Adrenal Inclusion in Testicular about Two Cases

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Abstract The adrenal enzyme deficiency leads pseudopuberty in later diagnosis or in the absence of treatment. The existence of testicular enlargement in boys can be related to adrenal inclusion. We report two observations about this pathology: A boy of 10 years old with 11β hydroxylase and another patients of 6 years old with 21 hydroxylase deficiency. The reason of consultation was the development of the penis and pubic hair with a testicular enlargement. Hormonal balance was in favor of early pseudo puberty. Testicular ultrasonography objectified increased volume and testicular hypoechoic nodules. Tumor markers (βHCG, ACE) were negative. Replacement and suppressive therapy by glucocorticoids is undertaken. The evolution was marked by regression of secondary sexual characteristics, reduced testicular size, increased its echogenecity and loss of nodules. During a reevaluation ten years later, a large heterogeneous testicular nodule is found in one patient. Tumor markers were elevated. Orchidopexy is decided. Histological study was in favor of bilateral Leydig tumor. The intratesticular adrenal inclusion is rare. It is the result of a cortical defect with a delay in diagnosis. Reduction of testicular volume after glucocorticoid therapy is a good predictor of disease control. However, a long term of follow up is necessary because a possibility of tumor degeneration.

Keywords Congenital adrenal hyperplasia, Adrenal inclusion Intratesticular, Ultrasound, Tumor leydig, Glucocorticoids

1 Introduction

The adrenal enzyme deficiency is a rare monogenic disorder caused by an abnormality in the biosynthesis of adrenal hormones. It is a complex disease that includes several clinical, biological and genetic forms. In most cases, there is a deficit in 21 hydroxylase deficiency rarely covers the 11β hydroxylase. When the diagnosis and suppressive treatments are not early, they cause virilization in girls and a pseudo precocious puberty in both sexes. The concomitant existence of testicular enlargement in boys should suggest adrenal inclusion.

2 Observations

Case 1: BS 06 years; was hospitalized in 2000 for a suspected precocious puberty. The clinical exploration tests found the development of secondary sexual characteristics, bilateral testicular enlargement (Figure 1), stature advance (Size: Either 3 DS/M+2.5 SD/CT) also a bone advance (AO: 13 years). Hormonal balance found a pseudo puberty secondary to congenital adrenal hyperplasia 21-hydroxylase (Table 1). Testicular ultrasound revealed hypoechoic, confluent and bilateral masses (Figure 2). The abdominal CT scan found adrenal hyperplasia (Figure 3).

Case 2: MK 10 years old; was brought into consultation for suspected precocious puberty. The clinical examination revealed the development of secondary sexual characters with an inhomogeneous testicular enlargement, skin pigmentation, hypertension, stature advance (Size:+2 DS/M+3 SD/CT) and bone advance (AO: 15). The biological assessment
was in favor for a congenital hyperplasia 11β hydroxylase complicated by pseudopuberty (Table 1). Testicular ultrasound showed hypoechoic circumscribed lesions and abdominal CT found bilateral adrenal hyperplasia.

The tumor markers (β HCG, ACE and α fetoprotein) were negative in both patients (Table 1). Replacement therapy and suppressive glucocorticoids is initiated which allowed the regression of secondary sexual characteristics, stabilization of bone maturation, normalization of hormonal balance and testicular volume, with a normalization of its echogenicity.

However, radiological control revealed a large and heterogeneous nodularisation in the patient BS 10 years after diagnosis. The other patient was stabilized.

Orchiectomy was performed in the patient. Histological study was in favor of bilateral Leydig tumor (Figure 4). The staging did not revealed any secondary locations. Close monitoring is recommended.

3 Discussion
Intratesticular adrenal inclusions have an origin from ectopic adrenal cortical tissue in testicles stimulated

Table 1 Hormonal results

| Parametre                          | Patient1 | Patient2 |
|-----------------------------------|----------|----------|
| Cortisol nmol/L (N: 138-690)      |          |          |
| Before Synactene immediat         |          |          |
| After                             | 26,29    | 20,10    |
|                                  | 30       | 26       |
| ACTH PlasmatiquePg/mL (N: 0-100)  | >2000    | >2000    |
| 17 OH Plasmatique nmol/L (N: 1,5-7)|          |          |
| Before Synactene immediat         | 17,06    | 135      |
| After                             | 28       | >1000    |
| FSH mU/mL (N: 1-9)                | 0,29     | 0,12     |
| LH mU/Ml (N: 1-5)                 | 0,24     | 0,15     |
| Testosterone nmol/L (N: 8, 20~34, 6)| 16,99   | 24       |
| Test au LH RH                     |          |          |
| FSH                               | 0,20; 0,50| 0,20;0,90|
| LH                                | 0,24;0,87|          |
| βHCGUI/L (N: 0, 00-4)             | 1,74     | 1,2      |
| ACE ng/mL (<10)                   | 1,59     | 1,2      |
| AFPng/mL (<09)                    | 1,09     | 1,1      |

