Eur Radiol
DOI 10.1007/s00330-012-2520-4

UROGENITAL

Testicular microlithiasis: is there a need for surveillance in the absence of other risk factors?

Jonathan Richenberg · Nick Brejt

Received: 8 December 2011 / Revised: 15 April 2012 / Accepted: 25 April 2012

Abstract
Objective Ultrasound surveillance of patients with testicular microlithiasis (TM) has been advocated following the reported association with testicular cancer. The aim of this study was to assess the evidence base supporting such surveillance.
Methods Formal literature review identified cohort studies comprising at least 15 patients followed up for at least 24 months. Combining an institutional audit with the identified studies in a pooled analysis the incidence of new cancers during the surveillance period was evaluated.
Results Literature review identified eight studies. Our institutional audit comprised 2,656 men referred for scrotal ultrasound. Fifty-one men (1.92 %) with TM were identified, none of whom developed testicular cancer (mean follow-up: 33.3 months). In a combined population of 389 men testicular cancer developed in 4. Excluding 3 who had additional risk factors, only 1 of 386 developed testicular cancer during follow-up (95 % CI 0.05–1.45 %).
Conclusions Ultrasound surveillance is unlikely to benefit patients with TM in the absence of other risk factors. In the presence of additional risk factors (previous testicular cancer, a history of maldescent or testicular atrophy) patients are likely to be under surveillance; nonetheless monthly self-examination should be encouraged, and open access to ultrasound and formal annual surveillance should be offered.

J. Richenberg (✉) · N. Brejt
Department of Radiology,
Brighton and Sussex University Hospitals NHS Trust,
Eastern Road,
Brighton BN2 5BE, UK
e-mail: Jonathan.Richenberg@bsuh.nhs.uk

J. Richenberg
Honorary Senior Lecturer,
Brighton & Sussex Medical School,
Brighton, UK

Published online: 19 June 2012

Key Points
- *The literature reports a high association between testicular microlithiasis and testicular cancer.*
- *Our study and meta-analysis suggest no causal link between microlithiasis and cancer.*
- *In the absence of additional risk factors surveillance is not advocated.*
- *In the presence of additional risk factors surveillance is recommended.*
- *Such surveillance is primarily aimed at engaging patients in regular follow-up.*

Keywords Testis · Testicular · Lithiasis · Microlithiasis · Testicular microlithiasis

Introduction

Testicular microlithiasis (TM) is a condition in which calcium deposits form in the lumina of seminiferous tubules [1–3] or arise from the tubular basement membrane components [4]. These deposits have a characteristic appearance using high-resolution ultrasound and are seen as multiple, speckled echogenic foci within the substance of the testis [5]. The calcifications usually affect both testes, but may be unilateral, and can be focal or diffuse.

The generally accepted definition of TM is the presence of five or more small echogenic foci within the testis measuring 1–3 mm in diameter [6, 7]. The prevalence of TM (amongst symptomatic men) has been quoted as being between 0.6 % to 9 % [2].

The incentive for investigating TM is the reportedly high association with testicular cancer, with co-occurrence rates of TM and germ cell tumours (GCT) reported to be from 6 % up to a striking 46 % [8]. This co-occurrence is based on a series

of retrospective studies from the late 1990s and early 2000 [9–13]. Miller and Sidhu reviewed previously published studies, quoting a range of prevalence of primary testicular tumours in patients with TM from 15 % to 45 % [14].

The high co-occurrence raised the profile of this new diagnosis, a diagnosis 'exclusive' to ultrasound. Recommendations followed that TM might be a pre-malignant condition justifying close scrutiny. Based on these observations, ultrasound surveillance of TM cases for tumour was endorsed by various centres [15, 16]. However, the evidence base supporting this intervention is questionable. Recommendations flowed from case reports and retrospective studies [2, 7, 13, 16–20] with their inherent limitations, blurring the undoubted association of TM with testicular cancer into a causal link. Moreover, multivariate analysis of the studies has been confounded by inconsistency in the definition of TM and inadequate documentation of confounding risk factors.

Nevertheless, in January 2000, our institution decided to instigate an annual surveillance programme for patients with TM with the intention of auditing the detection rate over a 5-year period. The aim of this study was to assess the evidence-base supporting continuation of the surveillance programme by undertaking a pooled analysis that combined the data from the audit with the results of similar studies identified by a formal literature review.

