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Leiden
The Netherlands

Testicular microlithiasis and undescended testis

Goede, J.

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Chapter 2.2

Prevalence of testicular microlithiasis in asymptomatic population males aged 0-19 years

J Goede
WWM Hack
LM van der Voort-Doedens
K Sijtermans
FH Pierik

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Abstract

Purpose

We assessed the prevalence of testicular microlithiasis via ultrasound in asymptomatic males 0 to 19 years old.

Materials and methods

We studied only patients with two scrotal testes at birth and at examination. We excluded boys with a history of undescended testis, hydrocele, varicocele or syndromes associated with testicular microlithiasis. To assess for testicular microlithiasis, we scanned the scrotum ultrasonographically by recording transverse and longitudinal images of each testis. Classical testicular microlithiasis was defined as 5 or more echogenic foci in either or both testes. Boys with fewer than 5 microliths (but with at least 1) were deemed to have limited testicular microlithiasis.

Results

We examined 694 asymptomatic boys between October 2007 and July 2008, of whom 670 participated in the study. Classical testicular microlithiasis was present in 16 boys (2.4 %) and limited testicular microlithiasis in 12 (1.8 %), yielding a total prevalence of 4.2 %. Classical testicular microlithiasis was found in 1 boy younger than 6 years, 8 boys 6 to 12 years old and 7 boys older than 12. There was a significant difference in prevalence among the 3 age groups ($p = 0.032$). Testicular malignancies were not found in any patient. In the 24 boys excluded from the study testicular microlithiasis was seen in 4.

Conclusion

The prevalence of classical testicular microlithiasis in asymptomatic boys is 2.4 % and increases with age.

Introduction

Testicular microlithiasis (TM) is characterised by multiple echogenic foci (< 3 mm) without acoustic shadowing within the testis parenchyma. The presence of 5 or more foci is defined as classical testicular microlithiasis, while the presence of fewer than 5 microliths meets the criteria for limited testicular microlithiasis.¹ In adults testicular microlithiasis is presumably related to testicular malignancies and infertility, while reports of associated testicular tumors in children are scant.² The prevalence of classical testicular microlithiasis is reportedly 0.6 to 9% in symptomatic adults and 2.4 to 5.6% in asymptomatic populations.³⁻⁶ The prevalence of TM varies among ethnical groups and is generally increased in blacks.⁵

In boys several benign conditions, including cryptorchidism, Down syndrome, varicocele and Klinefelter syndrome are associated with TM,⁷ which may indicate that TM is a predictor of future testicular disorders. However, this association is difficult to assess, since the prevalence of TM in asymptomatic boys has not yet been established. One recent study revealed a 1.9% prevalence of CTM in symptomatic boys.⁸ We prospectively studied asymptomatic males ultrasonographically from birth to adolescence to determine the prevalence of TM.

Materials and methods

Study design

Boys were recruited from the general population surrounding the Medical Centre Alkmaar. Patients were part of a cohort that was constructed to obtain normative values for testicular volume measured by ultrasound in a general population. To invite participation in the study, an information letter was sent to 2,600 boys and their parents (100-200 letters for each year of age) randomly selected from the records of the Youth Health Care Institutions of the Gemeenschappelijke Gezondheidsdienst Hollands-Noorden en Eeven-Gezondheidszorg. Several media were used to invite boys to participate in the study, including regional newspapers and a local radio and television station. A local secondary school also participated in the recruitment. The letter stated that only boys with 2 scrotal testes and no known scrotal pathologies could participate. The study is part of a trial for obtaining normative values for testicular volume measured by ultrasound, and was approved by the ethical committee of the hospital (reference number: M06-056).

Inclusion and exclusion criteria

Healthy boys with 2 scrotal testes at birth and at examination were included in the study. Boys with retractile testis were also included.

Boys with UDT at physical examination or at birth were excluded, as were boys who suffered from syndromes or other conditions possibly associated with TM.⁷ Patients with hydrocele and varicocele at examination were also excluded.

