Rare histopathological diagnosis of malakoplakia and Rosai-Dorfman disease in the same uterus mimicking malignancy: A case report

SUHA SHRAIM[1], WEJDAN AL-ETTEWI[1], ISMAIEL ABU MAHFOUZ[2], MAIS AL-ATTAR[1] and ANWAR AL-MASRI[3]

[1]Department of Obstetrics and Gynecology, Specialty Hospital, Amman 11194, Jordan; [2]Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Balqa Applied University, Al-Salt 19117, Jordan; [3]Department of Histopathology, Specialty Hospital, Amman 11194, Jordan

Received February 7, 2024; Accepted September 2, 2024

DOI: 10.3892/etm.2025.12794

Abstract. In the present case, a 66-year-old woman presented to the Specialty Hospital (Amman, Jordan) with recurrent post-menopausal bleeding. A pelvic ultrasound scan showed an abnormal endometrial thickness of 8 mm and no adnexal masses. An endometrial biopsy revealed abundant foamy histiocyte infiltration features suggestive of xanthogranulomatous endometritis. Subsequently, a total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed, before histopathology confirmed the co-existence of uterine malakoplakia (MP) and Rosai-Dorfman disease (RDD). The patient had recurrent admissions for abscess drainage and pneumonia. MP and RDD of the uterus are both rare inflammatory diseases characterized by the histiocytic infiltration of the endometrium, which can occasionally be misdiagnosed as cancer and associated with an increased risk of systemic infections. The present case report shows that surgical resection provides a definite diagnosis and treatment guidance of this disease, potentially reducing the inflammatory process and recurrence rate. To the best of our knowledge, the present case report was the first of the coexistence of uterine RDD and MP.

Introduction

Xanthogranulomatous endometritis (XE) is a rare, histiocyte-rich and inflammatory disease that may affect the endometrium, mimicking malignancy, with <25 cases reported to date (1-3). XE is a histopathologically benign entity characterized by inflammatory cell infiltration and foamy macrophages (1). The mean age of presentation is 72 years and vaginal discharge is the most common presentation (1). Malakoplakia (MP) rarely involves the female genital tract with <40 reported cases up to 2021 (4) and the vagina being the most affected site (4). Although the etiology of MP is generally considered to be non-specific, immune suppression through conditions such as diabetes has been documented to contribute in numerous reported cases (5-8). The mean age of presentation is 66 years (2) and vaginal bleeding is reported as the most common presentation (4). However, histopathological samples are frequently positively stained with von Kossa special stain and have pathognomonic Michaelis-Gutmann bodies (4,5). MP is rare and the knowledge remains limited, for which there are no established treatment methods. Antibiotics and surgical resection are considered to be optimal for the treatment of this disease (4,5).

Rosai-Dorfman disease (RDD) is another non-common benign idiopathic disease, with a prevalence of 1 in 200,000 (9), that rarely involves the female genital tract (10,11). RDD commonly affects the lymph nodes but could be extranodal and affect the skin, bones and orbital tissues as common sites (11). The affected tissue is typically positively stained with S100, CD68 and CD163, whilst negatively staining for CD1a and Langerin (CD207) (10,11). To the best of our knowledge, the co-existence of MD and RDD in the same patient has never been reported. The present study reported the unique existence of disease entities that could be mistaken for malignancy and that a targeted histopathological diagnosis would facilitate handling of unexpected outcomes.

Case report

A 66-year-old multiparous, with type 2 diabetes, hypertensive woman who previously had no surgical operations, presented to the Specialty Hospital (Amman, Jordan) in February 2023 with recurrent episodes of post-menopausal bleeding over a 1-year period. Physical examination

Correspondence to: Dr Ismaiel Abu Mahfouz, Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Balqa Applied University, 60 Al Salt Street, Al-Salt 19117, Jordan
E-mail: ismaiel.mahfouz@bau.edu.jo

Key words: uterine malignancy, xanthogranuloma, endometritis, malakoplakia, Rosai-Dorfman disease

