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Dr. Usha Sharma
President, 2020-22

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Dr. Vandana Walvekar
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Senior Members of ISOPARB and Friends,

At the outset, I thank the almighty by whose grace we have all joined webinar for ISOPARB Midterm National Conference 2020.

Thank you all for entrusting me to lead ISOPARB from 2020 to 2022.

ISOPARB was formed in 1978 by stalwarts of our country, Late Prof. G. Achari, Late Prof. Kamala Achari, from Patna and Late Dr. (Professor) Tarun Banerjee, Professor K.M. Gun, from Kolkata with a handful of members. My senior predecessors have nurtured ISOPARB with their dedicated good work in the past. Today we have 2445 members and 26 city chapters.

I hope 2021 will be a landmark year for progress and growth of ISOPARB.

Our progress in acquiring recent advancement in prevention, diagnosis and treatment in the field of perinatology will continue with our regular clinical meetings, CME Programs, workshops and awareness camps. Our services to adolescent girls, women and children will be rendered by free medical camps in city and villages alike.

Our theme for 2020-22 is
"Say No to Birth Defects"

As per World Health Organization (2016) an estimated 303,000 newborns die within 4 weeks of birth globally due to congenital anomalies. This figure has not changed much since then. Congenital anomalies contribute to long term disability which may have significant impact on individuals, families, healthcare system, societies and the country, so we will focus on ways for reducing birth defects.

Obstetricans, Neonatologists play a vital role in preventing and managing birth defects.

Our Strategy –

Mass educational campaigns –
- Family planning strategies, reproduction before 35 years
- Avoidable risk factors of birth defects
- Preconception, prenatal & neonatal care

Preventive strategies
- Folic acid supplementation
- Rubella Vaccination
- Restrict alchohol consumption
- Avoidance of teratogenic medications

Parental guidance
- Organisations which provide rehabilitatory support to such children
- Psychological support to parents and child with birth defects

Providing best medical care
- Medical
- Surgical

Provision of genetic screening
- Cost effective
- sensitive, easily available programmes

Epidemiological Data collection
- Extent of the problem
- Intervention priorities

Preconception Counseling

Preconception counseling involves education, risk assessment and intervention before pregnancy to reduce the chances of poor perinatal outcomes.

Preconception care often remains neglected owing to multiple reasons such as lack of understanding and acceptance of objectives of preconception care, secrecy about pregnancy planning, lack of prevailing culture of 'preparing for pregnancy', and unawareness about realities of unplanned pregnancies. This results in negligence towards preconception risk assessment, family planning and preconception care. Thus, benefits of preconception care remain unrecognized in India.

To improve preconception care in India and bridge the gap in preconception care and poor neonatal outcome, it is essential to inculcate healthcare precautionary measures in adolescents and emphasis should be given to antenatal care. Following measures could help in improving preconception care in India.

- Information on preconception health should be made widely available particularly in schools and family planning clinics
- More provisions should be made for preconception assessment or care from any health professional
- Preconception health should be promoted more routinely in a positive way even in women who are not immediately planning pregnancy. Importance of preconception health should be taught to all the women once they reach reproductive age
- Men should also be actively involved in preconception care and counselling as their health is an equally important determinant of neonatal well-being
- Access to GPs should be enhanced, particularly for young people and women who are less disposed to seeing their GP/ male practitioners

Frequent awareness camps across all cities and villages of India regarding prevention, detection and treatment of congenital anomalies which will help in reducing the numbers of birth of abnormal babies. This will result in healthy babies and healthy future India.

We will join hands with other organizations to conduct programs all over India.

This year ISOPARB is blessed with a galaxy of dynamic and dedicated office bearers. Our four Vice Presidents Dr. Sulekha Pandey, Dr. Shashi Kala Kola, Dr. Saswati Sanyal Choudhury and Dr. Parul Kotadawala will play an important role in all activities of ISOPARB.

Secretary General Dr. Meena Samant and Treasurer Dr. Pragya Mishra Choudhary with all the office bearers and all ISOPARB members will work together to best of their capabilities for progress and growth of ISOPARB.