Definitions

TM was defined as classical if 5 or more echogenic foci 1 to 3 mm in diameter were present in either or both testes.⁹ Patients who had at least 1 microlith but did not meet the criteria for CTM were considered to have LTM. CTM grade I was defined as presence of 5 to 10 microliths; grade II, 10 to 20 microliths; and grade III, more than 20 microliths.

Study protocol

At the pediatric outpatient clinic a questionnaire was used that included the items medical problems, medication, major surgery, prior groin surgery, gestational age, birth weight and ethnicity. Ethnical background was divided into white, Turkish, North-African, Asian or black. Adenotonsillectomy, middle ear drainage and acquisition method regarding study enrolment were not taken into account.

Examination of the left-sided testis was performed first, followed by the right-sided testis, with the patient in the supine and crossed-legged position. Testis position was classified as low scrotal, high scrotal, inguinal or absent and was categorized as descended, retractile or undescended.

To assess for TM, the scanner was placed on the scrotum, and transverse and longitudinal images of each testis were recorded. We documented the testicle involved, the number of calcifications and whether calcifications were focal or diffuse. Color Doppler ultrasound of the testis was not performed.

All 694 scans were performed by the same physician (JG) with the same equipment (Falco Auto Image, Tomsk, Russia, and 12 MHz linear array transducer).

If TM was diagnosed, boys were referred to our outpatient clinic. All patients underwent a full physical examination. Scrotal US examination was repeated to confirm the diagnosis of TM. No further investigations were performed if physical examination and US demonstrated no indications for testicular malignancy. Brothers of patients diagnosed with TM were also requested for scrotal ultrasound.

Statistics

Chi-square tests were performed to compare gestational age/birth weight, groin surgery and other medical problems in boys with and without LTM and CTM. Chi-square tests

were also used to compare the frequency of CTM in different age groups. A p value below 0.05 was considered significant.

Results

A total of 670 asymptomatic boys with a median age of 8.6 years (range 0.2 to 18.9) were included in the study. Testicular microlithiasis was present in 28 boys with a median age of 10.6 years (range 4.6 to 17.6 years), yielding a prevalence of 4.2 %. CTM was seen in 16 boys (2.4 %) with a median age of 11.7 years (range 5.5 to 17.6), and LTM in 12 boys (1.8 %) with a median age of 8.6 years (4.6 to 13.0).

Patients were grouped according to age in 3-year (table 1) and 5-year (table 2) increments. There was a statistically significant difference in the prevalence of CTM between the age groups when divided by 5-year increments ($p = 0.032$). Table 3 lists the distribution of TM with respect to the number of testicles and side involved. Images representative of CTM and LTM in our series are shown in the figure.

Table 1

Prevalence of classical and limited testicular microlithiasis by age (2 to 3-year increments).

Pt Age (yrs)	No. Pts	No. CTM	No. LTM
0-2	99	0	1
3-5	115	1	2
6-8	138	2	3
9-11	142	6	3
12-14	107	4	3
15-17	62	3	0
18-19	7	0	0
Totals	670	16	12

Table 2

Prevalence of classical and limited testicular microlithiasis by age.

Pt Age (yrs)	No. Pts	No. CTM (%) [*]	No. LTM (%) [#]
5 or Younger	214	1 (0.5)	3 (1.4)
6-11	280	8 (2.9)	6 (2.1)
12 or Older	176	7 (4.0)	3 (1.7)
Totals	670	16	12

^{*} $p = 0.032$

[#] $p = 0.823$

Figure A

Classical testicular microlithiasis in an eleven-year-old asymptomatic boy. The transverse ultrasound image of the right testis shows more than five microliths per sonographic plane. The microliths are without acoustic shadowing and are diffusely scattered throughout the testicular parenchyma. The left testis also shows CTM, diffusely scattered throughout the parenchyma.

Figure B

Limited testicular microlithiasis in a twelve-year-old asymptomatic boy. The transverse ultrasound image of the left testis shows four microliths per sonographic plane. There is no acoustic shadowing and the microliths are clustered in the testicular parenchyma. The right testis also shows a maximum of four microliths per sonographic plane.

