Case Reports in Women's Health 32 (2021) e00354

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

# Thrombotic microangiopathy following a minor gynaecological procedure in the setting of endometrial cancer: a case report

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ARTICLE INFO

*Keywords:*
Diagnostic hysteroscopy
dilatation and curettage
Thrombotic microangiopathy
Macroangiopathic haemolytic anaemia

ABSTRACT

Hysteroscopy dilatation and curettage is a common minor gynaecological procedure utilised for diagnostic or therapeutic purposes. A 62-year-old woman underwent a hysteroscopy, dilatation and curettage for investigation of prolonged post-menopausal bleeding. Unexpected uterine haemorrhage was encountered without evidence of uterine perforation causing haemodynamic instability. A thrombotic microangiopathy was triggered, leading to microangiopathic haemolytic anaemia, thrombocytopaenia and evidence of micro-thrombosis causing stroke and end-organ dysfunction, including acute renal failure. The histopathology confirmed stage 1 endometrioid adenocarcinoma. This is the first case report of a thrombotic microangiopathy leading to microangiopathic haemolytic anaemia in a patient with endometrioid adenocarcinoma FIGO grade 1, stage 1B following a minor gynaecological procedure.

## 1. Introduction

Hysteroscopy is a common gynaecological procedure which is utilised for diagnostic or therapeutic purposes. A diagnostic hysteroscopy is commonly performed with dilatation and curettage (D&C) in order to assess the endocervical canal, endometrium and tubal ostia, while allowing a sample of endometrial tissue to be taken for further investigation in women with abnormal uterine bleeding [1]. Causes of abnormal uterine bleeding include hormone-related disorders such as polycystic ovary syndrome, uterine-related problems or blood clotting disorders [2]. Uterine-related problems include leiomyomas, uterine polyps, adenomyosis, endometrial hyperplasia or endometrial cancer [2]. Operative hysteroscopy is used to treat some causes of abnormal uterine bleeding (polypectomy, myomectomy, endometrial ablation) or for adhesiolysis in the setting of Asherman's syndrome. Complications following hysteroscopy are rare. Operative (therapeutic) hysteroscopies carry higher risk of complication, with one study reporting a 0.61% risk of haemorrhage [3]. Diagnostic hysteroscopies have a lower complication rate, with another study reporting 0.16% of patients experiencing haemorrhage after diagnostic hysteroscopy; however, this was only in the setting of uterine perforation [4].

This case describes unexpected haemorrhage and a rare haematologic complication following a diagnostic hysteroscopy D&C.

## 2. Case presentation

A 62-year-old nulliparous woman underwent an elective hysteroscopy, D&C for investigation of prolonged post-menopausal bleeding. She had a background of hypertension well controlled by amlodipine, hypercholesterolaemia, previous cataract surgery, body mass index (BMI) of 30 kg/m$^2$ and was a smoker (20 packs per year). No other significant personal history was noted. The patient was reviewed routinely pre-operatively by the anaesthetics team. The patient was anaesthetised with a general anaesthetic and the cervix was hydrodilated with saline. Following this, she became hypotensive and bradycardic, likely secondary to vagal stimulation from cervical dilatation, which required metaraminol and atropine. Her blood pressure and heart rate returned to normal.

Dense polypoidal growth in the entire uterine cavity was seen at the time of hysteroscopy, with copious suspicious tissue removed with curettage and polyp forceps. Significant per vaginal bleeding was encountered. Transabdominal ultrasound was performed and there was no free fluid as evidence of uterine perforation. The uterus was compressed with bimanual pressure and tranexamic acid was administered intravenously. A Foley catheter with 10 mL of water was inserted into the uterus; however, ongoing brisk bleeding around the catheter was noted, so it was removed and replaced with a urological wide-bore 3-way catheter with 60 mL of water. Haemostasis was confirmed. The

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https://doi.org/10.1016/j.crwh.2021.e00354
Received 26 July 2021; Received in revised form 17 August 2021; Accepted 18 August 2021
Available online 20 August 2021

estimated blood loss was 500 mL. The patient underwent CT examination of the chest, abdomen and pelvis post-operatively, which confirmed no evidence of uterine perforation and the tip of the catheter terminating at the fundus. No free fluid was evident in the pouch of Douglas. Aside from the initial episode of hypotension with dilatation of the cervix, the patient remained haemodynamically stable throughout the procedure.

Urgent blood tests were done intraoperatively and the patient was found to be thrombocytopenic (platelets 74 $\times$ $10^9$/L) but to have a normal haemoglobin level. Electrolytes were normal. Coagulation studies were initially concerning for disseminated intravascular coagulation (DIC), with an APTT of 81 s (elevated), PT of 16.6 s (elevated), fibrinogen of 1.4 g/L (low) and INR of 1.2.