Materials and methods

Consent and ethics

As the study was not prospective clinical research but an audit of an ongoing clinical service combined with a literature review, following an interview with the chair of the institutional ethics committee, formal ethics committee review was deemed unnecessary.

Patient consent was obtained at the time of the initial ultrasound.

All patients entering the surveillance programme were given an information leaflet about TM, taught monthly self examination and offered regular ultrasound review with open access to ultrasound imaging whenever they felt it necessary.

Institutional audit

A prospective clinical decision was made to offer surveillance to men diagnosed with TM because of the reported co-occurrence with testicular cancer [16, 20]. The intention was to monitor interval development of cancers over a 5-year period between January 2000 and December 2005. The surveillance population comprised men undergoing scrotal ultrasound in the catchment area (population 1.2 million).

All staff performing scrotal ultrasound were primed to look for TM, defined as five or more microcalcifications within the body of a testis. Each patient diagnosed with TM on presenting ultrasound underwent re-imaging by a consultant uroradiologist. All surveillance imaging was performed using a 7.5-MHz linear transducer (ALOKA Holding Europe AG SSD2000 ultrasound platform).

At entry in to the surveillance programme, the extent of the microcalcification was graded.

The grading system was based on the number of microliths per testis.

- Grade 1: 5–10 microliths
- Grade 2: 11–20 microliths
- Grade 3: 21–30 microliths
- Grade 4: more than 30 microliths

The patients were subsequently annually followed up by a single radiologist.

In patients with a past history of testicular cancer, follow-up ultrasound was performed 6-monthly with an annual urology outpatient review.

The data recorded included: age, number of ultrasounds performed per patient, time period over which the imaging was performed (in months), indication for the original ultrasound and any previous history of testicular cancer.

The results recorded were: presenting TM grade, unilateral or bilateral TM, adjunctive pathological features detected, change in grade on follow-up and the development of testicular cancer.

Literature search method

The authors and a superintendent university librarian independently performed a computer-assisted literature search of medical databases: MEDLINE (January 1951 to date) and EMBASE (January 1974 to date). The search parameters are summarised in Table 1.

All the references were imported into Reference Manager Professional Edition Version 10© *ISI researchsoft* and each study reviewed. The literature search was restricted to the English language and studies including patients with and without additional risk factors were included.

Articles that fulfilled the following inclusion criteria were retained: cohort size of 15 or more, a cohort of 15 was deemed the minimum number from which a valid conclusion might be drawn minimising statistical noise; median follow-up of 2 or more years; case reports and review articles were excluded; articles concerned solely with a paediatric population and articles looking at the association between TM and infertility, in which testicular cancer was not addressed, were not included.

The identified studies were included in a pooled analysis evaluating, over the combined population, those who developed

Table 1 Literature search parameters

Search parameter	MEDLINE	EMBASE
Keyword	TM *or* lithiasis *or* microlithiasis *or* microcalcification	TM *or* microlithiasis *or* lithiasis *or* microcalcification
And keyword	Testicular *or* testic$4 *or* testis	Testic$4 *or* testis
And keyword	Adult *or* adult (age group)	Adult *or* adult (age group)
Mesh	Lithiasis	Testis disease
	Testicular diseases	
	Testis	

a new testicular cancer whilst under surveillance. Co-existent risk factors (atrophy, previous testicular cancer and orchidopexy) were considered. The incidence of new cancers together with 95 % confidence intervals was determined for all studies.

Results

Institutional audit

A total of 2,656 patients underwent scrotal ultrasound, of whom 57 had TM diagnosed at initial ultrasound. All 57 agreed to participate in the surveillance programme and subsequently underwent imaging by a consultant uroradiologist. Fifty-one satisfied the definition of TM giving a prevalence of 1.92 %. Their age range at presentation was 15 to 83 years (median 41 years). The number of follow-up ultrasounds performed on each patient ranged from 1 to 8 (median 3.33). Patients were followed up between 12 and 72 months (median 33.29 months) until December 2005. None had testicular cancer at presentation (95 % CI 0–7 %).

The indications for the original ultrasound were ‘mass in testis’ (17/51; 33 %), ‘tender testis’ (23/51; 45 %), ‘infertility’ (2/51; 4 %) and ‘scrotal mass’ (including epididymal mass: 9/51, 18 %). Four of the patients had previously undergone an orchidectomy for a malignant testicular tumour. One patient had bilateral testicular atrophy. The ultrasound findings in the remainder are revealed in Fig. 1.

