Journal of Andrology, Vol. 27, No. 1, January/February 2006

Age-Related Epididymis-Like Intratesticular Structures: Benign Lesions of Wolffian Origin That Can Be Misdiagnosed as Testicular Tumors

MANUEL NISTAL,*† MIGUEL A. GARCÍA-CABEZAS,* MARÍA C. CASTELLO,* MARÍA P. DE MIGUEL,*‡ AND JAVIER REGADERA†

*From the *Department of Pathology, La Paz University Hospital, Madrid, Spain; †Department of Anatomy, Histology, and Neuroscience, School of Medicine, Autonomous University of Madrid, Spain; and ‡Stem Cell Program, Institute for Cell Engineering, Johns Hopkins Medical Institute, Baltimore, Maryland.*

ABSTRACT: This study aims to characterize the epididymis-like intratesticular structures (ELITSs), a rare lesion found in elderly men. ELITSs were identified in 6 patients from a review of 1442 autopsies and 271 surgical specimens of adult men. Bilateral lesions were seen in 5 cases. The lesion was located in the proximity of the mediastinal rete testis (6 testes) and at the testicular periphery (4 testes), and at both central and peripheral locations in 1 case. The lesion is characterized by a pseudostratified cylindrical epithelium, with a robust pankeratin and 8, 18, and 19 keratin expression, focal vimentin expression, and apical CD 10 expression, similar to what is proper of the normal human epididymidis. The epithelial layer of ELITSs was surrounded by a thin layer of smooth-muscle cells. The adjacent testicular parenchyma was atrophied and the rete testis showed some associated degenerative lesions related to arteriosclerosis. The ELITSs are distinct from atrophic seminiferous tubules with a Sertoli cell-only pattern and from the benign glandular teratomatous component of an involution of a malignant testicular germ cell tumor, the so-called burn-out germ cell tumor. Clinical and histopathological data suggest that this lesion represents a late Wolffian differentiation similar to the initial segment of the epididymal duct, which represents an unusual manifestation of the aging process.

Key words: Testis, rete testis, cysts, aging.

J Androl 2006;27:79–85

Intratesticular cystic structures are frequently observed in testicular tumors, including teratomas, dermoid cysts (Broggi et al, 1991; Ulbright and Srigley, 2001), sex cord stromal tumors (eg, juvenile granulosa cell tumor) (Nistal et al, 1988; Harms and Kock, 1997), cystadenomas, and sertoliform cystadenomas of the rete testis (Jones et al, 2000), and rete testis adenocarcinomas (Stein et al, 1994). Simple or multilocular intratesticular cysts may be found in the testes of fetuses or prepubertal children and are considered congenital malformations of the rete testis, including the so-called rete testis dysgenesis (Nistal and Jimenez-Heffernan, 1997), and dysplasia of the rete testis (Nistal et al, 1984). In adults, epidermoid cysts (Price, 1969; Shah et al, 1981), cysts of the tunica albuginea with intratesticular growth (Nistal et al, 1989), and cystic transformation of the seminiferous tubules associated with testicular microlithiasis (Nistal et al, 2004) are benign cystic lesions incidentally seen in autopsy or surgical testicular specimens.

The recent approach of systematic echographic exploration of the testes in all urological patients has increased the frequency of intratesticular cystic lesion detection. These cystic lesions are frequently located within or near the mediastinum testis and include adenomatous hyperplasia of the rete testis (Nistal et al, 2003), cystic transformation of the rete testis secondary to ischemic epididymal atrophy (Nistal et al, 1996b), pseudohyperplasia of the rete testis (Ulbright et al, 1997), rete testis hyperplasia with hyaline globules (Ulbright and Gersell, 1991), and rete testis cystic transformation with calcium oxalate deposits associated with renal insufficiency (Nistal et al, 1996a). However, to our knowledge, the presence of tubular structures mimicking epididymal ducts inside the testicular parenchyma has not been reported in the literature. In the present work, we describe the presence of epididymis-like intratesticular tubular structures (ELITSs) that are morphologically and immunohistochemically similar to the epididymal duct of normal men.

Supported in part by Grant PI 021188 of the Fondo de Investigaciones Sanitarias, the Spanish Ministry of Health.

Correspondence to Dr Manuel Nistal, Departamento de Anatomia, Histologia y Neurociencia, Facultad de Medicina, Universidad Autonoma de Madrid, Calle Arzobispo Morcillo, 2. 28029, Madrid, Spain (e-mail: mnistal.hulp@salud.madrid.org).

