

Testicular Adrenal Rest Tumours in Males with Congenital Adrenal Hyperplasia: Clinical And Progressive Characteristics

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I. Introduction

Testicular adrenal rest tumours (TART) are benign tumors made of ectopic adrenal cortex tissue. They are frequently found in males with congenital adrenal hyperplasia (CAH) with a reported prevalence of up to 94% (1). In fact, all pathologies causing a rise ACTH levels may be associated with adrenal inclusions. They are found mainly in patients with congenital adrenal hyperplasia (CAH) of untreated or poorly treated. In adult patients with congenital adrenal hyperplasia (CAH) the presence of testicular adrenal rest is an important cause of gonadal dysfunction and infertility par apparition de troubles de la spermatogénèse (2). The objective of this study is to search the frequency of TART in CAH and clarify clinical and progressive characteristics

II. Materials and methods

It is a retrospective study of 40 patients with CAH in relation to a deficiency of 21 hydroxylase (n: 35) and 11 β hydroxylase (n: 5). All have undergone a clinical examination, an adrenocortical assessment (Dosage of 17OH Progesterone, ACTH) and an echo-Doppler testicular in search of TART. During the study, we assessed the age at diagnosis, the hormonal control and the characteristics of the TART: volume of testicle, presence of TART, their size, echogenicity and vascularity at diagnosis and during follow up

III. Results

Adrenal inclusions were found in 10 patients (25%). They were asymptomatic and bilateral in all cases. 30% of the tumours were detectable by palpation and 70% of the children with testicular tumours showed signs of gonadal dysfunction. Doppler ultrasound was suggestive in all patients (Table I). Mean diameter was 18 ± 1 mm (3- 40)

Table I: Results of Doppler ultrasound

Sign	Number(n:10) %
Hilar localization	10(100)
mitigating but not calcified appearance	10(100)
vascular architecture preserved	10(100)

Patients with TART were all diagnosed late at an average age of 8.6 ± 0.2 years (4-16). They were controlled very poorly. The mean ACTH was 65 ± 0.5 (16-89), the average 17 OH P was 26 ± 1.4 ng / ml (10-30) Treatment with glucocorticoides was taken irregularly in 68%. 40% were under dosage (Hydrocortisone average 12.5mg / m² body surface area.) After an enhanced education, emphasizing the necessity of continuous treatment and therapeutic readjustment, Partial regression was noted in 95% of cases. In two cases the adrenal inclusion continued to grow requiring orchidectomy. Histological study was in favor of a Leydig cell tumors. Aucun autre cas de dégénérescence n'a été observé

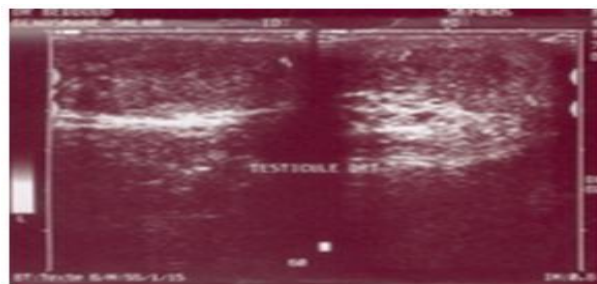


Fig 1: Sonographic features of adrenal inclusions intratesticular: Multifocal, large, heterogeneous and generally hypoechoic mass, lesions without calcifications



Fig2: The intra testicular adrenal inclusions are responsible for an increase in the size of the testicles in boys with congenital adrenal hyperplasia

IV. Discussion

The aetiology and pathogenesis of TART in CAH patients are not completely understood. Several studies documented the production of adrenal-specific steroids or the presence of adrenal-specific enzymes in these tumours (. Therefore, TART are thought to arise from aberrant adrenal cells in the testes. In the embryological period, cells destined to become adrenal or gonadal cells derive from neighbouring areas of the coelomic epithelium and are morphologically identical (3)(4). During further development, a limited number of ‘adrenal’ cells may migrate together with the descending testis (5)(6). Aberrant adrenal tissue within the testes is reported with an incidence of 7.5–15% (autopsy and surgical findings) in healthy neonates and normally regresses in early infancy (3)(5). Our data suggest that the incidence of aberrant adrenal tissue in the testes is probably underestimated, because under unstimulated conditions aberrant adrenal tissue is difficult to detect. In CAH patients, aberrant adrenal tissue may grow due to chronically elevated levels of adrenocorticotrophin (ACTH) or other unknown growth promoting factors, and may explain the increase in tumour detection by ultrasound during childhood. Tumors more common in patients with congenital adrenal hyperplasia who are noncompliant with treatment (8) Biologically, the lesions represent hyperplasia of aberrant rests rather than a true neoplastic tumor however, persistence of tumors despite ACTH suppression indicates role played by other factors TART also reported in patients with adequately controlled hormone levels(4) . Angiotensin II may have role in growth of them (9) TART have not been reported in late-onset CAH without clearly elevated ACTH or Angiotensin II levels(10)

Most of the TART were detected in children above 10 years old. It can be suggested that hormones whose levels are increased in puberty, such as LH, are additional stimulators of tumour growth. The presence of LH receptors in testicular tumour tissue supports this hypothesis (11) . Effects of TART are most important . there is a mechanical effects: size and duration dependent blockage of rete testis with resulting atrophy of seminiferous tubules , a Paracrine effects: steroids produced by tumor cells may be toxic to Leydig cells or germ cells (12)

The irreversible end-stage of longstanding TART is tubular hyalinization with obstruction of the lumen and complete loss of germ cells and Sertoli cells; differs from ischemic hyalinization by relative preservation of Interstitial Leydig cells (12) It is known that TART have no malignant features. Therefore, there seems to be no need to treat or remove the tumours at an early stage. However, because of the localisation of the tumours in the rete testis, the tumours may compress the seminiferous tubules leading to obstructive azoospermia and irreversible damage of the testes (2, 13). Therefore, it is important to detect and treat the tumours before permanent damage of the testis has occurred. Because the growth promoting factors are still unclear, strategies to prevent tumour growth are difficult to define. It has to be investigated whether testis-sparing surgery at an early stage may prevent irreversible testicular damage in later life (13).

Diagnosis is suspected on clinical features and ultrasound examination of scrotum and confirmed with a biopsy or surgical excision. Tumors are uniformly hypoechoic with well defined margins .multifocally and bilaterality is common (~75%) (14). Early tumors are responsive to glucocorticoid therapy, which suppresses ACTH levels .Surgery is reserved for tumors non-responsive to glucocorticoid therapy, or if differential diagnosis with other tumors exists .Testicular sparing surgery is preferred to preserve fertility, as tumor is

benign(15)(16) Histologically, TARTs are characterized by the presence of hypertrophied adrenal cells, grouped in islets, within the normal testicular parenchyma. Differential diagnosis arises with Leydig cell tumors. If it is indeed an adrenal inclusion, the histological analysis shows the presence of seminiferous tubules and the absence of Reink crystalloids. Risk of cancerization is very low, however, cases of malignant tumors (Leydig cell tumors and seminoma) and benign (myelolipomas) associated with ISIT have been reported in patients with HCS (17) (18) (19).

V. Conclusion

Tart are common in CAH (between 27% and 94%). Related to chronic stimulation by ACTH, they often reflect an insufficient suppressive treatment with glucocorticoid. The Doppler allows the characterization. They must be systematically sought and monitored They usually regress or stabilize with replacement glucocorticoid treatment. Sometimes they can grow, while raising the problem of the histological nature and risk of subfertility related to the mass effect of the TART and toxic effects of adrenal steroids and hypogonadotropic hypogonadism

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