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Original Article – Pediatric Urology

Testicular Microlithiasis in Pediatric Patients

Pediatrik Hastalarda Testiküler Mikrolitiazis

Short Title: Pediatric Microlithiasis (Pediatrik Mikrolitiazis)

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Abstract

Objective: Testicular microlithiasis (TM) is characterized by parenchymal calcifications, identified as hyperechoic, shadowless foci measuring between 1 and 3 mm in diameter within the testicular parenchyma. This condition is typically detected incidentally through ultrasonography in rare inguinal-scrotal disorders in pediatric patients. TM has been linked to various pathological conditions of the testis, notably an elevated risk of tumor development. A retrospective review of TM cases was conducted to assess clinical features and long-term follow-up outcomes.

Materials and Methods: This retrospective analysis was conducted over a 12-year period involving children diagnosed with TM through scrotal Doppler ultrasonography at our outpatient clinic. Medical records were examined to evaluate patient age, indications for ultrasound, associations with inguinal-scrotal pathologies, and follow-up findings.

Results: In this study, fifty-six patients aged between 2 and 17 years (median age of 9 years) were included. Bilateral TM was observed in all cases, except for 15 patients who exhibited unilateral foci. Among the participants, 27 patients (48.2%) presented with concomitant inguinal-scrotal pathology, while 3 patients (5.3%) had systemic disease. Notably, microlithiasis and Leydig cell tumors were identified in one patient who underwent ultrasonography due to testicular pain.

Conclusion: TM is predominantly bilateral and of the classic type, with testicular pain potentially indicating its presence. Ultrasonography is generally adequate for both the diagnosis and monitoring of testicular microlithiasis. An association with testicular tumors is noted, particularly within the pediatric population. Given that both benign and malignant lesions are linked to TM, studies involving larger populations and extended follow-up periods are warranted.
Keywords: Child, Leydig cell tumor, testicular microlithiasis, ultrasonogrphy

Özet

Amaç: Testiküler mikrolitiazis (TM), testiküler parankim içinde çapı 1 ila 3 mm arasında değişen hiperekoik, gölgesiz odaklar olarak tanımlanan parankimal kalsifikasyonlarla karakterizedir. Bu durum tipik olarak çocuk hastalarda nadir görülen inguinal-skrotal bozukluklarda ultrasonografi yoluyla tesadüfen tespit edilir. TM, başta yüksek tümör gelişimi

riski olmak üzere testisin çeşitli patolojik durumlarıyla ilişkilendirilmiştir. Klinik özellikleri ve uzun dönem takip sonuçlarını değerlendirmek için TM olgularının retrospektif bir incelemesi yapılmıştır.

Gereçler ve Yöntemler: Bu retrospektif analiz, kliniğimizde skrotal Doppler ultrasonografi ile TM tanısı konulan çocukları içeren 12 yıllık bir süre boyunca gerçekleştirilmiştir. Hasta yaşı, ultrason endikasyonları, inguinal-skrotal patolojilerle ilişkileri ve takip bulgularını değerlendirmek için tıbbi kayıtlar incelendi.

Bulgular: Bu çalışmaya yaşları 2 ile 17 arasında değişen (ortanca yaş 9) elli altı hasta dahil edildi. Tek taraflı odak gösteren 15 hasta dışında tüm olgularda bilateral TM gözlendi. Katılımcılar arasında 27 hastada (%48,2) eşlik eden inguinal-skrotal patoloji mevcutken, 3 hastada (%5,3) sistemik hastalık vardı. Özellikle, testis ağrısı nedeniyle ultrasonografi yapılan bir hastada mikrolitiazis ve Leydig hücreli tümörler tespit edildi.