Received for publication December 20, 2004; accepted for publication August 5, 2005.

DOI: 10.2164/jandrol.04190

*Clinical and pathological data of the ELITSs**

Case	Age (y)	Intratesticular Location	Testicular-Associated Lesions	Rete Testis–Associated Lesions	Epididymal-Associated Lesions	General Pathology and Associated Lesions
1	75	Center	Ischemic tubular hyalinization Decreased Leydig cell number	Atrophy	Efferent ducts focal atrophy	Cirrhosis and hematemesis Severe arteriosclerosis
2	72	Periphery	Obstructive focal tubular hyalinization	NPCCT	Epididymal duct ectasia Intradiverticular stone in cauda epididymis	Massive mesenteric thrombosis Urinary bladder carcinoma
3	70	Center and periphery	Ischemic focal tubular hyalinization Decreased Leydig cell number Hydrocele	Microlithiasis	Efferent ducts focal atrophy	Metastatic pancreatic carcinoma Severe arteriosclerosis
4	73	Center	Ischemic focal tubular hyalinization Decreased Leydig cell number	Atrophy Microlithiasis NPCCT	Efferent ducts focal atrophy Microlithiasis in corpus and in intradiverticular cauda epididymis	Aortic aneurysm Myocardial infarct Severe arteriosclerosis
5	70	Center	Ischemic focal tubular hyalinization Decreased Leydig cell number	Atrophy	Efferent ducts focal atrophy	Metastatic lung epidermoid carcinoma Severe arteriosclerosis
6	69	Periphery	Obstructive focal tubular hyalinization	Atrophy	Efferent ducts focal atrophy Epididymal duct ectasia	. . .

* ELITSs indicates epididymis-like intratesticular structures; NPCCT, nodular proliferation of calcifying connective tissue of the rete testis.

Materials and Methods

Six cases with ELITSs were found after retrospective review of testes from 1442 autopsies of male adults and 271 surgical specimens, obtained from 1994 to 2004 at the Pathology Department at La Paz Hospital. Five cases were found in testes from autopsies and 1 case in testes from surgical specimens. The lesions were bilateral in the 5 autopsied patients and unilateral in the surgical case. Clinical data are presented in the Table.

For histological studies, all testes and epididymis were fixed in buffered formalin for 24–48 hours. Three 2-mm-thick tissue slices were obtained from each specimen for microscopic examination. Tissues were embedded in paraffin, serially sectioned at 5 μm, and stained with hematoxylin and eosin, periodic acid-Schiff stain (PAS), Alcian blue, Orcein, and Masson's trichrome stains. For immunohistochemical studies, the avidin-biotin-peroxidase complex method was used. The primary antibodies and optimum dilutions used for these studies were 1) monoclonal anti-human pankeratin AE1/AE3 antibody (Shandon Immunon, Waltham, Pittsburgh, Pa), at 1:500 dilution; 2) monoclonal antikeratins 8, 18, and 19 antibody (Dakopatts, Glostrup, Denmark) at 1:200; 3) monoclonal anti-vimentin antibody (Progen, Heidelberg, Germany), at 1:200; 4) monoclonal anti-human smooth-muscle actin antibody (Dakopatts), at 1:500; 5) monoclonal anti-collagen type IV antibody (Euro-Diagnostica, Amhem, Sweden), at 1:200, and 6) monoclonal anti-CD 10 antibody (Novocastra, Newcastle, United Kingdom), at 1:20 dilution. The secondary antibody was a goat anti-mouse (Zymed). The immunoreaction was developed with diaminobenzidine (Sigma, St Louis, Mo), and the sections were counterstained with Harris' hematoxylin. As negative controls, adjacent control sections were subjected to the same immunohistochemical method, but the primary antibodies were omitted. No positive staining was observed in these control sections. For positive controls, 5 testes and epididymis obtained from the autopsy of young patients who had not died from endocrinological conditions or undergone treatment potentially affecting spermatogenesis were used.

Results

Gross Pathology

Testicular size was decreased in all cases. In macroscopic sections, the testicular parenchyma showed multiple irregular areas of firm, white tissue alternating with normal testicular tissue (Figure 1). The albuginea surface was smooth, and a small hydrocele was found in all cases. No macroscopic alterations were observed in the epididymis and paratesticular tissues.

