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CASE REPORT

TESTICULAR REGRESSION SYNDROME AND EXTREMELY ELEVATED ANTI-THYROID ANTIBODIES ON A PATIENT WITH LARGE UNILATERAL POLYCYSTIC RENAL MASS

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Summary

Vanishing testes syndrome (or bilateral anorchia), as part of 46, XY differences of sex development, may be early detected during life or partial gonadal dysgenesis are discovered during adult years with mild forms of hypogonadism. Testicular regression may have a genetic background, as mutations of steroidogenic factor 1 (SF 1), but it may be potentially related to other syndromes and anomalies as mental retard, renal anomalies, etc. We aim to introduce a complex male case with a long medical history, including late diagnosis of vanishing testes syndrome. This case introduces the challenges of distinguishing between testicular regression syndrome and ectopic testes on an adult male with mild form of hypogonadism. Particularly, the vanishing testes syndrome was associated with a compressive form of chronic thyroiditis of fibrous type, with aggressive elevation of anti-thyroid antibodies including after thyroidectomy, a large apparently benign unilateral multi-cystic mass at kidney level.

List of abbreviations: ATG = Anti-thyroglobulin antibodies, cm = centimetre, CT = computed tomography, TPO = Anti-thyreoperoxidase antibodies, TSH = Thyroid Stimulating Hormone

Key words: testicular regression, chronic thyroiditis, renal cyst

Résumé

Syndrome de régression testiculaire et anticorps anti-thyroïdiens extrêmement élevés chez un patient présentant une grande masse rénale polykystique unilatérale

Le syndrome de disparition des testicules (ou l'anorchidie bilatérale), dans le cadre de 46, les différences XY de développement sexuel, peut être détecté tôt au cours de la vie ou la dysgénèse gonadique partielle sont découverts pendant les années adultes aux formes légères d'hypogonadisme. La régression testiculaire peut avoir des antécédents génétiques comme des mutations du facteur stéroïdogène 1 (SF 1) mais elle peut être potentiellement liée à d'autres syndromes et anomalies comme un retard mental, des anomalies rénales, etc. Nous visons à introduire un cas masculin complexe avec une longue histoire médicale y compris le diagnostic tardif de la disparition du syndrome des testicules. Ce cas introduit les défis de distinguer entre le syndrome de la régression testiculaire et les testicules ectopiques chez un mâle adulte présentant une forme légère d'hypogonadisme. En particulier, le syndrome des testicules disparaissant était associé à une forme compressive de thyroïdite chronique de type fibreux avec élévation agressive d'anticorps anti-thyroïdiens incluant aussi après la thyroïdectomie une grande masse multi-kystique unilatérale apparemment bénigne au niveau du rein.

Mots-clé: régression testiculaire, thyroïdite chronique, kyste rénal

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Introduction

Vanishing testes syndrome (or bilateral anorchia), as part of 46, XY differences of sex development, may be early detected during life or partial gonadal dysgenesis are discovered during adult years, with mild forms of hypogonadism. (1,2,3) Testicular regression may have a genetic background, as mutations of steroidogenic factor 1 (SF 1), but it may be potentially related to other syndromes and anomalies as mental retard, renal anomalies, etc. (4,5,6)

We aim to introduce a complex male case with a long medical history, including late diagnosis of vanishing testes syndrome in association with severe chronic thyroiditis, and tumour-like polycystic kidney tumour.

Case presentation

The specific panel of thyroid and gonad axes are displayed. The patient agreed to present his medical data by signing the informed consent. He was first evaluated at different medical centres from Transylvania, Romania then he was seen as an outpatient on a private centre from Bucharest, while the final diagnosis and recommendations were established at National Institute of Endocrinology "C.I. Parhon", from Bucharest, Romania.

He is a 40-year old non-smoking man admitted for an endocrine check-up. His medical history was irrelevant. The documents regarding his birth and childhood were not available. He was diagnosed with bilateral cryptorhydism since youth, but no particular investigations were done. He had no children.