Table 2 summarises the distribution and extent of the TM.

During follow-up no testicular cancer developed (incidence 0 %, 95 % CI 0–7 %).Fifty out of 51 patients had no change. One patient increased in grade from 3 to 4.

Literature review

From our literature search, 144 references were identified. Of these, 128 were excluded. Reasons for exclusion are summarised in Table 3.

Sixteen articles [6, 8, 12, 13, 16, 21–31], in predominantly adult populations, were concerned in whole or in part with the natural history of TM, exploring the occurrence of GCT in patients with TM.

Excluding studies with cohorts of less than 15 patients, or in which follow-up was less than 24 months or not specified, 9 papers comprised the kernel of the analysis [6, 8, 12, 13, 16, 21–24]. In one paper [22], a retrospective audit of 4,529 patients with a mean follow-up of 33.9 months of 29 patients with TM, two interval testicular cancers developed. It is unclear whether in these two patients coexisting risk factors for the development of testicular cancer existed and as such they were excluded from the main bulk of our pooled analysis.

Pooled analysis

Incorporating our study, a total of 389 patients were included in the pooled analysis. Four patients (1 %; 95 % CI 0.4–2.6 %) developed interval testicular cancer during follow-up. Of these four patients, three had coexisting risk factors (one atrophied testis; two with previous GCT). Excluding these patients from the final analysis, one patient in 386 with TM and no coexisting risk factors developed cancer during follow-up (0.26 %; 95 % CI 0.05–1.45 %) .

The cohort size, follow-up interval, mean age, prevalence of TM, cancer at outset and 95 % confidence intervals are summarised in Table 4.

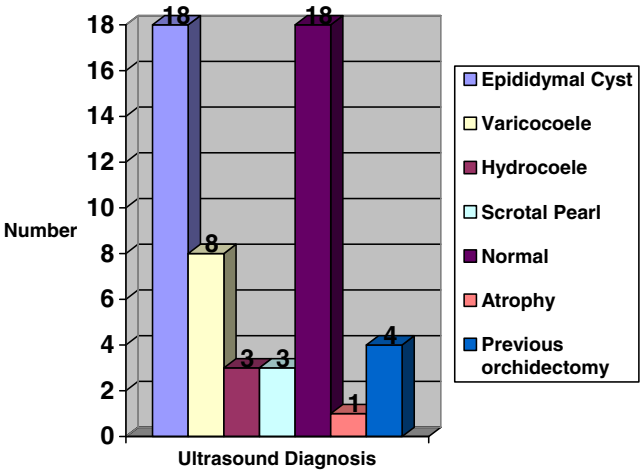

Fig. 1 Ultrasound diagnosis in patients with testicular microlithiasis (some patients had two pathological conditions)

Table 2 Distribution and extent of testicular microlithiasis

	Grade 1	Grade 2	Grade 3	Grade 4	Total (average)
Unilateral	12	2	2	0	16/51 (31 %)
Bilateral	12	7	2	14	35/51 (69 %)
Total (percentage)	24/51 (47 %)	9/51 (18 %)	4/51 (8 %)	14/51 (27 %)	51

Discussion

The finding of a 0.26 % (95 % CI 0.05–1.45 %) rate of interval cancer from the pooled analysis suggests that surveillance is unlikely to be of benefit for patients without coexistent risk factors. This stark conclusion pertains to a study population that is comparable to others, e.g. 1.92 % prevalence of TM. The prevalence of TM in *symptomatic* patients has been quoted with variation between 0.6 % to 9 % [2, 9, 13, 14, 16, 26]. However the 9 % prevalence was in a patient group referred to a tertiary cancer care centre and reflects its referral pattern [9]. More usually the figure quoted is between 1.5 % and 2.3 % [13, 26].

Two papers looked at *asymptomatic* men. A study of 2,179 Turkish male army recruits (17–42 years old, mean age 24) reports a prevalence of 2.4 % [29].

In an American population of 1,504 asymptomatic men aged between 18 and 35, the prevalence of TM has been recorded as 5.6 %. Paradoxically there was a disproportionately higher prevalence of TM in black men compared with other races (14.1 % in blacks, 8.5 % incidence in Hispanics, 5.6 % in Asians and 4 % in whites). This calls into question the association of TM with testicular cancer because the incidence of testicular cancer in black men is significantly lower than in other racial groups at 0.9/100,000 versus 5/100,000 per annum [32].

