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REVIEW

ULTRASOUND ASPECTS ON FEMALE PRECOCIOUS PUBERTY: SHORT COMMENTARY

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Summary

Introduction: Precocious puberty represents a challenging condition. The golden standard for diagnosis of central precocious puberty (CPP) is Gonadotropin-Releasing Hormone (GnRH) test but its use does not limit the ultrasound value as a very good screening and prognosis tool.
Cases report: An 8-year girl with right nipple pain was examined using a 15 MHz linear probe which revealed an image of 10 mm under the skin, consistent with an incipient breast having 2 ducts. The ovaries were analyzed with a 7 MHz curved probe and revealed a right ovary with a length of 15 mm. Left ovary has a length of 21 mm. A Caucasian girl aged of 7 years and 9 months has idiopathic CPP based on clinical aspects (height +1.9 SD above the normal limit for age, breast Tanner stage of 2/3), bone age of 10 years and GnRH test results (peak LH after 4 hours of 2mUI/mL, respective peak of estradiol after 24 hours of 112 pg/mL). Breast ultrasound revealed right mammary gland of 2 mm with inhomogeneous aspect and left mammary gland of 6.1 m. The uterus at ultrasound examination had 28.5/11/18 mm, associating visible endometrial area of linear pattern, and multi-follicle aspect of both ovaries sized of 25.5 by 15 mm.
Conclusion: Different ultrasound windows are needed for girls with precocious puberty; the lack of correlation between observations related to breast and uterus ultrasound gives us the opportunity to affirm that the breast is more sensitive to ovarian stimulation that the uterus.
Key words: breast, precocious puberty, uterus, ovaries, ultrasound

Résumé

Aspects échographiques sur la puberté précoce des femmes: bref commentaire

Introduction: La puberté précoce représente une condition difficile. La norme d'or pour le diagnostic de la puberté précoce centrale (CPP) est gonadolibérine (GnRH) test, mais son utilisation ne limite pas la valeur de l'échographie quie est très outil pour dépistage et pronostic.
Cas rapport: Une jeune fille de 8 ans avec la douleur au mamelon droit a été examinée à l'aide d'une sonde linéaire de 15 MHz qui a révélé une image de 10 mm sous la peau, en conformité avec une poitrine naissante ayant 2 canaux. Les ovaires ont été analysées à l'aide d'une sonde courbe 7 MHz et ont révélé un ovaire droit d'une longueur de 15 mm. Ovaire gauche a une longueur de 21 mm. Une jeune fille de race blanche âgé de 7 ans et 9 mois a CPP idiopathique basée sur les aspects cliniques (hauteur +1,9 SD supérieures à la limite normale pour l'âge, du sein stade Tanner de 2/3), l'âge osseux de 10 ans et les résultats des tests de la GnRH (pointe LH après 4 heures de 2 mUI / mL, le pic respectif de l'estradiol après 24 heures de 112 pg / mL). L'échographie mammaire révélé glande mammaire droite de 2 mm avec aspect inhomogène et glande mammaire gauche de 6,1 m. L'utérus lors de l'examen échographique avait 28.5/11/18 mm, associant la zone visible de l'endomètre motif linéaire, et l'aspect multi-folliculaire des deux ovaires de taille de 25.5 par 15 mm.
Conclusion: Différentes fenêtres d'échographie sont nécessaires pour les filles avec la puberté précoce; l'absence de corrélation entre les observations liées au sein et de l'utérus échographie nous donne l'occasion d'affirmer que le sein est plus sensible à la stimulation ovarienne que l'utérus.
Mots-clés: sein, puberté précoce, l'utérus, les ovaires, l'échographie

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BACKGROUND

Precocious puberty represents a challenging endocrine condition and new triggers more or less described seem to act as endocrine disruptors. The golden standard for diagnosis of central precocious puberty (CPP) is Gonadotropin-Releasing Hormone (GnRH) test but its use does not limit the ultrasound value as a very good screening and prognosis tool. The most important echographic aspects are related to mammary gland and pelvic area, namely uterus and ovaries. (1)

Pelvic ultrasound

A study published in 2016 on 192 girls aged less than 8 years with early puberty and associated advanced bone age presented CPP (51.6%), respective exaggerated thelarche. (2) The uterine volume was higher in the first group (4.31±2.79 mL versus 3.05±1.97 mL, p=0.03) but the other uterine echographic parameters were similar. The best predictor of CPP was a volume of the uterus larger than 3.3mL. (2)

Other observations are based on 100 girls presenting signs of precocious puberty to whom GnRH test was performed, as well as ultrasound assays. (3) The statistical analysis showed that the best predictors for CPP are based on hormonal panel (LH values and LH/FSH ratio and peak during stimulation) and on echographic features (the fundal/cervical ratio, the uterine length as well as the volume of ovaries). (3)

