
Non-palpable testicular lesion: the case for testicular preservation

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ASSAF GJ. Non-palpable testicular lesion: the case for testicular preservation. *The Canadian Journal of Urology*. 2006;13(2):3034-3038.

Objectives: To report our experience in the management of patients with non-palpable lesions of the testis with a review of published studies. Even though radical orchiectomy remains the golden standard treatment for solid testicular masses there is an increasing role for testes-sparing surgery in a select group of patients with non-palpable tumors.

Patients and methods: Between April 2000 and October 2004, a non-palpable testicular lesion was discovered on ultrasonography in six patients. Ultrasonography was performed for infertility in two patients, for testicular pain

in three patients, and in one case for previous history of seminoma in the contra-lateral testis.

Results: Radical orchiectomy was performed in two patients, testis-sparing surgery with microsurgical excision and frozen-section examination (FSE) in two patients, and a conservative watchful waiting attitude was adopted in two patients.

Conclusions: In a select group of patients, testis-sparing surgery with microsurgical dissection and FSE or a watchful waiting attitude can be safely adopted as an alternative to radical orchiectomy in the presence of incidentally discovered non-palpable testicular lesion.

Key Words: testis ultrasound, non-palpable testicular lesion, Leydig cell tumor, testis-sparing surgery

Introduction

Due to the increased use of high-resolution trans-scrotal ultrasound for indications other than evaluating palpable tumors it is not surprising that small impalpable tumors are detected unexpectedly. Scrotal ultrasonography has become widely used in the diagnostic evaluation of testicular or epididymal pain, epididymo-orchitis, scrotal trauma, infertility and contra-lateral testicular evaluation in patients with testicular cancer. This has caused an increase in the detection of focal testicular lesions without any

diagnostic information. Intra-testicular non-palpable lesions have been reviewed by a number of authors in small series of patients and have shown a surprisingly high percentage of benign lesions for which organ-sparing surgery could have been considered.¹⁻⁷ We can raise the question whether it is reasonable to consider testis-sparing surgery in small non-palpable and even malignant testicular tumors with adequate localization, complete excision and accurate FSE.

We report our small series of six patients with non-palpable tumors identified by ultrasonography.

Materials and methods

During a 4-year period, non-palpable testicular lesions were discovered sonographically in six patients. The indication for scrotal ultrasonography was: infertility

Accepted for publication March 2006

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in two patients, testicular pain in three patients (two with a previous history of epididymo-orchitis and one with a previous history of testicular trauma) and in one patient, previous seminoma in the contra-lateral testis. Preoperative tumor markers were obtained for all patients. Two patients underwent a standard radical orchiectomy. Two patients underwent testis-sparing surgery with inguinal exploration of the testis and occlusion of the spermatic cord vessels with a tourniquet. The patient with a solitary testes and a previous history of seminoma was offered semen cryopreservation prior to surgery. After adequate ultrasonographic identification, the lesion was sharply excised with 3 mm of normal-appearing tissue around it using 3.5 optical magnification. The lesion was sent for FSE. The testis remained on the ice slush throughout the procedure. Two patients were managed expectedly and the lesions were followed up with serial ultrasound.

Results

Patient age ranged from 26 to 52 (mean age 37). The non-palpable testicular lesion was unilateral in all cases. It was hypoechoic in five patients and heterogeneous in one patient. The size of the lesions varied between 4 mm and 20 mm. Tumor markers were negative in all patients.

Of the six patients, two underwent radical orchiectomy. The pathologic examination revealed a seminoma in one patient and scar tissue in the other one. Two patients underwent testis-sparing surgery. One patient had a 7 mm benign Leydig cell tumor. The other patient had an 8 mm seminoma in a solitary testis. In both cases, microsurgical excision was done with a 3 mm rim of normal tissue surrounding the lesion. Multiple random biopsies of the remaining parenchyma were done. FSE revealed in the first case a benign Leydig cell tumor with negative surgical margins and normal random biopsies. This patient consulted initially for male infertility and 3 months post-op his wife became pregnant. In the second patient FSE revealed an 8 mm seminoma with negative