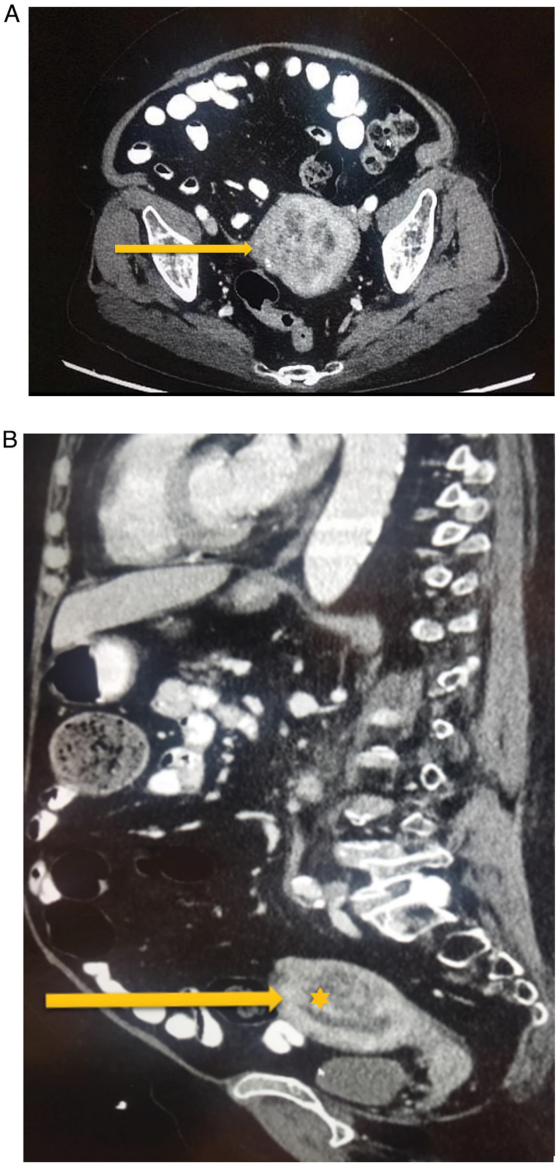

Figure 1. CT showing a heterogeneous lesion occupying the posterior wall of the uterus, compressing the endometrial cavity. (A) Sagittal view. (B) Cross-sectional view of the uterus. The arrows point to the uterus and the star indicates the thick endometrium previously measured by ultrasound at 8 mm.

revealed a normal body mass index of 27 kg/m^2 and lower abdominal tenderness. A transvaginal ultrasound scan (images not captured) showed a bulky uterus, an abnormal endometrial thickness of 8 mm and no adnexal masses or free fluid in the pelvis. A cervical smear was collected and the result was normal with no cytological indicators of cancerous/pre-cancerous lesions. Furthermore, an abdominopelvic CT scan was performed to identify any possible other types of lesions. The results showed a heterogeneous lesion occupying the posterior wall of the uterus involving two-thirds of the myometrium measuring 5.0x4.5x4.0 cm, compressing the endometrial cavity, with few retroperitoneal lymph nodes and no pelvic free fluid (Fig. 1A and B).

An endometrial biopsy was collected by dilatation and curettage and the tissue was processed for histological analysis. The tissue was fixed in 10% formalin at room temperature for

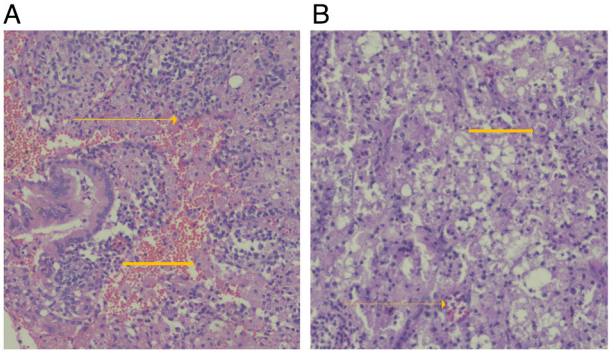

Figure 2. Histopathological analysis (magnification, x100) shows abundant inflammatory foamy histiocytes (thick arrow) and chronic inflammatory cells (thin arrow). (A) Histopathological finding of endometrial biopsy. (B) Histopathological finding of the endometrium post hysterectomy.

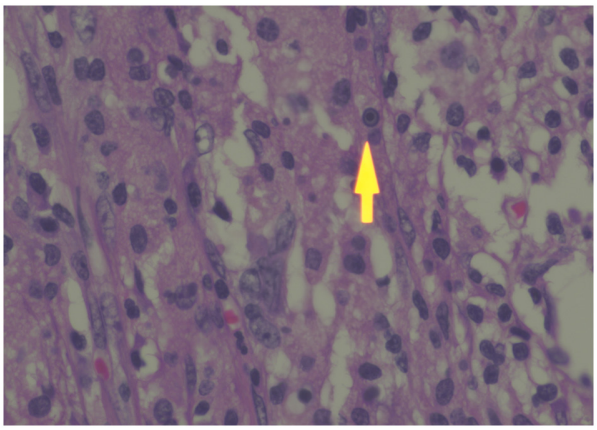

Figure 3. Michaelis-Gutmann bodies (arrow), a pathognomonic feature of malakoplakia (magnification, x100).