Critique of evidence base inferring a causal link between TM and GCT

The evidence base used to predict the risk of developing a testicular malignancy in a testicle with concurrent TM comprises three categories.

These are:

- Sporadic case reports
- Series—no interval cancer
- Series—interval cancer documented in men with and without other risk factors

Table 3 Reason for exclusion of references from meta-analysis

Reason for exclusion	Number
Association of TM with GCT not explored	55
Review articles	23
Case reports and letters	22
Exclusively paediatric population	14
Other, not TM	14
	128

Case reports

These are very biased as they under-represent most patients with TM who do not develop cancer. They constitute low-level evidence and as such are not considered.

Series of men with TM in which testicular cancer does not develop

There are five surveillance studies comprising at least 15 patients in which no patient with TM developed cancer [6, 13, 16, 21, 24]; these resonate with our patient population.

In our study group, contrary to the reported high co-incidence, none of the patients discovered with TM had testicular cancer at presentation. However, four (8 %) had undergone orchidectomy for a testicular malignancy and these four patients could be said to have had TM at the time of their initial cancer presentation. This would suggest a co-incidence of TM and GCT of 8 % in our cohort. The study groups under these circumstances could be accepted as being biologically comparable.

Bennett et al. [6] followed up 72 patients (mean 45 months, range 12–90 months). Of these 72 patients, 2 progressed with regard to the extent of microcalcification; however none showed interval cancer development.

Ou et al. [24] identified 150 patients with TM; 48 were followed up (mean 29.3 months, range 3–74 months). No interval cancers were detected and only one patient progressed with regards to the extent of microcalcification.

Similarly Pourbagher et al. [21] followed-up 36 patients, none of whom developed interval cancer (median 34 months, range 1–96 months); Ganem et al. [16] followed up 22 patients, 9 with ultrasound (mean 32 months , range 1–96 months) and 13 clinically (mean 31 months, range 1–108 months), none of whom developed interval cancers.

Series of men with TM in which testicular cancer develops

Three studies satisfying the inclusion criteria are considered here [8, 12, 23].

In a 5-year study DeCastro et al. followed up 63 out of 84 asymptomatic army volunteers with TM [23]; 1,504 men were

Table 4 Summary of testicular microlithiasis cohort studies

Publication	Date	Population size	Cohort size	Mean age (years)	Median follow-up (months)	Prevalence TM in population	Cancer at outset	New cancers	95 % CI range	Notes
[16]	1999	1,100	22	29 (8–63)	See notes	22 of 1,100 (2.2 %)	8 of 22 (36 %)	0	0 to 14.9 %	Follow up (mean): US: 32(1–96), clinical: 31(1–108)
[13]	2000	2,215	27	34* (23–78)	41 months (19–54)	34 of 2,215 (1.4 %)	5 of 34 (15 %)	0	0 to 12.5 %	
[12]	2001	3,026	39	34* (12–83)	36 (12–81)	54 of 3,026 (1.8 %)	16 of 54 (30 %)	2 (5.1 %)	1.4 to 16.9 %	New cancers: 1, ectopic testis & 1 history of GCT, history of GCT
[8]	2001	1,535	31	39.2 (16–69)	61.8 (16–105)	63 of 1,535 (4.1 %)	29 of 63 (46 %)	1 (3.2 %)	0.6 to 16.2 %	
[6]	2001	Unknown	72	39.5 (15–75)	45** (12–90)	104 in unknown population	8 of 104 (7.7 %)	0	0 to 5 %	104 with TM, 31: classic TM 41-limited TM 4
[21]	2005	5,263	36	31 (1–61)	34 (1–96)	40 of 5,263 (0.76 %)	4 of 40 (10 %)	0	0 to 9.6 %	of 40 excluded as presented
[24]	2007	1,978	48	30 (1–85)	29.3** (3–74)	150 of 1,978 (7.6 %) 84 CTM 66 LTM	9 of 150 (6 %)	0	0 to 7.4 %	with cancer, 48 with TM, 32-classic TM 16- limited TM
[23]	2008	1,504	63	(18–35)	60	84 of 1,504 (5.6 %)	0 of 84	1 (1.6 %)	0.3 to 8.5 %	No risk factors in patients with new cancer, 4 previous GCT, 1 atrophy
This study	2005	2,656	51	41*	33.3 (12–72)	51 of 2,656 (1.9 %)	0 (0 %) of 51	0	0 to 7 %	
All studies above	————		389				79 of 602 (13 %)	4 (1 %)	0.4 to 2.6 %	
[22]	2007	4,259	29	42.6 (17–82)	33.9** (3–72)	32 of 4,259 (0.75 %)	3 of 32 (9.4 %)	2 of 29	1.9 to 2.2 %	No risk factors documented

