Episodes of severe menorrhagia at menarche in a girl with von Willebrand disease

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Abstract

We describe a case of a 14-year-old girl with von Willebrand disease (vWD) and episodes of severe menorrhagia at menarche, necessitating hospitalization and requiring blood transfusions and administration of purified von Willebrand factor. Further episodes of menorrhagia were successfully prevented with the use of oral contraceptives and uterine bleeding at menses was regulated with the combination of nasal desmopressin and tranexamic acid per os.

Key words: von Willebrand disease, menorrhagia, menarche, contraceptive therapy, case report.

Introduction

Von Willebrand disease (vWD) is a common inherited bleeding disorder which is found in approximately 1% of the general population [1]. There is a prevalence of vWD of between 5% and 20% in women with abnormal uterine bleeding [2]. However, 60-95% of women with vWD experience menorrhagia [2]. Severe menorrhagia, necessitating hospitalization, usually occurs during the first few years after menarche in women with vWD. Management of menorrhagia includes hormonal treatment, desmopressin and antifibrinolytic agents. Despite the high frequency and the severity of this complication, no consensus on optimal management of menorrhagia in vWD currently exists.

Case report

A 14-year-old girl, previously diagnosed with vWD, was transferred to our department from her local hospital because of severe menorrhagia at menarche. vWD was diagnosed at the age of 2 after an episode of heavy gingival bleeding (von Willebrand Factor (vWF) – 14%, vonWillebrand factor:Ristocetin Cofactor (wWF:RCo) – 9.8%). In addition, she had had petechiae and ecchymoses during infancy. Both parents were found to have vWD following the diagnosis in our patient (mother: vWF – 64%, vwF:RCo – 40%; father: vWF – 5.1%, vwF:RCo – 5%). Her father experienced recurrent episodes of epistaxis and one episode of gastrorrhagia. Her mother presented with easy bruising and petechiae on mild pressure, however she had experienced normal menses, three uneventful pregnancies and uncomplicated childbirths. One cousin had previously been diagnosed with

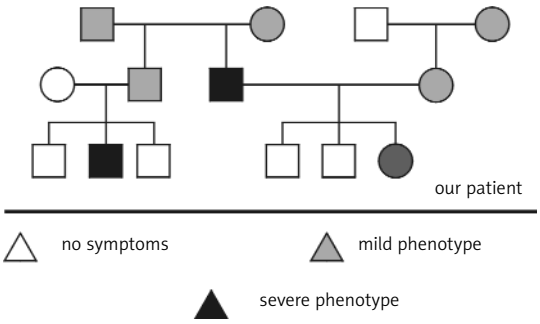

Figure 1. Family pedigree of the patient

severe vWD, whilst four other individuals from her family had mild bleeding diathesis (Figure 1). From the age of 2, the index case had been followed up in our paediatric haematology clinic, with episodes of epistaxis, easy bruising and gingival bleeding during teeth eruption.

At menarche episode, the girl had severe and prolonged (>6 days) uterine bleeding. She was initially admitted to a local hospital where she was transfused with 1 unit of cryoprecipitate and 1 unit of packed red blood cells due to low haematocrit (Ht) levels (16%). On admission to our department, haemoglobin (Hb) levels were 5.6 g/dl and the serum ferritin concentration 6.2 ng/ml. Pelvic ultrasound was normal. She required two extra units of red blood cells and also received purified vWF at a dose of 1000 units every 12 hours for 5 days. Menorrhagia was successfully controlled and the girl was then treated with hormone therapy. This consisted of conjugated oestrogens from day 1 until the 25th day of her cycle and dydrogesterone from day 15 until day 25, at doses of 1.25 mg/day and 20 mg/day, respectively. Additionally, she was given nasal desmopressin at a dose of 150 μg, BID for 3-5 days, and tranexamic acid per os, at a dose of 1500 mg for 7-10 days starting at the first day of her next menses. Finally, supplemental iron was given at a dose of 6 mg/kg/day for 3 months. Despite this treatment, the patient presented with heavy uterine bleeding at her next menses. She was re-admitted to our unit; Hb level was 6.9 g/dl and Ht was 22%. She was transfused with 3 units of packed red blood cells and she received purified vWF, for 3 days. After bleeding been controlled, she was advised to receive oral contraceptives (combination of ethinyl-oestradiol and drosiperinone) from day 1 until day 21 of her cycle. Following this regimen, her next menses were normal and bleeding was successfully regulated with the use of desmopressin and tranexamic acid. Oral contraceptive treatment was discontinued after 3 normal cycles, with no recurrence of menorrhagia. To date, 10 months after the first episode of menorrhagia, the patient remains free of complications.

Discussion

VWD is an autosomally inherited condition. Despite this, a high frequency of symptomatic vWD is reported in women due to the hemostatic challenge of menses and childbirth. Menorrhagia is reported by 60-95% of women with vWD [3, 4], whilst vWD is diagnosed in women with menorrhagia with a prevalence that extent from 5 to 20% in different studies [5, 6]. Although management of abnormal uterine bleeding has traditionally been the domain of gynaecologists, only 4% of them consider wVD in the differential diagnosis of menorrhagia [7], whilst the prevalence of haematologists identifying menorrhagia as an indication for testing for vWD reaches 91% [8]. Several studies indicate a cycling variation of vWF concentrations during menstrual cycles. This is mainly attributable to the fluctuating levels of oestrogens [9]. The latter was emphasized in a study showing that women undergoing in vitro fertilization had increased levels of vWF following supraphysiological levels of estradiol after ovarian stimulation [10]. Due to fluctuating vWF levels during the menstrual cycle, women of reproductive age, suspected of having vWD, should be tested during menses or in the first few days after a period. Our patient had already been diagnosed with vWD. However, wVF was repeated a few days after her period and confirmed the diagnosis of vWD (vWF – 13.2% and vWF:RCo – 9.6%).

Menorrhagia may be most severe during the first few years after menarche, both in adolescents with vWD and in unaffected individuals. This is related to immaturity of the hypothalamic-pituitary-ovarian axis and should be considered as a normal phenomenon. However, in adolescents with vWD, uterine bleeding at menarche can become severe. Transfusion of packed red blood cells may be required to correct haemoglobin levels and administration of purified vWF should be considered for haemostatic purposes. Menorrhagia at home can be managed with the use of desmopressin and antifibrolytic agents, alone or in combination. Desmopressin increases vWF and FVIII levels both in patients with vWD and in unaffected individuals. It has been widely used in vWD and menorrhagia with good results [11]. Antifibrolytic agents (tranexamic acid) inhibit the local fibrinolytic effect, whereas drugs interfering with prostaglandin synthesis (non-steroidal anti-inflammatory agents) block platelet inhibitory effect. Studies have shown that tranexamic acid is more effective in regulating menorrhagia compared to both mefenamic acid [12] and progesterone [13].

In order to prevent heavy bleeding in our patient during her next period, an alternating combination of conjugated oestrogens and dydrogesterone were given. However, this treatment was not successful and heavy menstrual bleeding, re-occurred. At this point, oral contraceptives were prescribed with good results. Contraceptive pills suppress ovulation and

consequently inhibit endometrial proliferation. By suppressing ovulation, oral contraceptives can also prevent recurrent haemoperitoneum in women with bleeding disorders [14]. Additionally, oestrogens, contained in oral contraceptives, enhance haemostasis as they increase the levels of vWF and FVIII [15]. However, in our patient, the natural maturation of hormonal axis have been a factor contributing to the regulation of her menses. This was supported by the fact that 3 months after the initial administration, oral contraceptives were discontinued and our patient is still experiencing normal menses.

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