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Mayer-Rokitansky-Kuster-Hauser syndrome accompanied by invasive ductal carcinoma: a case report

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Summary

Müllerian agenesis and the absence of organs of Müllerian canal origin are referred to as Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome. Invasive ductal carcinoma constitutes 47-75% of all breast carcinomas and is the most common type. The authors report the first case of invasive ductal carcinoma associated with MRKH syndrome in the literature to their knowledge. A 25-year-old woman with a palpable mass in her right breast for three months presented to the presented clinic. On physical examination a mobile, firm mass measuring 2×2 cm was detected in right breast, at a region close to axilla. A fine needle aspiration biopsy from the lesion revealed malignant cells and thus a segmental mastectomy operation was performed. All genital tract and endocrinological system should be thoroughly examined before administering hormone replacement therapy to patients presenting with primary amenorrhea.The co-occurrence MRKH syndrome of with invasive ductal carcinoma is regarded as coincidental. Confirming the absence of a common etiology, however, requires further genetic studies.

Key words: Mayer-Rokitansky-Kuster-Hauser syndrome; Invasive ductal carcinoma; MRI.

Introduction

Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is the second leading cause of primary amenorrhea and it affects one in every 4500 live births [1]. Mullerian agenesis and the absence of organs of Mullerian canal origin are referred to as MRKH syndrome. These women have normal female karyotypes and functioning ovaries while congenital renal and skeletal anomalies may be present [2]. The secondary sexual characteristics are normally developed and MRKH syndrome is not diagnosed until the cause of primary amenorrhea is investigated. This syndrome differ with respect to the extent of the vaginal aplasia, which ranges from a virtually absent vagina to a shorter one that is two to five cm in length (normally eight to 12 cm).

Breast cancer is the most common cancer in women. Invasive ductal carcinoma (IDC) constitutes 47-75% of all breast carcinomas and is the most common type [3].

The authors report the first case of invasive ductal carcinoma associated with MRKH syndrome in the literature to their knowledge.

Case Report

A 25-year-old woman with a palpable mass in her right breast for three months presented to the present clinic. No abnormality was noted in her biochemistry profile. On physical examination a mobile, firm mass measuring 2×2 cm was detected in the upper outer quadrant of the right breast, at a region close to axilla. There were also two conjoined lymphadenopathies having a diameter of one and 1.5 cm in right axilla. There was also a solid, heterogeneous mass lesion measuring 15×6 mm by ultrasonography and that was suggestive of malignancy in the upper outer quadrant of the right breast, in a region close to axilla. A fine needle aspiration biopsy from the lesion revealed malignant cells and thus a segmental mastectomy operation was performed to excise an elliptic skin portion over the mass in the outer quadrant of the right breast. The sample was sent for frozen examination and the result returned as a malignant tumor that lateral margin was positive on frozen section and was re-excised. Wide excision with additional axillary lymph nodes was carried out. The patient had an uneventful postoperative period; three days after the operation she had her drain removed and was discharged. A postoperative histopathological examination revealed invasive ductal carcinoma (both, modified Bloom and Richardson grade II: tubule and gland formation 3, nuclear grade of pleomorphism 2, and mitotic count 1) (Figure 1). There was positive lymphovascular and perineural invasion in histology specimen. Four of the nine lymph nodes sampled were metastatic. Estrogen receptors were 20% (+), progesterone receptors 5% (+), C-erb B-2 100% (+++), Ki-67 60% positive, and p53 3% (+).The clinical stage was determined T2N1M0 (Stage II) and the surgical therapy was followed by adjuvant chemo-, radio-, and hormonal therapy.

