Testicular Microlithiasis: How Concerned Should We Be?

***Okere PCN, *Ani N, *Iloanusi NI, *Itanyi DU, *Okoye IJ, #Olusina DB.**
Departments: *Radiation Medicine and #Morbid Anatomy, University of Nigeria Teaching Hospital, Enugu, Nigeria.
Correspondences: *Dr Okere PCN. E-mail pcnokere@yahoo.com

ABSTRACT
Testicular microlithiasis is a rare condition of the testis with characteristic sonographic features. It is thought to come with an increased risk of testicular tumors among other associations. Our objective is to present three cases of testicular microlithiasis (TM). All patients were referred for scrotal ultrasound scan which detected multiple non-shadowing intra-parenchymal testicular microliths. Upon detection of TM, relevant clinical and laboratory data of patients were reviewed and collated. Patients were young males with average age of 26years. The clinical presentations of two patients were found to include known associations of TM including testicular tumors, male infertility and intra-abdominal tumors. The third and youngest patient (18 years) presented with a short history of scrotal pain only. Scrotal sonography plays a role in the detection of TM and should be routinely offered to all males whenever opportuned. Increased surveillance in the form of scrotal ultrasound scans should be undertaken for all cases of asymptomatic TM.
Key words: Testicular microlithiasis, testicular tumors, ultrasound.

CASE REPORTS:
Case 1
Mr. H.N, a 29 year-old trader presented with a 3-month history of progressive abdominal distension and a swollen and painful right lower limb. There was associated vomiting post-ciba, poor bowel motions, anorexia, fever and weight loss. The patient had a right orchidectomy two years previously in another hospital. The patient had presented with a right hemi-scrotal swelling for which the surgeon suspected an inguino-scrotal hernia. No pre-op scrotal ultrasound was done. At operation the surgeon found a testis harboring a large right intra-testicular tumor. This intratesticular tumour appeared suspicious and a right orchidectomy was promptly done. After the surgery the patient was informed that his right testis was removed as there was a 'mass' within it. The specimen was not followed up to histology and the patient was discharged home after an uneventful recovery.
On examination the patient was chronically ill-looking, febrile to touch and in painful distress. He had a swollen, tender and warm right lower limb. The abdomen was enlarged, tense and there were visible and prominent abdominal wall vessels. Ill-defined masses were felt on deep palpation of the abdomen. Coarse crepitations were heard in his right lower lung zone on auscultation. A working diagnosis of abdominal Koch's to rule out intra-abdominal malignancy was made. Radiologic and laboratory work up was ordered. Ultrasound revealed extensive discrete and coalesced abdominal lymphadenopathy. This involved the porta hepatis, right renal hilum, para-aortic and retro-caval regions and spanned from the level of the pancreas to the aortic bifurcation, straddling the common, external and internal iliac vessels. These lymph nodes were considerably larger in size on the right causing significant vascular compression. Most of them were rounded and had no hilar notch suggesting possible infiltration. Other large masses of slightly heterogeneous echotexture were seen in the same region. The scrotum was examined using high frequency (7.5mHz) linear aray transdulacer. The right testis was not found, it had been removed at operation tow years previously. However, the left testis was found. It measured 3.6cm x 2.2cm and contained multiple small non-shadowing intra-parenchymal reflectors. No intra-testicular mass was seen. No hydrocoele was observed. Other findings were hepatomegaly (17.7cm liver span), cholelithiasis and right hydronephrosis most likely caused by a large para-pelvic lymph node. In view of the past history of orchidectomy for a testicular mass and the significant relationship between microlithiasis and testicular

malignancy (20-fold increased risk), a diagnosis of extensive retroperitoneal metastatic lymphadenopathy secondary to a probable right testicular malignancy was made. The unilateral (right-sided) lymphoedema was attributed to compression of the right iliac veins by the

Table 1 showing patient 1 tests results.

