Renal endometriosis mimicking a malignancy– a rare case of Reno-Mullerian fusion?

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Abstract

Endometriosis is a common gynaecological condition characterised by ectopic endometrial tissue growth beyond the uterine cavity. Urinary tract endometriosis represents only 1.2% of all cases, with renal endometriosis accounting for less than 1% of urinary tract involvement. An asymptomatic, 49-year-old, perimenopausal Irish female was found to have an incidental mass at the upper pole of the right kidney on imaging studies. Histological analysis was recommended to outrule a renal malignancy and an open radical nephrectomy was performed following multidisciplinary input. Histological analysis surprisingly revealed the presence of endometriosis and endosalpingiosis, accompanied by a significant smooth muscle component, which mimicked a renal neoplasm. The aetiology of renal endometriosis remains unclear. However, given the lack of a history of endometriosis and the absence of other foci of disease in this patient, together with the smooth muscle predominant phenotype, this may represent a case of reno-mullerian fusion or endometrial displacement during gestational development. Keywords Endometriosis, smooth muscle, reno-mullerian fusion, malignancy

Introduction

Endometriosis is a common gynaecological condition characterised by ectopic endometrial tissue growth beyond the uterine cavity (1). There are several hypotheses as to how endometriosis originates, including the implantation theory (retrograde menstruation), coelomic metaplasia (metaplastic processes of the peritoneal mesothelium) and even Mullerian duct abnormalities during embryogenesis (2).

Endometriosis is the second most common pathology in the female pelvis, affecting 15% of women of reproductive age (3). While most cases occur in the pelvis, extra-pelvic endometriosis can rarely involve sites such as the urinary tract and skin (4). Urinary tract endometriosis represents only 1.2% of all cases and typically occurs in the bladder and ureters, with renal endometriosis accounting for less than 1% of urinary tract involvement (3). Here, we report a rare case of renal endometriosis that mimicked a malignancy and explore its possible aetiology.

Case Report

An asymptomatic, 49-year-old, perimenopausal Irish female underwent abdominal ultrasound imaging for workup of abnormal liver function tests. Sonographically, a 4.2 cm mass in the upper pole of the right kidney was incidentally identified.

Following Computed Tomography imaging (Image 3), which characterised this lesion as a nodular, thick-walled, enhancing mass with possible central necrosis and perinephric fat stranding, the differential diagnoses included a renal malignancy or a haemorrhagic cyst. On Magnetic Resonance Imaging (Image 3), the lesion demonstrated different signal characteristics compared to the renal cortex and significant enhancement following contrast administration, therefore histological analysis was recommended to exclude a neoplasm.

Following review of imaging studies at a multidisciplinary team meeting and subsequent patient counselling, the decision was made to proceed directly to an open radical nephrectomy. An open approach was preferred given the adherence of the lesion to the inferior vena cava and diaphragm. The procedure was completed without any intraoperative complications and the patient had a successful postoperative recovery.

On gross dissection in the Histopathology laboratory, the resected nephrectomy specimen weighed 516 g and measured 154 x 105 x 55 mm. At the upper pole and adjacent perinephric fat, sectioning revealed an ill-defined, fibrosing mass lesion with variegated golden yellow deposits, primarily involving the perinephric fat with a minimal focus of attachment to the renal parenchyma.

Histological analysis surprisingly revealed the presence of endometriosis and endosalpingiosis with an accompanying histiocytic inflammatory reaction and prominent lymphoid aggregates (Image 1), supported by immunohistochemical staining with PAX8, AE1/3, CD10, CK7 and p16. Endometrial glandular tissue was accompanied by endometrial stroma and a significant smooth muscle component (Image 2), as demonstrated by actin immunostain positivity. There was no evidence of atypia or malignancy.

On histological analysis, the lesion demonstrated glandular structures accompanied by endometrial stroma with a prominent smooth muscle component, associated with a histiocytic inflammatory reaction and prominent lymphoid aggregates. Although endometrial glands and stroma were identified and a renal cell carcinoma excluded, the key differential diagnoses that remained were an angiomyolipoma (a differential diagnosis encountered in previous similar case reports (5)) or a mixed epithelial/stromal tumour. Renal angiomyolipomas are mesenchymal tumours that often present in the kidneys on a background of underlying Tuberous Sclerosis, a rare autosomal dominant disease (6), of which our patient had no history. Angiomyolipomas contain variable amounts of smooth muscle but also adipose tissue and dystrophic blood vessels; the latter were not present in this case. In addition, they typically stain positively for HMB45 (a melanocytic marker), which was negative. In the consideration of mixed epithelial/stromal tumours, they are known to have similar combinations of smooth muscle and glandular structures as endometriosis, but are typically well circumscribed with prominent cysts and centred on the renal medulla, which was not the case here.

