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GYNAE SPECTRUM

Dear Doctor,
Greetings from Micro Labs. We are happy to bring you "Gynae Spectrum", which contains latest and interesting news in the field of Obstetrics and Gynecology.

This issue contains:

1. **Evaluation of Prolactin levels in functional hypothalamic amenorrhea.**
2. **Assessment of the androgen receptor expression on disseminated tumor cells in early breast cancer patients.**
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Best Regards,
Medical Team, Micro Labs Limited



Evaluation of Prolactin levels in functional hypothalamic amenorrhea

Introduction

Prolactin levels in FHA women are mainly influenced by metabolic causes.

Functional hypothalamic amenorrhea (FHA) is a prevalent cause of both primary and secondary amenorrhoea among women of reproductive age. Chronic anovulation and absence of menstruation were the main characteristics. This was because of insufficient hypothalamic gonadotropin-releasing hormone (GnRH) secretion, which impaired pituitary gonadotropin and gonadal steroids release.¹ Prolactin levels may elevate physiologically as a result of extreme stress and exercise, which has previously been reported. Given that both FHA and hyperprolactinemia were triggered by physical and psychological stress, it would seem obvious that there would be a causal relationship. Secondly, polycystic ovarian morphology (PCOM), which has a prevalence ranging from 30 to 50% was often associated with FHA.² Thus, the purpose of this study was to assess the levels of prolactin in both FHA patients and controls with a focus on components that may act as "sensors" of hypothalamic-pituitary dysregulation.

Methods

A retrospective cohort study was conducted on, all women with FHA. 140 women with FHA were included in this study and were compared with 70 healthy, normally ovulating women matched for age. Hyperprolactinemia is defined by the Endocrine Society as prolactin serum levels over 25 µg/L. Furthermore, prolactin levels were used to subdivide the patients into three groups: < 7 µg/L, 7–12 µg/L, and > 12 µg/L. The main outcome parameter to evaluate was prolactin. A multivariable binary logistic regression model was used to evaluate factors related to the presence of prolactin levels >12 µg/L.

Results

Remarkably, excessive exercise (45.7%) was the most common cause of FHA, followed by stress (37.9%). The median prolactin level was 11.5 µg/L. Prolactin levels >25 µg/L were present in only two women (1.4%). As FHA patients were divided into 3 different groups according to their prolactin levels, only 26 women (18.6%) had prolactin levels below 7 µg/L, 53 women (37.3%) had prolactin levels between 7 and 12 µg/L, and the largest group of 61 women (43.6%) had prolactin levels above 12 µg/L. When FHA women were compared to healthy, ovulating controls, the latter had significantly increased levels of FSH, LH, and estradiol. Prolactin levels >12 µg/L had a significant association with eating disorder, excessive exercise and TSH in a multivariable binary logistic regression model (Figure 1).