*Median

**Mean

screened and 84 cases of TM detected (5.6 % prevalence). Two-year follow-up of 63 of the 84 cases showed none had developed testicular cancer. At 5-year follow-up one man had developed a GCT 64 months after initial screening, implying a significantly increased risk of developing testicular cancer (1.6 %) compared with the general population.

The sample size and solitary case call into question the statistical validity of extrapolating widely. The authors themselves note that despite this increased risk, testicular cancer would not develop in most men with TM. In any case, the index tumour was serendipitously detected on ultrasound following concern raised by a spermatocele detected on self-examination.

In the second study, 3,026 men were enrolled, 54 having TM (1.8 % prevalence) [12]. Thirty-nine had bilateral TM, of which 9 (23 %) had testicular cancer at presentation. The bilateral TM group was followed up for a median of 36 months. Two patients (5.2 %) developed interval testicular cancer: one had presented with an atrophic testis and developed a seminoma; the other had metastatic embryonal cell carcinoma at initial diagnosis and was found to have seminoma 4 years later. In other words, both men had coexisting risk factors justifying surveillance regardless of TM. Moreover, of the men with no coexistent risk factors, no testicular cancer developed during surveillance.

In the third cohort of 31 patients, one patient developed a combined teratoma and seminoma in his right testis 35 months after TM was diagnosed [8]. This patient had been cryptorchid for both testes and had been treated with an orchidectomy and chemotherapy for a prior embryonal carcinoma in his left testis. This was a high-risk patient in a population with a high TM prevalence of 4.1 % (63/1533) and a very high co-incidence of TM and GCT at presentation (46 % of those with TM).

In the retrospective study of 4,259 men by Ahmad et al. [22], mentioned in the results section, 32 men had TM, of which 3 had tumour at presentation. During the follow-up of 29 men with TM (mean 33.9 months, median 40 months), 2 developed a tumour. Crucially, the paper does not elaborate on these two cases and does not identify any possible risk factors. Interestingly, the authors conclude that ultrasound and tumour marker follow-up become financially prohibitive and advocate regular self-examination in following up these patients.

One further series reporting interval development of GCT merits discussion: a retrospective analysis of scrotal ultrasound performed in 1,399 infertile men and 219 normally fertile men [26]. Of the 14 men with TM followed up by ultrasound, testicular tumours developed in 2 patients. In both cases, the testes were reduced in volume. The authors concluded that diagnosis of TM, if present in an atrophic testis, demands a diagnostic biopsy or at least ultrasound follow-up.

Combining the total number of cases in the literature search with our study, confidence intervals can be gauged. The statistical parameters are summarised in Table 4. If all 389 men eligible for inclusion are considered, including patients with coexistent risk factors, 1 % (4 out of 389) developed cancer during follow-up (CI 0.4 to 2.6 %). If selection is refined to exclude the three with risk factors, there is only one documented case of interval malignancy amongst the 386 men (CI 0.05 to 1.45 %). This gives an indication of the likelihood of a man with TM developing a testicular tumour if there are no other risk factors being at worst 1 in 100.

Limitations of the analysis

A pooled analysis has its inherent limitations. Through pooling data the analysis lacks the power of a single randomised trial. Secondly individual study characteristics are ignored, and heterogeneity of study populations and study design can lead to questioning the validity of the analysis.

In the referenced studies, patient populations are generally small, with most comprising symptomatic patients. A significant limitation is the length of follow-up. Given that 50 % of intratubular germ cell neoplasias take 5 years to progress to malignancy [33, 34], only one study had a median follow-up of 60 months [23], detecting the one case of interval cancer at 64 months.

Despite our audit being one of the largest cohort groups, it is nonetheless limited by small patient numbers comprised of symptomatic patients. A further limitation is the short median length of follow-up of 33.3 months; we are, however in the process of a 7-year postal follow-up survey aiming to address this limitation.