The patient had primary amenorrhea, for which she applied to an outside center and received an unknown hormone replacement therapy for a long period five years ago. The physical examination of the patient was characterized by the presence of normal secondary female sexual characteristics (pubic hair and breast development were of Tanner stage 5). A karyotype analy-

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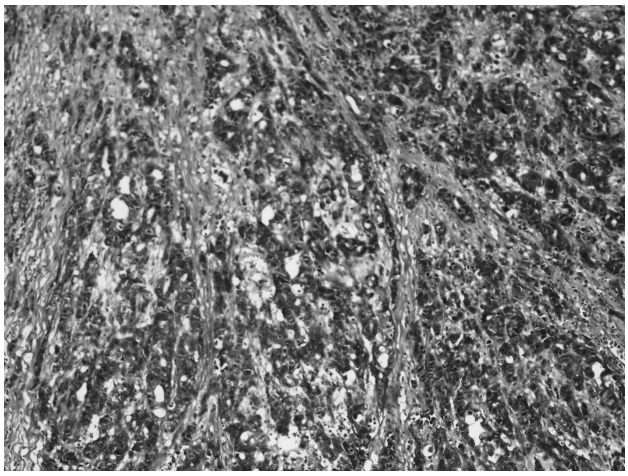

Figure 1. — Invasive ductal carcinoma, grade III (H&E ×100).

sis revealed a genotype of 46, XX. Hormonal parameters in blood tests were normal. Abdominal and pelvic ultrasonography and magnetic resonance imaging (MRI) were performed in the patient (Figures 2A-D). She was considered as having Type II MRKH syndrome since her both kidneys had an ectopic-ptotic location (Figure 2A) and there was an ovoid formation with an approximate diameter of 4.5×2.5 cm near the opening of the inguinal canal, immediately beneath the peritoneum, close to the anterior abdominal wall (Figures 2B-D). The lesion contained a thin linear hyperintensity consistent with endometrial tissue. The aforementioned formation was considered compatible with an ectopic-rudimentary uterus. Urethra could be visualized at the sagittal plane although no typical image of a vaginal canal could be located. Both ovaries were visible with normal morphology but they were localized more superiorly (Figures 2a, b). She had a vaginal remnant of two cm in length.

Discussion

Müllerian agenesis is a congenital malformation in women characterized by developmental failure of the Müllerian ducts, resulting in absence of the uterus and fallopian tubes, and varying malformations of the upper part of the vagina. There are two forms of MRKH syndrome: Type I results in isolated absence of the vagina and uterus, and Type II also affects other parts of the body includes various associated malformations related to vertebral, cardiac, urological (upper tract), and otological anomalies [4]. The present patient had a rudimentary uterus and short vaginal stump, although the fallopian tubes and ovaries were normal. She was considered as having Type II MRKH syndrome since her both kidneys had an ectopic-ptotic location.