Histopathology

The lesions were found as groups of 4–8 tubular structures resembling the typical histology of the epididymal duct intermingled between the seminiferous tubules. No capsule or fibrosis reaction was associated with these intratesticular tubular structures. In 6 testicular specimens, these groups of tubular structures were located in the central portion of the testis, proximally to the mediastinum testis (Figure 2). In 4 specimens, the epididymis-like structures were located at the periphery of the testicular

parenchyma (Figure 3), although no contact with the albuginea capsule was noted. Both central and peripheral lesions were found in 1 testis (case 3, Table). The tubular diameter of the structures ranged from 60 μm to more than 500 μm. The tubules were lined by a pseudostratified epithelium of basal and cylindrical cells. The cylindrical cells had elongated irregular nuclei with intranuclear eosinophilic inclusions, clear cytoplasm, and stereocilia (Figures 4 and 5). Neither mitoses nor cytological atypia were seen in the epithelial cells. The lumen of these tubular structures contained eosinophilic granular or fibrillar material (Figure 4) strongly positive for PAS and Alcian blue stains, but no cells were found within the lumen.

The tubules were surrounded by a well-defined tunica propria that contained a thick basal lamina, variable amounts of extracellular matrix, and several layers of elongated myoid-like cells (Figures 4 and 17). These histological features are similar to those of the epididymis of normal adult men (see Figure 6 for comparison).

The testicular parenchyma surrounding the tubules showed variable lesions related to aging. Seminiferous tubules were completely hyalinized in cases 1, 3, and 5 (Figure 2), whereas in cases 2, 4, and 6, an irregular mosaic pattern consisting of hyalinized seminiferous tubules intermingled with dilated seminiferous tubules with moderate or intense atrophy of the germinal epithelium were observed (Figure 3). Leydig cell numbers were decreased in 4 out of the 6 cases and were normal in the other 2 cases, but no specific lesions of these cells were observed. The small arteries located in the interstitium (the centripetal intratesticular arteries) showed intense intimal fibrosis in all cases.

The rete testis was atrophied in all cases. In 2 cases (cases 2 and 4), it showed intracavity protrusions of partially calcified connective tissue (not shown). Microliths were observed in the rete testis of cases 3 and 4. Additionally, multiple microliths located within diverticular formations in the epididymis were found in cases 2 and 4 (Table). In case 4, large, well-structured microliths were observed within the ELITSs (Figure 7). Focal atrophy of efferent ducts was seen in 5 out of 6 cases (Table).

Immunohistochemical study

All epithelial cells of ELITSs showed intense expression of AE1/AE3 cytokeratins (all cytokeratin subtypes) (Figures 8 and 11). This staining is different from that of normal caput epididymis (Figure 9), where only basal cells exhibited a strong immunostain with AE1/AE3 cytokeratin antibody, and more similar to the normal corpus epididymis (Figure 10), where all epithelial cells stained strongly. Similarly, keratins 8, 18, and 19 expression was strong and homogeneous in the epithelial cells of the ELITSs (Figure 12), similar to the staining of normal corpus epididymidis (not shown).

The ELITSs were positive for CD10 (a mesonephros derivatives marker) in the apical cytoplasm of the epithelial columnar cells and the lumen material (Figure 13). Similar CD10 immunoexpression is shown in the stereocilia of the principal cells of normal epididymis (compare Figures 13 and 14).

Vimentin expression (demonstrating mesodermal origin) was observed in some basal cells and in a very small number of columnar cells of the ELITSs (Figure 15), which is typical of normal human corpus epididymis (compare Figures 15 and 16).