The medical history included a history of chronic thyroiditis one year before, which associated a progressive enlargement of thyroid gland, with inhomogeneous pattern at ultrasound and local compressive symptoms, requiring total thyroidectomy. The pathological report confirmed Hashimoto's thyroiditis, fibrous variant. Post-operatory, the patient was treated with levothyroxine substitution therapy. The surgery was also complicated, with transitory hypoparathyroidism requiring vitamin D and calcium supplements and transient paresis of left recurrent nerve.

Recently, the patient allowed to be evaluated for his previous medical condition related to bilateral cryptorhydism. Ultrasound and urologic assessments did not identify the testes at the level of scrotum, thus the patient was referred to a tertiary centre of endocrinology to distinguish between vanishing testes syndrome and potential ectopic testes and their localisation. (7)

On current admission, the patient's physical exam revealed male phenotype, facial hair with slow grow rate, a body mass index of 20 kg/sqm (a height of 172 cm within the midparental height), the testes were not palpable at scrotum level, the penis length of 7 centimetre (cm). Axillaries and pubic hair had normal velocity growth and distribution.

Endocrine panel of investigation pointed a relative normal thyroid function under 150 μg of daily oral levothyroxine. (table 1) Yet, extremely elevated values of anti-thyroid specific antibodies were still positive. (table 1) The gonad ax was evaluated and hypergonadotropic hypogonadism was confirmed. (table 2) The karyotype was 46, XY. Anti-Mullerian Hormone (AMH) was not detectable. Bone evaluation showed normal results of Bone Mineral Density at Dual-Energy X-Ray Absorptiometry and Trabecular Bone Score. (fig. 1 a,b) A small decrease of vitamin D level was detected: a blood level of 25-hydroxyvitamin D of 22 ng/mL (normal values above the level of 30 ng/mL).

Ultrasound and computed tomography (CT) examinations were performed. Bilateral mammary ultrasound did not reveal gynecomastia. (fig. 2) Testicular ultrasound identified bilateral testes pointing a potential testicular small regression. (fig. 3) In situ testes remnants were confirmed at CT scan. (fig. 4) Moreover, abdominal ultrasound detected a large kidney mass with polycystic appearance and no other anomaly consistent with ectopic testes or tumour transformation. (fig. 5) CT scan also revealed the polycystic renal aspect. (fig. 6) No renal function anomaly was detected at routine biochemistry assays.

Since testicular regression was highly suggestive due to investigations and abdominal CT did not indicate any lesion that might suggest an ectopic testes, no further exploratory surgery was considered necessary. Testosterone therapy was offered to the patient (intramuscularly undecanoat 1000 mg/4 mL, every three months) in addition to vitamin D supplements and levothyroxine substitution. The patient was referred for urological follow-up and management of kidney mass.

Table 1 - Thyroid panel of investigations in a 40-year old male with thyroidectomy of fibrous variant of chronic thyroiditis and vanishing testes. The assays are done under daily oral 150 μg of levothyroxine

Parameter	Value	Normal	Unit
TSH	6.3	0.5-4.5	μUI/mL
FreeT4	6.6	10.3-24.4	pmol/L
ATG	3,000	30-70	UI/L
TPO	286	0-35	UI/mL

