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Prepubertal menarche: A defined clinical entity

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Prepubertal vaginal bleeding is considered as isolated menarche when, in the absence of detectable abnormality, it is not accompanied by any evidence of sexual development. The etiology remains unclear and various hypotheses have been put forward. This is the first time that a series of ultrasound patients with prepubertal menarche whose investigation has included imaging with ultrasound has been described. This paper illustrates isolated prepubertal menarche without the presence of an endometrial echo.

Vaginal bleeding in a prepubertal child should always be investigated as it may be the presenting sign of a serious medical problem. Such bleeding can result from estrogen stimulation, infection, foreign bodies, tumors, and trauma.

Prepubertal vaginal bleeding is considered as isolated menarche when thorough medical examination does not show other signs of sexual development or any detectable uterine or vaginal abnormalities.[1] Isolated menarche is unusual, its frequency being less than one tenth that of cases of isosexual precocity in girls.[1] The etiology remains unclear and various hypotheses have been put forward. This is the first time that a series of patients with prepubertal menarche whose investigation has included imaging with ultrasound has been described. This paper illustrates isolated prepubertal menarche without the presence of an endometrial echo.

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Case reports

We describe 4 cases of patients with isolated menarche.

Case 1

A 10-year-old girl presented with a history of recurrent vaginal bleeding of 2 years' duration. The bleeding lasted for 2 to 5 days and occurred every 1 to 2 months. She had no secondary sex characteristics. Her weight was on the 91st centile and her height between the 75th and 91st centile. Hormonal investigations showed estradiol (E_2), luteinizing hormone (LH), and follicle stimulating hormone (FSH) in the normal prepubertal range, and normal thyroid function tests. Gonadotropin releasing hormone (GnRH) stimulation test showed a normal prepubertal response. Ultrasound showed normal prepubertal uterus with no endometrial echo and normal ovaries, 1 of which contained a small follicle less than 2 mm diameter.

Examination under anesthesia (EUA) showed no foreign body, infection, or tumor. She had annual follow-up. The vaginal bleeding continued and, at the age of 12 years, she underwent normal pubertal development.

Case 2

This 10-year-old girl had recurrent vaginal bleeding since the age of 8. The bleeding occurred every month in the form of spotting. She had no secondary sexual characteristics. Her height and weight were normal for her age. The results of hormonal investigations were within the normal prepubertal range. Ultrasound showed a prepubertal uterus and ovaries with no endometrial echo. EUA showed no local abnormality. She had annual follow-up and, at the age of 11, underwent normal pubertal development.

Case 3

This 7-year-old girl had vaginal bleeding in the form of irregular spotting with no obvious pattern for a year before referral. Her height and weight were appropriate for chronologic age. The results of hormonal investigations were in the normal prepubertal range. Ultrasound showed a normal prepubertal uterus with no endometrial echo and normal ovaries. EUA revealed no cause for the bleeding. She had annual follow-up and was last seen at the age of 8 years. She had normal development with no sign of puberty. The irregular vaginal bleeding continued.

Case 4

This 6-year-old girl had cyclical vaginal bleeding of 1 day's duration and brown discharge. She had no secondary sexual characteristics. Her height was on the 91st centile and weight on the 99.6 centile. GnRH stimulation test showed a small rise in peak FSH but a normal prepubertal LH. Estradiol levels were slightly elevated at 59 pmol/L. On ultrasound examination, uterine and ovarian volumes were appropriate for her age. There was no endometrial echo. An ovarian follicle smaller than 2 mm was present. EUA showed no local abnormality. She had annual follow-up and was last seen at the age of 9 years. Bleeding stopped at the age of 7. She had normal development with no signs of puberty.

Comment

Isolated menarche is a benign and self-limiting condition that is not well described in gynecologic literature. It is a relatively rare complaint but can be a source of fear or concern for the girl and her family.

Pubertal development in girls usually follows a recognized pattern of early breast and pubic hair development, followed by the growth spurt, further breast and hair development, with menarche being a relatively late feature. Vaginal bleeding that occurs outside this pattern should be investigated to rule out underlying pathology. Abnormal vaginal bleeding in prepubertal girls may result from estrogen stimulation that may be endogenous from estrogen-secreting tumors or, less commonly, exogenous, caused by ingestion of hormone tablets. Infection, tumors of the lower genital tract, ovarian tumors, vaginal foreign bodies, or trauma may also cause vaginal bleeding.

