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CASE REPORT

Testicular adrenal rest tissue in a patient with classical congenital adrenal hyperplasia: color Doppler findings

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Abstract Congenital adrenal hyperplasia (also known as congenital adrenogenital syndromes) refers to a group of autosomal recessive diseases characterized by altered cortisol production, which may be associated with aldosterone deficiency. The absence of cortisol synthesis stimulates corticotropin production by the adrenal cells and the accumulation of cortisol precursors, which will be diverted for the production of sex hormones. In affected males, ectopic adrenal tissue frequently develops, usually at the testicular level. This tissue is absolutely identical to that of the adrenal gland itself, and its functionality can be stimulated by ACTH and suppressed with glucocorticoid therapy. The authors report the case of a male patient with classic congenital adrenal hyperplasia, who was referred to our staff for evaluation of bilateral testicular tenderness and enlargement. Color Doppler sonography revealed mild enlargement of both gonads, widespread disruption of the testicular echostructure, and hypervascularization. Two months later, when the underlying disease had been controlled, repeat color Doppler ultrasonography revealed markedly decreased vascularity, although no change was noted on the B-mode examination. The color Doppler findings thus represent an early indicator of response to treatment.

Keywords Adrenal hyperplasia · Ultrasonography · Color Doppler

Riassunto Le sindromi adrenogenitali congenite sono un gruppo di malattie autosomiche recessive caratterizzate da un'alterata produzione del cortisolo, a cui si può aggiungere un'insufficiente produzione di aldosterone. Il blocco della sintesi del cortisolo porta a stimolazione della corticotropina sulle cellule surrenaliche, con accumulo di precursori del cortisolo, che sono deviati alla biosintesi degli ormoni sessuali. Nei maschi affetti è relativamente frequente lo sviluppo di tessuto surrenalico ectopico, il più delle volte a livello testicolare, tessuto del tutto identico a quello del surrene e la cui funzionalità può essere stimolata dall'ACTH o soppressa dalla terapia con glicocorticoidi. Presentiamo il caso di un paziente affetto da sindrome adrenogenitale congenita che, in seguito a dolenzia e modico aumento di volume dei testicoli, si sottoponeva a ecografia, che evidenziava testicoli modicamente aumentati di volume, con ecostruttura in gran parte sovvertita, ipervascolarizzati. Ben controllata la malattia di base, a distanza di due mesi, veniva effettuato un esame eco color Doppler dei testicoli che non rilevava variazione dell'aspetto in B-mode, mentre la vascolarizzazione era marcatamente diminuita rispetto al controllo precedente. Abbiamo pertanto ritenuto opportuno segnalare quest'aspetto per sottolineare che, come accade per altre terapie, la diminuzione dell'ipervascolarizzazione è precoce rispetto alle variazioni che si osservano con l'esame in B-mode.

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Introduction

Congenital adrenal hyperplasia refers to a group of autosomal recessive diseases (also known as congenital adrenogenital syndromes) characterized by deficient cortisol production, which is caused by the absence of one of the five

enzymes involved in its synthesis. The most common form is caused by mutation in the *CYP21A2* gene, which encodes an adrenal steroid enzyme called 21-hydroxylase (P450c21). This enzyme converts 17-hydroxyprogesterone (17-OHP) into 11-deoxycortisol and progesterone, the respective precursors of cortisol and aldosterone [1].

The absence of cortisol synthesis stimulates the production of corticotropin by the adrenal cells and the accumulation of cortisol precursors, which will be diverted for the production of sex hormones. It may also be associated with insufficient production of aldosterone. The incidence of this association varies from 1:10,000 to 1:20,000 with high figures in certain ethnic groups living in relatively remote areas of the world (e.g., the Yupik people of Alaska) [1].

The clinical manifestations vary: some patients are asymptomatic, but the syndrome can lead to forms of virilization in females and precocious puberty in both sexes. The aldosterone deficiency can cause concomitant fluid and electrolytic imbalances with hypovolemia and shock.

Ectopic adrenal tissue frequently develops in affected males, usually at the testicular level [2–4] and involvement of both gonads is common (testicular adrenal rest tissue). Indeed, both the gonads and the adrenal glands originate from the mesoderm of the urogenital tract. The ectopic tissue may also be present in other parts of the body, such as the celiac plexus, the broad ligament, and the ovaries. It is absolutely identical to that of the adrenal gland itself, and its functionality can be stimulated by ACTH or inhibited by glucocorticoid therapy.

Many authors have documented the sonographic appearance [1, 2, 5] of ectopic adrenal tissue in the testes, but, to the best of our knowledge, there have been no descriptions of the color Doppler features of this tissue, particularly during the post-treatment follow-up of these lesions.