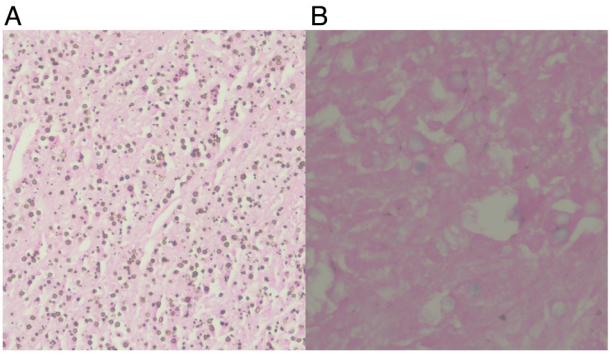

Figure 4. Positive staining for malakoplakia (magnification, x100). (A) Van Kossa-positive staining showing positive dark staining due to calcium content. (B) Iron-positive staining due to the calcium and iron salt content.

24 h, cut at a 5-μm thickness, stained with Harris H&E and observed under a light microscope. The histopathology results showed abundant inflammatory foamy histiocytes and chronic inflammatory cells (multinucleated giant cells formed from macrophage fusion), with no evidence of malignancy. The findings were suggestive of XE (Fig. 2A).

Considering the recurrence of postmenopausal bleeding and the results of histopathology being indicative of XE mimicking

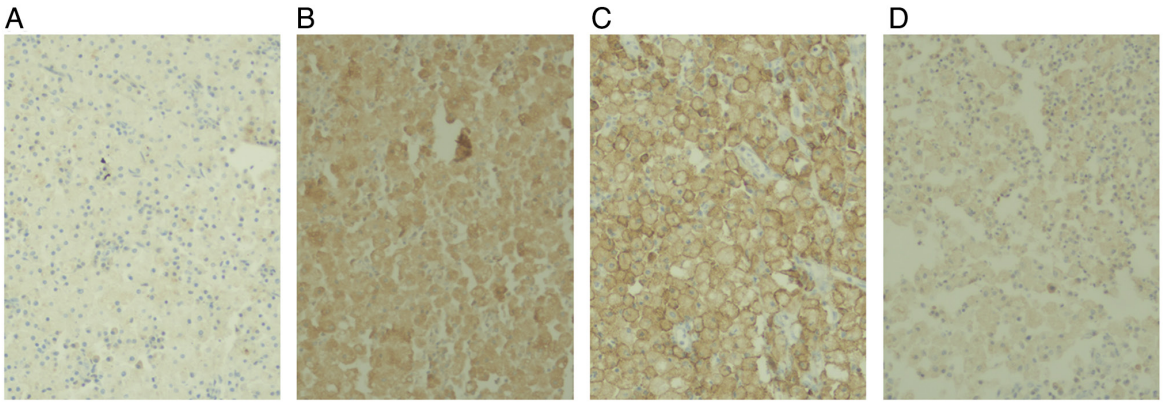

Figure 5. Histopathological immunostaining for Rosai-Dorfman disease (magnification, x100). (A) CD1a-negative, (B) CD68-positive, (C) CD163-positive and (D) S100-positive staining.

malignancy in it's presentation, a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH + BSO) were performed at the Specialty Hospital with the consent of the patient. Intraoperative findings showed a 10-week size uterus (10 cm) and no evidence of uterine fibroids, whereas both ovaries and Fallopian tubes were atrophic.