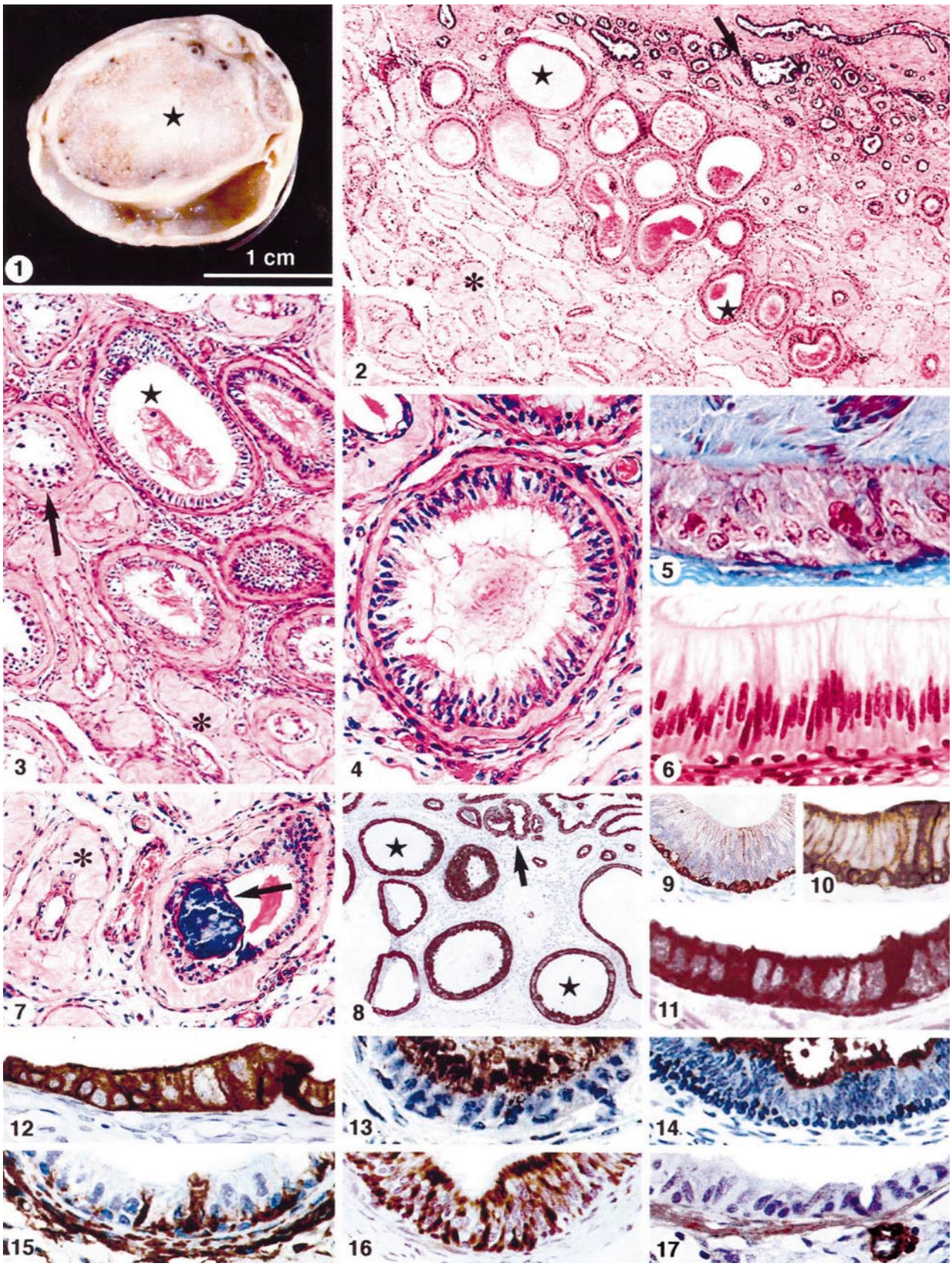
The basal lamina of the ELITSs gave an intense immunoreaction to collagen IV (not shown). A strong immunoreaction to vimentin was observed in the tunica propria cells of the ELITSs (Figure 15). The epithelium of ELITSs was surrounded by a thin layer of myoid-like cells, strongly α-actin positive (Figure 17). The thickness of this layer is more similar to that of normal caput epididymidis (not shown).

Discussion

Differential Diagnosis—The ELITSs can be difficult to distinguish from a well-differentiated benign glandular teratomatous component of an involuted germ cell tumor, the so called burn-out germ cell tumor (Azzopardi and Hoffbrand, 1965), as both lesions are frequently surrounded by hyalinized seminiferous tubules. However, the absence of fibrosis, macrophages with hemosiderin-positive bodies, and dystrophic calcification rules out the diagnosis of teratoma in a burn-out germ cell tumor in any of the patients studied.

The mean age of the patients of this study was 71.5 years, the youngest being 69 years old. Most of the seminiferous tubules in the proximity of ELITSs exhibited atrophied germ cells, hyalinization, and decreased tubular diameter with reduced Leydig cell numbers (cases 1, 3, 4, and 5). These characteristics are typical of seminiferous tubules from aging men (Nistal and Paniagua, 1997). This suggests that the ELITSs may be the result of an age-related acquired process and not a congenital disease because, to our knowledge, it has never been found in fetal or prepubertal testis.