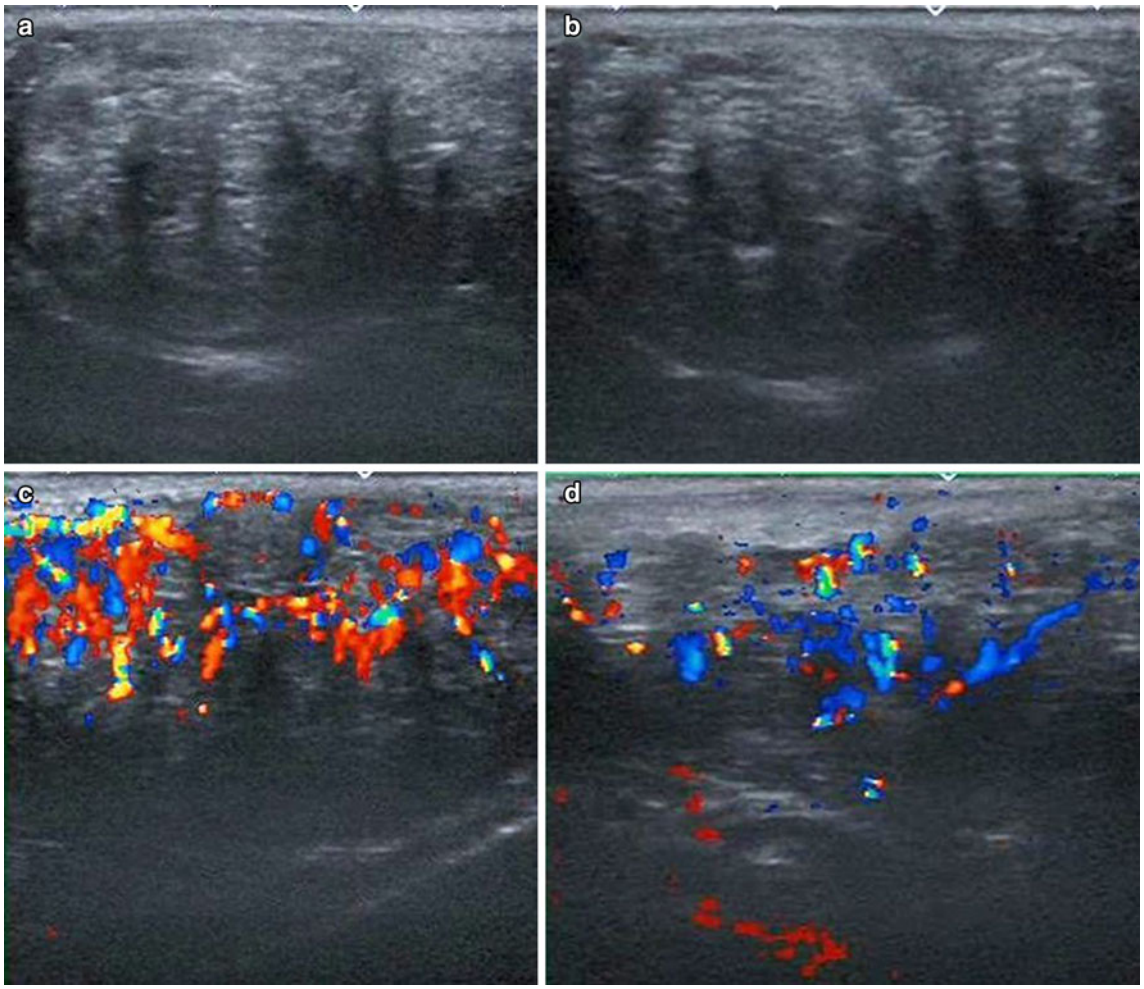

Fig. 1 Testicular sonography in a patient with decompensated androgenital syndrome. The testes are mildly enlarged with widespread alterations of their echostructure (**a**, **b**), which is predominantly hypoechoic with calcifications. The color Doppler examination reveals intense hypervascularization (**c**, **d**)

Case report

The patient was a 41-year-old male with congenital adrenal hyperplasia associated with salt wasting. He was being treated with dexamethasone and fludrocortisone, but took the drugs irregularly, arbitrarily suspending treatment during bouts of intercurrent diseases or failing to make the prescribed adjustments. He was referred to our staff for sonographic workup of tenderness and mild enlargement of the testes. The examination revealed slight enlargement and widespread alterations of the echostructure of both testes (Fig. 1a, b), which were predominantly hypoechoic with calcifications. The color Doppler examination revealed marked hypervascularization (Fig. 1c, d).

The sonographic appearance, the absence of tumor markers, and the elevated levels of ACTH were suggestive of ectopic adrenal tissue (testicular adrenal rest tumors), and appropriate therapy was started to control the underlying disease. Two months later, the underlying disease was under control and the patient was asymptomatic. Color Doppler ultrasonography was repeated. The B-mode examination revealed no change in the appearance of the testes (Fig. 2a, b). The vascularity was still increased, but markedly less so than it had been on the previous study (Fig. 2c, d). The color Doppler examination thus documented the correspondence between reduction of ACTH levels and diminished vascularization of the ectopic adrenal tissue.