The results of histopathology using H&E confirmed histiocytic-rich lesions in the endometrium but otherwise an unremarkable cervix and ovaries (Fig. 2B). Histopathological differential diagnoses included RDD, MP and histiocytosis X. Subsequently, special stains were performed, which were suggestive of MP. The tissue was positive for pathognomonic Michaelis-Gutmann bodies (H&E; Fig. 3). In addition, both van Kossa staining (Fig. 4A) and iron staining (Fig. 4B) revealed positive results. A second histopathological opinion was sought, where further immunohistochemical staining was performed to examine the potential presence of RDD. For immunohistochemistry, a tissue sample was embedded in paraffin and cut at a thickness of 5 μm. The sections were incubated in H_2O_2 solution and a ready-to-use antibody kit was used. Detection was performed using 3,3'-diaminobenzidine. The stained tissue sections were observed under a light microscope. Finally, the presence of RDD was confirmed in addition to MP through positive staining to CD68, CD163 and S100 and negative staining to CD1a (Fig. 5). All staining was performed using standard protocols on an automated machine with pre-prepared antibodies (BenchMark GX; Roche Tissue Diagnostics).

Postoperatively, the patient had multiple admissions to the same hospital (three times for 5-6 days each) due to recurrent retroperitoneal abscesses, pneumonia and sepsis, but eventually, the patient recovered completely. The blood and pus cultures were positive for *Escherichia coli*. Broad-spectrum antibiotics were administered (mainly meropenem 500 mg intravenously twice daily and levofloxacin 500 mg intravenously once daily for 10 days that were chosen according to blood and abscess aspirate culture sensitivity) and a multiple CT-guided drainage of the pelvic abscesses was performed.

Discussion

XE is a benign disease that most commonly involves the kidney and gallbladder, but it rarely involves the female genital tract (2). Whilst the pathogenesis of XE remains clear, it may include obstruction of the female genital tract, inflammation, ischemia and hemorrhage, which may lead to the generation of free radicals and lipid peroxidation as part of the inflammatory process (2). Furthermore, in the histopathological diagnosis of XE, there is either focal or diffuse histiocyte infiltration (3). In the present case, XE involved the endometrium and two-thirds of the myometrium, which may explain the posterior uterine wall lesion observed on the CT scan.

The development of XE may involve both Langerhans and non-Langerhans cell histiocytosis (12). The non-Langerhans cell histiocytosis may encompass various diseases, such as RDD (12), which the patient in the present case was also found to have.

The first reported case of XE was in 1978 (1) with <30 reported cases worldwide to date (3,13). The clinical interest of XE in gynecology is that the clinical presentation, imaging and pathology may mimic malignancy, thereby making management challenging and necessitating a definitive histopathological diagnosis (1,2). Since the endometrial biopsy in the present case indicated XE and considering that endometrial adenocarcinoma and XE may co-exist (2), the patient was advised to undergo TAH + BSO.

Risk factors for the development of XE include being postmenopausal, having diabetes mellitus and hypertension, which the present patient had. The majority of cases of XE resolve after antibiotic treatment (1,3,13). However, if untreated, XE may result in systemic inflammation and death; therefore, surgery forms the mainstay of the treatment (1,3,13).

The patient in the present case had several postoperative hospital admissions due to recurrent retroperitoneal abscesses, pneumonia and sepsis. This postoperative course is not uncommon in women who have XE and develop *Escherichia coli* infections, similarly to the present case (14). The abscesses were drained under CT guidance along with antibiotics treatment [mainly meropenem (carbapenem) and levofloxacin (third generation fluoroquinolone)], which were chosen according to the bacterial culture sensitivity.

RDD is a rare inflammatory disease characterized by non-Langerhans cell histiocytosis commonly affecting

the lymph nodes. Up to 2018, there have been only three reported cases of RDD involving the female genital tract (10). Histologically, RDD is characterized by positive staining of S100, CD68 and CD163 and negative staining of CD1a and Langerin (CD207) (11).

Surgical excision of the affected tissue may be indicated in a unifocal extranodal disease (11) as in the present case. Additionally, systemic therapy may include corticosteroids, whereas immunomodulators can be used for the treatment of a non-focal disease. A recurrence is reported in 70% of untreated RDD cases (10).

