



Rete testis adenomatous hyperplasia

Our experience



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Rete testis adenomatous hyperplasia: our experience

The word "adenomatous hyperplasia of rete testis" (AHRT) was used by M. Nistal et Al. for the first time in an article about the cystic dysplasia of the testis (1976). AHRT is a benign lesion of the testis.

The patient who came to our attention was studied with a testicular echo color Doppler that identified a solid, well circumscribed and hypoechoic mass of 4.5 x 3.8mm as diameter, localized in the upper third of the right testicle and with a perilesional vascularization pattern. The preoperative study was based on an accurate medical history, on an ultrasound with contrast and on a RMI.

The treatment consisted in an echo guided excisional biopsy of the testicular lesion, considering this as the best approach for those testicular neoformation difficult to define, with a lot of benefits for the patients, especially for those monorchid.

KEY WORDS: Adenoma hyperplasia, Rete testis pseudotumor, Testicular sparing surgery, Testis benign tumor.

Introduction

The term "rete testis adenomatous hyperplasia" (AHRT) was firstly used by M. Nistal and M. Garcia Villanueva et al. (1976) in an article concerning the testis cystic dysplasia. They described an epithelial proliferation in the testicular mediastinum composed of several tubular structures of different sizes; they were described as separated by a scant stroma and extended peripherally into the testicular parenchyma¹. Recently, adenomatous hyperplasia was described microscopically as a complex

interconnecting proliferation of tubulopapillary channels that may be focal or diffuse, with or without cystic dilatation^{2,3}.

Sometimes their lumen may be empty, it may contain sperm or it may have an eosinophilic secretion. The lining cells can be cuboidal or low columnar with benign cytology.

The pathologic tubulus continuity with the normal rete testis indicates that they take origin from the rete itself. However, the accidental presentation and the usual association with other testicular pathologies indicate a non-neoplastic nature³.

Macroscopically, instead, AHRT appears as a solid or a cystic mass in less than half of the cases³.

Moreover, it was described as a real or an apparent rete testis adenomatous hyperplasia. Testicular atrophy is one of the most frequent pathologies associated with AHRT^{3,4}. In these cases, the appearance is more similar to a tumefaction rather than a 'true' hyperplasia, but this distinction gains no sense if we consider its poor clinical importance.

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During the last thirty-five years, several Authors have reported many clinical cases of AHRT, sometimes supposing possible genetics causes for their origin ⁴. However, even if pathogenetic mechanisms are unknown, recent studies agree that these abnormalities are related to a disrupted mesonephric duct development during the ontogenesis ⁵.

The observation, the diagnostic problems and the treatment of a patient affected by this pathology lead us to do some observation about the need of a specific diagnostic approach that is aimed to a sparing testicular surgery, considering the benign nature of AHRT.

Case report

A 38 years-old man was admitted with a left testicular hypotrophy to the Department of Surgical Sciences of Sapienza University/Polyclinic "Umberto I" of Rome. His clinical history was negative for cryptorchidism; the patient was affected by second-degree obesity (BMI 38.8) and hypertension (Systolic Pressure 150 mmHg).

A low value of testosterone (2.36 ng/mL) was found at the endocrinological exams and the physical examination showed a left testicular hypotrophy.

The patient underwent a testicular color Doppler ultrasonography. A well circumscribed, hypoechoic and solid mass was detected in the upper third of left testis. The diameter of the mass was 4.5 x 3.8 mm with a perileisional vascular pattern.

No focal lesions were found in the right dydimus, that was morphologically normal, too. Epididymis were both of normal size, in seat and presented an homogeneous echotexture. Signs of varicocele were absent.

A contrast-enhanced ultrasound was performed. The lesion presented a hyperenhancement compared with the surrounding tissues.