Laboratory Test	Result
α-Feto Protein	Negative (Normal 0-15µg/L)
HIV	Negative to I and II
HBSAg	Negative
Urea	29mg/dl Normal value (10-40)mg/dl
Creatinine	1.0 mg/dl Normal value (0.5- 1.6)mg/dl
Total bilirubin	0.6mg/dl Normal value (<1)mg/dl
AST	24 Normal value(<12)
ALT	13 Normal value (<12)
ALP	316 Normal value (25-92)
Mantoux	Negative
Hb	8g/dl (9-15) g/dl
ESR	>150mm/1st hour
WBC total	12,600/mm3

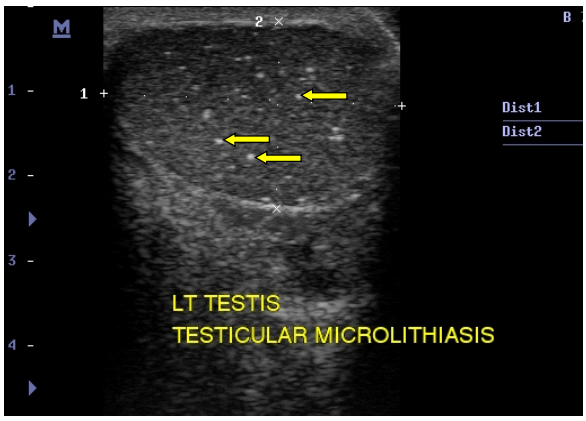


Figure 1 Left testicular sonogram of patient 1 showing multiple non shadowing microliths. (Short arrows) seen here as multiple intra-parenchymal echogenic specks.

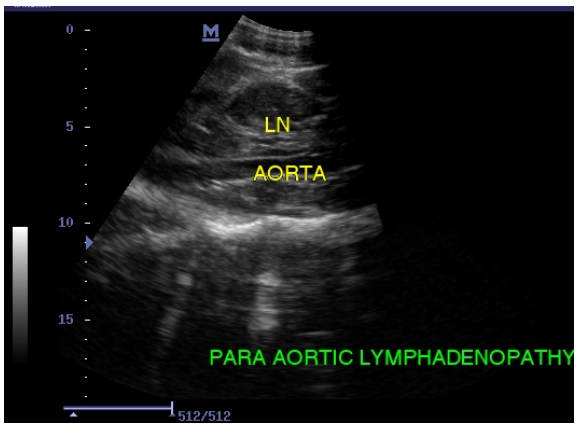


Figure 2. Abdominal sonogram of patient 1 showing enlarged para-aortic lymph node (LN).

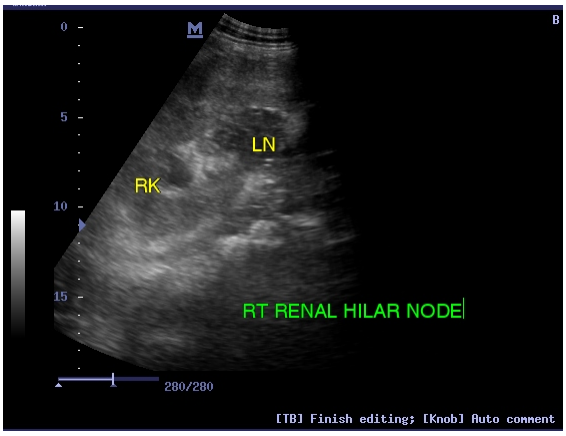


Figure 3. Abdonimal sonogram of patient 1 showing right renal hilar lymph node (LN). RK= Right kidney

Case 2

This is 31 year old unmarried patient who presented on 13/9/2010 with a 15 month history of inability to sustain erection during coitus and absent early morning erection. He did not smoke cigarettes but drank alcohol only occasionally. He denied being on any regular drugs and was neither diabetic nor hypertensive. On examination he was healthy looking and a review of his systems showed nothing remarkable. A Hormonal assay was ordered and done on the 18/9/2010. This showed markedly elevated prolactin (28.0). In addition, seminal analysis done showed non viscous semen, 20% actively motile forms and 40% abnormal spermatozoa and a sperm count of 5,000,000 sperm cells per ml. His referring physician suspected bilateral varicocoele and therefore referred him for sonographic evaluation.