Journal of ISOPARB is the mirror of the society. It is our pride that IJOPARB is an indexed journal since 2017, under the able leadership of Professor Hiralal Konar. We need to improve the quality of the Journal further and we need to go with other indexing agencies. Our work is on.

I quote Henry Ford – *Coming Together is Beginning, Keeping Together is Progress and Working Together is Success.*

I request all ISOPARB members to make at least one new member which will enable us to have a robust ISOPARB 2021. Once the numbers of ISOPARB members doubles, joins hands together for ISOPARB activities then we will definitely achieve success in all our pursuits.

JAI HIND

Long Live ISOPARB

Dr. Usha Sharma

Original Article - Obstetrics

A Study to Corroborate Early Onset Pre-Eclampsia with Uterine Artery Notch Depth Index in Pregnant Women

Tirthankar Sinha,[1] Sajal Datta[2]

Abstract

Objective – to corroborate uterine artery notch depth index with development of early onset pre-eclampsia

Method – study was carried out on 100 uncomplicated primigravida women and uterine artery notch depth index was measured at 20-22 weeks of pregnancy.They were later followed up till delivery to look for development of pre-eclampsia and also perinatal outcome — 1) development of SGA, 2) NICU admission etc.

Results – Of the 100 patient we examined 7 of them developed pre-eclampsia of which 4 were early onset disease. A notch was found in 44 patients of which 50% was unilateral and 50% bilateral. Risk of pre-eclampsia was 8.68 times more among patients having a notch.All the patients with early onset pre-eclampsia had a notch in their uterine artery Doppler which was higher than patients with late onset disease. The cut off value of NDI to predict early onset disease was 0.081 and risk of early onset pre-eclampsia was 9 times more in those who had NDI value> 0.081. However no significant association was found between presence of a notch and development of SGA and NICU admission rates.

Conclusion – NDI values measured in between 20-22 weeks of pregnancy can be a useful predictor for development of early onset pre-eclampsia.

Introduction

Pre-eclampsia is a hypertensive disorder of pregnancy with incidence in nulliparous women ranging 3-10%.[1] It accounts for a major share of maternal, fetal as well as neonatal mortality and morbidity. Hence, some way to predict it early and thus prevent its potentially grave complications remains a challenge. It is divided into early onset disease (<34 weeks POG) and late onset disease (>34 weeks POG).[2] It is early onset pre-eclampsia which is associated with greater risk of perinatal morbidity and mortality.[3] During past two decades numerous biophysical and biochemical tests have been proposed for early detection of pre-eclampsia. Uterine artery Doppler velocimetry is a valuable tool for early detection of pre-eclampsia. Resistant to blood flow in uterine arteries can be important and effective method in predicting obstetric vasculopathies. Resistance to blood flows can be measured by presence of diastolic notch as well