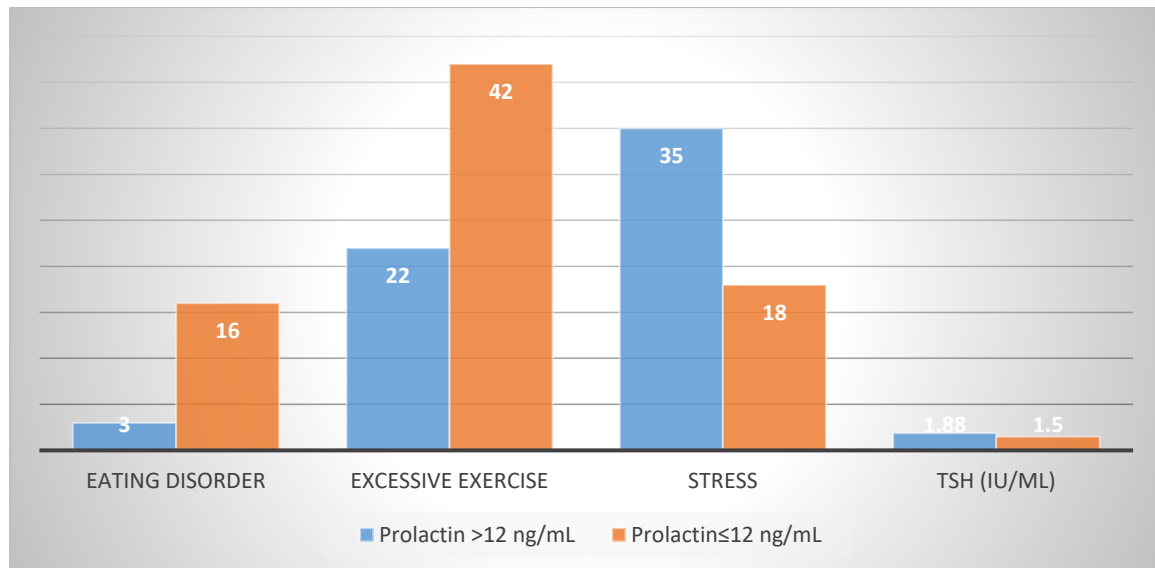


Figure 1. Factors associated with prolactin >12 ng/mL

Discussion

Women with FHA had prolactin levels that were similar to those of a group of healthy age-matched controls. About 1.4% of FHA patients had prolactin levels > 25 µg/L. Prolactin levels <12 µg/L were associated with eating disorders, which were linked with decreased calorie intake, and excessive exercise; in contrast, women with FHA had greater prolactin levels due to higher TSH levels. PCOM can be found frequently in this patient population has already been reported. Decreased AMH levels which was due to slower folliculogenesis seen in high rate of FHA women with PCOM and that of FHA patients without PCOM. In FHA women TSH levels were significantly higher than the control group.² Lee et al. findings suggested a possible relationship between PCOM and high TSH levels.³ Stress and PCOM appear to be associated with higher prolactin levels, which corresponds to prolactin being an important stress hormone and the recent study showed that stress induced FHA was associated with a higher prevalence of PCOM.⁴

Conclusion

Prolactin levels in women with FHA were similar to those of healthy, age-matched individuals. In FHA women, prolactin levels tend to be lowered by eating disorders and intense exercise, while prolactin levels >12 µg/L were linked to TSH. Women with FHA had significantly higher TSH levels, which may have been caused on by a higher PCOM prevalence among these women.

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Assessment of the androgen receptor expression on disseminated tumor cells in early breast cancer patients

Introduction

Androgen Receptor (AR) belongs to type I nuclear receptor and was expressed in many tissues in both

AR was considered a prognostic factor and potential predictive biomarker in breast cancer.

gender, including the breast.¹ Although AR was expressed in more than 70% of ER-positive and up to 45% of triple-negative breast cancer (TNBC), its exact function in breast cancer (BC) remains unclear. Depending on the co-expressed level of ER α and the availability of the respective ligand, the AR exhibits either proliferative or anti-proliferative activity in BC cells that are ER α positive. When compared to the primary tumour (PT), AR expression was higher in TNBC in early metastatic lesions, indicating that AR promoted tumour cell survival during metastatic dissemination. In BC patients, disseminated tumour cells (DTCs) in the bone marrow (BM) have been reported to serve as an indirect marker for minimum residual disease (MRD).² This study aimed to assess AR status of DTCs in a cohort of early BC patients and compared it with the AR status of the Primary tumor (PT).

Methods

About 62 DTC-positive patients were included in this study. Immunofluorescence staining was conducted using eFluor 615 conjugated monoclonal mouse AE1/AE3 Pan Cytokeratin Antibody. CK-positive, CD45-negative cells with an intact nucleus (DAPI positive) were recognised as DTCs. A single-pass filter for particular fluorochromes, such as FITC, Texas Red, or DAPI, and a triple-pass filter for FITC/TRITC/DAPI were used to screen for AR-positive DTCs. Immunohistochemistry was used to evaluate the AR expression of the primary tumour (PT) on formalin-fixed, paraffin-embedded (FFPE) tumour sections obtained from core biopsies and surgical specimens.

