Testicular Volume and Testicular Microlithiasis in Boys With Down Syndrome

Joery Goede,* Michel E. Weijerman, Chantal J. M. Broers, J. Peter de Winter, Laszla M. van der Voort-Doedens and Wilfried W. M. Hack

From the Departments of Pediatrics, Medical Center Alkmaar, Alkmaar (JG, LMvanderV-D, WWMH), Rijnland Hospital, Leiderdorp (MEW), VU University Medical Center, Amsterdam (CJMB) and Spaarne Hospital, Hoofddorp (JPdeW), The Netherlands

Abbreviations and Acronyms

DS = Down syndrome

TGCT = testicular germ cell tumor

TM = testicular microlithiasis

UDT = undescended testis

US = ultrasound

Submitted for publication July 4, 2011.

Study received hospital ethical committee approval (reference No. M08-001).

* Correspondence: Department of Pediatrics, Medical Center Alkmaar, Wilhelminalaan 12, 1815 JD Alkmaar, The Netherlands (telephone: 31-72-5-48-44-44; FAX: 31-72-5-48-21-90; e-mail: j.goede@mca.nl).

Purpose: Studies have suggested that testicular microlithiasis and Down syndrome are linked, yet a correlation remains unclear. We investigated the prevalence of testicular microlithiasis in patients with Down syndrome. We hypothesized that testicular microlithiasis is present at a higher rate in these patients. We further hypothesized that patients with Down syndrome have lower testicular volumes than normal age matched boys. We tested our hypothesis by ultrasound investigation in boys 0 to 18 years old with Down syndrome.

Materials and Methods: Testicular ultrasound was performed in 79 boys with Down syndrome. Mean patient age was 8.8 years (range 0.4 to 18.3). Testicular microlithiasis was assessed and testicular volume was measured according to the formula, $\pi/6 \times$ length $\times$ width $\times$ height.

Results: Testicular microlithiasis was present in 18 boys (22.8%). It was diagnosed in 6 of 28 boys younger than 7 years (21.4%), in 6 of 28 boys 7 to 12 years (21.4%) and in 6 of 23 boys 12 years or older (26.1%). No significant difference was found in the prevalence of testicular microlithiasis between these 3 groups. Mean testicular volumes in patients with Down syndrome (2.19 ml) were significantly smaller than the normative values.

Conclusions: This study demonstrated a 22.8% prevalence of testicular microlithiasis in boys with Down syndrome, which is significantly increased compared to normative values. In addition, testis volume is significantly smaller in boys with Down syndrome compared to normative values.

Key Words: Down syndrome, lithiasis, organ size, testis, ultrasonography

Down syndrome is one of the most common chromosomal disorders, occurring once in every 1,000 live births.[1] Patients with Down syndrome have an increased risk of childhood leukemia, gastrointestinal cancer and testicular germ cell tumors.[2–5]

TM is a condition in which multiple small calcifications are present in the seminiferous tubules, which may be indicative of a degeneration of the testicular parenchyma.[6–8] The prevalence of TM in patients with DS has only been documented in 1 study, which revealed a rate of 29%.[9] However, that study included adults as well as pediatric patients. Recently a prevalence rate for TM of 4.2% has been determined in boys without DS.[10]

We hypothesized that TM is present at a higher rate in boys with DS. We further hypothesized that boys with DS have lower testicular volumes compared to normal age matched boys.[11] We tested

0022-5347/12/1873-1012/0
THE JOURNAL OF UROLOGY®

Vol. 187, 1012-1017, March 2012
Printed in U.S.A.
DOI:10.1016/j.juro.2011.10.167

our hypothesis by ultrasound investigation in males 0 to 18 years old with DS.

MATERIALS AND METHODS

Study Design

Boys were recruited from the records and via the journal of the Dutch Down Syndrome Association (Stichting Downsyndroom), and via the records of the pediatric departments of 3 different hospitals. A total of 94 patients responded, of whom 81 enrolled in the study. The study was approved by the hospital ethical committee (reference No. M08-001).