Over the hours following the surgery, the patient developed abnormalities in her blood consistent with thrombotic microangiopathy (TMA), including persistent thrombocytopenia down to 22 $\times$ $10^9$/L (reference range 150-450 $\times$ $10^9$/L), evidence of microangiopathic haemolytic anaemia (MAHA) with haemoglobin down to 66 g/L requiring multiple blood transfusions, and clinical signs of a cerebrovascular accident with acute vision loss in one eye and drowsiness. Urgent medical evaluation was performed and she was transferred to a stroke unit. Urgent MRI showed multiple small acute infarcts in the cerebellum, both occipital lobes and right paracentral lobule, with a small amount of petechial haemorrhage related to the infarct in the right cerebellar hemisphere and occipital lobe. Her biochemistry and haematology continued to deteriorate and she was commenced on plasma exchange therapy, but with minimal effect. She was commenced on eculizumab in an emergency setting due to her worsening condition. She had a good response to eculizumab, with normalisation of her haemolysis markers, renal function and haemoglobin. She had complete recovery of her confusion. The balloon catheter was slowly deflated due to concerns for potential further hemorrhage in the setting of significant thrombocytopenia, but was removed almost 2 weeks post-operatively with no further episodes of per vaginal bleeding after improvement in the platelet count.

The histopathology of the endometrial curettings confirmed endometrioid adenocarcinoma FIGO grade 1. P53 and p16 showed heterogeneous staining. She remained in the ICU for a few weeks before being stepped down to the ward and was discharged home. She was referred to a specialist gynaecological oncology team. Further imaging showed no evidence of metastases. The patient underwent a total hysterectomy and bilateral salpingo-oophorectomy, which confirmed endometrioid adenocarcinoma FIGO grade 1, stage 1B, which invaded through 13 mm of the 15 mm myometrium. No lymphatic invasion, blood vessel invasion or cervical involvement was seen. Extrauterine extension was also not seen. The non-neoplastic endometrium was otherwise inactive. The estrogen receptor showed moderate staining of 80% of tumour nuclei with progesterone receptor showing moderate staining in 50% of tumour nuclei. The surgery was uncomplicated.

## 3. Discussion

Haemorrhage after diagnostic hysteroscopy has been reported only in the setting of uterine perforation. This is the first case report of haemorrhage requiring tamponade after a diagnostic hysteroscopy without uterine perforation in a patient with no coagulopathy known preoperatively. This case highlights the importance of being prepared for unexpected haemorrhage at the time of minor gynaecological procedures in patients thought to be at low risk. It is important to recognise abnormal bleeding, as it may be a sign of a triggered coagulopathy secondary to an underlying haematological cause not previously diagnosed.

In this case, a TMA was triggered, leading to microangiopathic haemolytic anaemia (MAHA), thrombocytopenia and evidence of microthrombosis causing stroke and end-organ dysfunction, including acute renal failure [5]. Thrombotic microangiopathies are rare, life-threatening conditions and can be either primary or secondary. Primary subtypes occur spontaneously, whereas secondary forms are triggered by surgery, medication or metastatic cancer or other causes [5]. There are no case reports in the literature of TMA triggered by stage 1 endometrial cancer [6]. The only known cancer-associated TMAs have involved metastatic cancer; however, there are no reports of TMA associated with metastatic endometrial cancer in the literature [6]. One literature review reported 95 cases of post-surgical TMA; however, most were secondary to major surgeries, with cardiovascular procedures being the most common [7]. No minor procedures were reported. One study reported MAHA as a paraneoplastic syndrome, with 9.2% of cancer-related MAHA being due to apparently non-metastatic cancer at the time of diagnosis [8]. On further investigation, all genitourinary cancers reported to be non-metastatic at the time of diagnosis were later found to be metastatic [8], with metastases being found in bone marrow and central nervous system [8]. While cancer-related paraneoplastic MAHA is documented, it appears to have been reported only in the setting of metastases in cancers of the genitourinary tract.

This case is significant in that it is the first case in the literature to report haemorrhage after diagnostic hysteroscopy without evidence of uterine perforation. While thrombotic microangiopathies are rare, it is important to consider that even minor procedures may trigger a first episode of a TMA, so recognising the signs of deterioration and implementing early treatment are important in improving outcomes for patients.

### *Contributors*

Lucinda Barry is the first author and undertook a literature review, wrote the initial manuscript, gained consent from the patient for the report to be published, and compiled the final manuscript for submission.

Helen Manning was involved in patient care, assisted in writing and editing the manuscript, and approved the final submission.

Emma Chesterman was involved in patient care, assisted in editing the manuscript, and approved the final submission.

Louis Izzo was involved in patient care, reviewed the manuscript, and approved the final submission.

Sacha Strockyj was the senior editor, assisted in preparing the manuscript, editing of the manuscript, and approved the final submission.

### *Conflict of interest*

The authors declare that they have no conflict of interest regarding the publication of this case report.

### *Funding*

No funding from an external source supported the publication of this case report.

### *Patient consent*

The patient gave written consent for the case report to be published.

### *Provenance and peer review*

This article was not commissioned and was peer reviewed.

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