Rare, Unexpected Condition of MRKH

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Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is one of the most common causes of primary amenorrhea, second only to gonadic dysgenesis, having a frequency of 1:4000–5000 women . This syndrome manifests as an aplasia or hypoplasia of the uterus and the upper two-thirds of the vagina, regular ovaries and tubes and a normal development of secondary sexual characteristics . The karyotype is generally normal (46, XX) and the manifestation is secondary to an abnormal development of the müllerian ducts.

Mayer-Rokitansky-Küster-Hauser leiomyoma pelvic mass torsion

1. Introduction

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is one of the most common causes of primary amenorrhea, second only to gonadic dysgenesis, having a frequency of 1:4000–5000 women [1]. This syndrome manifests as an aplasia or hypoplasia of the uterus and the upper two-thirds of the vagina, regular ovaries and tubes and a normal development of secondary sexual characteristics [2]. The karyotype is generally normal (46, XX) and the manifestation is secondary to an abnormal development of the müllerian ducts.

The syndrome has three different forms: type 1, typical form, is characterized by congenital absence of the uterus and the upper two-thirds of the vagina with regular adnexa; type 2, atypical form, manifests alterations to the genital apparatus (ovaries) and renal defects; type 3 shows aplasia or hypoplasia of the uterus and vagina in association with renal malformations (ectopic kidney, renal agenesis, horseshoe kidney) as well as skeleton, cardiac, ocular and hearing alterations, known as MURC syndrome [3]. In the past, the syndrome has been considered as a sporadic anomaly, but the increasing number of familial cases supports the hypothesis of a genetic cause. In these cases, the syndrome appears to be transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivity.

The presence of leiomyomas in patients with MRKH syndrome is rare and, according to a recent review, only one other case has been described in Italy [4]. The majority of leiomyomas develop in women with a mono or bilateral rudimental uterus; in the literature, a leiomyoma in the absence of a rudimental uterus is described only in two cases. In some cases, CT scans, as well as MRI, are not accurate in the diagnosis of leiomyoma or its anatomical delineation [5][6]. Therefore, in most cases, surgery is the only diagnostic tool to define the nature of the lesion.

Leiomyomas are benign tumors derived from smooth muscle cells forming the myometrium. They represent the most common benign female genital neoplasia with an estimated frequency of 20% of the population between 30-

and 60-year-old women [7]. In the current study, we would like to describe the case of a 50 year old patient with MRKH syndrome who was hospitalized with acute abdomen due to intraoperative evidence of a para-ovarian pelvic neoformation twisted on its own peduncles. Furthermore, the purpose of this study is to identify the number of cases of leyomyomas in patients with MRKH reported in the literature and how many of these manifested as an acute abdomen.

2. Materials and Methods

A search was carried out on PubMed and Scopus (until December 2020) to identify articles involving patients with MRKH and leiomyomatosis. The research was focused on original articles in English. Nine manuscripts were detected through the references of the works that had been identified with the research on PubMed and Scopus. A total of 35 cases were found describing the presence of myomatosis in patients with MRKH where 27 were not complicated and 8, instead, had an acute manifestation similar to our case.

3. Discussion

The presence of a pelvic mass in a woman with MRKH can be a diagnostic dilemma due to a subverted gynecologic anatomy and the frequent association with renal malformations. Specifically, our case falls within the classic form of the syndrome, with the presence of a rudimental unilateral uterus. Clinically, it seems that the mass can be completely asymptomatic until its volume reaches great dimensions (10–15 cm). This is probably due to the poor mobility and, therefore, to the reduced possibility of torsion of myomas of these sizes.

The age of onset is the same of the population with normal gynecologic development, and surgeons almost unanimously prefer the laparotomic approach in emergency cases such as the ones analyzed in the current review.

On ultrasound examination, leiomyomas are hypoechoic or heterogeneous masses. Sometimes there can be an internal cystic degeneration with necrosis or hemorrhage that appears ultrasonographically as a cystic component with internal echogenic material; differently, calcifications appear as hyperechoic foci [8].

The pre-surgical differential diagnosis between an ovarian lesion and a lesion of a rudimental uterus may be difficult since the usual anatomical landmarks are subverted. For example, a large pelvic mass with possible inner myxomatous degeneration may be easily confused with a cystic ovarian lesion [9].

If the mass is associated with pelvic pain, adenomyosis and other pathologies should be considered in the differential diagnosis, as described in rare cases [10][11]. In our case, the patient denied a history of pelvic pain, endometriosis and she declared that she never had a menstrual cycle. This excluded from the differential diagnosis the possibility of hematocolpos or pain related to the hormonal cycle.

