

Diagnostic ultrasound-guided excisional testicular biopsy for small (< 1 cm) incidental nodules. A single institution experience

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Summary

Introduction and objectives: The widespread use of scrotal ultrasound (SUS) has led to a marked increase in the number of incidentally detected testicular lesions. A small incidental nodule (STN) has defined as a non palpable (< 10 mm), asymptomatic solid lesion with normal levels of oncological testicular markers. Nowadays the lack of agreement on the topic causes managing problems to andrologists. We present our experience consisting in 8 cases of STN discovered by SUS performed for different clinical indications.

Material and methods: We retrieved from our ultrasonographic files the clinical information about 717 patients evaluated for andrological problems. Patients with STN underwent to a complete clinical history and physical examination as well as oncological testicular markers measurement and ormonal assessment and then received a diagnostic ultrasound guided excisional biopsy (DEB). Surgical approach was performed through an inguinal incision. Using the coordinates previously obtained from preoperative SUS, STN was localized by intraoperative SUS. The lesion was enucleated and sent to the Pathology department for frozen section examination (FSE). Biopsies of affected testis (TB) were also performed. Post-excision ultrasound has been used to confirm the complete removal of the nodule. Whether pathological findings were benign, testis sparing surgery (TSS) was performed. Immediate radical orchidectomy (IRO) was performed if FSE and TB findings suggested a malignant lesion.

Results: STNs were discovered in 8 patients (1,1%). Very small lesions (< 5 mm) were detected in 50% of cases. We performed four IRO and four DEB with consequent TSS. In one case we performed a delayed radical orchidectomy (DRO). At FSE pathologist reported 3 Leydig cell tumor and 3 seminoma and an inflammatory regressive lesion in one case. FSE on TB reported intratesticular neoplasia (TIN) in three cases. In one case nodule wasn't sent to FSE. We observed a concordance between FSE and definitive pathologic report in six cases (75%).

Conclusions: The management of STN is still a challenge for the surgical andrologist. A correct diagnosis has a crucial role in making the best treatment and patients outcome. Ultrasound guided excisional biopsy and the close collaboration with a dedicated pathologist are very useful in reducing errors..

KEY WORDS: Scrotal ultrasound; Small testicular nodules; Seminoma; Leydig cell tumor; Intratesticular neoplasia.

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No conflict of interest declared.

INTRODUCTION

The widespread use of scrotal ultrasound (SUS) has led to a marked increase in the number of incidentally detected small testicular nodules (STNs). STN is defined as a non palpable, asymptomatic solid lesion with normal levels of oncological testicular markers (1). STNs still represent an important diagnostic and therapeutic challenge for the surgical andrologist. It is difficult to decide the strategy to use with these lesions since there are no defined prognostic parameters. Many series in the literature revealed that the majority of non palpable intratesticular masses are malignant (2) while others suggested the benign nature of most of them (3). Nowadays the reported conclusions are difficult to compare due to a selection bias of the population studied. However, evidence deriving from well-conducted retrospective outcome studies with considerable follow-up suggests that the organ-sparing approach (TSS) stands for a viable treatment modality for testicular tumors of different histology and biology, both in the pediatric and adult population (4).

We herein present 8 cases of small (< 10 mm) incidental intratesticular nodules discovered by SUS performed for different clinical indications.

MATERIAL AND METHODS

We retrieved from our ultrasonographic data base files the clinical information of 717 patients referred for an andrological evaluation at Macerata Hospital, Surgical Department, Urology Unit during a 43 months period. STNs were discovered in 8 patients (1,1%). These patients underwent a diagnostic ultrasound guided excisional testicular biopsy (DEB) associated to a random testicular biopsies (TB). Each patient included in our study firstly underwent a complete clinical history and physical examination as well as oncological testicular markers measurement and ormonal assessment. Scrotal ultrasonography and Doppler examination were performed with a 7.5 Mhz B-mode linear array transducer with color Doppler capability (BK Medical, Denmark). After assessing testicular diameter and volume, focal intratesticular echostructural anomalies were described (site, dimensions and echotexture). All our patients, informed about

Table 1. Clinical and pathological findings of 8 patients with non palpable testicular nodules less than 10 mm diagnosed by several andrological ultrasound evaluation.