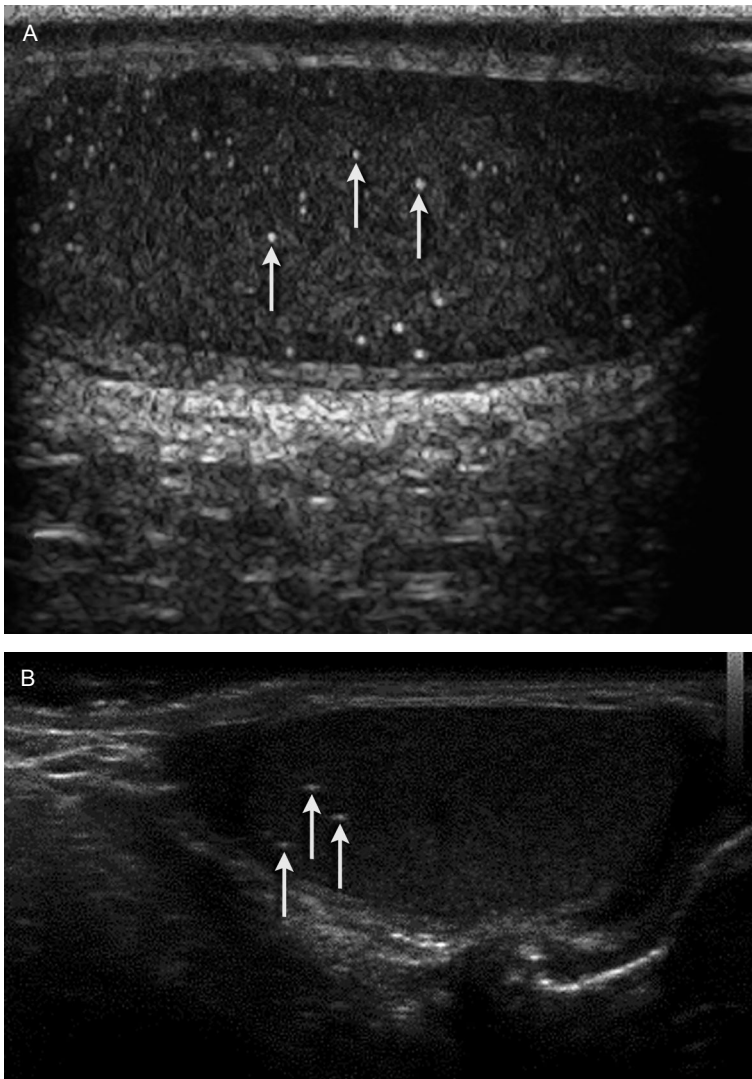


Table 3

Limited and classical testicular microlithiasis stratified by side.

	No. Rt (%)	No. Lt (%)	No. Bilat (%)	Total No. (%)
LTM	6 (21.4)	4 (14.3)	2 (7.1)	12 (42.9)
CTM:				
Grade I	0 (0)	0 (0)	0 (0)	0 (0)
Grade II	3 (10.7)	1 (3.6)	4 (14.3)	8 (28.6)
Grade III	0 (0)	0 (0)	8 (28.6)	8 (28.6)
Totals	9 (32.1)	5 (17.9)	14 (50)	28 (100)

The 16 boys with CTM were referred to our outpatient clinic, where another investigator confirmed the diagnosis of CTM. Among the patients 65 boys (9.7 %) with a median age of 6.5 years (range 1.0 to 13.0) had at least 1 retractile testis. None of these boys were diagnosed with CTM.

In our population, 656 boys (97.62 %) were white, 8 (1.19 %) were Turkish, 4 (0.60%) were North-African, 3 (0.80%) were Asian and 1 (0.15%) was black. Only 1 boy with TM was, while the others were white.

No testicular tumours were detected in any boy with or without TM. All boys with CTM had a normal genitourinary history and physical examination. Two boys with LTM had undergone groin surgery.