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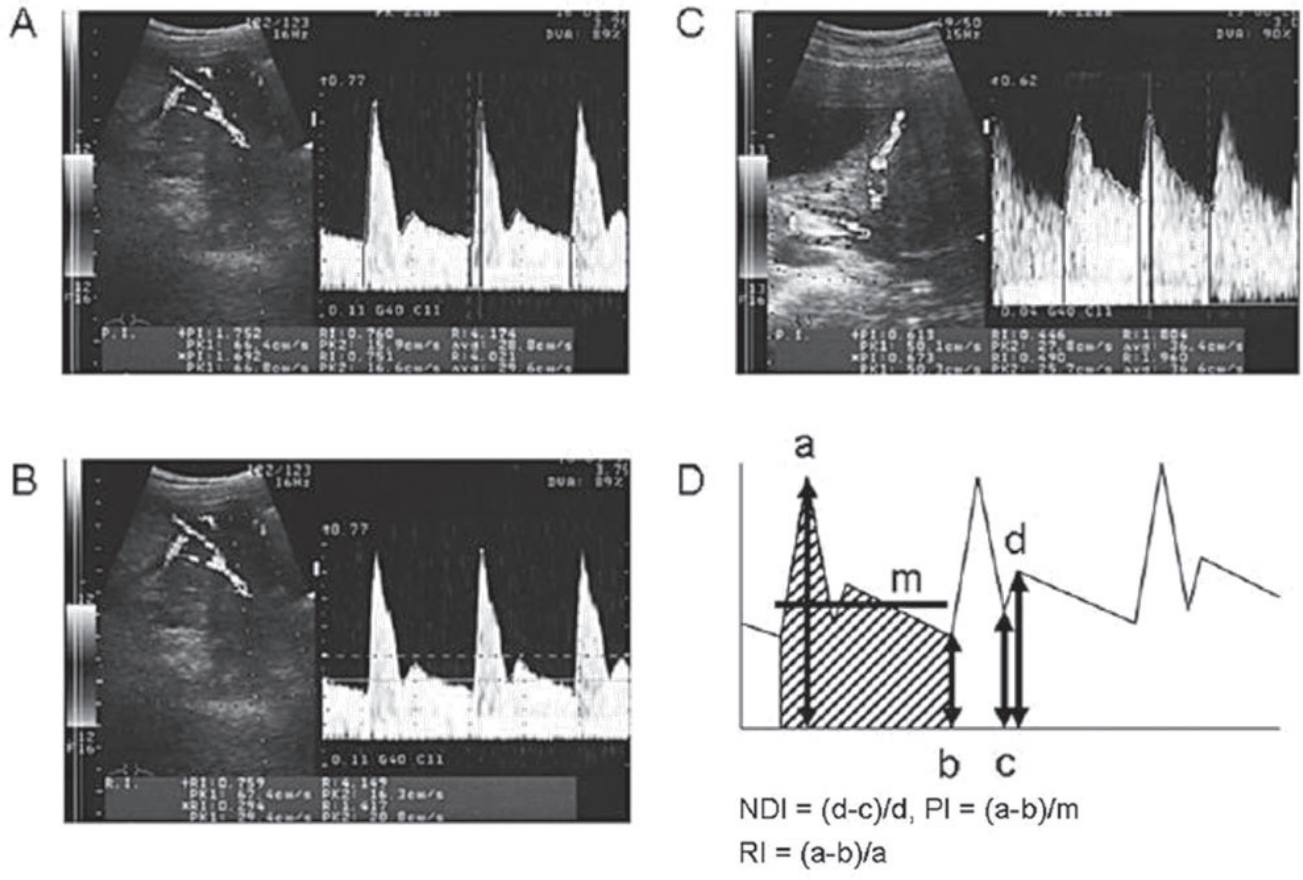

as standard colour Doppler indices namely Pulsatility index (PI), Resistance index (RI) and systolic : diastolic ratio (S:D).

One more concept that is being discussed currently in predicting obstetric vasculopathies is NDI (Notch Depth Index). Uterine artery Notch Depth Index values can be measured by Doppler velocimetry and may be used to detect early onset pre-eclampsia.0kuchi et al developed the NDI to evaluate its association with the risk of pre-eclampsia and SGA infant and to compare its usefulness with that of uterine artery RI and S/D ratio. They found that NDI value in the second trimester is clinically more useful than two other conventional indices.[4] Hence our study aims at corroboration of uterine artery NDI with development of early onset pre-eclampsia and to know the outcome of pregnancies.

Methods

A prospective observational study was conducted in Vivekananda Institute of Medical Sciences, Kolkata among 100 uncomplicated primigravidas. Uterine artery Doppler was performed along with anomaly scan at 20-22 weeks of pregnancy. Uterine artery Doppler velocimetry was performed and when three consecutive waveforms were obtained the NDI was measured and mean NDI of right and left arteries calculated.

The NDI was defined as (d-c)/d in the presence of a notch, or equal to zero in the absence of a notch. Patients were followed up till delivery and their obstetric outcome observed.

Results

Descriptive statistical analyses were performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. In the cases where one of the cell frequencies were less than 5 corrected Chi-square (χ^2) was used to find the association between variables. t-test was used to compare the means. Odds ratio (OR) with 95% confidence interval was calculated to find the risk factors. ROC (receiver operating characteristic curve) was used to find the cut-off value. $p<0.05$ was taken to be statistically significant.