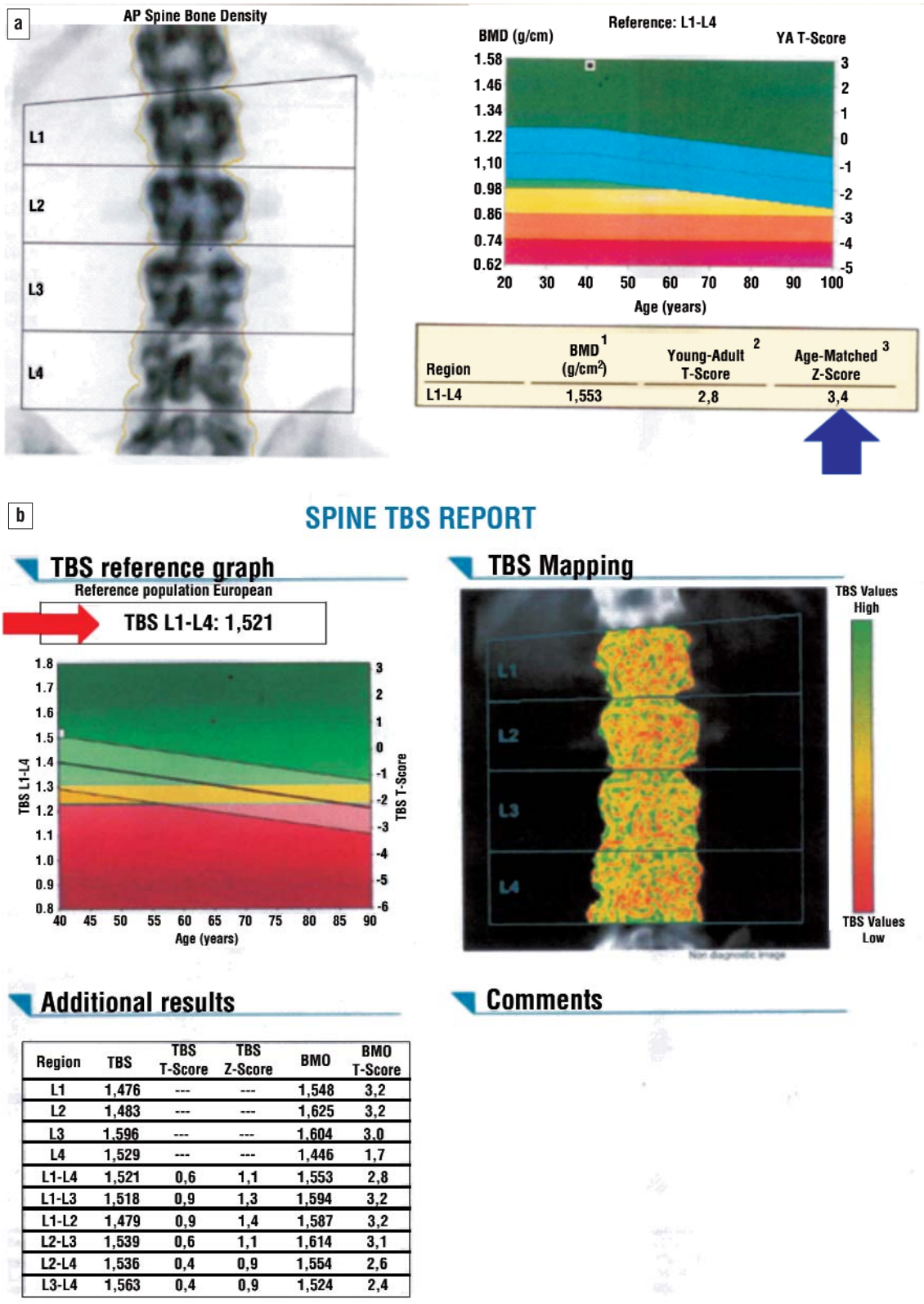
TSH=Thyroid Stimulating Hormone; ATG=Anti-thyroglobulin antibodies; TPO=Anti-thyreoperoxidase antibodies

Discussion

This is an atypical case of testicular regression: the

Table 2 - Gonad ax in a 40-year old male with late onset vanishing testes syndrome

Parameter	Value	Normal	Unit
Total plasma testostesterone	1.63	2.49-8.36	ng/mL
Prolactin	6.47	<21	ng/mL
FSH (Follicle Stimulant Hormone)	62	1.27-19.26	mUI/mL
LH (Luteinizing Hormone)	23	1.24-8.62	mUI/mL
SHBG (Sex Hormone Binding Globulin)	79	14.5-48.4	nmol/L
PSA (Prostatic-Sperific Antigen)	0.36	3-66	0-4



Region	TBS	TBS T-Score	TBS Z-Score	BMO	BMO T-Score
L1	1,476	---	---	1,548	3,2
L2	1,483	---	---	1,625	3,2
L3	1,596	---	---	1,604	3,0
L4	1,529	---	---	1,446	1,7
L1-L4	1,521	0,6	1,1	1,553	2,8
L1-L3	1,518	0,9	1,3	1,594	3,2
L1-L2	1,479	0,9	1,4	1,587	3,2
L2-L3	1,539	0,6	1,1	1,614	3,1
L2-L4	1,536	0,4	0,9	1,554	2,6
L3-L4	1,563	0,4	0,9	1,524	2,4