Most patients described in this study suffered from severe arteriosclerosis. We have found rete testis atrophy in cases 1, 4, 5, and 6; nodular proliferation of calcifying connective tissue in cases 2 and 4; and microlithic deposit in cases 3 and 4. These features have been previously reported in patients with decreased blood perfusion, including arteriosclerosis (Nistal et al, 2003, 2004). Chronic ischemia is related to the presence of hyalinized tubules, and the ELITs have been found in the vicinity of such tubules. The concomitant presence of ELITs and hyalin-


1
1 cm
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17

ized tubules is probably just an unusual finding of the aging process.

ELITSs Histogenesis—Several hypotheses may be proposed, including origin in i) the rete testis, ii) tubuli recti, iii) vaginal epithelium, iv) seminiferous tubules, v) mesonephric and Wolffian ducts.

i) Origin in the Rete Testis. In 4 lesions, the ELITSs were located in the central area of the testicular parenchyma, near the septal or mediastinal portion of the rete testis, suggesting an origin in the rete testis. In addition to the location, the epithelial cells of the ELITSs are histologically very similar to the columnar cells found in the normal rete testis, as well as those seen in cases with adenomatous rete testis hyperplasia and rete testis pseudohyperplasia (Nistal et al, 2003). Also, the presence of associated pathologies of the rete testis in the current series, including nodular proliferation of calcifying connective tissue in cases 2 and 4 (not shown; Nistal and Paniagua, 1989), suggests a possible origin of the ELITSs in the rete testis. However, the ELITSs showed a pseudostratified epithelium with a continuous layer of epithelial basal cells that are not present in the rete testis. Additionally, the rete testis epithelium strongly coexpresses keratins and vimentin (Kasper and Stosiek, 1989; Stosiek et al, 1990), whereas most epithelial cells of the ELITSs are vimentin negative. These data suggest another origin of the ELITSs different than the rete testis.

ii) Tubuli Recti. Some of the ELITSs of the present series are located in the central area of the testis that contains the tubuli recti (Trainer, 1997), which are formed by a single layer of keratin- and vimentin-positive modified Sertoli cells and a layer of myoid peritubular cells (De Kretser et al, 1982). The occurrence of stereocilia and the absence of vimentin expression in the ELITSs rules out the possibility of an origin in the tubuli recti.

iii) Vaginal Epithelium. In three cases, the ELITSs were located at the periphery of the testicular parenchyma, near the tunica albuginea, suggesting an origin as microcystic inclusions of the vaginal epithelium (Bryant, 1986). However, vaginal derivatives are lined by a single layer of squamous or cubic cells expressing vimentin, again discarding this possible origin.

iv) Seminiferous Tubules. The possible origin of ELITSs in the seminiferous tubules is based on similar tubule size and epithelial cell morphology to the epithelium of the Sertoli cell-only pattern of atrophic seminiferous tubules of infertile men (Sigg and Hedibger, 1981). However, the ELITSs exhibited strong keratin expression, which is absent in postpubertal seminiferous tubules. In addition, ELITSs epithelial cells were mostly vimentin

←

Figure 1. Morphological characteristics of ELITSs. Transversal section of the right testis (case 3) showing an irregular white fibrotic area (star) located in the testicular parenchyma, near the mediastinum testis. The tunica vaginalis and tunica albuginea are thickened and the vaginal cavity contains a gelatinous material.

Figure 2. Numerous well-defined intratesticular tubular microcystic structures (ELITSs) (stars) located in the vicinity of the rete testis (arrow) and hyalinized seminiferous tubules (asterisk) (case 3). Hematoxylin and eosin.

Figure 3. ELITSs showing dilated tubules and intraluminal secretion (star). The tubules are lined by a pseudostratified epithelium and a thin muscular layer. Note that some nearby seminiferous tubules show total sclerosis (asterisk) but others present Sertoli cells and partial germ cell differentiation (arrow) (case 5). Hematoxylin and eosin.

Figure 4. High magnification of a tubule of ELITSs lined by a pseudostratified epithelium containing basal cells and columnar cells with stereocilia and a fibrotic secretion in the lumen. The lamina propria is hyalinized and surrounded by a layer of myoid cells (case 5). Periodic acid-Schiff stain.