Sonuç: TM ağırlıklı olarak bilateral ve klasik tipte olup, testis ağrısı potansiyel olarak varlığını gösterir. Ultrasonografi testiküler mikrolitiazisin hem tanısı hem de takibi için genellikle yeterlidir. Özellikle pediatrik popülasyonda testis tümörleri ile bir ilişki kaydedilmiştir. Hem iyi huylu hem de kötü huylu lezyonların TM ile bağlantılı olduğu göz önüne alındığında, daha geniş popülasyonları ve uzun takip sürelerini içeren çalışmaların yapılması gerekmektedir.
Anahtar kelimeler: Çocuk, Leydig hücreli tümör, testis mikrolitiazisi, ultrasonografi

Introduction

TM is a pathological condition characterized by diffuse calcification within the seminiferous tubules [1,2]. Research on TM in pediatric populations is limited, and its association with testicular disease in children remains a subject of debate. [2,3,4]. TM is observed in 1.1-4.2% of asymptomatic males without urological disorders [3,4,5]. In the testicular parenchyma, it is usually detected by ultrasonography (US) and is typified by hyperechoic non-shadowing foci that are 1-3 mm in diameter. Although the exact cause of calcified material inside seminiferous tubules is unknown, several theories have been proposed, including inflammation, poor Sertoli cell phagocytosis, excessive immunological response, and rapid cell renewal [6]. Epidemiological studies have indicated an increased prevalence of TM in patients with risk factors for testicular tumor development. Its association with various benign or malignant pathologies has been documented, particularly testicular germ cell tumors, cryptorchidism, testicular torsion or atrophy, gonadal dysgenesis, varicocele, Klinefelter's

syndrome, Down's syndrome, infertility, male pseudo-hermaphroditism, carcinoma in situ, and a family or personal history of testicular cancer [7,8].

In asymptomatic patients, TM is typically identified incidentally during routine medical examinations or ultrasonography (US) performed for other diagnostic purposes. Symptomatic TM is defined as the presence of microliths on US, accompanied by testicular pain, testicular edema, increased testicular size, hydrocele, varicocele, or testicular atrophy, which can occur at any age [9,10].

We performed a retrospective analysis of the clinical characteristics, comorbidities, follow-up, and outcomes of patients with TM as observed on scrotal ultrasound (US). The objective of this study was to examine the relationship between TM and histopathological findings.

Materials and Methods

A retrospective analysis was conducted on 2.350 pediatric patients who presented with symptoms of testicular pain, scrotal swelling, and erythema at our outpatient clinic. These patients underwent scrotal ultrasonography (US) between January 2013 and December 2024. Doppler ultrasonography reports are documented within the hospital information system. The study included 56 patients diagnosed with TM, each of whom underwent a minimum of two scrotal ultrasound (US) procedures. During the US examination, the number and distribution pattern of testicular calcifications were assessed, with echogenic foci measuring less than 1-3 mm in a single plane and lacking acoustic shadowing being included. Additionally, the calcifications were categorized as diffuse or focal, bilateral or unilateral, and with or without associated nodules. Patients diagnosed with TM and monitored over time were evaluated concerning age, indications for US, association with inguinal-scrotal pathology, and follow-up findings. This study was conducted according to Kocaeli University Faculty of Medicine Ethics Committee (Decision date and number; GOKAEK-2025/08/09- E-80418770-020-765346).

Statistical Analysis

The statistical analysis was carried out using the latest version of IBM SPSS 29.0. The Kolmogorov-Smirnova test was employed to assess the normality of the data distribution, and it was found that the assumption of normal distribution was not met. Categorical variables are presented as frequencies (percentages), whereas numerical variables are reported as the median with the interquartile range (25th-75th percentile).

Results

The diagnosis of TM was established using ultrasonography (US) in all patients, with a prevalence of 2.3% among children. The patients had a median age of 9 years, with ages ranging from 2 to 17 years. TM was predominantly diffuse and bilateral (n=40, 71.4%), while unilateral TM was observed in 16 male patients (right: 6, left: 10), most frequently occurring in the 7-10 year age group (n=21, 37.5%). Twenty-seven patients (48.2%) presented with concomitant inguinal-scrotal pathologies (**Table 1**), and 3 patients (5.3%) had concurrent systemic diseases (**Table 2**).

