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Endometrial Adenocarcinoma with Synchronous Gastric Metastasis as the First Presentation, A Case Report and Literature Review

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Abstract **Case Report**

Background: Endometrial cancer is the most common gynecological malignancy in developed countries and the sixth most frequently diagnosed cancer among women worldwide (6). Although it usually presents at an early stage, distant metastases may occur, most commonly involving the lymph nodes, peritoneum, lungs, and liver. Isolated synchronous gastric metastasis is exceptionally rare. ***Case presentation:*** We report the case of a 57-year-old woman with diabetes and hypertension who presented with vague abdominal pain. Abdominal computed tomography revealed a gastric mass suspicious for a gastrointestinal stromal tumor (GIST). Following surgical resection, histopathological and immunohistochemical analyses identified the lesion as a metastatic adenocarcinoma of gynecological origin. Subsequent pelvic magnetic resonance imaging and hysteroscopy demonstrated an endometrial mass, and biopsy confirmed endometrioid adenocarcinoma. The patient was diagnosed with isolated synchronous gastric metastasis from endometrial cancer and was treated with first-line palliative paclitaxel–carboplatin chemotherapy after multidisciplinary discussion. ***Conclusion:*** Isolated synchronous gastric metastasis from endometrial carcinoma is an exceptionally rare presentation and may mimic a primary gastric tumor. Histopathological examination with immunohistochemistry is essential for establishing the diagnosis and guiding appropriate management.

INTRODUCTION

Endometrial cancer is the sixth most commonly diagnosed cancer among women worldwide and the most common gynecological malignancy in developed countries. According to the GLOBOCAN 2022 estimates, approximately 420,368 new cases and 97,524 deaths occurred globally, with an age-standardized incidence rate (ASR) of 8.4 per 100,000 women [6,7]. In Morocco, endometrial cancer represents an increasing public health concern, with approximately 1,000–1,100 new cases diagnosed annually and an ASR of approximately 5–6 per 100,000 women [8]. The incidence is expected to continue rising in both developed and developing countries owing to population aging, increasing obesity, diabetes mellitus, and other metabolic risk factors.

The majority of endometrial cancers are diagnosed at an early stage because abnormal uterine bleeding frequently prompts early medical evaluation, resulting in favorable survival outcomes following primary surgical treatment [10]. However, approximately 10–20% of patients experience recurrent disease, and those with advanced or metastatic cancer have a significantly poorer prognosis. Endometrial carcinoma most commonly metastasizes to the pelvic and para-aortic lymph nodes, peritoneum, lungs, and liver through lymphatic, hematogenous, or transcoelomic dissemination [12]. In contrast, gastrointestinal involvement is exceptionally rare, with metastases to the small bowel, duodenum, stomach, or colon reported almost exclusively as isolated case reports or small case series [14].

Several well-established risk factors contribute to the development of endometrial cancer, including obesity, diabetes mellitus, hypertension, prolonged exposure to unopposed estrogen, nulliparity, late menopause, tamoxifen therapy [9], and hereditary cancer syndromes such as Lynch syndrome. Recent advances in molecular characterization have transformed the management of endometrial carcinoma by enabling risk-adapted treatment strategies and the development of

targeted therapies and immune checkpoint inhibitors, which have significantly improved outcomes for patients with advanced and recurrent disease [13].

Despite these therapeutic advances, gastric metastasis from endometrial carcinoma remains an exceptionally uncommon clinical entity. The few published cases have almost exclusively represented metachronous recurrences occurring months to years after treatment of the primary tumor. Consequently, isolated synchronous gastric metastasis at the time of the initial diagnosis is extraordinarily rare and poses a significant diagnostic challenge, as it may mimic primary gastric adenocarcinoma both clinically and radiologically. Although contrast-enhanced computed tomography (CT) and 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) are valuable for detecting gastric lesions and evaluating the extent of metastatic disease, histopathological examination remains the diagnostic gold standard. Immunohistochemical analysis plays a pivotal role in distinguishing primary gastric adenocarcinoma from metastatic endometrial carcinoma [16], with the latter typically expressing Müllerian markers such as PAX8, estrogen receptor (ER), progesterone receptor (PR), and cytokeratin 7 (CK7), while showing absent or limited expression of gastrointestinal markers including CDX2 and CK20.