Patient	Age	Nodule diameter (mm) and testicular side	Nodule location	Ultrasonographic indication	FSE result on testicular biopsy	FSE result on nodule	Final pathology Biopsy-nodule	Type of surgery	Note
1	18	5 /left	Lower pole	Recent trauma	Normal tissue	Inflammatory and haemorrhagic infiltrate	Intratesticular Neoplasia (TIN)-hemorrhagic infiltrate	TSS	Patient underwent RO for seminoma 6 months later
2	36	4/left	Upper pole	Seminal infection	TIN	Seminoma	TIN-Seminoma	IRO	-
3	42	6/right	Lower pole	Scrotal discomfort	TIN	Seminoma	TIN-Seminoma	IRO	-
4	23	6,5 /left	Mesotesticular	Bilateral gynecomastia	Normal tissue	Leydig cell tumor	Normal tissue Leydig cell tumor	TSS	-
5	27	6/ right	Lower pole	Unilateral gynacomastia	Normal tissue	Leydig cell tumor	Normal tissue Leydig cell tumor	TSS	-
6	40	8 /left	Mesotesticular	Severe oligoasthenospermia	Normal tissue	Seminoma	Normal tissue Leydig cell tumor	IRO	Pre surgical CT findings of retroperitoneal lymphadenopathy
7	38	2,5/right	Mesotesticular	Azoospermia	Normal tissue	Leydig cell Tumor	Normal tissue Leydig cell tumor	TSS	Non obstructive azoospermia; bilateral small testicular volume
8	30	2,7/right	Lower pole	Follow-up of cryptorchidism	TIN		TIN- Seminoma	IRO	No nodule sent to FSE

TIN intratesticular neoplasia. RO radical orchidectomy. TSS testicular sparing surgery. IRO immediate radical orchidectomy. CT computed tomography. FSE frozen section examination

the chance of ruling out a malignant tumor, preferred surgery despite active surveillance. Surgical approach was performed through an inguinal incision with clamping of the spermatic funiculus. The gonad was exteriorized from the same access after sectioning the gubernaculum. Using the coordinates previously obtained from preoperative ultrasonographic study, the lesion was localized by intraoperative ultrasound (7,5 Mhz B-mode linear array transducer, BK Medical, Denmark) and a small caliber needle was placed adjacent to the lesion. The tunica albuginea overlying the lesion was then transversally incised and the nodule visualized by gently displacing the surrounding testicular parenchyma.

The lesion was then enucleated, leaving a rim of normal appearing testicular parenchyma and sent to the pathologist department for frozen section examination. Intratesticular biopsies was randomly performed in number of 4 specimen including perinodular testicular parenchyma and polar zone not involved by primary lesion. Biopsies was performed with the scissors through small incisions of the albuginea. Post-excision ultrasound has been used to confirm the complete removal of the nodules and the absence of intratesticular hematoma. If pathological findings were benign, the testis and wound were irrigated with sterile water, the vascular clamp on the spermatic cord was removed, and after achieving complete hemostasis, the tunica albuginea was closed with running 4-0 or 5-0 absorbable suture. If pathological findings of DEB and in TB suggested a malignant lesion, immediate radical orchidectomy (IRO) was performed.

RESULTS

During a 43 months period, 717 scrotal ultrasound examinations were performed for a variety of indications as

varicocele, echo-color-Doppler for fertility study, andrological screening, scrotal pain or discomfort or general clinical screening. Small (< 10 mm) incidental testicular nodules were discovered in 8 patients (1,1%). Very small lesions (< 5 mm) were detected in 50% of cases.

Clinical, ultrasound and pathological data are shown in Table 1. Figure 1a and 1 b show the ultrasonographic features of the small incidental testicular nodule in two different patients. Figure 2 shows the result after lesion removal at follow up control.

Figure 1a. Hypochoic mesotesticular lesion of right testicle in a 38 years old azoospermic man. Final histological report revealed a Leydig cell tumor.