Patients were invited to undergo ultrasound (US) examinations at least annually following their diagnosis. The median follow-up duration was 3.5 years, with a range of 1 to 8 years. During the follow-up of 32 patients without inguinoscrotal pathology, no new pathological findings were identified. Nine patients underwent inguinoscrotal surgery (undescended testis, n=6; acute scrotum, n=3). Orchiectomy was performed in three patients (5.3%): two due to testicular torsion and one due to testicular atrophy following surgery for an undescended testis. In one case, TM was identified during the diagnosis of a testicular mass on the same side. This patient was diagnosed with a Leydig cell tumor following biopsy and subsequently underwent testicular-sparing surgery (**Figure 1,2**). No recurrence was observed at the mean follow-up of 2 years.

Discussion

The precise etiology of TM, a pathological condition, remains unidentified. It is thought to result from the seminiferous epithelium's degeneration, which then spreads into the tubular lumen. Some researchers suggest that the development of microliths may result from malfunctioning Sertoli cells, potentially linked to abnormal gonadal embryogenesis [11]. Priebe and Garret documented radiographs of a healthy 4-year-old boy exhibiting TM, which was subsequently diagnosed by Doherty et al. in 1987 using ultrasonography [12,13].

The prevalence of TM in the pediatric and adult male populations ranges from 1.1% to 5.6% [5,10,14]. In our study, the incidence of TM among patients undergoing scrotal ultrasound for testicular pathology was 2.6%, aligning with existing literature.

TM is characterized by hyperechogenic foci of varying degrees within the testicular parenchyma, typically distributed bilaterally throughout the testes [3]. Diffuse testicular dysgenesis is associated with TM, which typically measures 1-2 mm in diameter on

ultrasonography (US). Both unilateral and bilateral TM are possible, as is a diffuse or localized distribution of calcifications [15,16]. In our study, a focal distribution was observed in sixteen cases (28.6%), while a diffuse distribution was noted in 40 cases (71.4%) of the ultrasound images diagnostic of TM. With the exception of two individuals who underwent unilateral orchiectomy, the calcifications were observed bilaterally.

Although TM is traditionally considered a static condition that neither progresses nor regresses over time, a limited number of studies have documented instances of increase, decrease, or complete resolution of the condition during patient follow-up [14].

Pain constitutes the primary cause for hospital admissions among children with TM [1,17]. Nonetheless, several studies have not reported on testicular pathology in individuals experiencing pain and TM diagnosed via ultrasound (US) [1,2,17]. In our study, TM was incidentally identified in 9 patients (16.0%), associated with pain in 20 patients (35.7%), and accompanied by inguinal-scrotal pathology, as detailed in **Table 1**, in 27 patients (48.2%). Our findings align with previous research, indicating an increased prevalence of TM in testicular pathology. TM may appear without patient-reported symptoms or may itself be the origin of pain.

The prevalence of TM may be heightened in benign illnesses such Klinefelter's syndrome, cryptorchidism, Down syndrome, hypospadias, and post-traumatic scenarios [5,9,18,19].

In our study, eight patients presented with undescended testes, ten with an acute scrotum, and two with epididymal cysts. Research has indicated that undescended testes are correlated with an increased prevalence of TM [2,19,20]. The prevalence of TM in an asymptomatic group, on the other hand, is similar to that seen in patients with undescended testes, according to research by Pedersen and Chiang et al [14,17]. In our analysis, six patients with cryptorchidism exhibited ipsilateral TM, while two presented with contralateral TM. All six patients underwent orchidopexy to address undescended testes at the age of one year. The etiology of TM remains uncertain, as it is unclear whether it is a consequence of cryptorchidism or if both cryptorchidism and TM are manifestations of tubular abnormalities. Additionally, it is plausible that surgical intervention itself may induce TM, or that it arises due to vascular damage to the testis.