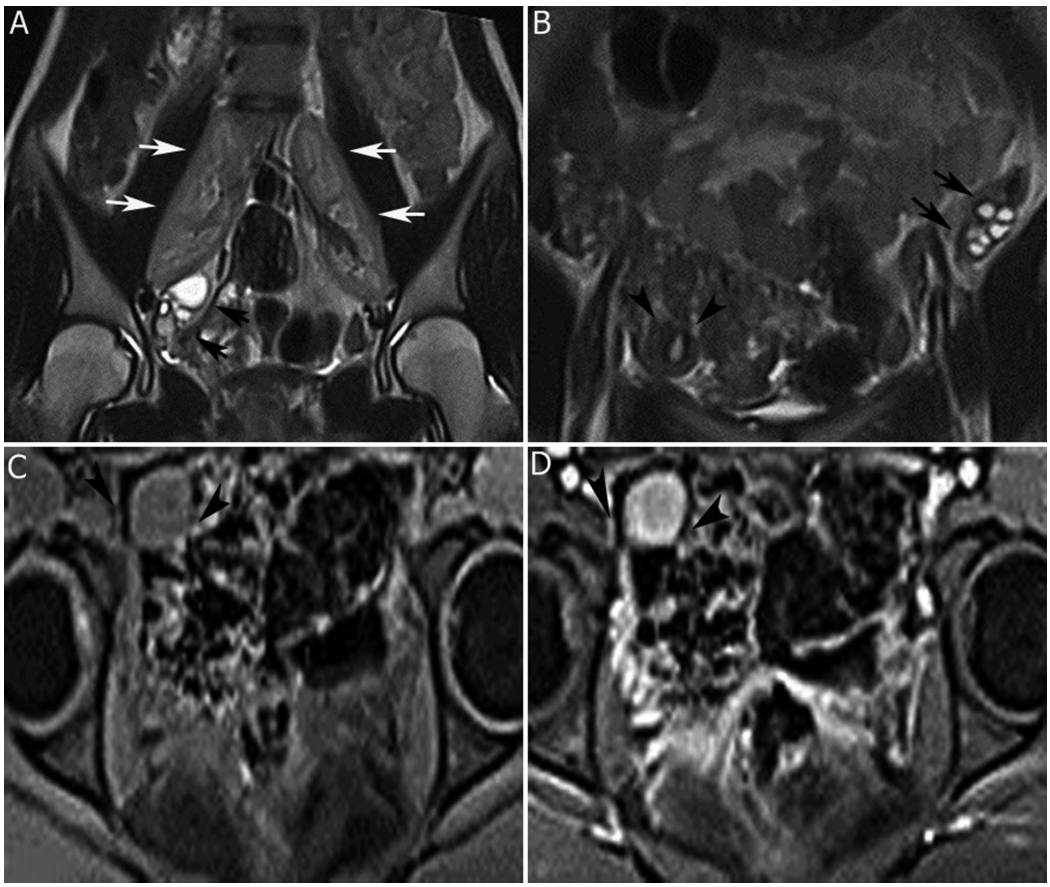

Figure 2. — Figure a-d: T2-weighted coronal images (A, B) show bilateral ectopic-ptotic kidney with normal morphology (A, white arrows) and bilateral ovaries (A, B, black arrows). Both ovaries are morphologically normal but localized more superiorly. In addition, ectopic rudimentary uterus with thin linear endometrium is observed near the opening of the inguinal canal (B, black arrowheads). Pre-contrast and post-contrast fat-supressed T1-weighted images (C, D) demonstrate enhancement of the rudimentary uterus (black arrowheads).

Renal anomalies are observed in 15% to 40% of the cases, while skeletal anomalies are seen in 30% to 45% of cases, with scoliosis being the primary skeletal anomaly [5]. Affected patients have 46 XX karyotype and a female phenotype. The syndrome is of unknown etiology, although its pathogenesis is thought to be secondary to an inhibited development of the Müllerian (paramesonephric) ducts [6]. Most cases are seen on a sporadic basis, although there are some families in which it is hereditary, suggesting an underlying genetic cause [7].

MRKH syndrome may also feature some form of malignancies. Nevertheless, all reports on the malignancies in this syndrome have indicated that they usually originate from the genital tract,such as ovaries (endodermal sinus tumor, a Sertoli cell tumor, and an immature teratoma of the ovary) [8]. Leiomyomas have also been reported in the literature [9]. As far as we know, this is the first case in the literature, which reported a co-occurrence of MRKH syndrome and invasive ductal carcinoma.

Breast cancer is the leading cause of cancer-related deaths worldwide [10]. Therefore, many studies have been conducted to date in an attempt to elucidate breast carcinogenesis. An increased risk has also been associated with early onset of menstruation, nulliparity or delayed first childbirth, short duration of breast feeding, late menopause, use of hormone replacement therapy, and increased bone density [11-12]. In addition, both environmental and genetic factors are believed to exert their influence by a hormonal mechanism [13, 14]. However, the etiological mechanisms of breast cancer have not fully understood and are thought to be multifactorial.

In conclusion, all genital tract and endocrinological system should be thoroughly examined before administering hormone replacement therapy to patients presenting with primary amenorrhea. The co-occurrence of MRKH with IDC is regarded as coincidental. Confirming the absence of a common etiology, however, requires further genetic studies.

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