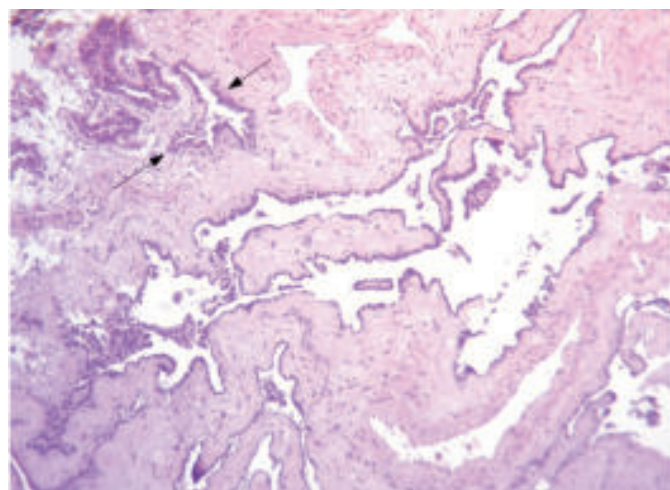


Fig. 1: Histological picture of the lesione with characteristic lumen similar to the rete testis, and adenomatous lumina (arrow). H&E, 100x.

The MRI confirmed the presence of a solid round mass of 4.32 x 3.17 mm diameter with regular margins, appearing hypointense in T2 weighted sequences and iso/hypointense in T1 sequences.

The seminal fluid examination revealed an astheno-oligoteratozoospermia (OATS).

The multiple serum markers dosage was: alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (beta-HCG), carcinoembryonic antigen (CEA), neuron-specific enolase (NSE) and placental alkaline phosphatase (PLAP), that were all normal.

Therefore, we performed an intraoperative US-guided biopsy of the testicular mass.

The extemporaneous histological analysis showed a cuboidal epithelium, with hyperchromic nucleus and few cytoplasm surrounded by a dense fibrotic stroma. No mitosis, atypical nucleus or necrosis were observed. As because these characteristics were compatible with AHRT, a conservative surgical approach was adopted.

The patient was discharged from the hospital the day after the procedure and then he underwent a six months follow-up. The definitive hystological examination confirmed the AHRT diagnosis, too.

Discussion

Rete Testis Adenomatous Hyperplasia (AHRT) is a nosological entity described by many Authors during the last thirty-five years, trying to find its possible etiology ⁴.

M. Nistal and R. Panigua, in 1988, supposed a pathogenic mechanism based on the influence of local factors; these factors may have an autocrine or paracrine actions and may be produced by the seminiferous tubules or by the epithelial cells of rete testis ⁶.

Observing one of their patient who underwent chemotherapy for a concomitant breast carcinoma, they finally suggested a probable implication of chemotherapy in the pathogenesis of AHRT ⁶, but it does not explain AHRT/its etiology, according to our point of view.

Considering the frequent association of AHRT with testis atrophy and hypospermatogenesis, in 1991-92 R.W. Hartwick and D.M. Butterwood described in two different articles the possible role of a hormonal embalance as its etiology ^{3,7}. AH. Lee and J.M. Theaker (1994) suggested atrophy, hypospermatogenesis, hormonal effects, cryptorchidism and tumour invasion as pathogenic hypotheses for AHRT, also supposing the pagetoid spread of malignant cells ⁸.

N.A. Hasan et al. (1995) agreed with AH. Lee and J.M. Theaker (1994) that pagetoid spread might have been a causal mechanism ⁹. H. Gruber et al. (1997) published the first case in the literature of a patient who developed a primary adenocarcinoma of the RT after having received an AHRT diagnosis ten years before ¹⁰.

M. Nistal and J.A. Jiménez-Heffernan (1997) ¹¹ classified RT dysgenesis in three different types:

- diffuse hypoplastic (37.5%);

- hypoplastic-cystic (50%).

- adenomatous pseudohyperplastic (12.5%).

The latter lesion corresponds morphologically to AHRT, as described by E.C. Jones et al. and S.K. Murray et al. (2000) who reported that the most common diseases associated with AHRT were:

- testicular atrophy;

- hypospermatogenesis;

- cryptorchidism;

- epididymal cribriform change (named “hyperplasia” by D.M. Butterworth and D.L.; – Bissettel in 1992 ⁷;

- bilateral kidney dysplasia;

- breast carcinoma;

- germ cell tumour with or without pagetoid spread or stromal invasion of the RT as the most.

Recent studies are confirming that these abnormalities are related to a disrupted mesonephric duct development.