Results

Hormone receptor (HR)+/HER2- tumor was diagnosed in 50 patients, 6 cases (10%) had immunohistochemistry staining indicating HR+/HER2+ tumor as determined by immunohistochemistry, and 5 patients (8%) had a TNBC. 21 out of 62 patients were initially DTC-positive and additional analysis detected at least 1 DTC in the BM. DTC numbers ranged from 1 to 20 cells. Further, 19 of the 21 DTC-positive patients (90%) had only 1 DTC in BM. 9 of the 21 further DTC-positive patients (43%) had detectable AR-positive DTCs. No correlation was found between AR status of DTC and any of the clinicopathological factors.

AR status of the PR in the 21 DTC positive patients was determined. 13 patients (62%), 12 out of 16 HR+/HER2– patients (75%), 1 out of 3 HR+/HER2+ patients (33,3%), and none of the 2 TNBC patients had tumors that tested positive for AR. The concordance percentage between the corresponding PT and DTC's AR expression was 33%. The DTC-AR status did not find correlation with clinicopathological factors, nor study didn't observe a significant correlation between the AR status of the PT and other established prognostic factors for BC.

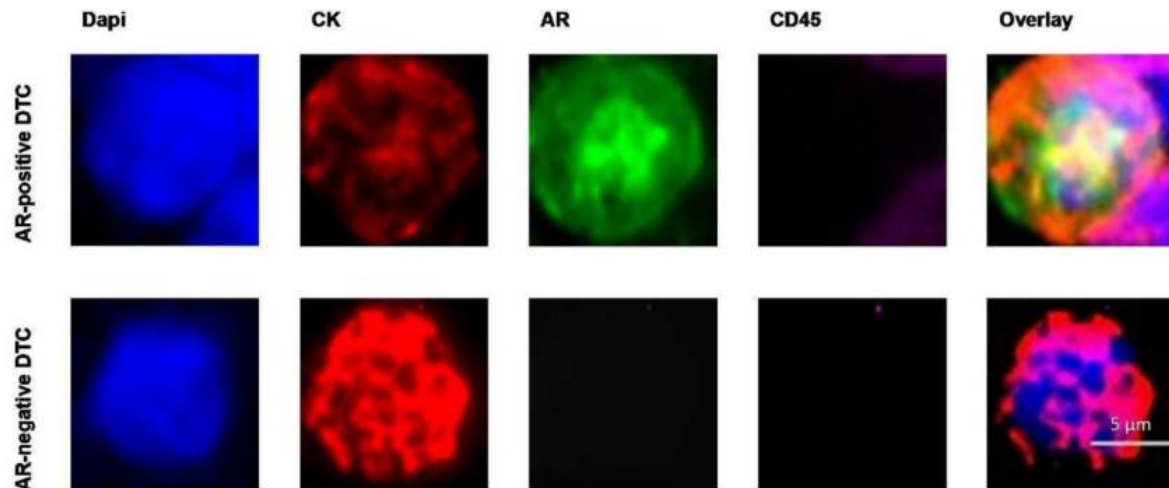


Figure 1. Androgen receptor (AR) staining of DTCs in patients with primary breast cancer: (A) AR-positive staining (B) AR-negative staining

Discussion

In BC, AR was considered to be a prognostic factor and possibly a predictive biomarker, while its exact function remains unknown. While AR expression was found to increase tumour proliferation in TNBC and HER2+BC, its impact in ER α -positive BC was unclear, as it can have either pro- or anti-proliferative effects depending on the level of co-expressed ER α and the presence of the specific ligand.² A study reported androgen receptor was more frequently expressed in diverse BC subtypes. AR may be a prognostic or predictive component as well as a potential therapeutic target in BC, according to accumulating data. The most affordable technique and one that was frequently used in BC to define AR positive was immunohistochemistry (IHC).³

Conclusion

AR-positive DTCs can be found in the bone marrow of early BC patients with a significant discrepancy in the AR status between DTCs and corresponding PTs.