Figure 5. Close view of the ELITs epithelial characteristics, showing a highly filamentous cytoplasm and abundant stereocilia at the apical border. The basal cell layer is discontinuous and the extracellular matrix shows abundance of collagen. Mason's trichrome.

Figure 6. Corpus segment of a normal epididymal duct (control case), showing a pseudostratified epithelium with columnar cells with abundant stereocilia and a cubic basal cell layer, surrounded by a thick layer of elongated myoid cells. Hematoxylin and eosin.

Figure 7. One tubule of ELITSs showing a large intraluminal microlith (arrow) (case 4). Hematoxylin and eosin.

Figure 8. Strong AE1/AE3 keratin expression in the epithelium of ELITSs (stars) and in the epithelial cells of the rete testis (arrow) (case 3). Diaminobenzidine and Harris' hematoxylin.

Figure 9. AE1/AE3 keratin immunoexpression in normal caput epididymidis (control case), showing intense expression only in basal cells. Diaminobenzidine and Harris' hematoxylin.

Figure 10. AE1/AE3 keratin immunoexpression in normal corpus epididymidis (control case), showing intense expression in all epithelial cells. Diaminobenzidine and Harris' hematoxylin.

Figure 11. Detail of AE1/AE3 keratin immunoexpression in the ELITSs epithelial cells, demonstrating a strong reaction in the basal and in the columnar cells (case 3). Diaminobenzidine and Harris' hematoxylin.

Figure 12. Keratins 8, 18, and 19 immunoexpression in the ELITSs epithelial cells, demonstrating a strong reaction in the basal and in the columnar cells. Diaminobenzidine and Harris' hematoxylin.

Figure 13. CD10 immunoexpression in the apical cytoplasm of the columnar cells of the ELITSs (case 5). Diaminobenzidine and Harris' hematoxylin.

Figure 14. CD10 immunoexpression in the apical cytoplasm of the columnar cells of the normal corpus epididymis (control case). Diaminobenzidine and Harris' hematoxylin.

Figure 15. Vimentin expression in all basal cells but only in some columnar cells of the ELITSs epithelium, and also in the lamina propria fibroblastic and myoid cells (case 5). Diaminobenzidine and Harris' hematoxylin.

Figure 16. Irregular vimentin expression in basal and columnar cells of the epithelium of normal corpus epididymis (control case). Diaminobenzidine and Harris' hematoxylin.

Figure 17. Muscular actin expression in the myoid cell layer of the ELITSs, demonstrating a thin muscular layer. Diaminobenzidine and Harris' hematoxylin.

negative, which contrasts with the robust expression of vimentin in normal and pathological Sertoli cells (Stosiek et al, 1990). In our opinion, these immunohistochemical differences, together with the absence of sperm in the lumen of the ELITSs, discards the possibility of an origin for the ELITSs from seminiferous tubules.

v) Mesonephric and Wolffian Ducts. The origin of ELITSs from mesonephric and Wolffian vestigial remnants is also feasible, as these remnants can mimic the histology of the efferent, epididymal, or deferent ducts. Embryonic remnants show a pseudoglandular or microcystic appearance, consisting of several small tubules lined by a cubic epithelium and lacking a muscular layer (Nistal et al, 1987; Rosai, 1996). The presence of embryonal remnants is not a rare finding in prepubertal or adult male genital organs. They are usually located in paratesticular regions, including the tunica vaginalis, epididymis, spermatic cord, and hernia sacs, and appear very rarely in the testicular parenchyma (Wollin et al, 1987; Satoh, 1991; Rosai, 1996; Steigman et al, 1999; O'Rahilli and Müller, 2001).

To determine if these structures originate from mesonephric or Wolffian remnants is very difficult, as these types of structures have never been documented together with ELITS in the testicular parenchyma. In rodents, efferent ducts and proximal epididymal regions derive from the mesonephros, whereas the distal epididymal regions derive from the Wolffian duct (Turner et al, 2003). However, it is not known if such developmental origins maintain from rodents to humans.

The mesonephric origin of the ELITSs is less probable, as these structures histologically never resemble efferent ducts, typical structures derived from the mesonephros in humans. The fact that the epithelium of the ELITSs is pseudostratified suggests that they are not similar to efferent ducts, which typically display a single epithelium. The absence of keratin-negative clear cells, typical of efferent ducts (Regadera et al, 1993), from the epithelial layer of all cases of ELITSs further suggests that they are not originated from mesonephric remnants.