In a proportion of cases with central precocious puberty, menstrual bleeding may be the first clinical manifestation. However, girls with central precocious puberty usually present with acceleration in linear growth, advancement in skeletal age, and breast development. The height and weight of 2 girls in this study were above average. Neither of them went on to show any other signs of pubertal development. Rarely, isolated menarche may be the initial presentation of the advanced sexual development relative to bone age, which may be seen in patients with juvenile hypothyroidism. Thyroid function tests were normal in the 4 girls in this series.

Diagnosis requires careful history, complete clinical examination, and assessment of pubertal development, taking into account both the physical and psychosocial factors. Pelvic ultrasound is mandatory to establish normal anatomy and exclude tumors. Hormonal profile, including a GnRH stimulation test, is necessary to exclude precocious puberty. Examination under anesthesia should be carried out to exclude vaginal or cervical lesions, foreign bodies, or infection. In the presence of normal investigation results, annual follow-up is advisable to ensure normal pubertal development and to provide support and reassurance in what is an extremely difficult situation for the girl and her family to cope with.

The 4 girls described here had unexplained recurrent vaginal bleeding, with no evidence of secondary sexual development, and with no local causes identified. A diagnosis of isolated menarche was made.

Two girls in our series have gone on to have normal pubertal development at an appropriate age. A follow-up of 9 girls in 1 series showed normal puberty and no sign of precocious sexual activity.[2] There was no acceleration of growth, bone age, or any signs of precocious puberty in follow-up study of 2 patients.[3] Twelve women had normal menstrual cycles and were fertile by ages 16 to 34 years after having developed isolated menarche during childhood.[4]

There have been few reports in literature describing this entity. In 1 published report, the accompanying signs of transient breast development make a diagnosis of transient sexual precocity more likely.[1] The first report in 1979 described 4 girls with cyclical vaginal bleeding in the absence of other signs of precocious secondary sexual development.[5] Investigation showed low estrogen levels in 2 of them, with basal gonadotrophin levels in the upper part of the prepubertal range. No information about ultrasound findings was given.

In 1985, Matilde Marcia described 17 prepubertal girls aged 1 to 8 years with isolated menarche. Eleven girls had 2 or more apparent menstrual periods, and 6 experienced only 1 period.[2] Hormonal investigation showed no increase in gonadotrophin secretion, but demonstrated elevated levels of estradiol in the early pubertal range. Ultrasound examination was performed but no measurement of the endometrial thickness was made.

Nearly all of the hypotheses regarding the etiology of this condition that have previously been put forward fail to address the absence of an endometrial echo, and this paper is the first one that illustrates this. This refutes the suggested hypotheses of increased sensitization of endometrium to estrogens as a causative factor.

The accepted view is that isolated menarche is related to the increased sensitivity of the endometrium to estrogens, similar to increased breast sensitivity to estrogens in premature thelarche.[5] This, however, would be expected to result in endometrial thickening. None of the published series have included information about uterine size or endometrial thickness. All the girls in our series had ultrasound examination that showed normal prepubertal uterine size and no identifiable endometrial echo. The absence of endometrial thickening cases does not fit in with the theory of increased sensitization of endometrium to estrogens.

It is suggested that in isolated menarche a partial and transient activation of the hypothalamo-pituitary-gonadal axis could be present.[3,6] In 1990, Saggese et al studied gonadotrophin pulsatile secretion in 5 girls with premature menarche.[6] During sleep, 3 girls showed LH pulses with low amplitude and a pubertal pattern of frequency, whereas FSH increased without demonstrable episodic secretion. In these 3 girls, menstruation ceased during the follow-up period and repeat testing in 1 girl showed a return to an apulsatile prepubertal LH pattern.

In our series, the hormonal investigations, including the GnRH stimulation test, were normal. The girl reported in case 4 showed a small rise in peak FSH and slightly elevated estradiol levels, which may suggest release of follicular estrogen, stimulating the pituitary-gonadal axis. Transient activation cannot entirely explain the persistent cyclical bleeding in the other girls in our series. This once again has not been the consistent finding in all the cases described in literature.

Prepubertal vaginal bleeding is a relatively rare condition but can be a source of fear and concern for the girl and her family whether it occurs as a single, transient event or is recurrent. Psychologic and social barriers that arise as a result of misinformation and fear may lead, in some cases, to patient delay in seeking medical aid.

Careful investigation is imperative to exclude underlying pathology. Long-term follow-up of these girls is advisable, mainly for reassurance, as there is no evidence that precocious puberty is an associated feature. Girls and their families can be reassured that isolated menarche a defined clinical syndrome, is a benign and self-limiting condition, and that the normal onset of puberty should be anticipated. The etiology of premature menarche remains unclear, and more research is needed to establish causation.

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