On the 28th of September 2010, a high frequency scrotal ultrasound scan (using 7.5MHz probe on an ALOKA 3500 machine) showed numerous widespread pin-head sized non-shadowing echogenic miliaries in both testes. The left testicular volume was 25.63cm^3. It harbored a 5.2mm simple cyst. The right testicular volume was 16.07cm^3.

No varicocoele was evident bilaterally. The liver, spleen and both kidneys were sonographically normal. No para-caval or para-aortic mass lesions were detected.

An impression of classical testicular microlithiasis was made and patient was advised to have annual ultrasound screening and regular testicular self examination.

Figure 3. Sonogram of left testis of patient 2 showing microliths (thick arrows) as well as a small testicular cyst (thin arrow).

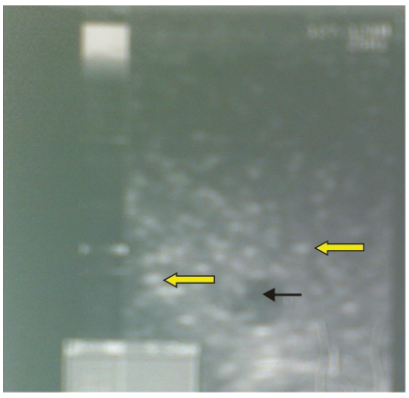


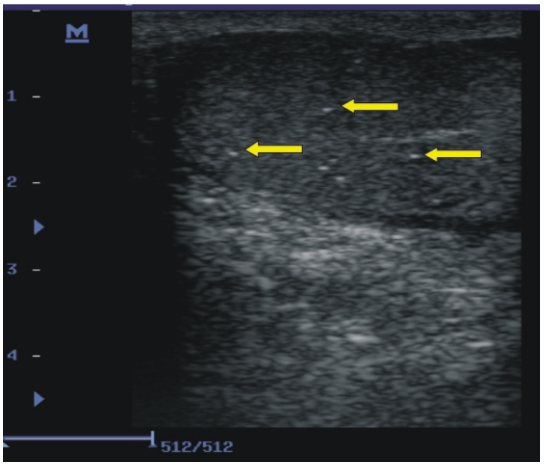
Table 2 showing laboratory seminal fluid analysis and hormone profile test results of patient 2

Test	Result
Serum prolactin	28ng/ml (Normal 1-20ng/ml)
Semen quality	Non viscous
Sperm motility	20% active forms
Morphology	40% abnormal forms
Sperm count	5million cells/ml (Normal 20-60million/ml)

Case 3

AV is an 18 year old student who presented on the 16th of November 2010, with a complaint of a two day history of intermittent, sudden onset suprapubic pain which he claimed radiated to the scrotum. He denied any history of previous urinary tract infections. At present he denied any associated fever, dysuria, vomiting or urinary frequency. A review of his systems was unremarkable. On examination, the referring physician recorded that both testes were slightly tender to palpation. He made a working diagnosis of probable testicular torsion and referred the patient for ultrasound. Two days later on the 18th of November 2010, patient underwent real time high-resolution ultrasound scrotal scan. The left and right testicular volumes were 9.8 and 7.9cm^3 respectively. The tunicae albuginea were not thickened. However, small, echo-free fluid was noted beneath the tunica vaginalis bilaterally. The Doppler signals within the spermatic cords suggested no vascular compromise. There was no varicocoele. However in each testis small non-shadowing echogenic specks were observed (about 13 on the left and 11 on the right). No other intra-testicular lesions were demonstrable. Abdominal scan revealed no additional findings. The pelvis was unremarkable. A diagnosis of testicular microlithiasis was made and the referring physician was advised to ensure yearly sonographic evaluation as well as counsel patient on self examination of his testis.

Figure 4 shows the right testis of patient. Note the non-shadowing microliths (arrows).