Herein, we report an exceptionally rare case of isolated synchronous gastric metastasis from endometrial carcinoma, emphasizing the diagnostic challenges, the crucial role of immunohistochemistry in establishing the diagnosis, and the therapeutic implications of this unusual metastatic presentation. A comprehensive review of the current literature is also presented to place this rare clinical entity into context and to highlight the available evidence regarding its diagnosis and management.

Case Report

A 57-year-old woman (gravida 1, para 1) with a medical history of type 2 diabetes mellitus and hypertension, both controlled with medical treatment, presented in July 2025 with progressive abdominal heaviness and vague epigastric discomfort.

A contrast-enhanced abdominal CT scan performed on 9 October 2025 demonstrated a predominantly cystic gastric mass measuring approximately 11 cm, arising from the gastric wall with a large extraluminal component, highly suggestive of a gastrointestinal stromal tumor (GIST). The examination also revealed a polymyomatous uterus with a lesion interpreted as probable aseptic degeneration.

The patient underwent distal gastrectomy (antrectomy) with gastrojejunostomy and segmental transverse colectomy on 28 November 2025. Histopathological examination demonstrated a high-grade poorly differentiated adenocarcinoma infiltrating the muscularis propria and subserosal layers of the stomach without mucosal involvement. Surgical margins and all resected lymph nodes were free of tumor.

Immunohistochemical analysis showed diffuse positivity for AE1/AE3, CK7, and PAX8, while CD117, DOG1, CD34, CK20, and TTF1 were negative. This immunophenotypic profile excluded GIST and strongly supported a metastatic adenocarcinoma of Müllerian origin, most likely arising from the uterus.

Following multidisciplinary discussion, the patient was referred to the Medical Oncology Department for identification of the primary tumor.

A thoraco-abdomino-pelvic CT scan performed on 7 January 2026 revealed an endometrial mass with cervical extension and parametrial fat invasion, without evidence of distant metastatic disease. A cervical biopsy performed on 23 January 2026 showed no evidence of malignancy.

Pelvic magnetic resonance imaging (MRI), performed on 13 March 2026, demonstrated a locally advanced endometrial tumor with deep myometrial invasion, serosal involvement, cervical stromal invasion, extension to the upper third of the vagina, and right internal iliac lymphadenopathy. Based on the available imaging findings, the multidisciplinary tumor board classified the disease as FIGO stage IIIC according to the staging system used at our institution.

Hysteroscopy with endometrial biopsy confirmed a high-grade poorly differentiated endometrioid adenocarcinoma, consistent with the immunophenotype observed in the gastric lesion. After multidisciplinary review, the final diagnosis was primary endometrial carcinoma presenting with isolated synchronous gastric metastasis. The patient was planned to start on first-line palliative chemotherapy consisting of immune check point inhibitors plus paclitaxel (175 mg/m²) plus carboplatin (AUC 5) every 21 days for six planned cycles according to the recommendations [11] but due to non-accessibility to immune check point inhibitors for the patient she will receive the chemotherapy only.