Figure 1 - Bone assessment on a 40-year old male with hypergonadotropic hypogonadism (a) shows Dual-Energy X-Ray Absorptiometry report with bone mineral density according to sex and age based on Z-score (arrow). (b) displays the Trabecular Bone Score (TBS) result which is normal (arrow)

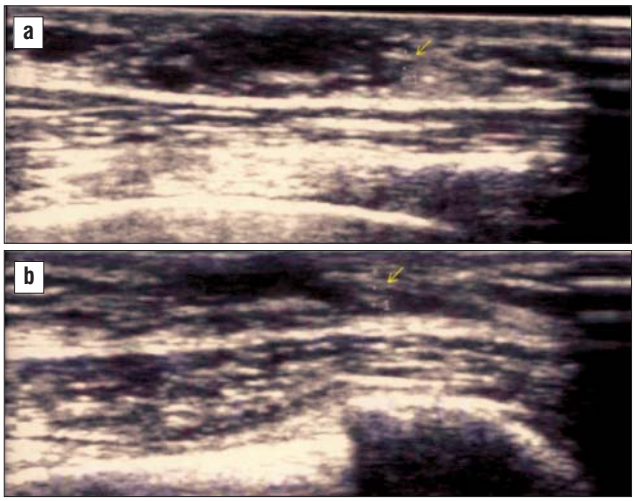


Figure 2 - Bilateral breast ultrasound showing lack of gynecomastia in a adult hypogonadic male: breast tissue of 0.3 cm on the right, of 0.2 cm on the left side (arrow)

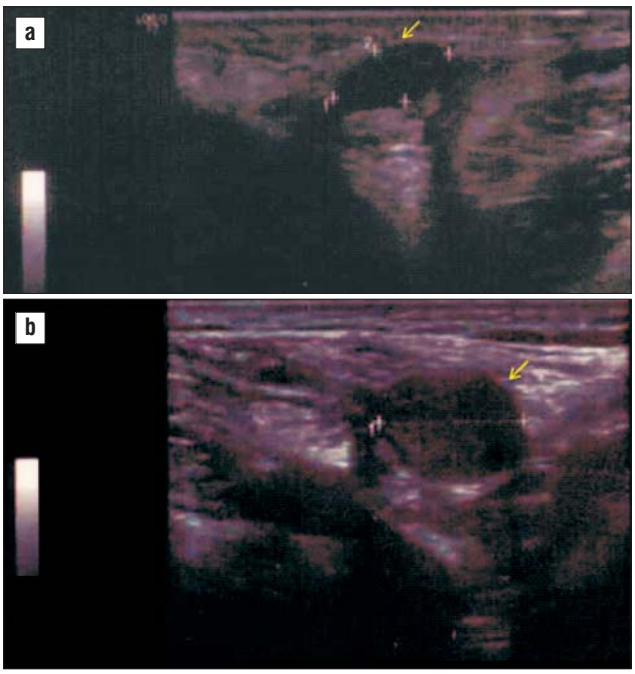


Figure 3 - Testicular ultrasound showing bilateral remnants at the level of scrotum, suggestive for testicular regression syndrome: right testicle of 1 cm, respectively left testicle of 1.24 cm (arrow)

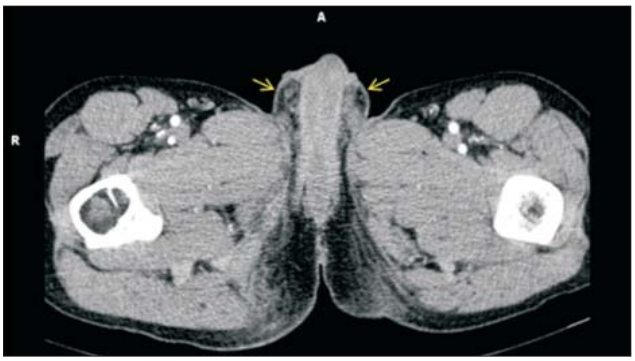


Figure 4 - Computed tomography (transversal plane) aspects showing a right scrotal mass of 0.7/1.7 cm (right testicle) and a left scrotal mass of 2.03/1.07 cm (left testicle) – arrow