There was no significance difference between gestational age/birth weight and actual weight and height in boys with or without CTM and LTM. There was also no difference in the number of patients treated with groin surgery or suffering from other medical problems between the groups with or without CTM and LTM (all p-values greater than 0.05).

Nine of the 16 boys with CTM had brothers (6 boys had 1 brother and 3 had 2 brothers). Scrotal US was performed in all of the brothers (median age 12.0, range 4.6 to 24.9) and revealed no TM.

Among the 24 boys (median age 10.0 age range 3.7 to 18.8) excluded from the study LTM was diagnosed in 3 and CTM in 1. All of the excluded boys were white.

Discussion

To our knowledge this study represents the first series on the prevalence of TM in asymptomatic boys. In our screening population CTM was present in 2.4 % of patients and LTM in 1.8 %, yielding a total TM prevalence of 4.2 %. The youngest boy diagnosed

with CTM was 5 years, and the youngest with LTM was 4 years.

The prevalence of CTM in our series was slightly lower than the prevalence of 5.6 % prevalence reported in a study of asymptomatic men.⁵ This result may be due to the different ethnic groups in our study. Since we saw an increased prevalence in older boys, TM may originate at a later age. Another study in asymptomatic men demonstrated a prevalence of CTM of 2.4%, which is comparable to our series. The reported prevalence of CTM in boys with UDT and Down syndrome seems higher than in our asymptomatic population.

TM exhibits characteristic sonographic findings of multiple hyperechogenic, non-shadowing foci, which can occur unilaterally or bilaterally. The microliths consist of hydroxyapatite deposits surrounded by concentric layers, and they can be segmented or scattered diffusely throughout the testicular parenchyma. Suggested sources of TM are the tubuli seminiferi as well as the layers outside these structures.¹⁰ Although the exact cause of TM is unknown, the origin of the microliths is presumably be related to Sertoli cell dysfunction.¹ Recently TM was reported in otherwise healthy siblings, suggesting a common risk factor, and in siblings with fragile X and pseudoxanthoma elasticum.¹¹⁻¹³ In our population the brothers of the boys with CTM were screened but no TM was found.

Age of onset of TM is largely unknown and only a few cases have been reported in infancy. To our knowledge the youngest patient with documented TM was 6 months old.¹⁴ TM has also been described in 2 boys as young as 2 years, of whom 1 was diagnosed with pseudoxanthoma elasticum and 1 with yolk sac tumor.¹³ Two studies of scrotal ultrasound in boys aged 0 to 6 years old did not discuss TM, which suggest that TM is extremely rare in young boys, probably manifesting later in childhood.^{15,16}

Generally only CTM is used to determine TM prevalence rates.⁵⁻⁷ CTM may be considered more important, because LTM is probably not associated with other testicular pathologies. Moreover, it is likely that patients with CTM are more closely monitored than those with LTM because of the greater prevalence of CTM in testicular tumors.¹⁷ Further grading of CTM (I to III) shows no effect on the prevalence of associated testicular tumors and, therefore, might not be useful in follow-up.¹⁸ It is unclear whether LTM can progress into CTM, and until now no further progression into CTM has been described. Since LTM is probably not associated with other testicular pathologies, boys with LTM were not further monitored in our series.

CTM seems to be associated to testicular cancer. Among adults a higher prevalence of testicular tumor is seen in symptomatic patients with CTM. However, testicular tumors develop in adults and boys with preexisting CTM only incidentally. So far the longest follow-up has been 6 years, which may be too short to detect testicular malignancies.¹⁹ Consequently the risk of tumor development in a testis with CTM is unknown, and, therefore, it is controversial to give recommendations for follow-up.²⁰

There is still no convincing evidence that CTM alone is premalignant. The 2.4 % prevalence of CTM in our asymptomatic patients compared to the much lower incidence

of testicular cancer in a normal population may disprove an epidemiological association with testicular malignancies. We believe that followup of CTM with routine US every 6 to 12 months plus computerised tomography of the abdomen and chest should only be considered in patients with other potentially premalignant features such as UDT. Screening of tumor markers in asymptomatic men with CTM appears normal and likewise seems unnecessary.⁵ We advise testicular self examination every 3 months in asymptomatic boys with CTM beginning at age 15, since testicular malignancies can occur from this age onward.

