Patient with Menorrhagia Secondary to MHY9 Related Disorder - May Hegglin Syndrome

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Abstract

May Hegglin syndrome is a very rare genetic disorder leading to clotting disturbances. This case report describes the management of a woman with May Hegglin syndrome (MYH9 related disorder), presenting with menorrhagia. The patient was managed in line with the national guidance with an MDT input, leading to very good results.

Keywords: Menorrhagia, MYH9 Related Disorder, May-Hegglin Syndrome.

Background

Menorrhagia is defined as excessive menstrual bleeding that impacts the physical health, social life and overall quality of life of women within the reproductive age.[1] It is defined as excessive bleeding greater than or equal to 80ml and lasting over seven days in research settings. However, it is diagnosed in clinical settings following a patient's self-assessment of symptoms.[2] Menorrhagia accounts for approximately 18-30% of all gynaecological referrals, with 80,000 women in the UK seeking help for their symptoms per year.[1,2] The causes of menorrhagia include uterine fibroids, endometriosis or coagulation disorders, with 90% of women with coagulation disorders being affected.[3] The treatment of menorrhagia, particularly in those with coagulation disorders, usually combines hormonal and haemostatic management that is tailored to each patient.[3]

In this article, we present a case of a 53-year-old woman who was referred to gynaecology with a long-standing history of menorrhagia on a background of May-Hegglin Anomaly (MYH9 related disorder). We aim to contribute to the existing knowledge of menorrhagia treatment and emphasise the importance of detailed history taking and the importance of a multi-disciplinary approach in managing patients with coagulation disorders in the gynaecological settings.

Case Presentation

A 53-year-old lady was referred from haematology for ongoing menorrhagia since menarche. She has a background of MYH9 related disorder. Previously, she tried tranexamic acid to control her bleeding. However, this had limited effect, as she could not tolerate it due to nausea. She was prone to easy bruising and had recurrent complaints of tiredness. She was found to be anaemic and started on iron tablets. As she did not tolerate these either, she had regular iron infusions, under the care of Haematology team.

Due to concerns regarding the bleeding, which had recently become heavier, the decision was made to attempt to visualise the source of the bleeding, with hysteroscopy. This would be able to exclude pathologies such as an endometrial polyp, which would be resistant to the medical management of menorrhagia. Due to the high risk of intra-operative bleeding, the informed decision

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to do the procedure under general anaesthetic was made. A multidisciplinary team meeting was held, and the following plan was made: if the procedure did not involve a polypectomy, the procedure could be covered with 1g tranexamic acid immediately prior to the procedure. If it involved removal of a polyp, she would need cover with one unit of platelets. As the possibility of polyp removal could only be confirmed after the diagnostic hysteroscopy, the unit of platelets was requested to be ready beforehand. The patient was admitted for a hysteroscopy under general anaesthetic with endometrial biopsy and polypectomy if indicated.

Visualisation of the uterus was challenging because the patient was menstruating at the time of the procedure. However, the procedure was successfully completed and there were no anatomical abnormalities noted. To help alleviate her symptoms, a Levonorgestrel Intrauterine System (Mirena IUS) was inserted too.

The biopsy subsequently showed late secretory-phase menstrual tissue, with no evidence of hyperplasia or atypia. The patient's symptoms of menorrhagia resolved to her satisfaction, but she had some spotting. This is not an uncommon side effect in the initial months following Mirena IUS insertion, therefore the patient was prescribed additional progesterone for a brief period.

