Management and Follow-Up of Pediatric Asymptomatic Testicular Microlithiasis
Are We Doing It Well?

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Purpose: To define timing and methods for a balanced follow-up of testicular microlithiasis (TM) in pediatric age.

Materials and Methods: We retrospectively reviewed medical records of 21 pediatric asymptomatic patients (42 testicular units) diagnosed with TM and without associated risk factors. Microliths were found bilaterally on ultrasonography in all the patients. Distribution of microliths (focal or diffuse) inside the parenchyma was evaluated as well as its eventual variation over time. Every six months, each patient underwent clinical and ultrasonography evaluation, as well as serum chemistry markers (α-fetoprotein and β-human chorionic gonadotropin) measurement to detect potential malignancy. In the interval between the follow-ups, parents and/or patients themselves were asked to control eventual enlargement of the gonads or scrotal swelling. Testicular biopsy was not performed in any of our subjects.

Results: Of 21 patients, 6 had unilateral undescended testis, 4 varicocele, and 1 patent processus vaginalis with scrotal swelling while 10 patients did not show associated anomalies. The distribution pattern of microliths on ultrasonography remained unchanged in all follow-ups in every patient, showing a predominance of diffuse pattern in the undescended testis series. Tumor markers remained within normal limits. In no subject, we observed a shift toward a malignant condition.

Conclusion: In the pediatric population with an incidentally diagnosed TM and without any associated risk factor, a slight follow-up is suggested, consisting of clinical evaluation every 6 months, without any justifiable recommendation to perform a testis biopsy and a measurement of serum tumor markers.

Keywords: testis, testicular diseases, testicular neoplasms, child, lithiasis

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INTRODUCTION

Testicular microlithiasis (TM) is a relatively rare clinical entity characterized by the existence of microliths located in the seminiferous tubules and composed of hydroxyapatite.[1] A relatively large number of benign and malignant conditions, such as testicular torsion or atrophy, cryptorchidism, gonadal dysgenesis, varicocele, Klinefelter syndrome, and male pseudo-hermaphroditism are strictly related to microlithiasis.[2,3]

Giving complete information about clinical implications of TM to parents, the opportunity of a clinical and instrumental endless

follow-up is experienced as a "Sword of Damocle" for the whole life-time.

We studied asymptomatic pediatric patients with TM to verify risks and benefits of a closed, aggressive instrumental and clinical follow-up since an early age opposite to an individualized and balanced one according to well-known risk-factors.

MATERIALS AND METHODS

Data from 21 patients who suffered from an incidentally discovered TM were retrospectively reviewed. They were all observed at our institution since January 2002.

Microliths were found bilaterally in all the patients (42 testicular units). All of them underwent ultrasonography performed with high frequency (10 to 17 MHz) linear transducers. Distribution of microliths (focal or diffuse) inside the parenchyma was evaluated as well as its eventual variation over time.

Every six months, each patient underwent a clinical and ultrasonographyevaluation as well as serum chemistry markers (α-fetoprotein and β-human chorionic gonadotropin) determination to detect potential malignancy. In the interval time between the follow-ups, parents and/or patients themselves were asked to control, throughout regular examination or self-examination, eventual enlargement of the gonads or scrotal swelling. A testicular biopsy was not performed in any of our subjects according to recommendations for asymptomatic and apparently healthy patients.[4]

RESULTS

Mean age of the patients and the mean follow-up duration were 10.5 years (range, 8 months to 18 years) and 41.2 months, respectively. As Table shows, of 21 patients, 6 had unilateral undescended testis, 4 varicocele, and 1 patent processus vaginalis with scrotal swelling while 10 patients (two of them twins) did not show associated anomalies.

The younger patient was an 8-month-old boy with a left undescended testis and an underlying bilateral partially diffuse microlithiasis (Figure 1). All the patients who resulted as normal were referred to us after they underwent a scrotal ultrasonography to detect an adolescent

Twenty-one pediatric patients with testicular microlithiasis

Patient	Age at Diagnosis	Right Testis	Left Testis	Tumor Markers	Ultrasonographic Distribution Pattern	Associated Pathology
1	8 mos	Yes	Yes	NL	Diffuse	Undescended testis
2	9 yrs	Yes	Yes	NL	Diffuse	Undescended testis
3	18 yrs	Yes	Yes	NL	Focal	Varicocele
4	4 yrs	Yes	Yes	NL	Focal	Hydrocele
5	11 yrs	Yes	Yes	NL	Focal	-
6	11 yrs	Yes	Yes	NL	Focal	-
7	8 yrs	Yes	Yes	NL	Diffuse	Undescended testis
8	17 yrs	Yes	Yes	NL	Focal	-
9	9 yrs	Yes	Yes	NL	Focal	Varicocele
10	16 yrs	Yes	Yes	NL	Focal	-
11	15 yrs	Yes	Yes	NL	Diffuse	-
12	10 yrs	Yes	Yes	NL	Focal	-
13	11 yrs	Yes	Yes	NL	Focal	-
14	13 yrs	Yes	Yes	NL	Focal	-
15	11 yrs	Yes	Yes	NL	Focal	Varicocele
16	13 yrs	Yes	Yes	NL	Diffuse	Varicocele
17	15 yrs	Yes	Yes	NL	Diffuse	Undescended testis
18	17 yrs	Yes	Yes	NL	Focal	-
19	2 yrs	Yes	Yes	NL	Diffuse	Undescended testis
20	12 mos	Yes	Yes	NL	Focal	Undescended testis
21	9 yrs	Yes	Yes	NL	Focal	-

Mos indicates months; yrs, years; and NL, normal.