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Evaluation of vitamin D deficiency effect on urinary incontinence during the third trimester of pregnancy

Introduction

Urinary incontinence (UI), a common health issue affecting 44–57% of middle-aged females. In addition to age, pregnancy and childbirth were recognised risk factors. The pelvic floor's anatomy and innervation undergo modifications throughout pregnancy and childbirth.¹ Weight gain, increased uterine volume, elevated intra-abdominal pressure, pressure on the pelvic floor and bladder, and widening of the genital hiatus with increasing parity were risk factors for the development of UI during pregnancy. Vitamin D impacts the reproductive tissues of both men and women via receptors. Vitamin D was essential for the normal functioning of the pelvic floor muscles. Numerous studies have shown that in non-pregnant women, vitamin D insufficiency was linked to UI. Moreover, postpartum pelvic floor muscle dysfunction has been connected to vitamin D deficiencies during pregnancy.² Hence, this study aimed to investigate the prevalence of UI and examined the relationship between vitamin D deficiency and UI in full-term pregnant women.

Pregnant women with vitamin D deficiency had a risk of urinary incontinence.

Methods

A single-centre, cross-sectional study was conducted which included 250 healthy pregnant women with a singleton pregnancy over 28 weeks. The Incontinence Severity Index (ISI) was used to identify the severity of UI. The ISI includes 2 questions, “How frequently do you urinate?” and “How much of urine do you leak per day?”. The enzyme-linked immunosorbent assay was used to evaluate the amount of serum 25 (OH) D3. Concentrations of serum 25 (OH) D3 less than 20 ng/mL were considered inadequate. 40 women with acceptable vitamin D levels were included in the control group, while 210 women with insufficient levels included in the study group. The ISI scores were used to compare the two groups.

Results

A total of 40% (100) of all the pregnant women experienced UI at some point during their pregnancy. Based on subjective reports of incontinence, 42.4% (n = 89) of the study group's pregnant women and 27.5% (n = 11) of the control group's pregnant women reported having UI at least once during their pregnancies. Compared to 27.5% of pregnant women in the control group, 42.4% of pregnant women with vitamin D deficiency experienced UI. Further, compared to the control group, the pregnant women in the study group had significantly higher ISI scores (Figure 1).