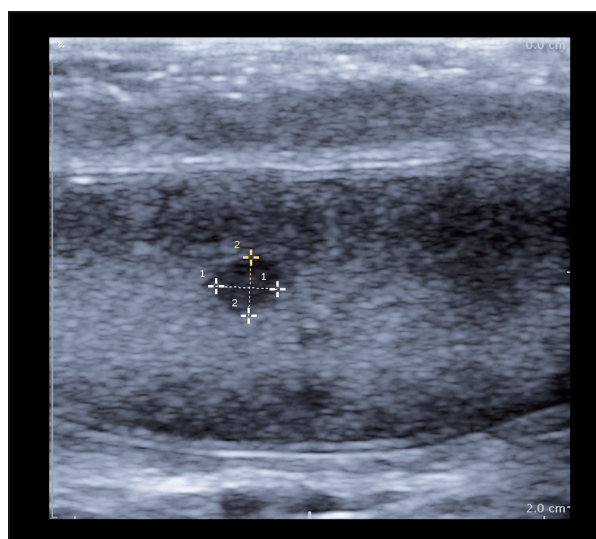
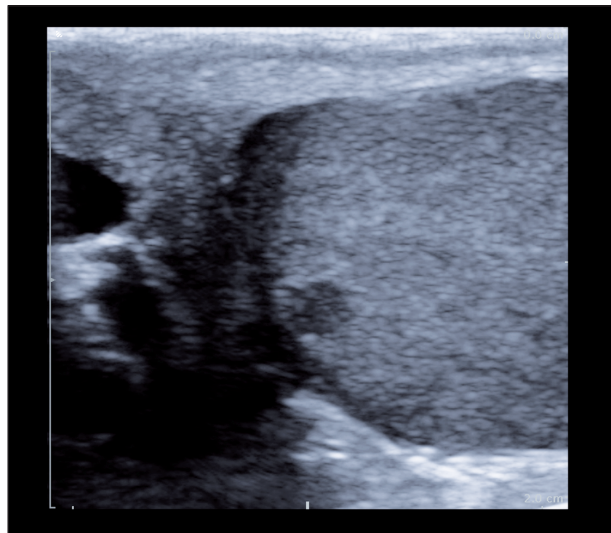


Figure 1b.

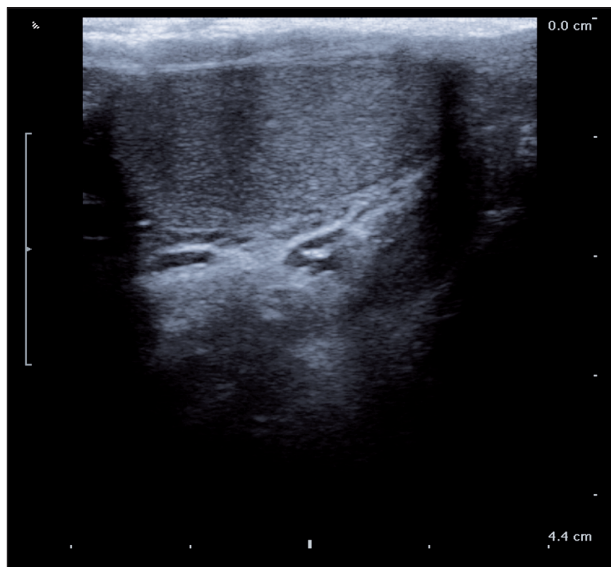
Hypoechoic lesion of lower pole in right testicle in a 30 years old normospermic man.

The ultrasonographic evaluation was performed for follow up of cryptorchidism.

**Figure 2a-b.**

Follow up of patient in figure 1a.

No residual or innovative lesions was found.