There are limitations to this study. To recruit boys for participation, an invitation letter was sent to 2,600 boys. Only a portion of these boys agreed to participate. The reasons for not participating were not analysed, which may have introduced a selection bias.

The prevalence of TM was assessed in boys from birth to adolescence. Age at onset of TM is largely unknown but may be later in childhood because the prevalence was significantly higher in our patients who were 9 years or older. Moreover, if we had selected only boys 5 and older, the prevalence would have been 3.2 %. The prevalence rate in this subgroup is also affected by the fact that the age distribution is skewed, in that more young boys were included than older boys.

It was impossible to assess the prevalence of TM by ethnic group, since only a few nonwhites were included in the study. To determine the overall prevalence of TM, we included boys from different ethnic backgrounds. It is possible that the rate of TM varies in different ethnical groups.⁵

Conclusions

This study reveals a 2.4 % prevalence of CTM and 1.8 % prevalence of LTM, yielding a total TM rate of 4.2 % in asymptomatic boys from birth to adolescence. The youngest boy diagnosed with CTM was 5 years old and the youngest boy with LTM was 4. The prevalence of CTM increases with age.

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Supplementary material

Review of the paediatric cases of testicular microlithiasis as reported in the literature.

Author	Group Investigated	Method	Patients TM	Tumor at presentation	Age range
			N	N	Years
Bieger et al. 1965	mainly cryptorchidism	testis biopsy	13(134)	0	5-14
Priebe et al. 1970	tenderness thigh	testis biopsy	1(1)	0	4
Weinberg et al. 1973	inguinal hernia	testis biopsy	1 (1)	0	6
Nistal et al. 1979	cryptorchism	testis biopsy	2 (2718)	0	6
Vegni-Talluri et al. 1980	cryptorchism	testis biopsy	2 (30)	0	10-11
Jaramillo et al. 1989	torsion testis	ultrasound	1(1)	0	14
Moran et al. 1993	different testicular size	ultrasound	1(1)	0	14
McEniff et al. 1995	different testicular size	ultrasound	1(1)	0	17
Kwan et al. 1995	torsion appendix testis	ultrasound	1(1)	0	8
Howard et al 1998	mediastinal germ cell tumour	ultrasound	1(1)	1	15
Furness et al 1998	different symptoms	ultrasound	26(?)	0	0.5-21
Dell'Acqua et al 1999	different symptoms	ultrasound	6(?)	0	4-12
Riebel et al. 2000	after orchidopexy	ultrasound	6 (68)	0	not mentioned
Leenen et al. 2002	different symptoms	ultrasound	16 (850)	2	6-18
Blau et al 2002	cystic fibrosis	ultrasound	3(12)	0	2-12
Drut et al 2002	different symptoms	testis biopsy	11(?)	2	3-15
Drut 2003	yolk sac tumour	ultrasound	1(1)	1	2

Author	Group Investigated	Method	Patients TM	Tumor at presentation	Age range
			N	N	Years
Pinto et al 2004	pseudoxanthoma elasticum	ultrasound	1(1)	0	14
Pourbagher et al 2005	fragile X	ultrasound	3(3)	0	13-21
Kocaoglu et al 2005	different symptoms	ultrasound	9 (?)	0	3-16
Coley 2005	scrotal pain	ultrasound	1(1)	0	8
Dagash et al. 2006	different symptoms	ultrasound	7 (623)	not mentioned	7-15
Goede et al 2008	cryptorchism and scrotal pain	ultrasound	3(3)	0	9-15
Thomas et al 2008	hydrocele	ultrasound	2(2)	0	5-6
Goede et al 2008	pseudoxanthoma elasticum	ultrasound	1(1)	0	2

() Number of boys investigated

(?) Unknown