However, aside from the pathogenic mechanisms, during these years, Authors agreed about the role of a hormonal imbalance (estrogenic stimulation, diethylstilbestrol, androgenic blockers, cryptorchidism) in the pathogenesis ²⁻⁵.

In 2003, Nistal M. et al. categorised AHRT in two different etiological types ⁴:

- Congenital AHRT associated with kidney and/or spermatid duct diseases (cryptorchidism);

- Acquired AHRT.

They considered a pathogenesis related to a possible hormonal imbalance role (estrogens and other hormonal products derived from a germ cell tumour) for the first group; whereas they considered a probable role of some drugs for the second group ⁴.

Among several studies regarding a possible pathogenesis of male infertility, in 2006, M. Lupien and A. Diévert et al. described an altered function of the Notch family proteins ⁶.

In particular, studying transgenic male mice expressing a constitutional mutation of the intracellular Notch ¹ domain, they discovered a particular phenotype characterized by hyperplasia and blockage of the efferent ducts, especially those placed in the interface between the rete testis and the efferent duct. At the end of the work, all the Tg mice presented the dilation of RT with the presence of spermatozoa and the absence of spermatozoa in highly hyperplastic epididymis and in the efferent ducts ¹³. Despite the RT histological alteration, a correct definition of genetic mechanisms of pathogenesis is very difficult: surely there are many causal factors and many different ways that are responsible of a similar lesion.

In fact, we have already described a possible cystic presentation for AHRT, very similar to those determined by the expression of a Notch domain mutation.

However, a similar ectasy of RT can also be caused by testicular malignancies, such as teratoma: this shows the importance of a correct diagnostic approach.

Today, high frequency ultrasonography (US) is considered the gold standard exam in order to evaluate the scrotal pathology ^{12,14}.

It is important to remember that only 18% of male patients shows a normal rete testis on high-frequency US imaging ¹⁴.

Unfortunately, AHRT has no significant US characteristics to discriminate this lesion from many others. In fact, we have already described a less common, even if possible, RT cystic transformation coexisting with AHRT ⁴. For this reason, as stated by M. Nistal et al. and E.C. Jones et al. ^{4,12} AHRT differential diagnosis should at least include three different conditions.

1) The first condition includes tumour-like lesions, such as RT ectasic/cystic transformations with epithelial metaplasia ⁴. Tubular ectasy, also known as cystic transformation of rete testis, is a dilatation of RT, as the result of a partial or a complete obliteration of the efferent ductules ^{14,16}.

It usually affects over 50-years-old men and it is generally bilateral and asymmetric; in this typical location in or around the mediastinum testis, often it is associated with ipsilateral spermatoceles. These characteristics makes very difficult to differentiate this benign lesion from malignant cystic tumours ^{14,16}.

In this group we want to include smooth muscle hyperplasia too. It is a non-neoplastic smooth muscle proliferation which occurs in a variety of circumstances in many organs, including skin, breast, oral cavity, trachea and lungs, vascular system, the gastrointestinal and the urological epithelium, including the spermatic cord or the rete testis, causing a cystic testicular clinical picture ¹⁷.

2) The second condition, instead, is characterized by benign lesions, like the cystic testicular dysplasia (CDT), often associated with renal and other genitourinary tract anomalies during childhood, even if the literature reported one case in a 63-years-old man ^{17,18}.

Having origin in the mediastinal area, CDT consists of multiple irregular small cystic spaces and affects either a part or the whole testis, resulting in an enlargement of the testis and in an atrophy of the residual parenchyma. Rarely, it appears as a solid mass. Sometimes, it can result in a spontaneous regression ¹⁷⁻²⁰.

Even if CDT and RT ectasy have similar histological and sonographical appearance, these disorders have different etiologies. In fact, CDT generally derives from a congenital defect, whereas RT ectasy could be determined from acquired obstructive processes ¹⁹.

3) The last nosological entities going on differential diagnosis with AHRT could be the adenoma or the papillary cystadenoma that are rare types of benign tumors with a restricted growth in the testicular mediastinum. Cases reported in literature are all unilateral ⁴. Adenomas and benign papillary tumours are circumscribed small-sized formations with solid appearance. Cystadenomas may involve the whole RT and they are generally larger than adenomas and benign papillary tumours ⁴. Another possible differential diagnosis is with the Leydig cell neoplasm ¹⁷.