We have performed four (4/8) *immediate radical orchidectomy* (IRO) and four (4/8) excisional biopsy with consequent *testis sparing procedure* (TSS). In one case (1/8) we have performed a *delayed radical orchidectomy* (DRO). At intraoperative FSE, both Leydig cell tumor and seminoma have been diagnosed in three cases and flogosis with hemorrhagic infiltration in one case. In this last one case, six months after TSS we have performed a RO due to the discovery during the follow up of a new nodular lesion revealed as seminoma. At FSE of testicular biopsies, pathologist diagnosed in three cases an *intratesticular neoplasia* (TIN). In one case we were not able to identify the

nodule to send to the pathologist for FSE. We had observed a concordance between intraoperative frozen section examination and definitive pathologic report in six cases (6/8). No complication was observed in each patient.

DISCUSSION

The recent marked increase in the number of incidentally detected and small testicular nodules is to be attributable to the widespread use of scrotal ultrasound. The management options of these type of lesion represent a problematic challenge for the uro-andrologist and include *radical orchidectomy*, immediate (IRO) or delayed (DRO), *diagnostic excisional biopsy* (DEB) or active surveillance. Although high resolution ultrasound can reliably detect solid intratesticular masses, benign lesions cannot be conclusively distinguished from malignant ones (5-6) The widely accepted surgical maxim that “*a solid intratesticular mass, even if non palpable, must be considered malignant until proven otherwise*”, must be partially revisited. The old dogma that equaled diagnosis of any testicular mass to immediate radical orchidectomy has been confuted by the clinical experience accumulated in the last decade. Several series are now available reporting an unremarkable follow up when, because of non palpable testicular nodules, patients received either TSS or RO (4) An aggressive approach to a non palpable testicular lesion is reasonable in case of the presence of other risk factors of testicular tumor (7). It must be minimized the risk of performing a radical orchidectomy and the related patient overtreatment in the case of a benign nodule. On the other hand, in the case of a malignant nodule, the diagnostic excisional biopsy could lead to an alteration of the predictable pattern of lymphatic spread or determine a positive margin, without neglecting the possibility of unrecognized lesions or TIN in the remaining testis. The last option management may be the active surveillance. General consensus for this approach exists only in the presence of a recent inflammation (7). The risk of an active surveillance is that the disease could progress to a higher stage in the case of a malignant lesion (8). In the management of small testicular nodules, it could be avoided these risks with use of the clinical and instrumental information obtained during the diagnostic work-up. However the known prognostic factors are still inaccurate (7).

In patients with small testicular lesions a prevalence of benign tumors has to be expected, compared to patients with palpable testicular lesions which are malignant in over 90% of cases (9). In a series of 27 patients with ultrasound detected testicular lesions Carmignani *et al.* (1) reported an overall 51.8% prevalence of benign disease at definitive histology, with 80% of non-palpable lesions being benign.

Similarly, Sheynkin *et al.* (10) reported a 75% prevalence of benign lesions among eight non-palpable testicular masses. It is noteworthy that up to 100% of non-palpable testicular lesions are benign Leydig cell tumor. It has also been shown that smaller lesions (< 2 cm) are more likely to be benign (7).

In our series of 8 small testicular nodules, we found 37.5% of benign tumors. At the definitive pathological

report, seminoma was diagnosed in 3 cases and a definitive diagnosis of TIN has been made in 1 case. In case of lesions less than 5 mm (4/8), we founded a seminoma in two case (50%) and a benign Leydig cell tumor in one case (25%). Muller *et al.* (11) reported a series of 20 men diagnosed with a tumor mean diameter of 3.5 mm with four patients (20%) who underwent an IRO because the lesions were found to be malignant. In all case, the resected specimen revealed a multifocal TIN. According to this previous report, our limited experience did not confirm that the benign lesions are smallest than malignant ones.

Moreover, in our small series, clinical information or imaging data was not always useful for predicting the benign or the malignant nature of testicular lesion. Two patients with gynecomastia had a definite diagnosis of Leydig cell tumor. On the other hand, although the presence of retroperitoneal lymphadenopathy was considered an indication to immediate radical orchidectomy, in our patient it has not been associated with a malignant neoplasia.

Moreover inflammatory and hemorrhagic infiltrate in a clinical setting of recent trauma lead us to a sparing surgical approach, but definitive pathological examination revealed intratesticular neoplasia (TIN) and patient underwent radical orchidectomy 6 months later for a new testicular mass (seminoma) detected after ultrasound follow-up.

