Menstrual-like vaginal bleeding in prepubertal girls: an unexplained condition

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Abstract

Unexplained menstrual-like cyclic vaginal bleeding, lasting for several days and without any uterine and vaginal anomaly, is a rare condition in prepubertal girls. Only small series (containing four to eleven cases) have been described in literature. We report our in nine girls presenting with vaginal bleeding without any abnormality at gynaecological, hormonal and echographic examination.

Key words: Prepubertal vaginal bleeding, menarche, telarche, isolated menses, environment.

Introduction

Recurrent vaginal bleeding is a rare symptom in prepubertal girls. When the vaginal bleeding is cyclic and lasts for two to five days, isolated menses should be considered. The first menstruation normally appears approximately two and a half years after the onset of breast development. The occurrence of a menstrual-like bleeding before telarche is very rare and has also been defined as premature menarche analogous to premature pubarche and premature telarche. These conditions are considered as an incomplete form of precocious puberty since no other signs of puberty are present.

The pathophysiology of cyclic vaginal bleeding in prepubertal girls is not well understood and is thought to be due to unusual sensitivity of the endometrium to very low prepubertal levels of oestrogens (Stanhope, 2006; Traggiai et al., 2003). In one study a seasonal effect was suspected (Blanco et al., 1985). It is possible that a range of environmental factors can influence the prepubertal endometrium and thus be involved in abnormal bleeding patterns (Croes et al., 2009; Degen et al., 2004; Mouritsen et al., 2010; Munro et al., 2010; Nebesio et al., 2005).

We report on nine girls who presented with menstrual-like cyclic vaginal bleeding during the last three years.

Materials and Methods

From a retrospective case review in four Medical Centers (St Pieter Hospital Brussels, ULB Erasmus Hospital Brussels, Queen Paola’s Children Hospital Antwerp and UZ Brussels) we retrieved nine girls with a diagnosis of menstrual-like unexplained vaginal bleeding over a period of three years (between 2009 and 2011).

In all girls a complete clinical examination, including body height, body weight and Tanner staging was performed. Bone age was determined by X-ray of the left hand and wrist, according to the Greulich and Pyle atlas.

Basal concentrations of LH, FSH, E2, DHEAS, progesterone, 17-OH-progesterone, IGF1, PRL, TSH,
T4 were measured. In all patients a GnRH stimulation test (2.5 micrograms/kg bodyweight) was performed (Cesario et al., 2007; Perry et al., 2008). Uterine length, thickness of the endometrial lining, uterine artery flow and ovarian volumes were measured by ultrasound (Badouraki et al., 2008; Munro et al., 2010; Zierissen et al., 2001).

Results

Table 1 and 2 give an overview of the findings in our nine patients.

The included patients were from different ethnic origins and their chronological age at examination ranged from three to ten and a half years. The number of menstrual-like vaginal bleedings varied from one to eight. The duration of bleeding varied from one to five days and in most patients less than three pads were used. No seasonal pattern was evident. Only one girl showed vaginal bleeding at the moment of gynaecological examination. None of the girls had breast development. The vulvar aspect was normal for their age. One girl showed a café-au-lait spot. Growth data, including the BMI, were normal (Rosenfeld et al., 2009). Bone age was not significantly different from normal. Pelvic ultrasound showed a normal prepubertal sized uterus without endometrial proliferation and with a prepubertal uterine artery flow, with the exception of one girl who had an endometrial lining of 3 mm. Two girls with more than two episodes of vaginal bleeding underwent a vaginoscopy but no anomaly was seen. Serum concentrations of oestradiol (< 20 pg/ml), LH (< 1 mIU/ml) and FSH (< 5 mIU/ml) were all within the prepubertal ranges. The peak LH response at GnRH testing was lower than 4.5 mU/L, which also corresponds to a prepubertal state. None of the girls had clinical or hormonal signs of an exaggerated adrenarche.

Discussion

There are rather scarce data in the literature on prepubertal menstrual-like bleeding (Berberoglu et al.,

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**Table 1.** Symptomatology and clinical findings.

| Patient number | 1st bleeding month | Age at 1st bleeding (yr) | N° of bleeding events | Duration (N° days) | Ethnic origin | BMI (kg/m²) | Vulva | Pub. Status (Tanner) |
|----------------|--------------------|--------------------------|-----------------------|-------------------|--------------|------------|-------|--------------------|
| 1              | April              | 7                        | 2                     | <2                | Burkina Faso | 14,8       | Infantile | A1P1M2             |
| 2              | May                | 3                        | 3                     | <2                | Sierra Leone | 14,9       | Infantile | A1P1M1             |
| 3              | October            | 8                        | 2                     | <3                | Morocco       | 20,7       | Infantile | A1P1M1             |
| 4              | November           | 8                        | 1                     | 4                 | Belgium       | 21,3       | Infantile | A2P2M2             |
| 5              | August             | 4                        | 8                     | 2-3               | Turkey        | 17,2       | Infantile | A1P1M1             |
| 6              | September          | 7                        | 2                     | 5                 | Congo         | 17,1       | Infantile | A1P1M1             |
| 7              | August             | 7 ½                     | 1                     | 2                 | Belgium       | 18,1       | Infantile | A1P1M1             |
| 8              | September          | 7                        | 2                     | <3                | Turkey        | 16,9       | Infantile | A1P1M1             |
| 9              | December           | 3 ½                     | 2                     | <2                | Guinea        | 15,0       | Infantile | A1P1M1             |