Of the 100 patients we examined 44 patients had notch, of which 22 (50%) had unilateral notch and 22 (50%) had bilateral notch. In overall 7% patients developed pre-eclampsia of which 4 (57.1%) were early onset pre-eclampsia and 3 (42.9%) were late onset pre-eclampsia.

Maternal Outcome and NDI

Table 1. Pre-eclampsia and Notch Depth Index of the patients

Pre-eclampsia	Notch Depth Index		TOTAL
	>0 (Present)	0 (Absent)	
Yes Row % Col %	6 85.7 13.6	1 14.3 1.8	7 100.0 7.0
No Row % Col %	38 40.9 86.4	55 59.1 98.2	93 100.0 93.0
TOTAL Row % Col %	44 44.0 100.0	56 56.0 100.0	100 100.0 100.0

χ^2=5.31; p=0.021 S-Significant.

Corrected chi square test showed that there was significant association between pre-eclampsia and presence of notch among patients (p=0.021). The risk of pre-eclampsia was 8.68 times more among the patients with notch as compared to the patients without notch and the risk was significant [OR-8.68 (1.01,75.07); P=0.021].

Table 2. Type of Pre-eclampsia and Notch Depth Index of the patients

Type of Pre-eclampsia	Notch Depth Index		TOTAL
	>0 (Present)	0 (Absent)	
Early Row % Col %	4 100.0 66.7	0 0.0 0.0	4 100.0 57.1
Late Row % Col %	2 66.7 33.3	1 33.3 100.0	3 100.0 42.9
TOTAL Row % Col %	6 85.7 100.0	1 14.3 100.0	7 100.0 100.0

For all the patients with early onset of Pre-eclampsia (100.0%) NDI was present which was significantly higher than that of the patients with late onset of Pre-eclampsia (66.7%) NDI (Z=3.27;p<0.001).

For all the patients with early onset of pre-eclampsia NDI was present (100.0%). But none of the patient without NDI developed early onset Pre-eclampsia (Z=14.32;p<0.001).

Receiver operating characteristic curve (ROC) was used to calculate cut-off value for both pre-eclampsia overall and early onset pre-eclampsia. For early onset pre-eclampsia the cut-off value of NDI was 0.081 and for overall preeclampsia it was 0.064.

Table 3. Early onset pre-eclampsia and Cut-off value of Notch Depth Index for early onset pre-eclampsia of the patients

Cut-off value of Notch Depth Index for early onset pre-eclampsia	Early Onset pre-eclampsia		TOTAL
	Yes	No	
≥ 0.081 Row % Col %	3 23.1 75.0	10 76.9 25.0	13 100.0 29.5
<0.081 Row % Col %	1 3.2 25.0	30 96.8 75.0	31 100.0 70.5
TOTAL Row % Col %	4 9.1 100.0	40 90.9 100.0	44 100.0 100.0

χ^2=4.36; p=0.03 S-Significant

Chi-square (χ^2) test showed that there was significant association between Early onset pre-eclampsia and Cut-off value of Notch Depth Index for early onset pre-eclampsia (p=0.03).

However, the risk of Early onset pre-eclampsia was 9.00 times more among the patients with NDI ≥ 0.081 as compared to the patients with NDI <0.081 and the risk was significant [OR-9.00 (1.03, 96.63);p=0.03].

Table 4. Pre-eclampsia and Cut-off value of Notch Depth Index for pre-eclampsia of the patients

Cut-off value of Notch Depth Index for pre-eclampsia	Pre-eclampsia		TOTAL
	Yes	No	
≥ 0.064 Row % Col %	6 19.4 85.7	25 80.6 67.6	31 100.0 70.5
<0.064 Row % Col %	1 7.7 14.3	12 92.3 32.4	13 100.0 29.5
TOTAL Row % Col %	7 15.9 100.0	37 84.1 100.0	44 100.0 100.0

χ^2=0.93; p=0.33 NS-Not Significant

Chi-square (χ^2) test showed that there was no significant association between Pre-eclampsia and Cut-off value of Notch Depth Index for pre-eclampsia (p=0.33).