The ultrasound data varies, for instance, 125 girls (aged between 0 to 10 years) with premature puberty were matched with 143 healthy girls in one study highlighting the pelvic measurements. (4) The results proved that uterine length and volume (as well as fundo-cervical ratio) were statistical significant different between subjects with CPP and those with premature thelarche or adrenarche if the girls were younger than 8 years (in the group between 8 and 10 years the statistical significance was lost) while the data related to the ovarian parameters were inhomogeneous within the studied groups. (4)

Breast ultrasound

A retrospective ultrasound study on 90 female subjects (37.7% of them with CPP) having a mean age of 7.8 years showed that breast ultrasound grading is associated with age, bone age, and baseline gonadotropes, as well as bud diameter, but neither of them reveals the discrepancy between bone age and chronological age so the use of ultrasound to distinguish between CPP and premature thelarche is limited unless other data are provided. (5)

The periodic check-up of the ultrasound breast changes over time represents a useful parameter for the progression of endocrine anomalies. (6) A study on 60 girls with precocious puberty found an ultrasound breast volume of ≥0.85 cm^3 correlated with a rapidly progressive CPP. The same prediction was offered by a uterine volume of ≥5 cm^3, or presence of an endometrial echo. (6)

Other authors consider that the breast development is the hallmark for investigating the CPP versus isolated premature thelarche but the distinction between these two conditions is based on GnRH test results, bone age and some parameters from pelvic ultrasound, not necessarily the results of mammary echography. (7)

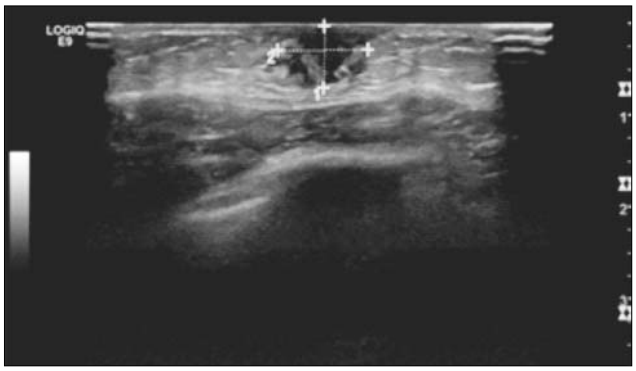

Figure 1 - Ultrasound aspect of the right breast in an 8-year old girl with precocious puberty (15 MHz linear probe, Logiq E9 machine): image of 10/6.7 mm under the skin, consistent with an incipient breast having 2 ducts

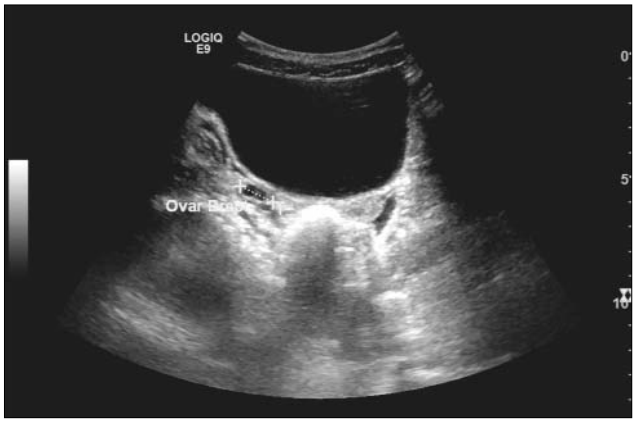

Figure 2 - Ultrasound of right ovary in a 8-year old girl with precocious puberty (7 MHz curved probe; Logiq E9 machine). Note the development of two follicles

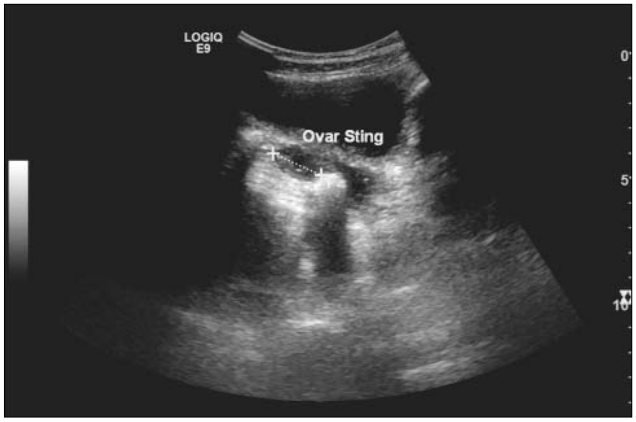

Figure 3 - Ultrasound of the left ovary in an 8-year old girl with precocious puberty (7 MHz curved probe; Logiq E9 machine). Note 4-6 small follicles