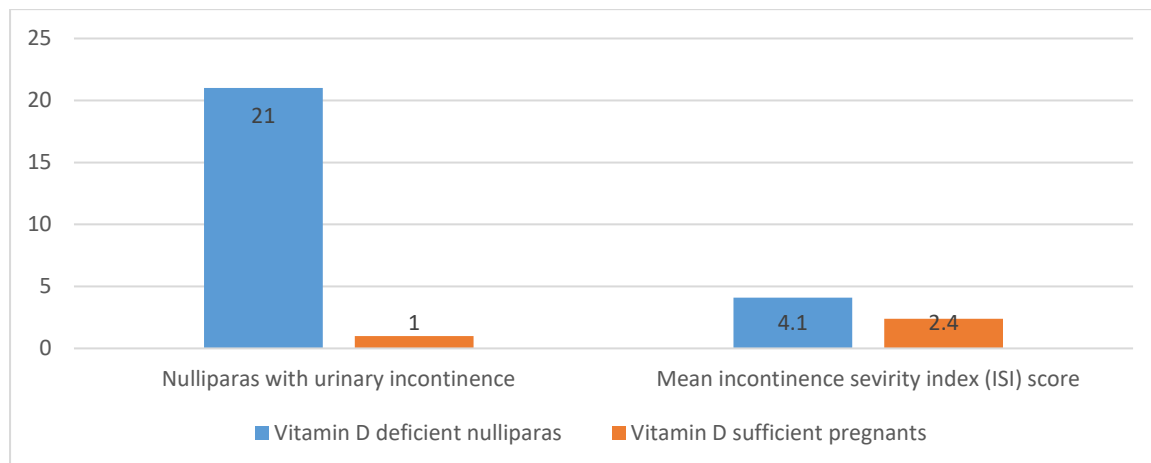


Figure 1. Nulliparous women's incontinence frequency and severity

Discussion

The present investigation examined how vitamin D insufficiency affected UI in pregnant women in their third trimester. According to the results of this study, 40% of the women had a history of urinary incontinence, and 84% of them were vitamin D deficient. Compared to women with normal vitamin D levels, pregnant women with low vitamin D levels experienced considerably more UI problems. Vitamin D receptors were found in the bladder and pelvic floor muscles. Consequently, urinary continence and pelvic floor function may be impacted by vitamin D deficiency.² Stafne et al. reported that the prevalence of UI, especially stress incontinence, was higher in pregnant women with vitamin D insufficiency and that it affected 27% of healthy, nulliparous, mid-trimester pregnant women.³

Conclusion

The severity of UI was significantly higher in patients with vitamin D deficiency. Urinary incontinence was found to be significantly associated with vitamin D deficiency in pregnant women.

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Case report on umbilical vein thrombosis during second trimester with associated portal vein thrombosis after childbirth

Introduction

Umbilical cord vessels thrombosis is a rare event, occurring 1 in 1500 deliveries.¹ The probability of umbilical

cord venous thrombosis was higher, but umbilical cord artery thrombosis was more likely to lead to adverse pregnancy outcomes.² The diagnosis and treatment of umbilical vein thrombosis (UVT) were difficult since it was not typically simple to find during standard antenatal exams. This report described a rare case of umbilical vein thrombosis (UVT) in a neonate that was detected prenatally via ultrasound examination, and portal vein thrombosis was identified after birth.

Regular prenatal ultrasound evaluation enables early detection and monitoring of any anomalies or vascular abnormalities related to the fetal umbilical vein.

Case presentation

A 33 years old primiparae was admitted to the hospital at 40 weeks of gestation. Patient was normal expect for gestational diabetes mellitus. Umbilical vein thrombosis was suspected following a routine obstetrical ultrasound at 21 week's gestation, which showed an atypical bean-like dilatation of the intra-abdominal umbilical vein. At 21 week's gestation, a fetal system ultrasound revealed no anomalies. umbilical cord exhibited normal morphology with two umbilical arteries and one umbilical vein, and normal blood flow waveform in the umbilical artery. An apparently healthy female baby weighing 2,830 grams was delivered. Soon after the infant was born, an abdominal ultrasound revealed possible thrombosis in the portal and umbilical veins. Further, abdominal ultrasound performed on the 2nd day of life confirmed the existence of a thrombus measuring 26×16 mm in the umbilical vein thrombosis and a thrombus measuring 21×5 mm in the portal vein (Figure 1). Upon admission, a laboratory examination revealed the following white blood cells at $14.21 \times 10^9/L$, hemoglobin at 175g/L, platelets at $183 \times 10^9/L$, and C-reactive protein (CRP) at 13.65mg/L. Additionally, prothrombotic states were assessed. Protein C 26%, antithrombin III 48%, lupus ratio 0.58, d-dimer 2.38µg/mL, and other indicators were within normal ranges. Treatment was started with anticoagulation with low-molecular weight heparin (enoxaparin) at a dose of 1.5mg/kg twice a day was started at day of life 3, targeting an anti-Xa between 0.5 and 1.0 IU/mL. On the 9th day of life, a third ultrasound revealed that the thrombus had reduced. In order to get the desired anti-Xa level, the dose of enoxaparin was gradually increased to 2.1 mg/kg twice a day, indicating that anticoagulant therapy was effective. A fourth ultrasound performed on the 16th day of life revealed that the thrombus had greatly reduced and the portal vein's degree of stenosis had dropped from 75% to 30% (Figure 2). Laboratory tests revealed that Protein C had increased to 40%. The infant was discharged in good clinical condition, with directions to

continue taking enoxaparin (2.1 mg/kg every 12 hours). On the 26th day of life, an ultrasound examination revealed nearly complete clearance of the thrombus. At day 33 of life, enoxaparin was stopped along with a 30-day treatment plan. Patient had no recurrence of thrombosis at the 10-month follow-up.