The histological pattern of the epithelium of the ELITSs resembles most that of the corpus epididymis of normal men. In the ELITSs, keratins immunostaining together with focal coexpression of vimentin filaments was seen in epithelial columnar cells. There was also strong keratin expression in the basal cells of the epithelium. This immunohistochemical pattern is similar to that described for the normal corpus epididymis (Palacios et al, 1993). In addition, the strong CD10 immunoexpression observed in the stereocilia and apical cytoplasm of the columnar cells of the ELITSs is similar to that found in the same regions of the principal cells of the epididymal epithelium, typical of Wolffian derivatives (Cerilli et al, 2003). However, the ELITSs are surrounded by a thin layer of α-actin-positive smooth muscle cells, similar to that seen in the normal caput epididymis (Lopez and Breucker, 1986; Palacios et al, 1993). Based on these results, we cannot clearly identify this pathological structure as caput or corpus epididymidis. The ELITSs are pathological features, with most epithelial cell characteristics similar to corpus, but some tubule characteristics, such as the small thickness of the myoid layer, similar to caput. Still, these data support the hypothesis of a Wolffian origin of the ELITSs, probably originated by a late differentiation process. In our experience of more than 2500 autopsies from fetal and prepubertal men studied in the last 30 years, we have never found a case of ELITSs. This suggests that these structures are developed later in life. However, the presence of isolated Wolffian duct-derived cells inside the testicular parenchyma of young men, which may have not been detected by microscopy, cannot be discarded.

In conclusion, our histological and immunohistochemical data suggest that these intratesticular structures are a benign lesion produced by a late differentiation process of intratesticular Wolffian derivatives that represents an unusual manifestation of the aging process.

Acknowledgments

The authors thank P. Rubio and R. Marcos for technical assistance and Philip Mason for linguistic assistance.

References

Azzopardi JG, Hoffbrand AV. Retrogression in testicular seminoma with viable metastases. *J Clin Pathol.* 1965;18:135–141.

Broggi G, Appetito C, di Leone L, Ciprandi G, Menichella P, Broggi M, Boldrini R, Zaccara A. Dermoid cyst in undescended testis in a 9-year-old boy. *Urol Int.* 1991;47:110–112.

Bryant J. Efferent ductule cyst of tunica albuginea. *Urology.* 1986;27: 172–173.

Cerilli LA, Sotelo-Avila C, Mills SE. Glandular inclusions in inguinal hernia sacs: morphologic and immunohistochemical distinction from epididymis and vas deferens. *Am J Surg Pathol.* 2003;27:469–476.

De Kretser DM, Temple-Smith PD, Kerr JB. Anatomical and functional aspects of the male reproductive organs. In: Bandhauer K, Frick J, eds. *Disturbances in Male Fertility.* Berlin: Springer-Verlag; 1982: 24–34.

Harms D, Kock LR. Testicular juvenile granulosa cell and Sertoli cell tumours: a clinicopathological study of 29 cases from the Kiel Paediatric Tumour Registry. *Virchows Arch.* 1997;430:301–309.

Jones EC, Murray SK, Young RH. Cysts and epithelial proliferations of the testicular collecting system (including rete testis). *Semin Diagn Pathol.* 2000;17:270–293.

Kasper M, Stosiek P. Immunohistochemical investigation of different cytokeratins and vimentin in the human epididymis from the fetal period up to adulthood. *Cell Tissue Res.* 1989;257:661–664.

Lopez ML, Breucker H. Ultrastructure of the lamina propria of the human ductuli efferentes and ductus epididymidis. *Andrologia.* 1986;18:133–146.

Nistal M, Castillo MC, Regadera J, Garcia-Cabezas MA. Adenomatous

hyperplasia of the rete testis. A review and report of new cases. *Histol Histopathol.* 2003;18:741–752.

Nistal M, García-Cabezas MA, Regadera J, Castillo MC. Microlithiasis of the epididymis and the rete testis. *Am J Surg Pathol.* 2004;28:514–522.

Nistal M, Iniguez L, Paniagua R. Cysts of the testicular parenchyma and tunica albuginea. *Arch Pathol Lab Med.* 1989;113:902–906.

Nistal M, Iniguez L, Paniagua R, Redondo E, Regadera J. Tubular embryonic remnants in the human spermatic cord. *Urol Int.* 1987;42: 260–264.