tumor margins. However the random biopsies revealed intra-tubular germ-cell neoplasia. The patient postponed radiotherapy for paternity reasons. He was followed regularly with periodical ultrasounds every 3 months. Nine months later he developed two recurrences in the lower pole of the testes. Chest x-ray, CT scan of the abdomen and pelvis were normal as well as the tumor markers. He refused a radical orchiectomy and a hemi-orchiectomy was done through an inguinal approach. Pathology revealed seminoma. Tumor margins were positive for intra-tubular germ-cell neoplasia. Radiation therapy was administered to the remaining testes and the retroperitoneal lymph nodes in order to spare him androgen replacement therapy. The patient was recently seen 8 months after completion of radiotherapy. Ultrasound of the testes is normal and he has spontaneous erections without any androgen replacement therapy. In the remaining two patients, a watchful waiting attitude was adopted. One patient with a previous history of testicular trauma and occasional bilateral testicular pain had a 4 mm hypoechoic lesion that remained unchanged over a 30 month period and one patient with a history of epididymo-orchitis 4 weeks before had a heterogeneous testis with two hypoechoic lesions (1.2 mm and 1.5 mm). The lesions were followed by serial ultrasound and 3 months later they were undetectable, Table 1.

Discussion

Due to the increased use of high-resolution trans-scrotal ultrasound for indications other than evaluating palpable tumors it is not surprising that small impalpable lesions are detected unexpectedly. The diffusion of scrotal ultrasonography in urology and andrology has caused an increase in the detection of focal testicular lesions that are not always easy to interpret. Most of these lesions are hypoechoic.^{3,6} Although ultrasonography is extremely effective for detecting an intra testicular mass with 96.6% sensitivity, the ability to differentiate between benign and malignant masses is disappointing at 44.4% specificity.^{8,9}

TABLE 1. Results

Benign lesion	Malignant lesion	Benign process
Radical orchiectomy	Scar tissue (1)	Seminoma (1)
Partial orchiectomy	Benign Leydig cell tumor (1)	Seminoma (1)
Observation		Post- infectious process (1)
		Post-trauma (1)

An incidental lesion is considered asymptomatic and non palpable with negative markers.³ In such cases there is the clinical dilemma of whether always to perform orchiectomy, adopt a more conservative surgical attitude while maintaining an inguinal approach without placing the patient at a higher oncological risk due to insufficient surgical eradication, or adopt a watchful waiting attitude.

Management guidelines for these non-palpable lesions are not well established because literature regarding the histology of these lesions is contradictory. One single series in the literature by Comiter et al¹⁰ has shown that 73% i.e. 11 of 15 non-palpable intra-testicular masses were malignant. However, in this report, the indications for ultrasonography in 7 of the 15 men were to establish the primary site for metastatic peritoneal or visceral masses.

Many other authors have shown that the majority of these lesions are benign. Buckspan et al¹ reported four cases of benign non-palpable Leydig cell tumors. Jarvi et al⁴ found no malignant tumors in three patients with non-palpable testicular lesions who underwent radical orchiectomy. Horstman et al³ noted that 7 of 9 incidental lesions found by ultrasound (78%) were benign neoplasms. In their series of ten patients with non-palpable nodules (diameter 4 mm to 16 mm), Carmignani et al⁶ found a benign lesion in 8 of 10 patients (80%) and two diffuse Leydig cell lesions in the remaining two patients. Sheynkin et al⁷ found a benign lesion in six of eight cases of non-palpable testicular lesions. Corrie et al² reported five cases of non-palpable testicular lesions all benign. Our series of six patients revealed a benign neoplasm in two patients, a benign process in another

two patients and finally a malignant tumor in the last two patients. If we consider the pathologic diagnosis of non-palpable testicular tumors we find that the majorities are benign mainly: Leydig cell lesions, fibrosis, and infarctions or infectious lesions, Table 2.

Organ sparing surgery has been reported by many authors in cases of intra-operatively proven benign non-palpable testicular lesions.^{1-3,5,6,11,12} The surgical approach is well described and includes the following: an inguinal approach, cold ischemia to protect spermatogenesis, precise ultrasound localization of the intra-testicular lesion, accurate FSE of adjacent tissue to confirm complete tumor excision and safe negative margins and finally random peripheral testicular biopsies to exclude intra tubular germ cell neoplasia (ITGCN).