The precise correlation between TM and both benign and malignant conditions remains undetermined, particularly within the pediatric demographic [5,9,21]. According to extant

literature, the prevalence of TM in children presenting with potential risk factors for primary testicular tumors (TT)—such as testicular pain, testicular masses, personal or familial history of TT, or undescended testis—ranges from 0.7% to 12%, and may reach up to 4.2% in asymptomatic children [1,5,22]. The age range of pediatric cases documented in the literature spans from 2 to 17 years. Pediatric instances of TM associated with tumors include gonadoblastoma, yolk sac germ cell tumor, metastatic mixed germ cell tumor, Leydig cell tumor, teratoma, choriocarcinoma, Sertoli cell tumor, and benign metachronous epidermal cyst [23].

Leydig cell tumors constitute up to 5% of testicular neoplasms and can occur across all age groups [24,25]. Approximately 20% of these tumors manifest between the ages of five and ten. In the present study, an 11-year-old patient was diagnosed with microlithiasis and a Leydig cell tumor and subsequently underwent testicular-sparing surgery. No recurrence was observed at the four-year follow-up. The diagnosis of a testicular tumor with microlithiasis was confirmed via ultrasound (US). Consequently, it cannot be conclusively stated that microlithiasis serves as a precursor lesion. However, literature reports a case of a 20-year-old patient with Down syndrome who developed a Leydig cell tumor due to microlithiasis over a four-year follow-up period [26]. Our patient did not present any additional conditions that could serve as risk factors, such as Down syndrome, McCune-Albright syndrome, gonadal dysgenesis, or undescended testes.

As TM is typically an incidental finding in the absence of associated risk factors, the European Association of Urology (EAU) and the European Society for Pediatric Urology (ESPU) guidelines do not advocate for routine ultrasonography (US) in cases of undescended or palpable testes [9]. Testicular microlithiasis (TM) is also associated with testicular pathologies, including testicular tumors and cryptorchidism. Consequently, it is imperative to exercise caution when managing patients presenting these risk factors. However, they do recommend regular follow-up with US, particularly if there is a family history of testicular malignancy, testicular pain, testicular enlargement, or Down's syndrome [2].

Previous studies have demonstrated that the determination of tumor markers or the performance of testicular biopsy in pediatric patients with TM does not provide additional clinical value, as it lacks clinical implications [9]. We did not routinely conduct tumor marker assessments in patients monitored with a diagnosis of TM. However, in the case of our patient diagnosed with a Leydig cell tumor, tumor markers, specifically AFP and B-HCG, were evaluated and subsequently returned to normal levels.

In the majority of studies, the reported follow-up period did not extend beyond adolescence, even in the presence of risk factors. The longest follow-up duration of seven years may be insufficient to detect testicular malignancies. In cases where a patient presents with isolated testicular microlithiasis (TM) but lacks identifiable risk factors, yet exhibits clinical symptoms, we advise conducting follow-up imaging at one-year intervals. It is crucial for patients to perform monthly testicular self-examinations during this period. For patients with risk factors such as cryptorchidism, infertility, testicular atrophy, and particularly a family or personal history of germ cell tumors, we recommend more frequent scrotal ultrasound examinations. Future research in the pediatric population would benefit from focusing on distinguishing cases of benign microlithiasis from those with a higher risk of malignant transformation. Incorporating a larger sample size and conducting longer studies with regular ultrasound surveillance may provide conclusive evidence regarding whether testicular microlithiasis in children is benign or premalignant.

The psychological impact of a TM diagnosis on children and their families is frequently an overlooked aspect of care. It is imperative that the emotional and developmental concerns of both parents and patients are more effectively addressed during follow-up care.

Of course, our study had some limitations. The limitations of our study were the retrospective nature of the study, the small number of patients and the short follow-up period.

Conclusion

TM is a rare and contentious condition frequently associated with various inguinoscrotal disorders. Long-term monitoring of TM cases is essential for the early detection of concomitant tumor development, particularly in the presence of predisposing conditions and accompanying undescended testes. Elevated TM levels may suggest an increased risk of malignancy and may guide decisions regarding imaging or surgical interventions. In this study, only one tumor lesion associated with TM was identified. Given the documented association between tumor lesions and TM in the literature, we assert that a long-term, multidisciplinary approach involving pediatric surgeons and urologists is warranted.