Figure 2 Sonographic features of adrenal inclusions intratesticular: Multifocal, large, heterogeneous and generally hypoechoic mass, lesions without calcifications

Figure 3 Color Doppler intratesticular adrenal inclusions have a regular vascular architecture
by ACTH excess. All pathologies causing a rise in ACTH levels may be associated with adrenal inclusions. The congenital adrenal hyperplasia (by 21-hydroxylase deficiency in 90% of cases) is by far the most common (Bricaire et al., 1970). The prevalence of adrenal intratesticular inclusions in these cases is between 27% and 94% of patients (Barka and Anderson, 1962; Bricaire et al., 1970; Luton, 1966; White et al., 1987).

They are found at the revelation of an increase testicular volume as was the case in our two patients or after a systematic testicular ultrasound performed in a patient with congenital adrenal hyperplasia. It can also be found later in adulthood during the exploration of infertility. Usually asymptomatic, they can generate a gravity scrotal or harmful pain. Typically bilateral (83%), their development is progressive, especially in untreated patients. Sometimes adrenal inclusions are firm at the touch palpation and raise the problem of differential diagnosis of malignancy (Avila et al., 1999; Rutgers et al., 1988).

In the Ultrasound, adrenal inclusions. They delimit hyperechoic areas within hypoechoic masses globally. They are multifocal, confluent, and bilateral and are close to the testicular hilum (Avila et al., 1999; Rutgers et al., 1988; Proto et al., 2001).

In color Doppler, they have a regular vascular architecture, often normovascular. Sometimes they are hypervascular, but without chaotic vascularisation, or deviation or mismatch at the arteries gauge through the lesions (Rutgers et al., 1988; Proto et al., 2001; Stikkelbroeck et al., 2003).

In magnetic resonance imaging, the inclusions are isointense to intratesticular parenchyma on T1 isointense or slightly hypo intense weighted T2. They are enhanced with gadolinium. It has not been found superiority of MRI over ultrasound for the differential diagnosis between adrenal inclusion and malignant tumors. The unique advantage is a better view of the limits of the tumor, which can sometimes be useful if orchiectomy is considered (Stikkelbroeck et al., 2003; Berg et al., 1996; Proto et al., 2001; Vanzulli et al., 1992).

Histological determination of these nodular masses cannot settle between a Leydig cell origin and adrenal one. Ultra structural study highlights define one cell type of intermediate degree of differentiation (Keely et al., 1993).

In fact, the clinical and hormonal congenital adrenal hyperplasia, bilateral hypoechoic testicular masses and regression after glucocorticoid treatment can easily ask the diagnosis. Indeed, the evolution is characterized by a decrease or stabilization in glucocorticoid correct treatment. However, despite prolonged administration, some adrenal inclusions are not altered but see their volume increased (Luton, 1966; Rutgers et al., 1988).

Complications related to intratesticular adrenal inclusion are represented essentially by subfertility constantly found in adulthood. It is the consequence of the mass of tumor nodules and toxic effects of adrenal steroids, also to an hypogonadotropic hypogonadism (Cabrera et al., 2001; Stikkelbroeck et al., 2001).

Sperm changes observed over time and consequent subfertility must consider precociously cryopreservation of gametes. Of this fact, the discovery of adrenal inclusions requires close and regular monitoring because of its association with cancer. The risk of degeneration is more frequent than in the general population (Burke et al., 1973; Srikanth et al., 1992). Cases of scrotal primary malignant tumors (adrenocortical) developed from adrenal tissue have been reported in men no carriers of congenital adrenal hyperplasia. Other primary malignant testicular tumors can be developed from adrenal tissue or at the periphery of adrenal inclusions.

It is mostly malignant Leydig cells and seminoma. A myélolipomes have also been described in the adrenal
intratesticular inclusions in patients with congenital adrenal hyperplasia (Morimoto et al., 1971; Crouch, 1958; Davis et al., 1995; Adesokan et al., 1997; Boudreaux et al., 1979; Murakami et al., 1992).

The increase in intratesticular masses despite suppressive treatment leads to eliminate neoplastic origin. Biopsy or spermatogenic samples are not reliable. The MRI provides more evidence that hardly ultrasound and even when orchiectomy is considered, the diagnosis of malignancy is difficult in the absence of secondary locations. Histological and immunohistochemical criteria above must be sought. It should be noted that the diagnosis is posed to the presence of secondary locations.

4 Conclusion
The intra testicular adrenal inclusion is a rare disease that must be known. It must be sought in any patient with adrenal hyperplasia. Its detection and management is important because it can be a source of infertility and malignancy. We retain their hypoechoic, bilateral, symmetrical character and centered on the hilum.

Treatment should be adapted and freezing procedures of gametes must be proposed. A regular monitoring must be adopted in these patients.

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