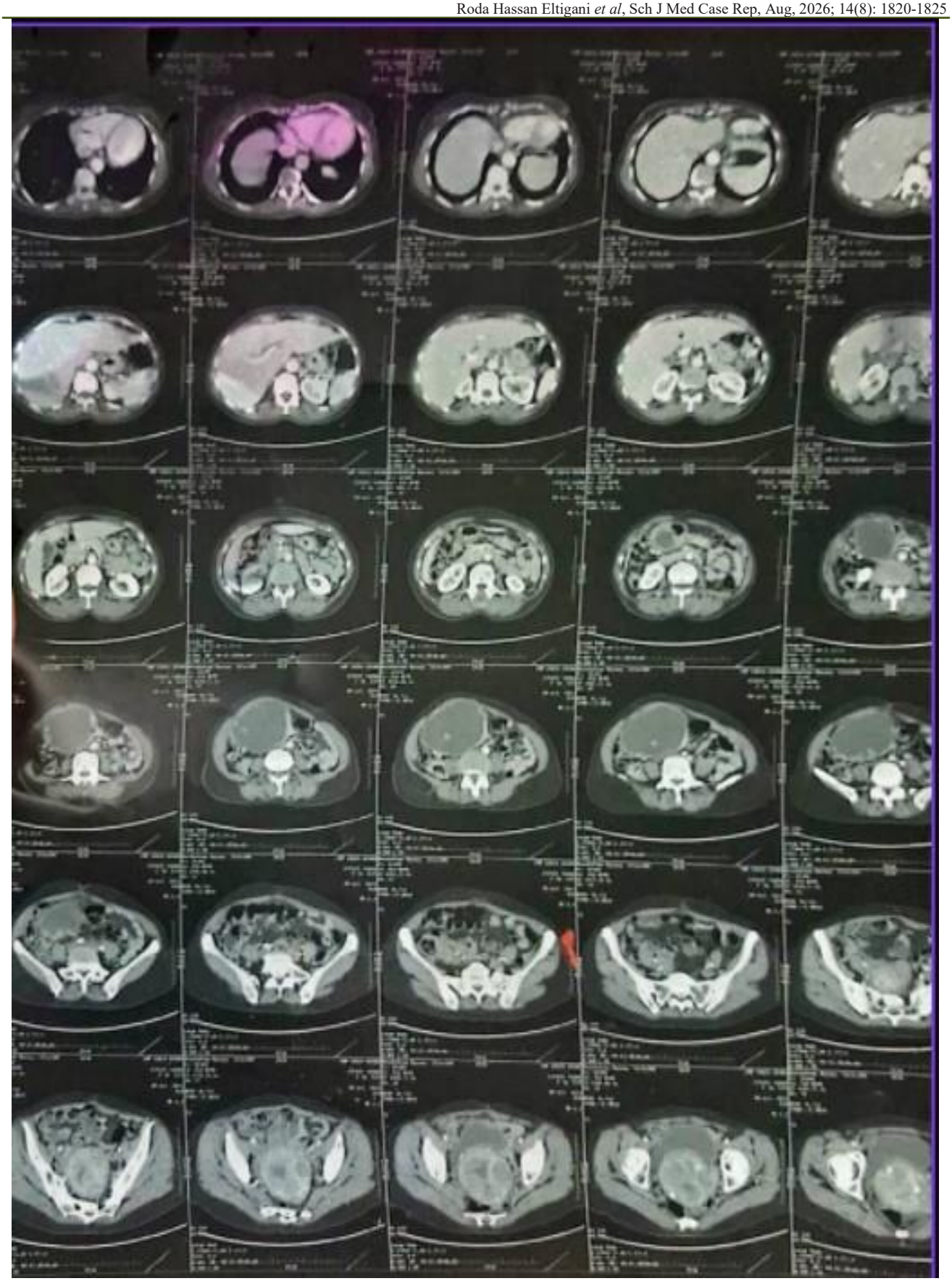
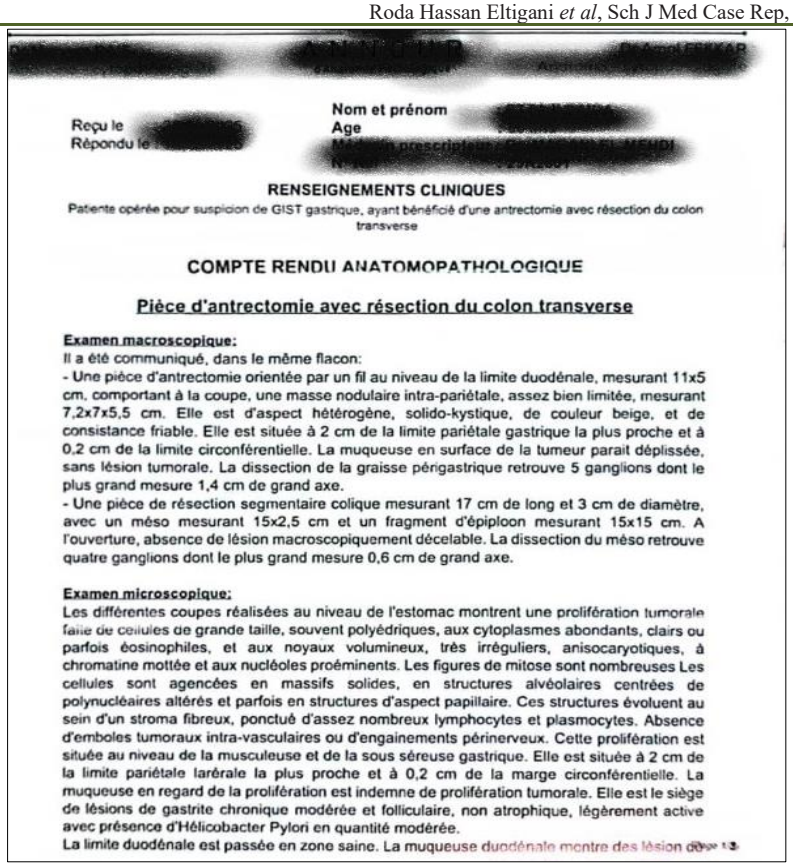