MP is another rare inflammatory disease that frequently occurs in immunocompromised individuals (5). It commonly affects the urinary system, but rarely involves the female genital tract (4). Up to 2021, a total of <40 cases of MP involving the female genital tract have been reported, with the vagina being the most commonly affected site (4). The etiology of MP is poorly understood and is considered to be associated with the defective bactericidal capacity of macrophages (5). Clinically, vaginal bleeding is the most common presentation (83%) of MP (4). Histopathologically, pathognomonic Michaelis-Gutmann bodies (calcified iron-containing intracytoplasmic inclusions) are characteristic of MP, whilst positive staining can also be observed with periodic acid-Schiff, Perls' stain and von Kossa stain (5). Due to the limited cases reported, the clinical management of this disease remains unclear. However, general principles of treatment include the use of systemic antibiotics, surgical excision and limiting the immunosuppression process (5). These overlapping inflammatory processes (XE, RDD and MP) can be misdiagnosed clinicoradiologically as malignancy. However, clinicoradiological methods are the primary methods for differential diagnosis until a histopathological diagnosis is made (1,3). Furthermore, immunostaining techniques are used to confirm the inflammatory and disease-specific process over the neoplastic one (1,3). Also, the presence of Michaelis-Gutmann bodies is pathognomonic for MP, which are absent in malignancy (1,3).

In conclusion, XE is a rare inflammatory disease, which rarely involves the endometrium. It may be misdiagnosed as cancer, where its presence may complicate a postoperative course with repeated infections. Therefore, knowledge of the disease may help in planning postoperative care. Surgical resection and antibiotics administration are the primary treatment strategy for this disease.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WAE and MAA clinically managed the patient, performed the surgery, and drafted and revised the manuscript. SS and IAM collected clinical data, wrote and edited the manuscript, and prepared the figures. AAM performed histopathological analyses and drafted the manuscript. IAM and SS confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Malik V, Chatterjee D, Goel B and Takkar N: Xanthogranulomatous endometritis: A benign uncommon masquerader of malignancy. J Midlife Health 10: 206-208, 2019.
2. Makkar M, Gill M and Singh D: Xanthogranulomatous endometritis: An unusual pathological entity mimicking endometrial carcinoma. Ann Med Health Sci Res 3 (Suppl1): S48-S49, 2013.
3. Merviel P, James P, Carlier M, Thomas-Kergastel I, Guilloique M, Conan-Charlet V, Bastard C, Marcorelles P, Jobic Y and Dupré PF: Xanthogranulomatous endometritis: A case report and literature review. Clin Case Rep 9: e04299, 2021.
4. Saco A, Rakislova N, Marimon L, Torne A, Diaz-Feijoo B, Salvador R, Alos S, Jordao D, Hurtado JC and Ordi J: Malacoplakia of the uterine cervix: A case report. Pathogens 10: 343, 2021.
5. Kwan E, Riley CA and Robinson CA: Malakoplakia. In StatPearls. StatPearls Publishing. Malakoplakia-PubMed (nih.gov), 2022.
6. Leão CA, Duarte MI, Gamba C, Ramos JF, Rossi F, Galvão MM, David-Neto E, Nahas W, Shikanai-Yasuda MA and Pierrotti LC: Malakoplakia after renal transplantation in the current era of immunosuppressive therapy: Case report and literature review. Transpl Infect Dis 14: E137-E141, 2012.
7. Medlicott S, Magi-Galluzzi C, Jimenez RE and Trpkov K: Malakoplakia associated with prostatic adenocarcinoma: Report of 4 cases and literature review. Ann Diagn Pathol 22: 33-37, 2016.
8. Kohl SK and Hans CP: Cutaneous malakoplakia. Arch Pathol Lab Med 132: 113-117, 2008.
9. Werneck Rodrigues DO, Wolp Diniz R, Dentz LC, Costa MA, Lopes RH, Suassuna LF, Cintra JRD and Domenge C: Case study: Rosai-dorfman disease and its multifaceted aspects. J Blood Med 15: 123-128, 2024.
10. Marie J, Alday M and Cortez AC. (n.d.): Case report: Rosai-Dorfman disease: Pelvic manifestation*.
11. Bruce-Brand C, Schneider JW and Schubert P: Rosai-Dorfman disease: An overview. J Clin Pathol 73: 697-705, 2020.
12. Bourm KS, Menias CO, Ali K, Alhalabi K and Elsayes KM: Spectrum of xanthogranulomatous processes in the abdomen and pelvis: A pictorial review of infectious, inflammatory, and proliferative responses. AJR Am J Roentgenol 208: 475-484, 2017.
13. Chandramouli R, Rajan N, Veerappan V, Venkatesan D and Balasundaram P: Xanthogranulomatous endometritis: A benign mimicker of malignancy. Int J Reprod Contracept Obstet Gynecol 13: 1858-1861, 2024.
14. Silva-Rengifo C, Asencio A and Salirrosas O: Xanthogranulomatous endometritis: A report of two cases. Cureus 15: e38226, 2023.