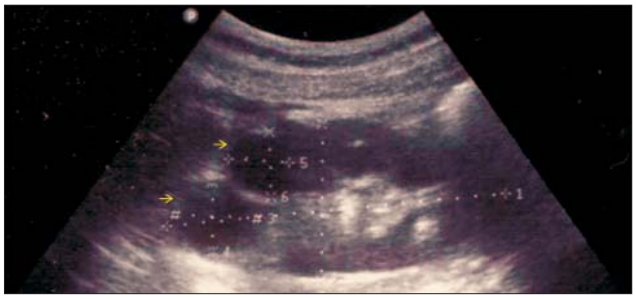


Figure 5 - Abdominal ultrasound showing a multiple cystely at left renal area of 2.4/2 cm, respectively of 1.8/1.9 cm, respective of 2.3/2.2 cm (arrow)

testes were underdeveloped since the diagnosis of bilateral cryptorchidism was done during the teenager years. Most probably, due to current testicular ultrasound and CT aspects, they were present into the scrotum, with reduced dimensions. The external genitalia and lack of typical complications of long-term hypogonadism as osteoporosis, cardio-metabolic complications (except for a level of total cholesterol of 237 mg/dL, with normal levels less than 200 mg/dL) indicate a small resource of testosterone which seemed enough over the years. (8) The current challenge of the case was to distinguish between vanishing testes syndrome and undescended testes to avoid the malignancy risk of non-scrotal testicular remnants, but the clarity of current assessments made unnecessary a surgical exploratory procedure. (9,10)

A particular aspect of the case is the co-presence of a

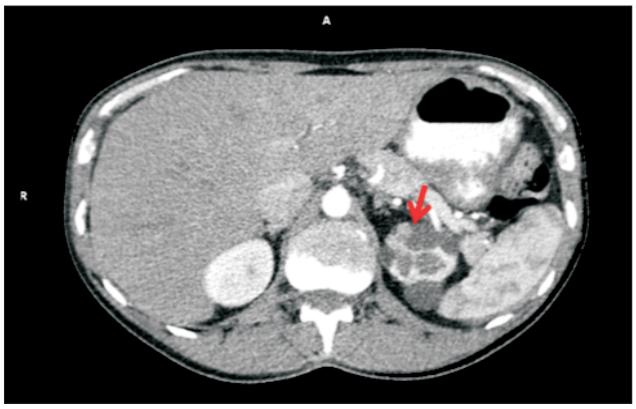


Figure 6 - Transversal plane of computed tomography in a 40-year old male diagnosed with vanishing testes syndrome: left kidney has multiple iodophile, dense cystic masses of 3/2.34 cm, of 1.9/2.8 cm, 0.8/1.1 cm, respectively of 0.7/0.6 cm (arrow)

rare thyroiditis type with compressive elements that finally required surgery. (11,12,13,14,15) Post-operative, underlying fibrous histological pattern was confirmed. (11,12,13,14,15) After surgery, the specific anti-thyroid antibodies remained extremely elevated. No other auto-immune condition was detected. The autoimmune mechanism is not related to testes regression so the two conditions seem incidental. (11,12,13,14,15)

The third observation is related to the presence of unilateral kidney cystic transformation (which seems independent of the classical polycystic renal condition due to advanced patient's age and unilateral lesion). (16,17,18,19,20) This might be related to testes anomalies due to common embryological origin and potential genetic background. (16,17,18,19,20) No surgery was considered necessary up to current evaluation, based on multidisciplinary opinion, since malignancy was not suspected by imaging and urologic examination and the renal function was not impaired. (16,17,18,19,20) However, close follow-up is needed.

Conclusion

This case introduces the challenges of distinguishing between testicular regression syndrome and ectopic testes in an adult male with mild form of hypogonadism. Particularly, the vanishing testes syndrome was associated with a compressive form of chronic thyroiditis of fibrous type, with aggressive elevation of anti-thyroid antibodies, also including after thyroidectomy, a large apparently benign unilateral multi-cystic mass at kidney level.

Conflict of interest

The authors have nothing to declare.

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