Fig. 1: Contrast-enhanced abdominal CT scan demonstrating a predominantly cystic gastric antral mass with a large extraluminal component, initially suggestive of a gastrointestinal stromal tumor (GIST)



Reçu le
Répondu le

Nom et prénom
Age

RENSEIGNEMENTS CLINIQUES

Patiente opérée pour suspicion de GIST gastrique, ayant bénéficié d'une antrectomie avec résection du colon transverse

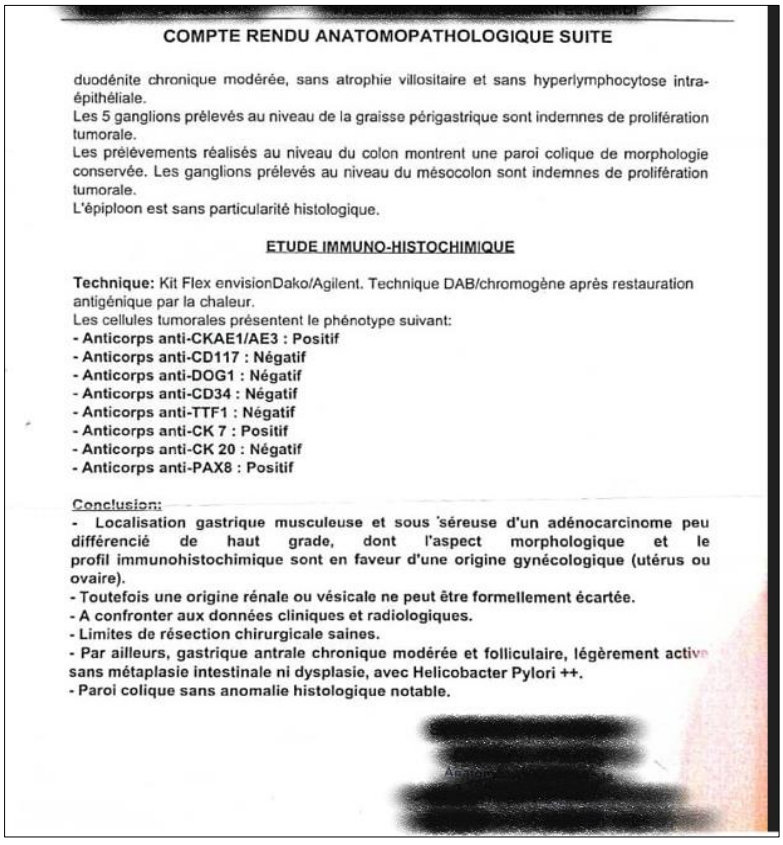
COMPTE RENDU ANATOMOPATHOLOGIQUE

Pièce d'antrectomie avec résection du colon transverse

Examen macroscopique:
Il a été communiqué, dans le même flacon:
- Une pièce d'antrectomie orientée par un fil au niveau de la limite duodénale, mesurant 11x5 cm, comportant à la coupe, une masse nodulaire intra-pariétale, assez bien limitée, mesurant 7,2x7x5,5 cm. Elle est d'aspect hétérogène, solido-kystique, de couleur beige, et de consistance friable. Elle est située à 2 cm de la limite pariétale gastrique la plus proche et à 0,2 cm de la limite circonférentielle. La muqueuse en surface de la tumeur parait déplissée, sans lésion tumorale. La dissection de la graisse périgastrique retrouve 5 ganglions dont le plus grand mesure 1,4 cm de grand axe.
- Une pièce de résection segmentaire colique mesurant 17 cm de long et 3 cm de diamètre, avec un méso mesurant 15x2,5 cm et un fragment d'épiploon mesurant 15x15 cm. A l'ouverture, absence de lésion macroscopiquement décelable. La dissection du méso retrouve quatre ganglions dont le plus grand mesure 0,6 cm de grand axe.

Examen microscopique:
Les différentes coupes réalisées au niveau de l'estomac montrent une prolifération tumorale faite de cellules de grande taille, souvent polyédriques, aux cytoplasmes abondants, clairs ou parfois éosinophiles, et aux noyaux volumineux, très irréguliers, anisocaryotiques, à chromatine mottée et aux nucléoles proéminents. Les figures de mitose sont nombreuses Les cellules sont agencées en massifs solides, en structures alvéolaires