics of a Leydig cell tumor, even found in the spermatic cord; those cells showed positivity to inhibin, MART-1 and vimentine.

KEY WORDS: Adrenogenital syndrome, Leydig tumor, Orchidectomy, Testis tumor.

Introduction

Adrenogenital Syndrome, more properly defined as Congenital Adrenal Hyperplasia (CAH), is related to the enzyme 21-beta-hydroxylase deficiency, with impaired glucocorticoids and aldosterone syntheses and increased ACTH synthesis. The true frequency of testicular masses in patients with the CAH is unknown, even if it has been reported that testicular adrenal rest is a rare clinical condition. The association of the CAH with Leydig cell tumor of the testis was described in 1940 and few cases have been reported in literature. This report describes a case of a monorchid patient suffering from Adrenogenital Syndrome and Leydig cell tumor of his testis.

Case report

A 24-yr-old man was admitted to our Unit because of lower abdominal pain extended to the right groin and testis. He was suffering from “salt-wasting” CAH, diagnosed early in neonatal period, and was in therapy with hydrocortisone (40mg/die) and dexamethasone (0.25mg/die). He was also affected from post-thyroiditis hypothyroidism, treated with levothyroxine, and phobic psychosis, treated with risperidone, carbamazepine and dolanzepam. Seven years before, the patient underwent orchidectomy for abnormal twisting of left testis and lab tests showed aspermia. No bacteria, fungi and flagellate protozoa were checked by sperm-culture. On palpation, right testis had hard consistency and irregular margins. Hormonal assay showed increase of plasma renin, FSH and 17-hydroxyprogesterone levels, low levels of DHEA-sulphate and total testosterone, borderline levels of free testosterone and delta-4-androstenedione, normal levels of aldosterone, prolactin and 17-beta estradiol.

Scrotal US, both standard grey scale and Colour Doppler, was performed by using 7.5 MHz linear array transducer.
with a commercially available sonographic equipment (model AUC50 unit, Esaote Medical System, Genova, Italy). The US detected a moderate increase size of the right testis that was dismorphous and inhomogeneous in consequence of a lesion measuring 40x27 mm, with irregular margins and poor vascularisation in peripheral portions. The patient underwent biopsies of testis with intraoperative histology that was negative for tumor. On the contrary, the postoperative immunohistochemical study showed a proliferation of large eosinophilic cytoplasm and low-grade nuclear pleomorphism cells which was organized in lobules, separated by fibrous septa. Therefore, the nodule was diagnosed as a Leydig cell tumor. Based on this diagnosis, a right orchidectomy (Fig. 1) with implantation of testis prosthesis was performed, after informing the patient on the consequences of his castration and obtaining his consent. The final histology showed a testis measuring 4x3x2.5 cm with a 6 cm long spermatic cord; there was a yellowish, well-defined nodule measuring 3.5x1.5 cm, surrounded by normal parenchyma. This nodule had morphologic and immunohistochemical characteristics of a Leydig cell tumor, even found in the spermatic cord; those cells showed positivity to inibine, MART-1 and vimentine (Figg. 2-4).

Discussion

The CAH is a congenital autosomal recessive disease, characterized by 21-hydroxylase deficiency, that leads to an inefficient cortisol and/or aldosterone production or function with over activity of the adrenal steroid-producing. Such deficient production of glucocorticoids and/or mineral corticoids results in rising levels of adrenocorticotropic hormone (ACTH) which causes hyperplasia of the adrenal glands. In 1940, Wilkins et al. 4 described in a male patient the association of the CAH with a bilateral Leydig cell tumor. This cancer can be unilateral and histology is characterized by steroid secreting cells, above all testos-
terone but also estrogens or derivatives. In these patients immunohistochemical assay shows receptors of estrogens and progesterone in Leydig cells that are physiologically lacking of them. Leydig cell tumor is considered to be originated from the aberrant adrenal tissue descended with the testis along its artery. Therefore Gotob et al. suggested a careful adrenal gland evaluation in presence of a Leydig cell tumor. It represents 1-3% of testicular tumors and only 3-10% are bilateral. There is no association with cryptorchidism and sometimes it was reported in patients with Klenechtler syndrome. Moreover this cancer is also related to high levels of ACTH, because the immunohistochemical assay demonstrates that tumor cells produce ACTH and angiotensin II receptors. Therefore it was hypothesized that angiotensin II and ACTH can assume an important role as Leydig tumor growth factors.

Leydig cell tumor can occur at any age, even if the higher incidence is from 20 to 60 years of age and 25% of cases were reported in prepubertal age. Leydig cell tumor is always benign before puberty, but in adults it may be malignant in 10-20% of cases (tumor size exceeding 5 cm in diameter) with an average survival time of 2-3 years after surgery. Tumor metastases are rare and predictive factors that emphasize the invasive behaviour are presented by the presence of atypical cells, necrosis, lymphatic invasion, numerous and atypical mitoses, extra testicular invasion. The tumor is often asymptomatic and detected incidentally during US of testis. In prepubertal age, symptoms include precocious puberty with short stature, extra testicular invasion. While in adulthood, testicular swelling, gynaecomastia, female hair distribution, sexual disorders with infertility, azoospermia and decreased libido may be observed. Hormonal assay is modified in 20% of tumors, with increased estradiol and testosterone serum levels, leading to signs of masculinisation and acquisition of female sexual characteristics, in adults and in children respectively. Endocrine changes usually come before the finding of palpable testis swelling. So these changes can also be a helpful marker of tumor recurrence in the follow-up. Usual treatment is orchidectomy followed by chemotherapy and radiotherapy for malignant tumors, although a chemo- and radio-resistance have been reported.

Conclusions

Our case was a typical association between the CAH and a unilateral Leydig cell tumor. It was characterized by the particularity that in this young patient a testicle had been previously removed for its torsion. So the orchidectomy for Leydig cell tumor was a surgical castration with consequent serious psychological effects.


