We report a rare case of three leiomyomas of the spermatic cord and testis in a 73-year-old man. Indirect, large, painful, non-reducible inguinal hernia was diagnosed at admission. During surgery, the hernia was revealed. Furthermore, two tumors were found, both attached on the spermatic cord, and a third tumor close to the testis. All the tumors were carefully removed and no orchidectomy was performed. Hernia repair was performed and the removed tumors were sent to the Pathology Department. All tumors were benign. At the first follow up, chromosomal analysis was also performed. Chromosomal lymphocyte analysis revealed increased fragility at site 4q31. Two years after surgery, the patient was admitted again with a new similar tumor, and underwent a new surgical treatment. In the case of large non-reducible inguinal hernias, surgeons have to consider tumors in the inguinal area in their differential diagnosis.

Key words: Leiomyoma; spermatic cord; testis; chromosomal analysis; 4q31 fragile site

INTRODUCTION

Epitheliod smooth-muscle tumors, or leiomyomas, are benign tumors more commonly found in the uterus, called fibroids, although there have also been cases reported at unusual sites. A very rare location of leiomyomas is at the testis and the spermatic cord. However, leiomyomas have been described in nearly every organ and every location in the soft tissue. Under the microscope, they look nearly identical in any organ. Clinically, leiomyomas are soft tissue tumors that sometimes present with pain.

The pathophysiology of leiomyomas is not well understood. Genetic predisposition, steroid hormones, and growth factors important in fibrotic processes and angiogenesis all play a role in the formation and growth of these tumors.

Leiomyomas may be viewed as a common phenotype resulting from a number of different genetic events. There are a variety of specific karyotypic subgroups that characterize myomas; however, the evolution of a cytogenetic abnormality appears to be a late event.

Herein, we describe a case of three leiomyomas of the spermatic cord and testis diagnosed as hernia. One of the tumors of the spermatic cord belongs to the symplastic or "bizzare" variety. Chromosomal analysis of the patient is also presented.

CASE PRESENTATION AND MANAGEMENT

A 73-year-old man presented to the emergency room, complaining of a painful enlargement of his left inguinal hernia. He mentioned that this hernia has been progressively enlarging, that it was initially reducible, but as it continued growing for the last eight months, it was getting sometimes painful and could not be reduced. It was his first time visiting a surgeon regarding this problem, so there was no previous estimation of the clinical condition. Upon further questioning (after surgery), the patient admitted that the inguinal mass was growing for much longer than eight months. During visual inspection with the patient coughing, a mass enlargement was observed on the respective side. Physical examination revealed an enlarged, hard, painful scrotum, particularly on the left side. The testicle was not clearly palpable as a separate part, because the entire scrotum was a painful mass. The preoperative diagnosis was chronic, non-reducible inguinal hernia; the preoperative feel was that the hernia sac contained bowel with hard adhesions. Therefore, the patient was moved to the operating room immediately after the pre-operative clinical examination.

On the operating table, an indirect inguinal hernia was revealed and the hernia sac contained small bowel, with no signs of necrosis. The sac turned out to be smaller than expected, whereas two tumors were found (one 9 cm and the other 5 cm in diameter) both attached on the spermatic
cord, resembling to beads on a string. A third tumor, of dimensions 13x5x3 cm, was found close to the testis. The tumors were carefully checked; their macroscopic characteristics were well-organized with clear macroscopic margins from the spermatic cord. No palpable lymph nodes were found in the inguinal area. Hernia repair was performed and the tumors were removed and sent to the Pathology Department. All the tumors were removed very carefully and no orchidectomy was performed. Follow up was every six months and included thorough clinical examination. At the first follow up, a right inguinal hernia was also diagnosed and repaired. No tumors were revealed on this side. At the two-year follow up the patient was doing well.

The histological analysis showed that the first tumor (9 cm) of the spermatic cord was a symplastic leiomyoma, which showed atypical multinucleated tumor giant cells and no mitoses (Figure 1a). The other two tumors were leiomyomas containing areas with characteristics of a sclerotic fibroma with extended hyalinization of the substrate and plasma cell infiltrations (Figure 1b). Histological features associated with malignancy were absent.

At the first follow up, chromosomal analysis was performed. Lymphocytes of the peripheral blood of the patient (0.4 ml) were cultured in Chromosome Medium B (5 ml) (Biochrom KG) for 72h at 37°C. Colcemide was added to all cultures at 70h, for further incubation of approximately 2h. Cell harvesting followed. G-banding and C-banding karyotyping analysis was carried out applying the standard protocols. Fifty metaphases were karyotypically analyzed for each individual in both banding techniques. When an abnormality was identified, a hundred metaphases were analyzed to avoid misdiagnosis. Chromosomal analysis of the patient was performed on 4 peripheral blood lymphocyte cultures. A total of 25 cells from each culture were karyotypically analyzed employing G and C banding techniques.

In 88.4% of analyzed cells the genotype was 46, XY. A terminal deletion in 4(q31.1) was noticed in 11.6% of analyzed metaphases (Fig. 2a,b). An acentric fragment representing 4(q31.1qter) was identified in some of the cells mentioned above. Therefore, the genotype of the patient is: 46, XY (88.44%) / 46, XY, del(4)(q31.1) (11.6%).

