Case Report

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Mesonephric Like Mullerian Adenocarcinoma Case Report: A Radiation Oncology Perspective

Mark E Bernard*[1], Virgilius Cornea[2], Waleed Mourad[1], Mahesh R Kudriomoti[1] and Marcus E Randall[1]

[1]*Department of Radiation Medicine, Lexington*

[2]*Department of Pathology, Lexington*

***Corresponding author:** Mark E Bernard, Department of Radiation Medicine, Lexington

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ABSTRACT

Mesonephric adenocarcinomas (MA) are rare tumors arising the Wolffian ducts [1]. These ducts (called mesonephric or wolffian) traverse in a parallel fashion to mullerian ducts during the embryonic period [1]. During female development, the mesonephric ducts degenerate with testosterone absence and in adult, only mesonephric remnants remain usually in the lateral cervical walls, broad ligament, although the ovarian hilum, mesosalpinx, and very rarely in the corpus uterus [2-4]. The remnants of Wolffian ducts sometimes become hyperplastic and give rise to adenocarcinomas [1]. Recently, reports on mesonephric-like adenocarcinomas have been presented [5-6]. These malignancies have immunophenotypic and morphologic characteristics similar to mesonephric carcinomas without an associated mesonephric remnant. While first reported in 2016, these are thought to behave more aggressively than endometrioid carcinomas. However, their biological potential is not yet clear. This case report presents our first experience with managing this rare malignancy along with justification for adjuvant treatment.

Abbreviations: MA: Mesonephric Adenocarcinomas; ER: Estrogen Receptor; TTF-1: Thyroid Transcription Factor 1; PMS-2: Postmeiotic Segregation Increased 2; MLH-1: MutL Homolog 1; MSH-2: MutL homolog 2; MSH-6: MutS Protein Homolog 6; IMRT: Intensity Modulated Radiation Therapy; LVI: lymphvascular Invasion; PORTEC: Post Operative Radiation Therapy in Endometrial Carcinoma; GOG: Gynecologic Oncology Group

Case

Patient was a 71-year-old gravida 2 para 2 woman who initially presented to her gynecologist with post-menopausal intermittent vaginal spotting for one month. Ultrasound showed a mass within the uterus which lead to total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pathology revealed a mesonephric-like adenocarcinoma measuring 3cm in greatest dimension and involving 85% of the myometrium (17mm out of 20mm). Lymphovascular aspace invasion was indeterminate and there was no assessment of the regional lymphatics. Estrogen Receptor (ER) showed, focal weak expression, Progesterone (PR) was negative, GATA binding protein 3 (GATA 3) and thyroid transcription factor 1 (TTF-1) showed strong patchy expression. MutL homolog 1 (MLH-1), Postmeiotic Segregation Increased 2 (PMS-2), MutL homolog 2 (MSH-2), and MutS Protein Homolog 6 (MSH-6) showed retained expression. If grading were to be in a manner similar to endometrioid carcinoma, it would be International Federation of Gynecology and Obstetrics (FIGO) II. Her case was discussed at a tumor board in a multidisciplinary fashion. The final consensus was for adjuvant radiation to the pelvis. She then completed 50.4Gy in 28 fractions to the pelvis using Intensity Modulated Radiation Therapy (IMRT) followed by 2 vaginal cylinder brachytherapy boost consisting of 6 Gy per fraction prescribed to the surface of the vaginal cuff.

Pathology

Discussion

Mesonephric-like adenocarcinoma was first reported by Mcfarland et al. [5]. They reported on a series of seven uterine corpus and

five ovarian neoplasms which distinct immunohistochemical and morphologic features. These tumors were negative for the estrogen receptor (ER) and progesterone receptor (PR), while being positive for GATA binding protein 3 (GATA 3) and thyroid transcription factor 1 (TTF-1). One neoplasm was negative for TTF-1. All the neoplasms showed glandular, tubular, papillary growth patterns. Mesonephric remnants were not seen in any of their cases. Our patient exhibited identical pathologic characteristics. The ER and PR stains were focally weak and negative, respectively. There was a mixture of solid, tubular, and papillary architecture, and staining was positive for both GATA-3 and TTF-1. These features push the differential diagnosis toward a mesonephric adenocarcinoma, and the lack of ER and PR positivity push the differential diagnosis away from an endometrial adenocarcinoma. However, the lack of mesonephric remnants in the pathology specimen or hyperplasia favor the mesonephric-like distinct entity. The questions of adjuvant treatment and, if so, what type are open questions

Management for early stage endometrial carcinomas is surgical staging which includes a decision to assess the pelvic lymph nodes [7]. Adjuvant treatment is then determined based on the pathologic features from the surgical specimen, extent of surgical staging, and patient age. Established risk factors for recurrence include patient age, depth of myometrial invasion, grade, and presence of lymphvascular invasion (LVI) [7-8]. If a patient meets criteria established by either Gynecologic Oncology Group (GOG) 99 or Post-Operative Radiation Therapy in Endometrial Carcinoma (PORTEC) trials, then adjuvant radiation therapy is recommended [7-9]. Adjuvant radiation therapy can consist of pelvic external beam, vaginal cuff brachytherapy, or both [7-10]. Which treatment to give has its controversies and practice patterns vary across the United States [11]. Regardless, GOG 249 showed radiation is standard of care for these patients [10]. Our patient was found to have an incidental carcinoma from an apparent type I hysterectomy and bilateral salpingo-oophorectomy. Her tumor invaded nearly all of the myometrium (85%), LVI was indeterminate, and her tumor was assigned a FIGO grade II. Although the grade was determined, as if it were an endometrial adenocarcinoma and there is no current grading system for mesonephric-like carcinomas. Given she is above 70 years of age, with outer third myometrium invasion, and a grade 2 malignancy, she met the high-intermediate risk category of GOG 99 [7].

Patients in this trial had a significant reduction in local recurrence with pelvic radiation when compared to observation (6 vs 26%). She also would have qualified for the high-risk category of PORTEC 1 given she was above the patient of 60 and had greater than 50% myometrium invasion [12]. The addition of pelvic radiation, when compared to observation, reduced the risk of local regional recurrence (5 vs 23%).Therefore this patient was thought to benefit from adjuvant radiation therapy. While the decision to use vaginal brachytherapy alone or whole pelvic radiation comes with its controversies, this patient was thought to benefit more than pelvic radiation given she did not have a nodal dissection or assessment. This is our first mesonephric- like adenocarcinoma case report. The pathologic results are in keeping with what has been previously reported and her adjuvant treatment was extrapolated from prior randomized control trials for endometrial primaries.

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