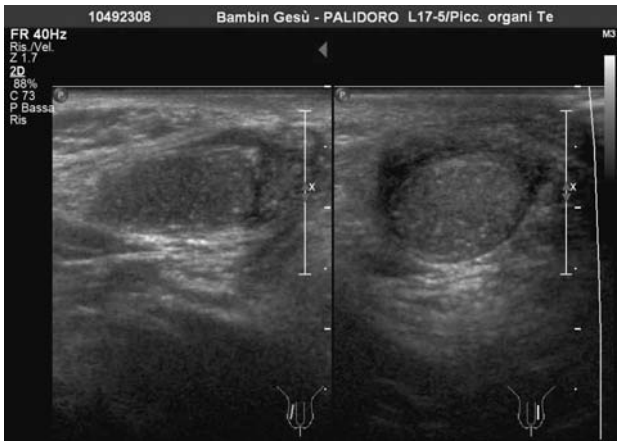

Figure 1. An 8-month-old boy with a left undescended testis and an underlying bilateral partially diffuse microlithiasis.

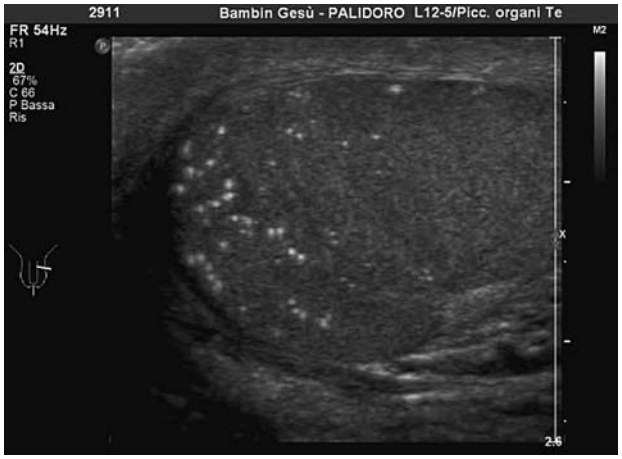

Figure 2. Focal distribution pattern of microliths.

varicocele. Two of them were monozygotic twins with a focal distribution pattern of microliths (Figure 2). The distribution pattern of microliths on ultrasonography remained unchanged in all the serial follow-ups in every patient, showing a predominance of diffuse pattern in the undescended testis series (n. 1, 2, 7, 17, and 19 of our series).

Tumor markers determination performed in all the patients, which were within normal limits. In no subject, we observed a shift toward a malignant condition.

DISCUSSION

The first description of TM and ultrasonography dates back to 1965[5] and 1987,[6] respectively. The first report of a pediatric case dates back to 1970.[7] Nowadays, state of the art of the literature on the argument tends toward a clear separation between incidentally discovered TM in a healthy patient and microliths accompanying a testicular tumor or found in a testis that suffered from a torsion and/or a hemorrhagic infarction.[4,8]

Furthermore, grading of TM as observed on ultrasonography seems to have no effect on the prevalence of associated malignancy.[9] A prevalent category of patients, in our opinion needing a high level of suspicion, includes those children with underlying pathologies, such as disorders of sex development, WT1 gene mutation related syndromes,[10] McCune–Albright,[11] and Klinefelter syndrome.[12]

However, the most common pediatric patient observed having a TM is that who underwent an ultrasonography examination for an associated cryptorchidism or varicocele. We believe that undescended testis and the varicocele itself may not be considered as a risk factor even if they are associated with TM. Subfertility related to varicocele and eventual hormonal therapies may, nevertheless, be judicious in a patient with TM. Associated risk factors determine the intensity of long-term follow-up period.

In a land of reports that associate TM from lentigines[13] to mediastinal germ cell tumor,[14] experts on the field are still debating if TM is a benign or a premalignant condition.[15-18] Obviously, not all the patients with a diagnosed TM are at risk for testicular cancer development, but association with already known risk factors, such as hypogonadism, intersexual conditions, WT1 gene-related syndromes, and familial history of testicular germ cell tumors (TGCT), renders it a really worrisome entity.

How to organize and plan a balanced follow-up since an early age in order to ensure a proper protection from malignancy is a challenging matter. There are not updated data suggesting that testicular tumors may arise in a pediatric population with an incidentally discovered TM. Furthermore, suggestions to perform a biopsy in a pediatric patient with the testis with microliths without any other risk factors, above all in a bilateral condition, seem really questionable.

As a matter of fact, in a recently published report,

two high-risk groups were identified fitting the decision to perform a biopsy: patients with unilateral TGCT and patients with extragonadal TGCT. [19] Adult patients with TM based on the scrotal ultrasonography might be possibly considered for biopsy when additional scrotal anomalies and/or infertility are present.

Measurement of serum tumor markers, even at an interval time of 6 months, has not proven to be a useful and justifiable method to ensure a safe surveillance, and this is also why the onset of a TGCT may require a less time than the interval to develop and grow.

A review of the literature on the incidence of testicular malignancy in pediatric patients revealed few case reports and two relevant case series with a definitive prevalence of 4.2% among asymptomatic boys.[7,8,20-23]

CONCLUSION

In a pediatric population with asymptomatic and incidentally discovered TM and without an association with well-known risk factors, a conservative approach is recommended. In this selected category of patients with TM, testicular biopsy and measurement of serum markers are not recommended.

CONFLICT OF INTEREST

None declared.

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