Among the few cases described in the literature, apparently only eight are reported to be the manifestation of the lesion as a twisted mass, and six patients had an acute abdomen. Furthermore, only in two reports, the torsion

involved the mass exclusively, sparing the adnexa [5][6], similarly to what happened in our case (Table 2), where both surgical procedure and histological examination highlighted that neither the uterus or ipsilateral Fallopian tube were involved in the torsion. This allowed us to save the ovaries, preserving the hormonal balance of the patient. Apparently, this is the second case in which it was possible to spare the patient's ovaries.

Table 2. Torsion of leiomyomas in Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome in the literature.

References	Age of Onset	Acute Abdomen	Surgical Approach	Imaging	Dimension of the Lesion	Mass Localization	Type of Surgery
YAN, et al. (2002) [6]	52	Yes	LPT	US + CT	15 cm	Rudimentary uterus	Hysterectomy and bilateral salpingo-oophorectomy
Galajova, et al. (2003) [37]	55	No	LPT	US	10 cm × 7.5 cm	Not reported	Mass only
Petric, et al. (2008) [36]	53	Yes	LPT	Not reported	Date not available	Not clear origin	Mass only
FLETCHER, et al. (2012) [5]	28	Yes	LPT Pfannenstiel	MRI	10 cm × 15 cm	Paraovarian mass	Mass only
VIDYASHREE, et al. (2014) [32]	40	No	LPT	CT + MRI	6 cm × 7 cm and 5 × 6 cm	Rudimental uterus	Bilateral salpingo-oophorectomy and excision of uterine remnant
KUNDU, et al. (2014) [33]	40	Yes	Vertical LPT	US + CT	10 cm	Rudimentary uterus	Right salpingo-oophorectomy, excision of right and left hemiuteri with pedunculated leiomyomas, and left salpingectomy
YI, et al. (2016) [34]	47	Yes	LPS	MRI	Date not available	Rudimentary uterus	Bilateral salpingo-oophorectomy and excision of uterine remnant
HOO, et al. (2016) [35]	45	Yes	LPT	US + MRI	15 cm × 13 cm × 13 cm	Right adnexa	Right salpingo-oophorectomy

References	Age of Onset	Acute Abdomen	Surgical Approach	Imaging	Dimension of the Lesion	Mass Localization	Type of Surgery
							and excision of uterine remnant
Case Described by This Article	50	Yes	LPT Pfannenstiel	US + CT	10 cm × 9 cm × 7 cm	Paraovarian mass	Mass only

Regarding the surgical procedure, the literature describes various approaches. Laparoscopic, as well as laparotomic techniques, have been chosen according to the patient's clinical evaluation, imaging, number of masses, mass localization and characteristics (size of the mass or complicated nature of its feeding arteries). a mono or bilateral salpingo-oophorectomy may be added to the procedure, according to the mass location or complication [12]. In conclusion, even if our case seems to be clinically similar to a few others described in the literature, in the current paper, we would like to share a particular immunohistochemical aspect we have discovered.

The current knowledge about it suggests that the pathogenesis of fibroids is a multistep process, starting with the recruitment of a smooth muscle stem cell from the myometrium that lacks receptors for the gonadal steroids. Subsequently, four key cell types that comprise fibroids (smooth muscle cells, vascular smooth muscle cells, fibroblasts and fibroid-associated fibroblasts) and the extracellular matrix (ECM) synergize with environmental and molecular stimuli to undergo growth acceleration and progression into clinical disease [13][14]. Therefore, the development of fibroids in an MRKH patient can be explained by the presence of smooth muscle cells in the proximal ends of the müllerian ducts, stimulated by the estrogen physiologically produced by the ovaries, resulting in the formation of leiomyomas; in these cells, the estrogenic receptors seem to be overexpressed [3]. However, Sharma et al. attribute low concentration or sensibility to the estrogenic stimulation by the receptors located on the rudimental uterine horns in women with MRKH [15].

4. Conclusions

In women with Mayer-Rokitansky-Küster-Hauser syndrome presenting with pelvic pain not responsive to the analgesic therapy, the presence of a gynecological complication should always be considered among the possible diagnosis. The use of ultrasonography is recommended, adding a CT or an MRI for higher anatomical detail and better pre-surgical stadiation. However, the proper and final diagnosis, due to the rarity and the anatomical complexity of these lesions, can be given only through surgical procedure and histological evaluation.

We demonstrated that the etiopathogenesis of leiomyomas still remains unclear, and the cluster of agonists and antagonists with their receptors involved in the development needs to be clarified.

Finally, from our review, it emerges that the occurrence of new myomatous neoplasms in patients with MRKH, starting or not from uterine rudiments, could cause an acute abdomen requiring urgent surgery. For this reason,

patients who undergo pelvic surgery could benefit from preventive remotion of uterine residues by minimally invasive surgery with minimal discomfort to the patients.

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