centrées de polynucléaires altérés et parfois en structures d'aspect papillaire. Ces structures évoluent au sein d'un stroma fibreux, ponctué d'assez nombreux lymphocytes et plasmocytes. Absence d'emboles tumoraux intra-vasculaires ou d'engainements périnerveux. Cette prolifération est située au niveau de la musculeuse et de la sous séreuse gastrique. Elle est située à 2 cm de la limite pariétale latérale la plus proche et à 0,2 cm de la marge circonférentielle. La muqueuse en regard de la prolifération est indemne de prolifération tumorale. Elle est le siège de lésions de gastrite chronique modérée et folliculaire, non atrophique, légèrement active avec présence d'Hélicobacter Pylori en quantité modérée.
La limite duodénale est passée en zone saine. La muqueuse duodénale montre des lésion de

Fig. 2: Histopathological examination showing a high-grade poorly differentiated adenocarcinoma infiltrating the muscularis propria and subserosal layers of the stomach (H&E staining)



COMPTE RENDU ANATOMOPATHOLOGIQUE SUITE

duodénite chronique modérée, sans atrophie villositaire et sans hyperlymphocytose intra-épithéliale.
Les 5 ganglions prélevés au niveau de la graisse périgastrique sont indemnes de prolifération tumorale.
Les prélèvements réalisés au niveau du colon montrent une paroi colique de morphologie conservée. Les ganglions prélevés au niveau du mésocolon sont indemnes de prolifération tumorale.
L'épiploon est sans particularité histologique.

ETUDE IMMUNO-HISTOCHIMIQUE

Technique: Kit Flex envisionDako/Agilent. Technique DAB/chromogène après restauration antigénique par la chaleur.
Les cellules tumorales présentent le phénotype suivant:
- **Anticorps anti-CKAE1/AE3 : Positif**
- **Anticorps anti-CD117 : Négatif**
- **Anticorps anti-DOG1 : Négatif**
- **Anticorps anti-CD34 : Négatif**
- **Anticorps anti-TTF1 : Négatif**
- **Anticorps anti-CK 7 : Positif**
- **Anticorps anti-CK 20 : Négatif**
- **Anticorps anti-PAX8 : Positif**