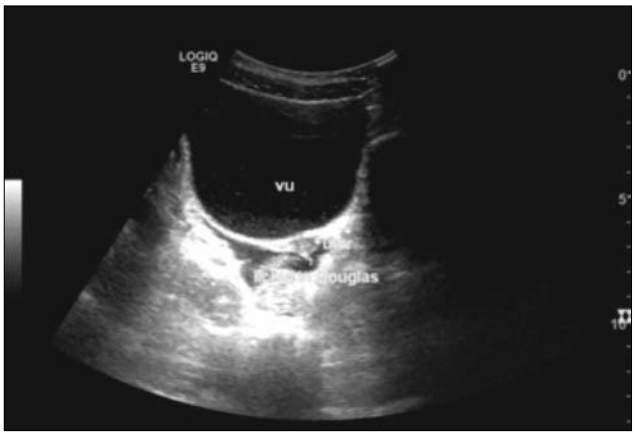

Figure 4 - Ultrasound of the uterus and the Douglas pouch on an 8-year girl with precocious puberty (7 MHz curved probe; Logiq E9 machine)

Focus: cases selection

An 8-year old girl with right nipple pain and a small bud palpable (Breast Tanner stage 1, with no adrenache, neither pubarche) was examined by ultrasound. The examination using a 15 MHz linear probe (Logiq E9 machine), revealed an image of 10/6.7 mm under the skin, consistent with an incipient breast having 2 ducts. (Fig. 1) The stage of breast development is "C" on Bruni scale. (6) The ovaries were analyzed with a 7 MHz curved probe (Logiq E9 machine) and revealed an inadequate ultrasound aspect patient's age: right ovary with a length of 15 mm, volume of 0.275 cm^3. (Fig. 2) Left ovary has a length of 21 mm, and a volume of 0.85 cm^3. (Fig. 3) The presence of both ovaries is suggestive for a central stimulation. The uterus had a hypoechoic image: length of 9 mm, volume of 0.075 cm^3. (Fig. 4) The uterus was accessible to examination due to a small posterior anechoic area which suggested liquid in Douglas' poach. This anechoid area was of 5/25 mm ant its ultrasound features suggest pelvic inflammation or increased ovarian permeability due to estrogen infusion. (8)

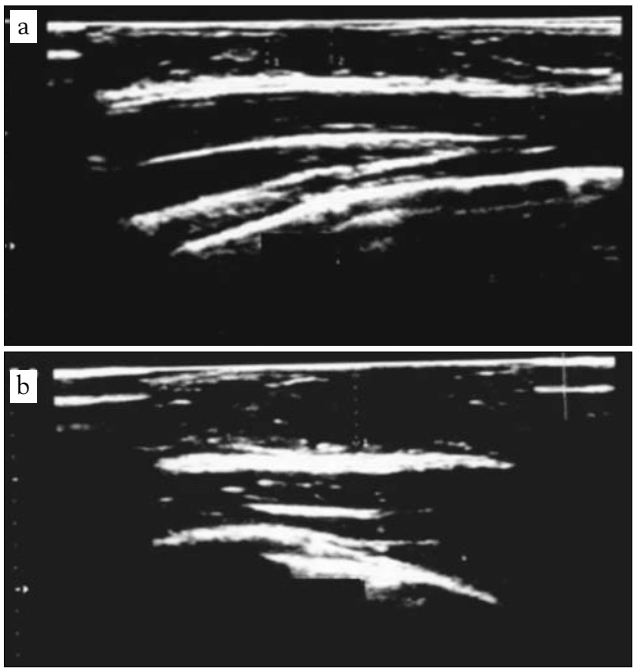

Figure 5 - Ultrasound aspects involving breast development in the context of idiopathic precocious puberty at age of 7 years and 9 months (Linear probe of 7.5 MHz)
a. Right mammary gland of 1.9 by 2.7 mm
b. Left mammary gland of 6.1 mm

A Caucasian girl aged of 7 years and 9 months has idiopathic central precocious puberty based on clinical aspects (height +1.9 SD above the normal limit for chronological age, breast Tanner stage of 2/3), bone age of 10 years and GnRH test results (baseline FSH, LH, estradiol of 2 mUI/mL, 0.2 mUI/mL, respective <20 pg/mL; peak LH after 4 hours of 2 mUI/mL, respective peak of estradiol after 24 hours of 112 pg/mL). Under these circumstances, breast ultrasound revealed right mammary gland of 2 mm with inhomogeneous aspect and left mammary gland of 6.1 m. (Fig. 5 a,b). The stage of breast development is "A" on Bruni