Discussion

Several case studies have identified the diagnostic difficulty posed by renal endometriosis, particularly in its differentiation from a neoplasm. Conventional imaging modalities are limited in discriminating between endometriosis and a cystic malignancy (7). The majority of previously reported cases were indeed cystic or demonstrated a cystic component. Although a cystic component was suspected radiologically in our case, this was not found at gross inspection, with the inflammation and associated edema possibly accounting for this radiological impression.

Clinically, endometriotic lesions with a prominent smooth muscle component may give rise to a significant mass effect, which can mimic a malignancy on imaging studies. Several reports have identified that endometriosis has the potential to mimic a neoplasm, as the disease presents with multiple components in varying quantities, such as smooth muscle (8). Large amounts of fibromuscular tissue are more associated with deeply infiltrating endometriosis (9). The fact that renal endometriosis is exceedingly rare, accounting for 0.1-1% of all cases (3), coupled with the knowledge that lesions with a smooth muscle predominance are atypical and difficult to separate from a neoplastic process, contributed to the diagnostic dilemma in our case.

Pre-operative distinction from an angiomyolipoma on core biopsy can be difficult in lesions that have a prominent smooth muscle component, with endometrial glands in endometriosis and entrapped renal tubules in an angiomyolipoma both demonstrating positivity for PAX8. In this situation, CD10 and ER/PR immunohistochemistry, confirming endometrial stroma, is necessary. In addition, smooth muscle predominant angiomyolipomas may be negative for HMB45, especially in a core biopsy.

The right kidney was involved in our case, and in previous case reports where laterally is indicated, the majority of the lesions were also right-sided (3, 5, 7, 10). Additionally, the concurrence or history of other foci of endometriosis outside of the kidney is mentioned in only two of the thirteen previous cases. The curious right-sided predilection and the frequent absence of endometriosis elsewhere suggests that renal endometriosis may develop from a residual Mullerian remnant in or adjacent to the kidney, rather than through retrograde menstruation or a metaplastic process. The proximity of the paramesonephric duct to the mesonephros during embryogenesis may account for this phenomenon. During embryonic development, the urogenital ridges eventually differentiate into the kidneys, ureters, reproductive ducts and gonads (11). The same primitive coelomic epithelium also invaginates near the anterior aspect of the mesonephros (foetal kidney) and expands caudally to form the Mullerian ducts, which are the origin of the female reproductive tract (11). The intermediate mesoderm eventually develops into the kidneys and parts of the reproductive system.

Another possible hypothesis for the occurrence of endometriosis in this case is ectopic implantation of endometrial tissue, known as Mullerianosis. The embryonic rest theory proposes that cells of Mullerian origin within the peritoneal cavity may be induced to form endometrial tissue, which can result in endometriosis at various locations along the migration pathway of the Mullerian system (12). In one study investigating this theory, 4 out of 36 foetuses examined at post-mortem demonstrated the presence of misplaced endometrium in five different ectopic sites (13). This suggests that one cause of endometriosis may be the dislocation of primitive endometrial tissue outside of the uterine cavity during gestational development, as opposed to retrograde menstruation.

Such ectopic misplacement or fusion of tissue at embryogenesis is recognised in other areas of human biology. For example, adrenal cortical rests in the testes and testicular adnexa occur frequently, not just in exclusive cases of congenital adrenal hyperplasia (14). In addition, splenogonadal fusion is a recognised anomaly, which is characterised by congenital fusion between the spleen and testicular tissue, often

presenting as a testicular mass. This specific congenital malformation is believed to occur due to the close proximity of the developing gonad and spleen during gestational development, resulting in an abnormal connection between these structures during early embryological development, which facilitates their fusion. Following this fusion, once gonadal descent begins, the attached splenic tissue subsequently follows the gonadal path (15). Misplacement of endometrial tissue or indeed fusion of the developing kidney and Mullerian ducts may account for the rare presence of renal endometriosis in our case.

In conclusion, this is a rare case of renal endometriosis, which clinically and radiologically mimicked a neoplastic process due to the prominent smooth muscle component and associated inflammation and edema. Histopathological correlation with multidisciplinary team input and collaboration was required to accurately diagnose this entity and ensure that an appropriate management plan was implemented. The aetiology of renal endometriosis remains unclear with several theories hypothesised (2); however, given the lack of a history of endometriosis and the absence of other foci of disease in this patient, together with the smooth muscle predominant phenotype, this may represent a case of reno-mullerian fusion or endometrial displacement during gestational development.

Declarations

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1. Diarmuid O’Connor: Primary author of the manuscript; editor of the manuscript; sourced and formatted all histology images utilised.
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5. Teresa McHale: Supervising consultant of the case report; selected the case as a case of interest; editor of the manuscript; vetted all images utilised.

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