Ethics Committee Approval: Ethical approval for this study was obtained from Kocaeli University Faculty of Medicine Ethics Committee before the study (Decision date and number; GOKAEK-2025/08/09- E-80418770-020-765346).
Informed Consent: An informed consent was obtained from all the patients.
Publication: The results of the study were not published in full or in part in form of abstracts.
Peer-review: Externally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept –O.V., M.A.A.; Design –O.V., M.A.A.; Supervision –O.V., Y.A.; Resources –O.V.; Materials –O.V., M.A.A., N.G.S., Y.A.; Data Collection and/or Processing –O.V., M.A.A., N.G.S; Analysis and/or Interpretation –O.V., M.A.A.; Literature Search –OV, M.A.A., Y.A.; Writing Manuscript –O.V., ; Critical Review –O.V, M.A.A.
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Table 1. Patients' symptoms and associated diagnosis with testicular microlithiasis

Patients	**%**	**Presenting symptoms and associated diagnosis**
20	35.7	Painful testis
10	17.8	Acute scrotum
9	16.0	Incidental
8	14.2	Undescended/retractile testis
4	7.1	Hydrocele
2	3.5	Varicocele
2	3.5	Epididymal cyst
1	1.8	Benign tumor

Table 2. Systemic diseases with testicular microlithiasis

Patients	**Systemic diseases**
2	hypothyroidism
1	rheumatoid arthritis

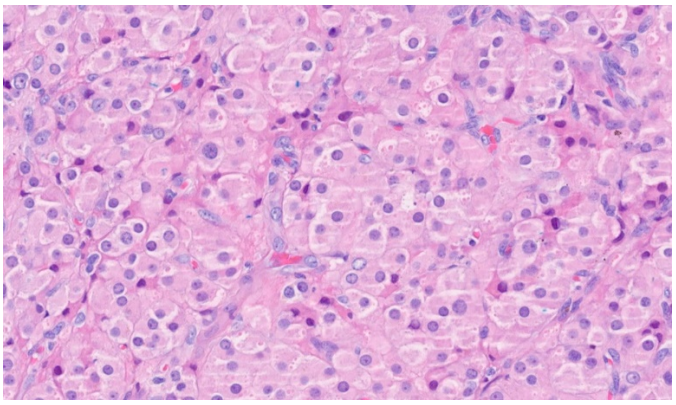

Figure 1. Tumor cells with eosinophilic large cytoplasm and round vesicular nucleus (H&E X40)

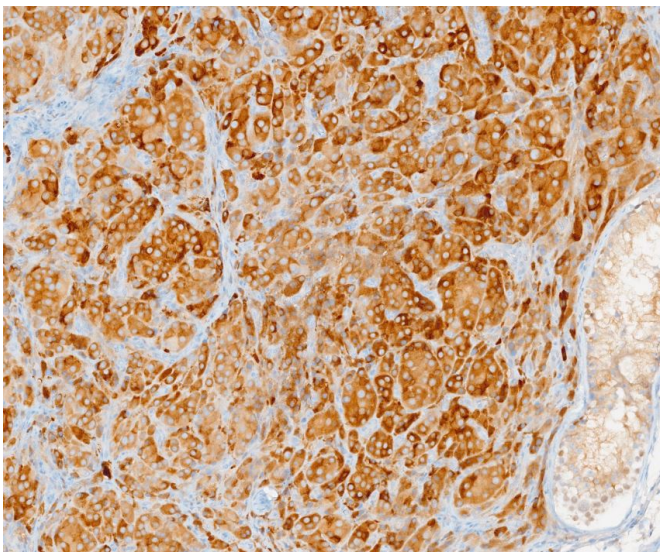

Figure 2. Inhibin positivity in tumor cells (Immunohistochemistry DABX20)