A large prospective study, inclusive of a control group, following up an asymptomatic population with TM for a median of 5 years would help reinforce our findings.

In summary, the evidence suggests that TM and GCT of the testis may be caused by a common defect, probably tubular degeneration. It follows that there is an increased association of GCT in men with TM. However the natural history seems that the development of cancer in TM patients is infrequent and thus TM can be considered a marker of, *not* a predisposing risk for, tubular degeneration. Miller and Sidhu made similar observations: the high prevalence of TM in testicular cancer predicts neither the future development of GCT nor whether TM predisposes to development of GCT [14].

Furthermore an overwhelming body of evidence shows that TM indicates premalignant changes only in those men with additional risk factors for germ cell cancer, such as previous testicular cancer, a history of testicular maldescent or the presence of an atrophic testis [26, 35–38].

Doubt also exists whether chance detection of a subclinical mass on annual screening ultrasound confers any survival advantage over early clinical detection achieved by regular self-examination [39].

We therefore advocate that all patients are well informed and educated to practice regular self-examination of the testes. No surveillance is warranted in men found to have TM alone. However for men with TM and coexistent risk factors annual surveillance is advised together with open access to scrotal ultrasound.

The aim of the annual surveillance not being the detection of subclinical masses but maintaining patient's engagement with the process as indefinite self-examination without intermittent contact with medical care is likely to fail.

Acknowledgements A thank you to Prof. Ken Miles, who was involved and provided advice in the early stages of this document.