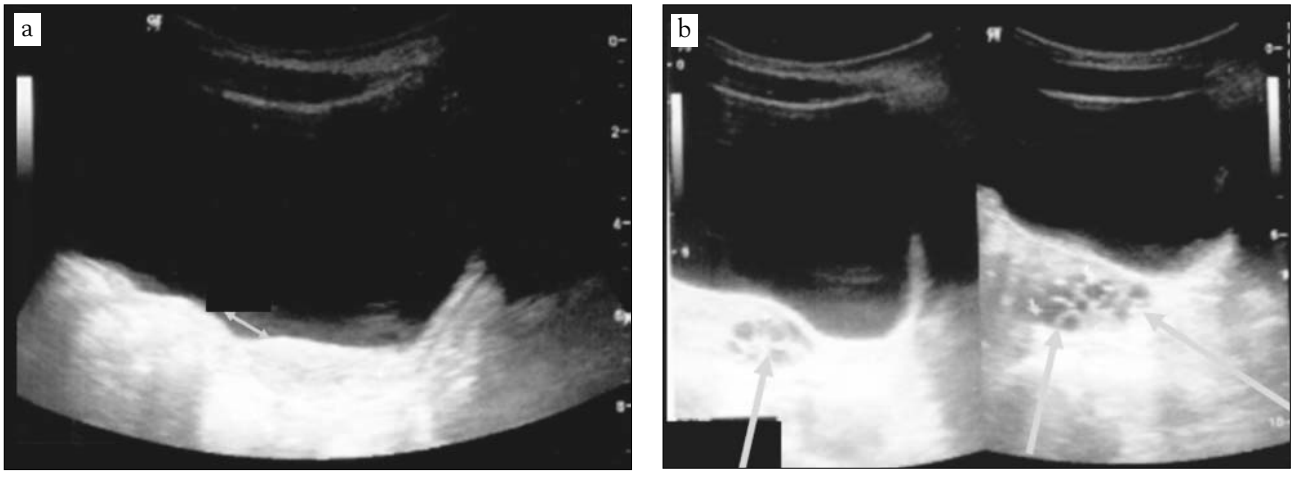

Figure 6 - Pelvic ultrasound aspects on a 7 years and 9 months girl with idiopathic central precocious puberty (Curved probe, 5 MHz)
a. Uterus has 28.5 by 11 by 18 mm, visible endometrial area of linear pattern
b. Multi-follicle aspect of both ovaries sized of 25.5 by 15 mm (right, respective left ovary)

scale. (6) The uterus at ultrasound examination had 28.5 by 11 by 18 mm, associating visible endometrial area of linear pattern, and multi-follicle aspect of both ovaries sized of 25.5 by 15 mm. (Fig. 6 a,b)

Insights

In Romanian Caucasian girls puberty's age is around 11 years. (9) Generally, the first clinical sign is the bud nipple (as seen in first case) followed by pubarche and adrenarche and after the development of external genitalia is registered. There are no central general ultrasound data for Romanian population. For other populations, for instance India, the process seems to be more rapid: at 8 years, the ovaries are from 0.62 to 1.11 cm^3; the uterus size is between 30-32 mm. (10) Therefore the physiologic puberty might begin at 8-9 years, within 2-3 years before than in Romanian Caucasian girls. (10) In India, the normal development of breast Tanner stage 1 corresponds appears at 0.52 cm^3 for ovaries and at 29 mm length for uterus. (10) Despite the differences between different populations, the ultrasound remained one of the best methods to assess precocious puberty in girls. The references for each geographic area are necessary to compare each individual since many genetic, environmental, social and economic factors are involved in puberty.

Our first patient had the largest ovarian diameter of 0.85cm^3, the uterus of 9 mm and the breast Tanner stage was 1. This observation points out on the fact that precocious puberty associates a discrepancy between the breast and the uterus development after ovarian stimulation. The uterus reacts later than the breast. (11) This means that the breast is more sensitive to the hormones in this syndrome. If this statement could be true during all the life-time, than the breast will suffer earlier from estrogen deprivation, process which characterizes the menopause. (12) Thus, in premenopausal state we need to protect the breast not to enter into the up regulation process of menopausal hyperechogenization. (13, 14) This process of up regulation could be responsible to increased prevalence of breast cancer in menopause women. (15)

CONCLUSIONS

Different ultrasound windows are needed for girls with precocious puberty; the lack of correlation between observations related to breast and uterus ultrasound gives us the opportunity to affirm that the breast is more sensitive to ovarian stimulation that the uterus.

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Conflict of interest

The authors have nothing to declare

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