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**Table 2.** Investigations.

| Patient number | Bone Age (yr) | LH (mIU/ml) | FSH (mIU/ml) | Oestradiol (pg/ml) | DHEAS (ng/ml) | Peak LH at GnRH (mIU/ml) | Ultrasound Max. uterine length (cm) |
|----------------|---------------|-------------|--------------|-------------------|---------------|-------------------------|------------------------------------|
| 1              | 7             | <0,1        | 0,9          | <5                | 230           | <4,5                    | 3,6                                |
| 2              | 3             | 0,5         | 1,6          | 10                | 150           | 3                       | 2,9                                |
| 3              | 8             | <1          | 3            | 10                | 664           | 2                       | 3,4                                |
| 4              | 9             | <0,2        | 1,3          | <20               | 312           | <2                      | 3,6                                |
| 5              | 4             | <1          | 1,2          | 7                 | 250           | 1,7                     | 1,3                                |
| 6              | 7 ½           | <1          | <1           | 12                | 230           | <2                      | 2,6                                |
| 7              | 8             | <0,2        | 1,6          | 6                 | 297           | 2                       | 3,3                                |
| 8              | 7             | <1          | 3            | <10               | 604           | 3                       | 3,4                                |
| 9              | 4             | <1          | 1,6          | 10                | 170           | <1                      | 1,5                                |
whether recurrent cyclic prepubertal vaginal bleeding can be defined as prepubertal menarche (Shanthi et al., 2006) or premature menarche (Murrum et al., 1983) can be a matter of debate. It could be argued that by definition menarche is one step in the chain of pubertal events and necessitates a certain level of cyclic hormonal changes, which is not the case in this study. Anyway, in all cases reported there was no impact on the subsequent menstrual pattern and fertility prognosis (Sterling, 2007).

Early menarche (before the age of ten years) can occur in case of central precocious puberty. This disorder is by definition gonadotrophin dependent and is caused by a precocious maturation of the hypothalamic pituitary axis, which results in physical and hormonal changes (Cesario et al., 2007). In none of our tested girls a pubertal response to GnRH was seen and no other signs of pubertal development were present.

The response to GnRH test was suppressed (no increase in basal gonadotrophins) in two cases, but this was not associated with an elevated oestradiol level. This might be due to a previous and transient follicular cyst although these transient ovarian cysts are often associated with breast development which was not the case in our patients. A suppressed response of gonadotrophins is seen in other causes of peripheral precocious puberty such as adrenal and ovary tumors. DHEAS values were normal in all our patients and none of them had an advanced bone age, which is classically seen in such cases of peripheral precocious puberty. Two girls were younger than four years of age. In case of uterine bleeding at a very young age (most often below the age of two) McCune Albright syndrome must be considered. This sporadic disorder is accompanied by café-au-lait spots and fibrous bone dysplasia. This triad can also fit into other endocrine pathologies like pituitary adenoma, hyperthyroidism. The ultrasound examination of these children typically shows voluminous ovarian cysts, which was not seen in our cases. Detailed history did not evoke any exposure to exogenous oestrogens in our patients. None of them had taken any herbal medicines or was having contact with a mother, grandmother or caretaker treated with dermal oestrogens.

A temporary activation of the hypothalamic pituitary axis was unlikely in our population of girls with menstrual-like vaginal bleeding, since there was neither an increase of gonadotrophins nor of oestradiol levels. Ultrasound showed a normal prepubertal state of uterine maturation and the absence of endometrial proliferation. In only one girl endometrial lining was evidenced, suggestive of an increased sensitivity of the endometrium as possible mechanism in this particular case.

Surprisingly, active bleeding was seen in only one girl in our study. We cannot exclude that some of these girls might suffer from the Munchhausen by Proxy syndrome. This psychiatric syndrome due to relational problems confirms the importance of an objective evaluation of the vaginal bleeding (Sterling, 2007). Some conditions and symptoms may be faked by the caregiver or the parents and even the child may inflict injury on itself to draw attention and sympathy.

Prepubertal vaginal bleeding is a source of anxiety not only for the girl, but also for her family. In each case a prompt evaluation is recommended and warranted. If no explanation can be found, only clinical observation and reassurance of the girl and parents are necessary (Golub et al., 2008; Posnet et al., 2006). The clinician should also be sensitive to the unspoken concern of possible sexual molestation. Harmful traditional practices of genital mutilation in foreign girls can be another cause of genital bleeding.

Conclusion

The aetiology of cyclic vaginal bleeding in prepubertal girls remains unknown in most cases. It must be differentiated form early pubertal timing and peripheral precocious puberty. More research is needed to clarify its pathophysiology.

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