Conclusion:
- **Localisation gastrique musculeuse et sous séreuse d'un adénocarcinome peu différencié de haut grade, dont l'aspect morphologique et le profil immunohistochimique sont en faveur d'une origine gynécologique (utérus ou ovaire).**
- **Toutefois une origine rénale ou vésicale ne peut être formellement écartée.**
- **A confronter aux données cliniques et radiologiques.**
- **Limites de résection chirurgicale saines.**
- **Par ailleurs, gastrique antrale chronique modérée et folliculaire, légèrement active sans métaplasie intestinale ni dysplasie, avec Helicobacter Pylori ++.**
- **Paroi colique sans anomalie histologique notable.**

Fig. 3: Immunohistochemical profile of the gastric lesion demonstrating PAX8 and CK7 positivity, with negative staining for CD117, DOG1, CD34, and CK20, supporting a gynecological origin and excluding GIST

DISCUSSION

Endometrial cancer is the most common gynecological malignancy in developed countries and its incidence continues to rise, largely due to increasing rates of obesity, population aging, and metabolic disorders. Established risk factors include obesity, diabetes mellitus, and hypertension, prolonged exposure to unopposed estrogen, tamoxifen use, nulliparity, late menopause, and hereditary cancer syndromes such as Lynch syndrome.

Although most patients present with early-stage disease and have a favorable prognosis following primary surgical treatment, approximately 10–20% will experience disease recurrence. Advances in molecular profiling, targeted therapies, and immune checkpoint inhibitors have improved clinical outcomes in advanced and recurrent disease [11,13].

Although endometrial carcinoma commonly recurs or metastasizes to the pelvic and para-aortic lymph nodes, peritoneum, lungs, and liver the gastrointestinal involvement is exceedingly rare. Metastatic lesions involving the small bowel, duodenum, stomach, or colon have been described only in isolated case reports and small case series, highlighting the exceptional rarity of this pattern of dissemination [4].

This case report represents; to our knowledge; one of the first reported cases of isolated synchronous gastric metastasis from endometrial carcinoma as the mentioned secondary lesions in literatures are metachronous [2,15].

Although abdominal contrast-enhanced CT and 18F-FDG PET/CT, upper GIT endoscopy are valuable imaging modalities for identifying gastric lesions and assessing the extent of metastatic disease, histopathological evaluation remains the diagnostic gold standard. Immunohistochemical staining plays a pivotal role in differentiating primary gastric carcinoma from metastatic endometrial carcinoma, particularly through the expression of Müllerian markers such as PAX8, estrogen receptor (ER), progesterone receptor (PR), and the absence or limited expression of gastrointestinal markers including CDX2 and CK20 [5].

Although radical surgery can be achieved in case of operable patients of only gastric recurrent site with previously treated endometrial cancer followed by systemic chemotherapy, but our patient was considered a metastatic non operable patient and to start a systemic palliative treatment.

For patients with primary advanced (FIGO stage III–IV) or recurrent endometrial carcinoma who are candidates for systemic therapy and are not amenable to curative surgery or radiotherapy, the current standard first-line treatment is the combination of an immune checkpoint inhibitor with carboplatin and paclitaxel, irrespective of mismatch repair (dMMR/pMMR) or microsatellite instability (MSI-H/MSS) status. Patients with dMMR/MSI-H tumors derive the greatest benefit, although a clinically meaningful benefit has also been demonstrated in pMMR/MSS disease [11,17].

COCLUSION

Isolated synchronous gastric metastasis from endometrial carcinoma is an exceptionally rare clinical presentation that may mimic a primary gastric neoplasm. This case highlights the importance of considering metastatic disease in the differential diagnosis of atypical gastric lesions in women, even in the absence of a known gynecological malignancy. Histopathological examination combined with immunohistochemistry remains the cornerstone for establishing the correct diagnosis. Early multidisciplinary evaluation is essential to guide appropriate therapeutic management and avoid unnecessary treatment.

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