Inclusion and Exclusion Criteria

Males 0 to 18 years old with DS confirmed by chromosomal analysis were included in the study. It proved impossible to measure testicular volume by US 3 times in all boys. Those whose testicular volume was measured fewer than 3 times were excluded from determination of testicular volume but not from determination of TM.

Definitions

Descent was defined as a spontaneous stable position of the testis at the bottom of the scrotum. UDT was defined as a testis that could not be manipulated into a stable scrotal position and where further tension on cord structures caused discomfort. UDT was classified as high scrotal, inguinal or nonpalpable.

TM was defined as classic TM if 5 or more foci measuring 1 to 3 mm in diameter were seen on ultrasound plane in 1 or both testes.[12] Patients who had at least 1 microlith but who did not meet the criteria for classic TM were considered to have limited TM. TM was differentiated as diffusely scattered throughout the parenchyma or segmented.

Study Protocol

Questionnaire. At the pediatric outpatient clinic a questionnaire was used that included the items diagnosis of DS confirmed by karyotype, age at diagnosis, medical problems, major surgery, prior groin surgery, medication use, diet, gestational age, birth weight, ethnicity and school level. Ethnic background was divided into white, Turkish, North African, Asian or black.

Physical examination. The physical examination and measurement of height and weight of each boy was performed by the same physician (JG). A full physical examination was not routinely performed. With the boy in the supine and cross-legged position, examination of the left testis was carried out, followed by examination of the right testis. Testis position was classified as low scrotal, high scrotal, inguinal or absent, and the testis was diagnosed as descended or undescended.

Testicular ultrasound. After the physical examination US of both testes was performed to assess the presence or absence of TM. All ultrasounds were performed with the same equipment (Falco Auto Image, Falco Software Co., Tomsk, Russia), using a 12 MHz linear array transducer. After that volume of the left testis was measured, followed by volume of the right testis.

To measure testicular volume, the scanner was placed on the testis with only light pressure to avoid distorting the testicular shape. If the testis could be brought into a scrotal position, volume measurement was performed on the scrotum. However, if the testis was positioned in the groin region, US was performed there. Three separate transverse and longitudinal images of each testis were recorded. The epididymis was not included. When maximum length, width and height had been obtained in the ultrasound, these were measured and the volume was calculated with the formula for an ellipsoid, $\pi/6 \times$ length $\times$ width $\times$ height. The highest value of the 3 testicular volumes was taken as the volume measurement. Parenchymal disturbances were not studied, and Doppler flow studies to assess testicular blood flow were not performed.

Data Recording and Statistical Methods

SPSS®, version 14.0 for Windows was used for all calculations and statistical analyses. Differences in age between boys with and without TM were tested with the Mann-Whitney test. The chi-square test was used to determine whether there was a relationship between patient age and presence of TM. The chi-square test was also used to assess whether there was a relationship between TM and any comorbidity. Finally, the Mann-Whitney test was used to compare testicular volumes for boys with DS and normative values.

RESULTS

Numbers of Patients and Ultrasounds

A total of 81 patients with DS enrolled in the study. Mean age was 8.8 years (range 0.4 to 23.0). Of these boys 79 (97.5%) 0.4 to 18.3 years old (mean 8.4) were included in the study. Two patients were excluded as they were older than 18.

General Characteristics

Of the 79 boys included in the study all diagnoses were confirmed by karyotype and all were diagnosed before age 3 months. One boy (6.2 years) had mosaic trisomy 21 and 78 had karyotype 47 XY + 21. A total of 15 boys (19.0%) had a birth weight less than 2,500 gm and 13 (16.5%) had been born prematurely.

Of the patients 74 (93.7%) were white, 3 (3.8%) were North African and 2 (2.5%) were Turkish. All patients with TM were white.

A total of 14 patients (17.7%) were educated at a normal primary or high school, while 42 (53.2%) were educated at a special needs school (23 boys were younger than 4 years and, therefore, not yet attending school). The history of relevant pathology of the included boys is summarized in table 1.

Height and weight were compared with the reference data for boys with DS.[13] This comparison yielded no significant differences.