Although intra-operative ultrasound of non palpable testicular lesions has been suggested, it is not routinely used in clinical practice.^{1,3,7,11,12} Hopps and Goldstein¹² followed more recently by Sheynkin et al⁷ reported the ultrasound guided needle localization of intra-testicular tumors and microsurgical tumor excision using an operative microscope with 6X to 25X magnification allowing less parenchymal damage and devascularization.

The role of FSE is essential in organ-sparing surgery. Most of the reports have shown FSE to be highly sensitive and specific in the histological examination of testicular tumors.^{1,5,6,11,13} Only one known report by Hopps and Goldstein¹² found frozen section to be inconclusive in two of four patients; permanent section examination later revealed respectively seminoma and ITGCN. Subsequently both patients underwent radical orchiectomy. Tokuc

TABLE 2. Distribution of non-palpable testicular lesions

Authors	Benign [n]	Malignant [n]	No tissue diagnosis [n]	Total [n]
Comiter et al ¹⁰	4	11		15
Buckspan et al ¹	4	0		4
Jarvi et al ⁴	3	0		3
Horstman et al ³	7	2		9
Carmignani et al ⁶	10	0		10
Sheynkin et al ⁷	6	2	1	9
Corrie et al ²	3	0	2	5
Hopps and Goldstein ¹²	2	2		4
Present study	2	2	2	6
Total	41	19	5	65

et al¹¹ correlated the results of FSE with permanent histological examination of the testes after orchiectomy and reported a correct diagnosis in all 26 cases. Buksan et al¹ found similar results in four patients with non palpable testicular tumor. In a large series, Elert et al¹³ evaluating 354 testicular tumors showed also that FSE can discriminate benign from malignant lesions with 100% accuracy. FSE has been increasingly used in testis sparing surgery.^{6,12} Carmignani et al⁶ reported on focal testicular lesions on ultrasound in 27 of a total of 1320 investigated patients. Seventeen patients had palpable lesions and ten patients had non-palpable lesions. All were surgically explored and they were able to discriminate benign from malignant tumors in all cases. In the first group, 8 of 17 patients (47%) underwent conservative surgery versus 7 of 10 patients (70%) in the latter group.

Our first patient who underwent testes-sparing surgery had a Leydig cell tumor. Leydig cell tumors comprise only 2% to 3% of all testes tumor. They are bilateral in 3% to 9% of cases. Only 10% are malignant.¹⁴ Concerning the criteria of malignancy in Leydig cell tumors of the testis, the study by Chevillet et al¹⁵ demonstrates that large size, morphologic features of tumor necrosis, angiolymphatic invasion, mitotic activity >5/10 high-power fields, atypical mitotic figures, infiltrative growth, invasion beyond the testicle, as well as DNA aneuploidy and increased MIB-1 (Ki-67) activity are predictive of malignancy and metastatic potential. This study confirms the findings of Kim et al¹⁶ in a detailed study of 19 Leydig cell tumors (five malignant cases) with an extensive review of the literature. Of the five malignant tumors in their series, all had four or more of these features, whereas most benign Leydig cell tumors had none.

Testis sparing surgery has been advocated in Leydig cell tumors with no criteria of malignancy, excluding diffuse Leydig cell hyperplasia with positive FSE.⁶ The reported series showed excellent results with no local recurrence.^{3,5,6} However, Wegner et al¹⁴ reported the first and only case in which testis sparing surgery was performed for a Leydig cell tumor and inguinal orchiectomy was subsequently done for local recurrence. This case is significant since the resection margins were tumor-free. This finding might suggest a possible multi-focal development of Leydig cell tumor and serves as a caution to the advocates of testis sparing surgery. Metachronous bilateral tumors have also been reported.¹⁶⁻¹⁸ For these reasons, routine follow up for long periods is recommended. In our opinion, the risk of metachronous contra lateral recurrence militates for a conservative surgery when possible.