References

1. De Jong BW, De Gouveia Brazao CA, Stoop H et al (2004) Raman spectroscopic analysis identifies testicular microlithiasis as intratubular hydroxyapatite. J Urol 171:92–96
2. Kim B, Winter TC, Ryu JA (2003) Testicular microlithiasis: Clinical significance and review of the literature. Eur Radiol 13:2567–2576
3. Renshaw AA (1998) Testicular calcifications: Incidence, histology and proposed pathological criteria for testicular microlithiasis. J Urol 160:1625–1628
4. Drut R, Monica R (2002) Testicular microlithiasis: Histologic and immunohistochemical findings in 11 pediatric cases. Pediatr Dev Pathol 5:544–550
5. Howlett DC, Marchbank ND, Sallomi DF (2000) Pictorial review. Ultrasound of the testis. Clin Radiol 55:595–601
6. Bennett HF, Middleton WD, Bullock AO, Teefey SA (2001) Testicular microlithiasis: US follow-up. Radiology 218:359–363
7. Backus ML, Mack LA, Middleton WD, King BF, Winter TC 3rd, True LD (1994) Testicular microlithiasis: Imaging appearances and pathologic correlation. Radiology 192:781–785
8. Derogee M, Bevers RF, Prins HJ, Jonges TG, Elbers FH, Boon TA (2001) Testicular microlithiasis, a premalignant condition: Prevalence, histopathologic findings, and relation to testicular tumor. Urology 57:1133–1137
9. Bach AM, Hann LE, Hadar O et al (2001) Testicular microlithiasis: What is its association with testicular cancer? Radiology 220:70–75
10. Byrne A, Al-Agha G, Torreggiani WC, et al (2003) Does testicular microlithiasis matter? (multiple letters). Clinical Radiology 58
11. Middleton WD, Teefey SA, Santillan CS (2002) Testicular microlithiasis: Prospective analysis of prevalence and associated tumor. Radiology 224:425–428
12. Otite U, Webb JAW, Oliver RTD, Badenoch DF, Nargund VH (2001) Testicular microlithiasis: Is it a benign condition with malignant potential? Eur Urol 40:538–542
13. Skyrme RJ, Fenn NJ, Jones AR, Bowsher WG (2000) Testicular microlithiasis in a UK population: Its incidence, associations and follow-up. BJU Int 86:482–485
14. Miller FN, Sidhu PS (2002) Does testicular microlithiasis matter? A review. Clin Radiol 57:883–890
15. Cast JEI, Nelson WM, Early AS et al (2000) Testicular microlithiasis: Prevalence and tumor risk in a population referred for scrotal sonography. Am J Roentgenol 175:1703–1706
16. Ganem JP, Workman KR, Shaban SF (1999) Testicular microlithiasis is associated with testicular pathology. Urology 53:209–213
17. Leenen AS, Riebel TW (2002) Testicular microlithiasis in children: Sonographic features and clinical implications. Pediatr Radiol 32:575–579
18. Berger A, Brabrand K (1998) Testicular microlithiasis—a possibly premalignant condition. Report of five cases and a review of the literature. Acta Radiol 39:583–586
19. Ihara H, Maruyama T, Kondo N, Shima H, Uematsu K (2003) Testicular microlithiasis: report of 14 cases. Hinyokika Kiyo 49:575–578
20. Miller RL, Wissman R, White S, Ragosin R (1996) Testicular microlithiasis: a benign condition with a malignant association. J Clin Ultrasound 24:197–202
21. Pourbagher MA, Kilinc F, Guvel S, Pourbagher A, Egilmez T, Ozkardes H (2005) Follow-up of testicular microlithiasis for subsequent testicular cancer development. Urol Int 74:108–112
22. Ahmad I, Krishna NS, Clark R, Nairn R, Al-Saffar N (2007) Testicular microlithiasis: Prevalence and risk of concurrent and interval development of testicular tumor in a referred population. Int Urol Nephrol 39:1177–1181
23. DeCastro BJ, Peterson AC, Costabile RA (2008) A 5-year followup study of asymptomatic men with testicular microlithiasis. J Urol 179:1420–1423
24. Ou SM, Lee SS, Tang SH et al (2007) Testicular microlithiasis in Taiwanese men. Arch Androl 53:339–344
25. Sakamoto H, Shichizyou T, Saito K et al (2006) Testicular microlithiasis identified ultrasonographically in Japanese adult patients: Prevalence and associated conditions. Urology 68:636–641
26. Von Eckardstein S, Tsakmakidis G, Kamischke A, Rolf C, Nieschlag E (2001) Sonographic testicular microlithiasis as an indicator of premalignant conditions in normal and infertile men. J Androl 22:818–824
27. Kosan M, Gonulalan U, Ugurlu O, Oztekin V, Akdemir O, Adsan O (2007) Testicular microlithiasis in patients with scrotal symptoms and its relationship to testicular tumors. Urology 70:1184–1186
28. Lam DL, Gerscovich EO, Kuo MC, McGahan JP (2007) Testicular microlithiasis: Our experience of 10 years. J Ultrasound Med 26:867–873
29. Serter S, Gumus B, Unlu M et al (2006) Prevalence of testicular microlithiasis in an asymptomatic population. Scand J Urol Nephrol 40:212–214
30. Hobarth K, Susani M, Szabo N, Kratzik C (1992) Incidence of testicular microlithiasis. Urology 40:464–467
31. Janzen DL, Mathieson JR, Marsh JI et al (1992) Testicular microlithiasis: Sonographic and clinical features. AJR 158:1057–1060
32. Peterson AC, Bauman JM, Light DE, McMann LP, Costabile RA (2001) The prevalence of testicular microlithiasis in an asymptomatic population of men 18 to 35 years old. J Urol 166:2061–2064
33. von der Maase H, Rorth M, Walbom-Jorgensen S et al (1986) Carcinoma in situ of contralateral testis in patients with testicular germ cell cancer: Study of 27 cases in 500 patients. Br Med J (Clin Res Ed) 293:1398–1401
34. Skakkebaek NE, Berthelsen JG, Muller J (1982) Carcinoma-in-situ of the undescended testis. Urol Clin North Am 9:377–385
35. Guzman Martinez-Valls PL, Hita VG, Fernandez AT, Minana LB, Martinez DF, Sanchez GF (2003) Significance and management of testicular microlithiasis. Arch Esp Urol 56:472–477
36. Nistal M, Paniagua R, Diez-Pardo JA (1979) Testicular microlithiasis in 2 children with bilateral cryptorchidism. J Urol 121:535–537
37. Patel MD, Olcott EW, Kerschmann RL, Callen PW, Gooding GA (1993) Sonographically detected testicular microlithiasis and testicular carcinoma. J Clin Ultrasound 21:447–452
38. Bieger RC, Passarge E, McAdams AJ (1965) Testicular intratubular bodies. J Clin Endocrinol Metab 25:1340–1346
39. Rashid HH, Cos LR, Weinberg E, Messing EM (2004) Testicular microlithiasis: A review and its association with testicular cancer. Urol Oncol: Semin Orig Inv 22:285–289