Discussion

Menorrhagia is a common gynaecological condition that is diagnosed following a detailed clinical history and imaging of the reproductive organs.[4,5] In the case above, the patient had a coagulopathy that significantly increased her bleeding risk and was the likely cause of her menorrhagia.[6]

May-Hegglin Anomaly is a very rare disorder of MYH9 gene often an autosomal dominant disorder, manifesting a spectrum of clinical features. MYH gene encodes the non-muscle myosin heavy chain IIA, a cytoskeletal contractile protein.[7] MYH9 gene mutations lead to premature release of platelets from bone marrow , macro-thrombocytopenia, and cytoplasmic inclusion bodies known as Dohle like bodies in leucocytes. The four conditions; May-Hegglin Anomaly, Epstein syndrome, Fechtner syndrome, and Sebastian syndrome are now understood to be included within the same category of MYH9 related disorder. MYH9 related disorder is characterised by macrothrombocytopaenia and therefore increased bleeding risk, as well as in some patients increased risk of sensorineural hearing loss, cataracts, and renal disease. Although macrothrombocytopaenia varying from 30,000/µL to 100,000/µL ,is sometimes asymptomatic, common bleeding symptoms that patients present with are menorrhagia, easy bruising and recurrent epistaxis.[5] The most possible explanation for bleeding is due to reduced clot stability due to impaired clot retraction of dysfunctional platelet cytoskeleton.[7] In female patients with menorrhagia , the leading symptom of MYH9 disorder is iron deficiency anaemia secondary to menorrhagia.[8]

During menstruation, there are multiple coagulation pathways involved in the shedding of the uterus lining that are influenced by progesterone levels. The increase in progesterone levels initiates fibrinolysis and cellular breakdown. The withdrawal of progesterone initiates the release of prostaglandins to allow shedding of the lining and menstrual bleeding to occur[3]. Research suggests that women with coagulopathies have increased fibrinolytic and collagenase activity along with increased prostaglandin levels which result in increased menstrual bleeding.[1,2]

Intrauterine structural abnormalities, such as fibroids, polyps or endometrial hyperplasia can also cause menorrhagia.[9] Other causes of menorrhagia include adenomyosis, ovulatory disorders, endometriosis and leiomyoma.[2] As per the National Institute of Clinical Excellence (NICE), it is recommended that patients with high suspicion of submucosal fibroids, polyps or who have been unsuccessfully treated for menorrhagia should be referred for an outpatient hysteroscopy with endometrial biopsy.[4] In the case of this patient, there were no anatomical abnormalities found and the biopsies were normal.

Anti-fibrinolytic medications are often used for symptomatic treatment of heavy bleeding.[10] Medications such as Tranexamic Acid competitively inhibit plasminogen activation, which reduces the breakdown of fibrin and stabilises clots.[10,11] Other non-hormonal medications can be used in conjunction with Tranexamic Acid to stabilise clots. NSAIDs such as Mefenamic Acid reduce prostaglandin synthesis and can also help to alleviate cramping and abdominal discomfort during menses.[10,11] The patient in this case received symptomatic treatment from her haematologist with limited effect. She could not tolerate the tranexamic acid due to side effects of nausea and required additional management under gynaecology. In general, patients with MYH9 related disorder should avoid use of NSAIDs.[5]

Hormonal therapies can be used in conjunction with anti-fibrinolytic medications to reduce menstrual loss and alleviate symptoms of menorrhagia.[12] Treatment aims to maintain the level of progesterone to reduce the inflammation of the uterus lining and reduce the amount of blood loss during menses. The modality of hormonal therapy is dependent on the individual. Combined oral contraceptive pills or progesterone-only oral tablets are often utilised in community settings but are heavily reliant on patient compliance to have affect.[12,13] The most effective modality is the Levonorgestrel IUD.[13] The IUD allows a localised slow release of progesterone whilst reducing systemic absorption and generalised side effects. Evidence suggests that IUDs can reduce menstrual loss by 71-95% within the first year of use.[9,12,13] Various studies have also shown the IUD is the most effective modality in alleviating menorrhagia in women with coagulopathies.[12]

Conclusion

Menorrhagia can be due to a range of causes, including rare bleeding disorders such as MHY9 related disorder, as our patient had. It is important to investigate the cause of menorrhagia, as this is essential in guiding its management. MHY9 related disorder is a rare cause of menorrhagia, and options for management of menorrhagia secondary to this have been summarised. A multidisciplinary approach is

also needed in management of patients with MHY9 related disorder, due to its multi-organ system complications. The options to manage menorrhagia secondary to MYH9 related disorder are tranexamic acid or hormonal therapy.[5]

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