Our second case was an 8 mm seminoma in a solitary testis. Testis sparing surgery has only recently become an accepted therapy even for malignant germ cell tumors of the testis in a small subset of carefully selected patients with a solitary testis or bilateral testicular tumors, or a suspected benign lesion.¹⁹ Strict guidelines are to be followed including cold ischemia, organ confined tumor less than 20 mm, multiple biopsies of the tumor bed, adjuvant local irradiation postoperatively to avoid local recurrence, close follow-up and high compliance. Associated ITGCN was diagnosed in 82% of patients¹⁹ for whom local radiation with 18 Gy was recommended. After a median follow-up of 91 months, 98.6% of patients had no evidence of disease. No local relapse occurred in patients with associated ITGCN treated with local radiation. However, local recurrence did develop in four patients who did not undergo radiation; all were cured after inguinal orchiectomy.¹⁹ In our case the patient had ITGCN but decided to postpone radiotherapy which resulted in local recurrence. Therefore postoperative follow-up must be performed closely for early detection of local recurrence in all patients who have not undergone local adjuvant radiation. Of the ten patients who postponed local radiation for paternity reasons, five had successfully fathered a child after organ sparing surgery.¹⁹ In the future, it will be surgically possible to resect small testicular tumors in the presence of a normal contralateral testis without harming the patient.¹⁹ This statement could possibly apply to non-palpable malignant tumors and additional studies with larger numbers of patients and long-term follow-up are warranted to evaluate this approach. In a recent editorial comment, Heidenreich²⁰ suggests that organ-preserving surgery can be safely performed in patients with small lesions that mostly present with a pseudocapsule facilitating tumor enucleation. The long term results after a median follow-up of 72 months and 91 months in benign and malignant testicular tumors respectively, reveal a local recurrence rate of 0% and 12% respectively. Partial orchiectomy could therefore be considered early in the management of testicular masses of uncertain histology. The procedure must be thoroughly discussed with the patient including, in case of malignancy, the limited outcome data, the long-term follow-up, the need for postoperative testicular radiotherapy that may be a problem for men with infertility.

The two remaining cases with a history of trauma and of epidymo-orchitis were treated conservatively without surgery. Concerning the watchful waiting attitude facing a non-palpable testicular lesion

incidentally discovered on ultrasonography, Corrie et al² support conservative management, including surveillance sonography. If the lesion remains stable or enlarges, inguinal exploration with frozen section is recommended. However this study concerns only five cases, two patients had a Leydig cell tumor, another two patients presented with suspected infectious processes, of which only one underwent orchiectomy, which revealed an orchitis and the other man was followed with repeat ultrasound and the lesion resolved spontaneously. In the remaining patient with a history of recent trauma the lesion resolved on surveillance studies. In the group of non-palpable nodules (diameter 4 mm to 16 mm) reported by Carmignani et al,⁶ seven of the ten patients (70%) with negative FSE underwent conservative surgery. The definite histological report showed focal Leydig cell hyperplasia in one patient (10%), fibrosis in three (30%), infarction in two (20%) and mesothelial hyperplasia in one (10%). The five patients with fibrosis and infarction could have been followed with serial ultrasound and possibly have been spared even conservative surgery. However we continue to believe that an active watchful waiting attitude with rigorous follow up and early intervention should be adopted only when a history of trauma or an infection process is suspected. Magnetic resonance imaging (MRI) might be of further assistance to differentiate malignant from inflammatory lesions.²⁰

Conclusion

Non-palpable lesions of the testes incidentally discovered by ultrasound are frequently benign. They should be explored through an inguinal incision unless there is a history of trauma or infection in which case they can be followed by serial ultrasound or by MRI.

In Leydig cell tumors, a conservative surgical approach is warranted when the lesion is benign according to well-defined pathologic criteria and negative tumor margins. Regular follow up is recommended considering the hypothetical risk of local recurrence or even metachronous tumor recurrence in the contra-lateral testes.

In case of a malignant tumor, radical orchiectomy is still the standard therapy. Testis-sparing surgery is considered in cases of a solitary testis or bilateral malignant tumors. It should also be considered early in the management of non-palpable testicular masses of uncertain histology after detailed counseling regarding the possible outcome, strict follow-up and or the need for postoperative testicular radiotherapy in case of malignancy. □

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