The differential diagnosis with malignant pathologies is more important for the patient's prognosis.

The first differential diagnosis has to be performed against cystic malignant tumours, that are commonly teratomas. These can be distinguished with US thanks to the presence of multiple cystic areas, often surrounded by a soft tissue rind. They are frequently unilateral and they are not limited to the testicular mediastinum¹⁴⁻¹⁶. Other malignant conditions deserving to be considered are the RT adenocarcinoma and the metastatic prostate adenocarcinoma⁴. This last type of adenocarcinoma can be confirmed by measuring serum tumour markers¹⁴. Therefore, four conditions should be present to diagnose AHRT:

- 1) True epithelial proliferation causing the enlargement of the testicular mediastinum;
- 2) Loss of RT architecture with the appearance of either gland-like, papillary or cribriform structures, replacing the normal flat superimposed cavities with scant content;
- 3) Continuity remaining between the AHRT and the normal RT epithelium;
- 4) Lack of malignancy signs.

It is possible to discuss about the best surgical treatment to adopt for these lesions. Many Authors are inclined to orchiectomy^{3, 14,15,17-20}.

As reported, it is very important to start with a complete clinical history of the patient. Moreover, it is desirable to obtain a support by radiologists expert on performing many US and testicular MRI; this last exam is used to complete the report of US in case of doubt¹⁴⁻¹⁶. Other Authors expressed their preference for a "wait and see approach", in particular for young patients^{19,20}.

In our experience we chose to perform an intraoperative US-guided biopsy of the testicular mass, taking about a 5 mm sample of parenchyma, considering this approach the best one in case of a not well defined testicular lesion, especially for monorchid patient or patients affected by OATS²¹⁻²⁷. Partial orchiectomy for benign lesions allows to preserve the endocrine and exocrine function and it reduces the risk of local recurrence because, supported by intraoperative echography and by extemporaneous histological exam, we can achieve the complete removal of the lesion.

Conclusion

Preoperative diagnosis of AHRT is not always easy; despite the considerable support of the modern imaging techniques such as ETG with contrast and MRI, the differential diagnosis with other lesions and in particular with some tumors of the testis is still difficult. For this reason, some authors strongly believe that orchiectomy is the safest treatment to perform, whereas others suggest the observation of the lesion as the best solution. Balancing the risks of a wait-and-see treatment in the event of a rete testis tumor with the benefits of a testis-

sparing surgery in case of benign lesion as AHRT, we considered appropriate to perform an excisional biopsy with ultrasound intra-operative support, in order to be sure of the complete excision of the lesion, also using the histological examination to confirm it.

The advantage of this type of treatment is the real possibility for the patients to preserve their endocrine and exocrine function, especially for those who are monorchid. Today, thanks to a multidisciplinary diagnose support, the conservative treatment we proposed is now possible, without precluding a diagnostic accuracy and a surgical radicality.

Riassunto

Per iperplasia adenomatosa della rete testis (AHRT) si intende una proliferazione epiteliale benigna a carico del mediastino testicolare, costituita da una complessa proliferazione di canali tubulo-papillari intercomunicanti fra loro, che può essere focale o diffusa e con o senza dilatazione cistica. In circa la metà dei casi si presenta come una massa macroscopicamente rilevata di consistenza solida o cistica. Tra le anomalie testicolari che spesso si associano alla AHRT, quella di più frequente riscontro è l'atrofia testicolare.

Il paziente venuto alla nostra osservazione è stato studiato con un ecocolordoppler testicolare che ha individuato nel terzo superiore del testicolo destro una massa solida localizzata del diametro di 4,5x3,8mm, ben circoscritta ed ipoecogena con un pattern di vascolarizzazione perilesionale. Lo studio preoperatorio, oltre che sull'accurata anamnesi si è basato su una ecografia con contrasto ed una RMI.

L'intervento è consistito nella biopsia escissionale ecoguidata della lesione testicolare, considerando questo approccio come il migliore per le neoformazioni testicolari non altrimenti ben definibili, con indubbi vantaggi per tutti i pazienti ma specialmente per quelli monorchidi.

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