Discussion and conclusions

Ectopic adrenal tissue is present in approximately 30 % of patients with classical congenital adrenal hyperplasia. It is identical to the tissue of the adrenal gland and its functionality can be stimulated by ACTH or suppressed by glucocorticoid therapy [1, 2]. Pseudotumoral ectopic tissue of this type in the testes is difficult to detect on clinical examination, but it can be readily identified with ultrasonography. It typically appears as an inhomogeneous, hypoechoic infiltration, which often contains calcifications, although these characteristic aspects are not pathognomonic of testicular adrenal rest tissue [5]. The bilateral nature of the lesions, however, together with the clinical findings and blood chemistry data, allows one to differentiate these lesions from other testicular masses (including tumors) [6].

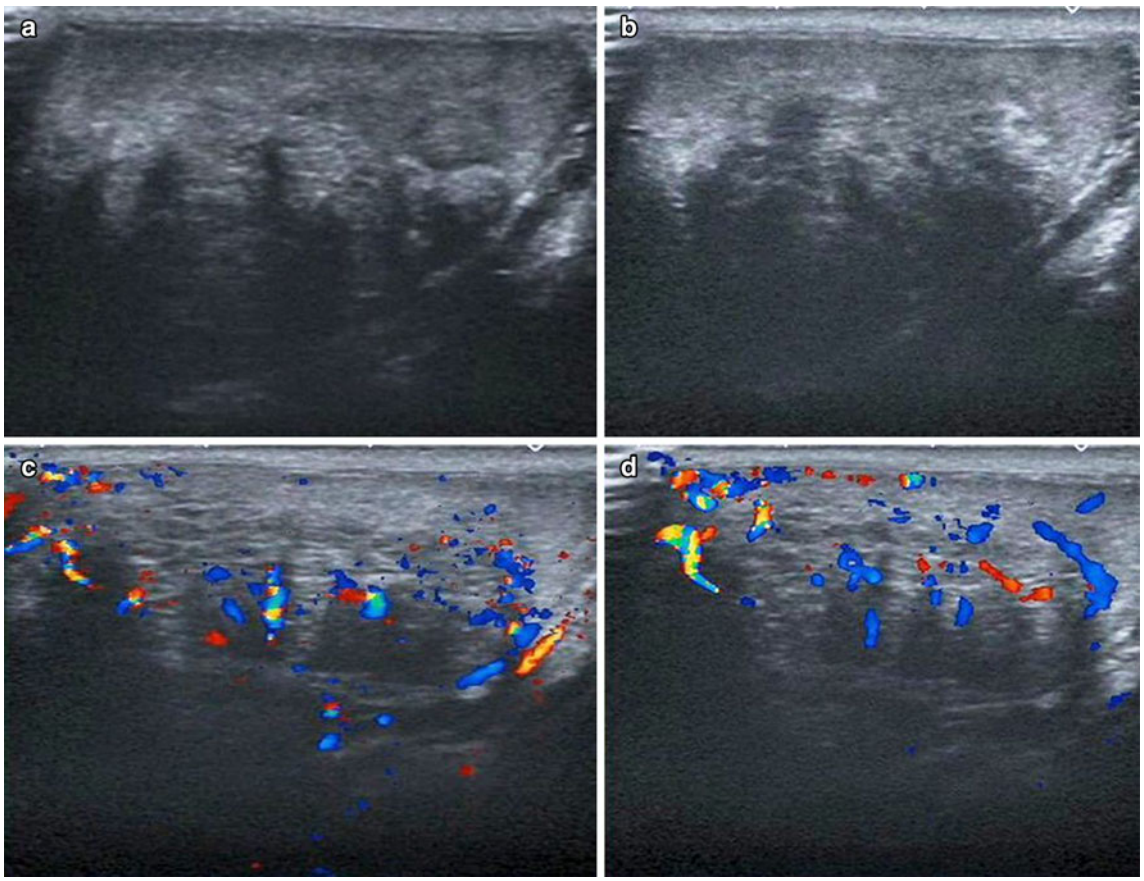

Fig. 2 Testicular sonography in the same patient shown in Fig. 1. After 2 months of appropriate therapy, repeat sonography reveals no changes in the B-mode examination (**a**, **b**). The hypervascularity is still evident, but much less intense than it was on the previous examination (**c**, **d**)

The follow-up is also based on clinical assessment, blood tests, and ultrasonography. Changes in the ultrasound appearance of the lesions are usually appreciable after approximately 6 months of therapy [1]. As observed with other types of treatment (e.g., chemotherapy of primary breast cancers), we noted that decreases in the hypervascularity of the tissue can be appreciated before changes are observed in the B-mode examination, and these decreases should be mentioned as an indicator of positive response to treatment.

Conflict of interest None.

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