Two years after the tumor excision the patient was admitted again with an enlargement of the testis. The U/S at the urology department revealed a solid mass which enclosed the testis. The patient underwent surgical excision of the tumor and the testis. The pathology report revealed again a symplastic leiomyoma, which showed atypical multinucleated tumor giant cells and no mitoses, similarly to the initial tumor. The patient is doing well after one month follow up.

DISCUSSION

There is a prevailing view that leiomyomas of deep soft tissue are rare or non-existent; however, data on this subject are limited. Extended clinical studies with long follow up information are lacking.

The benign leiomyoma is characterized by a circumscribed margin and hyalinization, whereas the clinically malignant one presents hypercellularity, nuclear atypia, increased mitotic activity and tumor cell necrosis [1]. The symplastic, or bizarre, leiomyoma is characterized by cells that are either multinucleated, or contain multilobed nuclei, and often have prominent intranuclear invagination of eosinophilic cytoplasm. Leiomyomas are more commonly found in the uterus, but there have been reports of it involving the vagina and, more commonly, the skin. The skin lesions reported are both pilo epitheliomas and hemangiomas².

The genitourinary leiomyomas are more commonly found in the renal capsule, but there are also reports of leiomyomas of the testis². Although masses other than hernias can occur in the inguinal region, the phenomenon is very rare. In our hospital, approximately 10% of the patients admitted with hernias have non-reducible hernias; from the total number of patients who underwent hernia repair, only 0.002% presented with a tumor. It was the
first time our patient visited a surgeon regarding his problem as an emergency case; therefore, there was no previous estimation of his clinical condition. One would expect that the firmer feel of separate, relatively large leiomyomas would have provided a hint on their existence at the original exam; however, this was not the case. Furthermore, the testicle could not be clearly palpated as separate, because the entire scrotum was a painful mass. Therefore, there was no suspicion about the tumors before surgery. When we realized their existence, we carefully checked them and also palpated for lymph nodes. We decided not to perform orchidectomy, at least until getting the final pathology report.

Follow up was every six months. It included thorough clinical examination and, if necessary, ultrasound. In our case, ultrasound at follow up was not deemed necessary by the surgical team. At the first follow up, a right inguinal hernia was also diagnosed and repaired. No tumors were revealed on this side. At the two-year follow-up the patient was doing well. To the best of our knowledge, this is the first case of a symplastic leiomyoma of the spermatic cord involving three independent tumors.

Chromosomal analysis from peripheral blood lymphocytes revealed a terminal deletion in chromosome 4 in 11.6% of analyzed cells. Several regions of the long arm of chromosome 4 have been implicated in structural abnormalities identified in uterine leiomyoma tissues. To the best of our knowledge, a cutaneous leiomyoma has never been connected with a heritable or de novo structural abnormality implicating chromosome 4. An autosomal dominant disorder consisting of multiple cutaneous leiomyomas and uterine fibroids (Reed syndrome) has been localized to a gene encoding for fumarate hydratase (FH) on chromosome 1q42.3-43. A case study has reported a severely mentally retarded adult female with 9p trisomy/18pter monosomy 46,XY,der(18),t(9;18)(p13; p11) presented with multiple cutaneous leiomyomas. Ring chromosome 12 mosaicism, 46,XX,t(12)(pl3.3q24.3)/46,XX has also been associated with a pedunculated uterine leiomyoma.

Terminal deletion of 4q (4q31 ter) produces a multiple congenital anomaly/mental retardation (MCA/MR) syndrome, in which the phenotype correlates with the amount of chromosome material missing. The patient of the present case report did not share any phenotypic features with an MCA/MR syndrome. This is probably due to the fact that there is not actually a partial monosomy of chromosome 4 present, since an acentric fragment was also found in most analyzed cells baring del4(qter). The GTG banding pattern of this fragment matched 4q31q35 region. Besides that, breakpoint site 4q31 is a common fragile site, which, as illustrated, exhibited increased breakage leading to a terminal deletion. Fragile sites are specific genomic loci that are especially prone to express genomic instability that is observed as an increased rate of sister chromatid exchanges, deletions and translocation breakpoints. Over the years, studies on fragile sites have illustrated their significant role in genome stability, tumorigenesis, cell cycle checkpoints, DNA repair and replication dynamics.

Site 4q31, a common fragile site, exhibited an increased degree of breakage leading to a terminal deletion in a portion of analyzed cells. The association of fragile sites with tumorigenesis has already been established, and thus, it is probable that the benign form of leiomyoma tumor identified in the present patient is connected with the presence of spontaneously increased breakage at site 4q31.

CONCLUSIONS

We describe a rare case of a spermatic cord symplastic leiomyoma associated with two other sclerotic leiomyomas originally presenting as a painful, non-reducible hernia. To the best of our knowledge, this is the first symplastic leiomyoma of the spermatic cord with three independent tumors. Despite their worrisome cytologic appearances, the clinical features and the follow up data support the benign nature of the lesions. Chromosomal analysis revealed that it is probable that the benign form of the leiomyoma tumor identified in this case is connected with the presence of increased fragility at site 4q31. Therefore,
in the case of large non-reducible inguinal hernias, surgeons have to consider tumors in the inguinal area in their differential diagnosis.

SUMMARY


Ključne reči: Leiomiom; spermatična vrpca, testis, analiza hromozoma

REFERENCES