DISCUSSION

Testicular microlithiasis (TM) is a rare condition of the testis that has characteristic sonographic features and is thought to be associated with an increased prevalence of testicular tumors[1-5], testicular malignancies[6-8,1-5,9], non neoplastic conditions including Klinefilter's syndrome[10], male infertility[11], cryptorchidism[12] and pulmonary alveolar microlithiasis.[13] As an entity, TM was first reported by Preibe and Garret[14] in 1970 in a healthy 4-year old boy. The first sonographic description was made by Doherty[5] *et al*. in 1987. With an incidence of 1in 21000 in adult males[9] TM is considered to be an asymptomatic condition, typically discovered incidentally at ultrasound scan for other testicular abnormalities and for this reason, it is difficult to determine its true prevalence.[15] This appears to be the case from the author's local experience as the three cases we have seen so far and present show that incidental discoveries of TM appear to be the rule. In our first (case1), TM was discovered in the remaining testis of a patient who had had a right orchidectomy two years previously for intra-testicular tumor at a local hospital, and was subsequently referred to us with suspicion of intraabdominal mass; our second case of TM was discovered during work up for erectile dysfunction and features of hypogonadism while the third was found during sonographic work up for suspected testicular torsion.

The association of testicular microlithias with increased risk of testicular maligancy finds some credence in patient 1. In this patient, although aggregates of retro-peritoneal masses and lymph nodes with malignant features were found during the abdominal ultrasound scan , we are yet constrained to the realm of speculation as to their true nature and whether there exists any relationship between these nodes and the excised "malignant" right testis whose histology was never done. The inability to submit specimen to histologic conclusiveness is not infrequent in the authors' local environment. In addition to the above, we do not have a pre-operative ultrasound of the testes especially the right testis to prove it harboured a testicular tumor in the setting of background microlithiasis. Finally, this patient opted to be discharged as soon as he learned he had multiple inoperable intraabdominal tumors. A biopsy of these retroperitoneal masses was therefore not done. We are therefore left with retroperitoneal masses and adenopathy in a patient with sonographic evidence of TM. Testicular microlithiasis is usually bilateral.[1] However it has been reported in a single testis.[16,17,3] This aside, TM has been reported in association with intraabdominal[18] germ cell tumors. A similar case to ours has been reported in a 37-year old man by Cast[19] *et al*.

The accepted typical sonographic appearance of TM has been enunciated by Backus[1] *et al*. These are multiple small nonshadowing echogenic foci up to 3mm in size, with five or more evident on a single sonogram. These criteria were fulfilled in the three patients we present.

Some workers have observed the mean age of patients presenting with TM alone to be 22.3 years[20], 31years.[19] Others have reported a range from 10 months to 70 years.[1,20] These appear to be in consonance with our study where the average age was 26 years, although it can be argued that our series is small.

The exact cause of testicular microlithiasis remains unclear.[19] However, the microliths shown by electron microscopy have been found to be intratubular bodies with a central calcified core and surrounding concentric laminations composed of collagen fibers.[21] The calcium which are deposited in the seminiferous tubules are thought to accumulate as a result of failure of Sertoli's cells to phagocytose degenerating cells within the tubules.[22,21] The clinical importance of TM remains controversial. It has been proposed

that TM is a manifestation of primary testicular dysfunction and that it is the primary dysfunction that leads to the increased prevalence of carcinomas.[2,22] This primary dysfunction may perhaps explain the features of hypogonadism as seen in our second patient. Some authorities insist that findings do not still prove a cause-effect relationship[19], however, surveillance of patients with TM appears mandatory.[19] Clearly, there is cause for concern considering the young age of the patients involved and the fact that we do not know the true incidence. Also we do not know if there are any differences in biology between local cases and those reported in literature in other environments. This in part may be due to the fact that few cases are reported. More local data is without doubt required. We therefore recommend annual and long term follow up scrotal and abdominal sonographic scans for identified cases of TM. Opportune scrotal scans in young males with unexplained low abdominal pain should be done.