Therefore, at the best of our knowledge, in small nodular lesions of the testes the intra-operative ultrasound excisional biopsy is mandatory.

The first description of the operative technique of ultrasound guided testicular nodule excision was made by Stoll *et al.* (12) and progressively developed until 2002, when Hopps and Goldstein codified the procedure introducing the use of a magnificant system, with the aim of improving the identification and complete excision of small non palpable lesions (13).

Rolle *et al.* (14) described their experience on a series of 14 hypoechoic testicular lesions that underwent surgical exploration with the aid of the operating microscope. With a mean size of the nodules of 5.7 ± 4.6 mm, they reported the identification and the complete excision of lesions in all patients. The intraoperative frozen section examination (FSE) showed a benign lesion in 12 cases and intratesticular neoplasia (TIN) in two who underwent RO.

The definitive histological analysis always confirmed the frozen section examination report. After a mean clinical and ultrasound follow-up of 15 months, they not reported complications. Valotto *et al.* (15) described a total of 25 patients with negative testicular cancer markers who underwent an inguinal surgical exploration for a testicular non palpable suspected lesion of a mean diameter of 16.1 mm (range 4-89 mm) without use of magnificant systems.

They identified and successfully removed all lesions. FSE revealed benign lesion in 21 cases (84%) but this findings was confirmed in 18/21 (84%). DRO was performed with a diagnosis of seminoma in two cases. And the pathological report was negative in one case. When FSE revealed a malignant lesion (4 cases), the definitive

pathological report on radical orchidectomy specimen confirmed this findings in 75%.

After a median follow up of 18 months they not reported relapse. Also in our series we used only intraoperative ultrasonography with needle lesion localization. We have not enough experience about lesion less than 5 mm in diameter (4 cases of 8) for considering microsurgery useless in such cases.

In any case a microsurgical approach to small testicular lesions can provide the opportunity to identify all lesion and remove it with appropriate margins in case of a solitary testis or bilateral malignancies (16). Ultrasound excisional biopsy has been very difficult for us in case of very small nodules. In particular, in one patient, we were not able to identify the lesion (diameter 2.7 mm) despite the use of intra operative ultrasound. Immediate radical orchidectomy was decided considering the diagnosis of TIN on testicular biopsies.

Definitive histopathologic evaluation reported a small seminoma. The use of a magnificant system could have helped the dissection improving the identification, the complete nodule excision and the accuracy of the diagnosis, especially during the intraoperative biopsy for frozen section examination. Intraoperative FSE could provide a diagnosis of nature with absolute certainty. FSE has demonstrated to be a highly reliable method to characterize testicular masses.

Subik *et al.* reported in 36 (83.7%) of 43 cases with benign frozen section assessments, the capability to successfully avoid a radical orchidectomy (17).

Therefore there is general consensus that FSE is useful for permitting testicular preservation, especially in men with small, non palpable, incidentally found masses as well as other benign lesions where a clinical diagnosis of malignancy is in doubt (17).

In our series we observed a concordance between FSE and definitive pathologic report in six cases (75%). Misdiagnoses were made in absence of the dedicated pathologist.

In addition to the need for magnification tools, we recognize, especially in cases of very small lesion, that diagnostic accuracy in FSE may be influenced by the expertise of the attending dedicated pathologist, which cannot be translated to every community hospital.

CONCLUSIONS

Small (< 10 mm) testicular nodules are nowadays commonly observed due to the widespread use of scrotal ultrasound evaluation. The management of this topic is still a challenge for the surgical andrologist and the pathologist.

Treatment options include radical orchidectomy, diagnostic excisional biopsy and active surveillance. In our single centre experience, ultrasound guided excisional biopsy with frozen section examination is the preferred option for initial management. Intra-operative ultrasound excisional biopsy is mandatory but very difficult in many cases, especially without use of magnificant systems, when lesion is very small (< 5 mm). Misdiagnosis is possible and close collaboration with a dedicated uro-pathologist is needed.

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