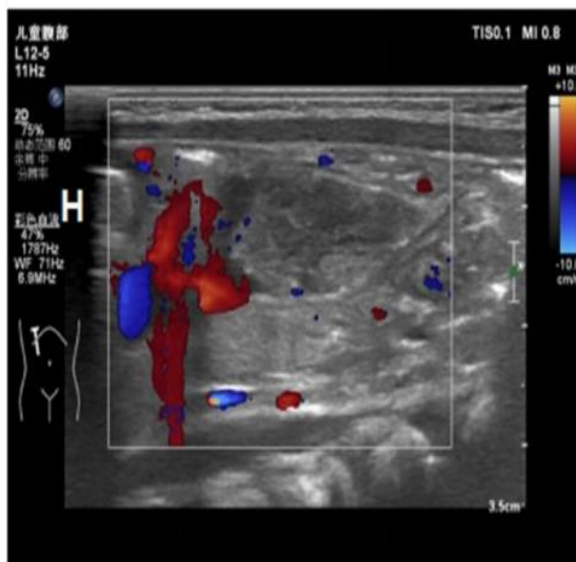


Figure 1. Umbilical vein thrombus at day 2

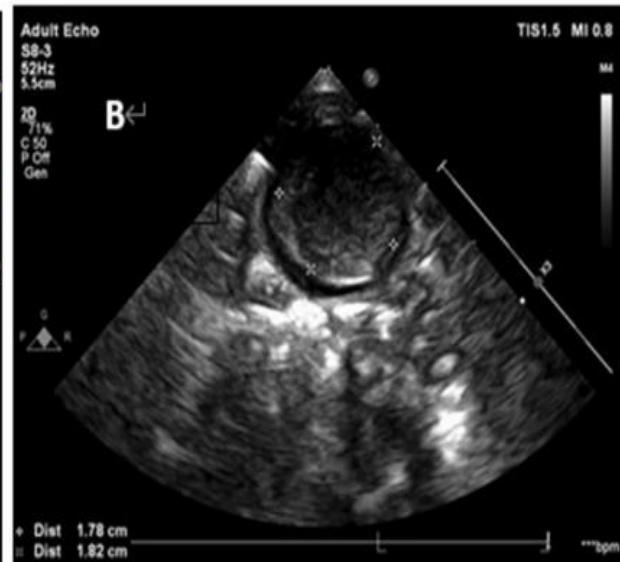


Figure 2. Signal of blood flow through umbilical vein thrombosis at day 16

Discussion

Umbilical vascular thrombosis is a rare pregnancy condition that was significantly linked to higher rates of perinatal morbidity and mortality. Compared to umbilical artery thrombosis (UAT), UVT happens more commonly. In the present case, there was no evidence of an acquired disorder linked to UVT or anatomical cord abnormalities, nor was there any indication of umbilical cord torsion. Additionally, the baby's thrombophilia tests were negative. Maternal gestational diabetes mellitus was the only related risk factor that was identified. Fritz suggested that irregular blood glucose levels in mothers can result in an unbalanced expression of endothelial vasodilatation and shrinking factors, which can cause coagulation problems and ultimately thrombosis.¹ A study suggested that umbilical vascular thrombosis may also be related to maternal pathology such as maternal diabetes, hypertension and smoking.³ Another study reported that maternal diabetes was a risk factor for developing thrombosis in two cases.⁴

Conclusion

Early detection of umbilical cord thrombosis can be enhanced by foetal heart monitoring, counting foetal movements, and attention to abnormal clinical symptoms during prenatal ultrasonography. This results highlighted the significance of routine prenatal ultrasound examination, which allowed for the early identification and observation of any anomalies or vascular abnormalities pertaining to the foetal umbilical vein.



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