Nistal M, Jimenez-Heffernan JA. Rete testis dysgenesis. A characteristic lesion of undescended testes. *Arch Pathol Lab Med.* 1997;121:1259–1264

Nistal M, Jimenez-Heffernan JA, García Viera M, Paniagua R. Cystic transformation and calcium oxalate deposits in rete testis and efferent ducts in dialysis patients. *Hum Pathol.* 1996a;27:336–341.

Nistal M, Mate A, Paniagua R. Cystic transformation of the rete testis. *Am J Surg Pathol.* 1996b;20:1231–1239.

Nistal M, Paniagua R. Nodular proliferation of calcifying connective tissue in the rete testis: a study of three cases. *Hum Pathol.* 1989;20: 58–61.

Nistal M, Paniagua R. Non-neoplastic diseases of the testis. In: Bostwick DG, Eble JN, eds. *Urologic Surgical Pathology.* 1st ed. St Louis, Mo: CV Mosby; 1997:457–465.

Nistal M, Redondo E, Paniagua R. Juvenile granulosa cell tumor of the testis. *Arch Pathol Lab Med.* 1988;112:1129–1132.

Nistal M, Regadera J, Paniagua R. Cystic dysplasia of the testis. Light and electron microscopic study of three cases. *Arch Pathol Lab Med.* 1984;108:579–583.

O′Rahilli R, Müller F, eds. *Human Embryology and Teratology.* 3rd ed. New York, NY: Wiley-Liss; 2001.

Palacios J, Regadera J, Paniagua R, Gamallo C, Nistal M. Immunohistochemistry of the human ductus epididymis. *Anat Rec.* 1993;235: 560–566.

Price EB. Epidermoid cysts of the testis: a clinical and pathologic analysis of 69 cases from the testicular tumor registry. *J Urol.* 1969;102:708–713.

Regadera J, Palacios J, Martín-Cordova C, Nistal M, Cobo P, Paniagua R. Enzymohistochemical and immunohistochemical study of the human efferent ducts. *Int J Androl.* 1993;16:315–323.

Rosai J. *Ackerman's Surgical Pathology.* 8th ed. St Louis, Mo: CV Mosby; 1996.

Satoh M. Histogenesis and organogenesis of the gonad in human embryos. *J Anat.* 1991;177:85–107.

Shah KH, Maxted WC, Chan B. Epidermoid cysts of the testis: a report of three cases and analysis of 141 cases from the world literature. *Cancer.* 1981;47:577–582.

Sigg C, Hedibger C. Quantitative and ultrastructural study of germ epithelium in testicular biopsies with ''mixed atrophy.'' *Andrologia.* 1981;13:412–424.

Steigman CK, Sotelo-Avila C, Weber TR. The incidence of spermatic cord structures in inguinal hernia sacs from male children. *Am J Surg Pathol.* 1999;23:880–885.

Stein JP, Freeman JA, Esrig D, Chandrasoma PT, Skinner DG. Papillary adenocarcinoma of the rete testis: a case report and review of the literature. *Urology.* 1994;44:588–594.

Stosiek P, Kasper M, Karsten U. Expression of cytokeratin 8 and 18 in human Sertoli cells of immature and atrophic seminiferous tubules. *Differentiation.* 1990;43:66–70.

Trainer TD. Testis and excretory duct system. In: Sternberg SS, ed. *Histology for Pathologists.* 2nd ed. Philadelphia, Pa: Lippincott-Raven; 1997:1019–1039.

Turner TT, Bomgardner D, Jacobs JP, Nguyen QAT. Association of segmentation of the epididymal interstitium with segmented tubule function in rats and mice. *Reproduction.* 2003;125:871–878.

Ulbright TM, Amin MB, Young RH. Tumors of the testis, adnexal, spermatic cord and scrotum. In: *Atlas of Tumor Pathology.* Washington, DC: American Forces Institute of Pathology; 1997:322–326.

Ulbright TM, Gersell DJ. Rete testis hyperplasia with hyaline globule formation. A lesion simulating yolk sac tumour. *Am J Surg Pathol.* 1991;15:66–74.

Ulbright TM, Srigley JR. Dermoid cyst of the testis: a study of five postpubertal cases, including a pilomatrixoma-like variant, with evidence supporting its separate classification from mature testicular teratoma. *Am J Surg Pathol.* 2001;25:788–793.

Wollin M, Marshall F, Fink M, Malhotra R, Diamond DA. Aberrant epididymal tissue: a significant clinical entity. *J Urol.* 1987;138:1247–1250.