REFERENCES

1. Backus ML, Mack LA, Middleton WD, King BF, Winter TC, True LD. Testicular microlithiasis: imaging appearances and pathologic correlation. *Radiology* 1994; 192: 781-785
2. Janzen DL, Mathieson JR, Marsh JI, et al. Testicular microlithiasis: sonographic and clinical features. *AJR* 1992; 158: 1057-1060
3. Kragel PJ, Delvecchio D, Orlando R, Garvin DF. Ultrasonographic findings of testicular microlithiasis associated with intratubular germ-cell neoplasia. *Urology* 1991; 37: 66-68
4. Roberts ISD, Loughran CF. Case report: the ultrasound appearances of testicular microlithiasis ("snow-storm" testis): a case complicated by testicular seminoma. *Clin Radiol* 1993; 47: 65-67
5. Doherty FJ, Mullins TL, Sant GR, Drinkwater MA, Ucci AA. Testicular microlithiasis *J Ultrasound Med* 1987; 6: 389-392
6. Bach AM, Hann LE, Hadar O, et al. testicular microlithiasis: what is its association with testicular cancer? Radiology 2001; 220: 70-75
7. Derogee M, Bevers RF, Prins HJ, Jonges TG, Elbers FH, Boon TA. Testicular microlithiasis, a premalignant condition: prevalence, histopathological findings, and relation to testicular tumor. Urology 2001; 57: 1133-1137
8. Ganem JP, Workman KR, Shaban SF. Testicular microlithiasis is associated with testicular pathology. Urology 1999; 53: 209-213
9. Patel MD, Olcott EW, Kerschmann RL, Callen PW, Gooding GAW. Sonographically detected microlithiasis and testicular carcinoma. *J Clin Ultrasound* 1993; 21: 447-452
10. Aizenstein RI, Hibbeln JF, Sagireddy B, Wilbur AC, O'neil HK. Klinefelter's syndrome associated with testicular microlithiasis and mediastinal germ-cell neoplasm. J Clin US 1997; 25: 508-510
11. Aizenstein RI, DiDomeninco D, Wilbur AC, O'Neil HK. Testicular microlithiasis associated with male infertility. J Clin Ultrasound 1998; 26: 195-198
12. Nistal M, Paniagua R, Diez-Pardo JA. Testicular microlithiasis in two children with bilateral cryptorchidism. J Urol 1979; 121: 535-537
13. Arsian A, Yalin T, Akan H, Belet U. Pulmonary alveolar microlithiasis associated with calcifications in the seminal vesicles. J Belge Radiol 1996; 79: 118-119
14. Preibe CJ Jr, Garret R. testicular calcification in a 4-year old boy. *Pediatrics* 1970; 46: 785-786
15. Bercovitch RS, Januario JA, Terry SF, Boekelheide K, Podis AD, Dupuy DE, Bercovitch LG. Testicular Microlithiasis in Association with Pseudoxanthoma Elasticum. Radiology 2005; 237: 550-554
16. Parra BL, Venable DD, Gonzalez E, Eastham JA. Testicular microlithiasis as a

predictor of intratubular germ cell neoplasia. *Urology* 1996; 48: 797-799

17. Frush DP, Kleiwer MA, Madden JF. Testicular microlithiasis and subsequent development of metastatic germ cell tumor. *AJR* 1996; 167: 889-890
18. Emberton P, Moody AR. Testicular microlithiasis (letter) *AJR* 1994; 162: 1002-1003
19. Cast JEI, Nelson WM, Early AS, Biyani S, Cooksey G, Warnock NG, Breen DJ. Testicular Microlithiasis: Prevalence and Tumor Risk in a Population Referred for Scrotal Sonography. *AJR* 2000; 175: 1703-1706
20. Miller RL, Wissman R, White S, Ragosin R. Testicular microlithiasis: a benign condition with a malignant association. *J Clin Ultrasound* 1996; 24: 197-202
21. Vegni-Talluri M, Bigliiardi E, Vanni MG, Tota G. Testicular microlithiasis: their origin and structure. *J Urol* 1980; 124: 105-107
22. Janzen DL, Mathieson JR. Testicular microlithiasis and seminoma (letter) *Clin Radiol* 1993; 48: 219-220