However, the risk of Pre-eclampsia was 2.88 times more among the patients with NDI ≥ 0.064 as compared to the patients with NDI <0.064 but the risk was not significant [OR-2.88 (0.31, 26.68);p=0.33].

Table 5. NICU admission and Notch Depth Index of the patients

NICU admission	Notch Depth Index		TOTAL
	>0	0	
Yes	4	2	6
Row %	66.7	33.3	100.0
Col %	9.1	3.6	6.0
No	40	54	94
Row %	42.6	57.4	100.0
Col %	90.9	96.4	94.0
TOTAL	44	56	100
Row %	44.0	56.0	100.0
Col %	100.0	100.0	100.0

χ^2=1.33; p=0.24 NS-Not Significant

Chi-square (χ^2) test showed that there was no significant association between NICU admission and NDI of the patients (p=0.24).

However, the risk of NICU admission was 2.70 times more among the patients with NDI as compared to the patients without NDI but the risk was not significant [OR-2.70 (0.47, 15.47); p=0.24

Table 6. SGA and Notch Depth Index of the patients

SGA	Notch Depth Index		TOTAL
	>0	0	
Yes	3	3	6
Row %	50.0	50.0	100.0
Col %	6.8	5.4	6.0
No	41	53	94
Row %	43.6	56.4	100.0
Col %	93.2	94.6	94.0
TOTAL	44	56	100
Row %	44.0	56.0	100.0
Col %	100.0	100.0	100.0

χ^2=0.09; p=0.76 NS-Not Significant

Chi-square (χ^2) test showed that there was no significant association between IUGR and NDI of the patients (p=0.76).

However, the risk of SGA was 1.29 times more among the patients with notch as compared to the patients without notch but the risk was not significant [OR-1.29 (0.24, 6.74); p=0.76].

Discussion and Conclusion

Of the 100 uncomplicated primigravidas 44 had a notch of which 50% was unilateral and 50% was bilateral. Total 7 patients developed pre-eclampsia of which 4 (57.1%) were early onset pre-eclampsia and 3 (42.9%) were late onset disease. The risk of pre-eclampsia was 8.68 times more among patients with notch and the risk was significant (p=0.021). For all the patients with early onset pre-eclampsia (100%) notch was present which was significantly higher than that of the patients with late onset disease (66.7%) and also none of the patients without notch developed early onset pre-eclampsia (Z=14.32: P<0.001).

The cut off value of NDI to predict early onset pre-eclampsia was 0.081. Risk of early onset pre-eclampsia was 9.0 times more among patients with NDI>0.081 and the risk was significant (p=0.03). The sensitivity, specificity and positive predictive value by using this cut off to predict early onset disease was 75%.75% and 23% respectively. There was no significant relationship found between presence of notch and development of SGA babies and also NICU admission rates.

In the study done by Okuchi et al, Nine (3.1%) of the 288 women developed pre-eclampsia and 18 women (6.3%) delivered an SGA infant. The NDI was associated with subsequent onset of pre-eclampsia. The optimal cut off value for the NDI in predicting pre-eclampsia was 0.14, giving a sensitivity, specificity and a positive predictive value (PPV) of 67, 92, and 22%, respectively. The PPV of the NDI was the largest of the three indices evaluated (12% for the RI and 16% for the A/C ratio).[4]

In a study done by R. Becker and R.Vonk to determine whether assessment of depth of notch in Doppler sonography of uterine arteries (DSUA) at 20–23 gestational weeks has the potential to predict the probability of adverse pregnancy outcome (APA) and degree of IUGR.The prevalence of one or several forms of APA increased with increasing depth of the notch from 4.7% (mNI =0) to 46.5% (mNI>0.3).Fetal growth restriction increased with increasing depth of notch from 1.0 MOM or 56th centile (mNI=0) to 0.84 MOM or 21st centile (mNI>0.3). So they came to the conclusion that assessment of depth of notch at 20-23 weeks seems to have the potential to predict

the probability of APA and extent of fetal growth restriction.[5]

Our study supports some of the findings of these previous studies and therefore we come to a conclusion that NDI values may have a role in predicting development of early onset pre-eclampsia and further studies are needed for establishing its role.

Acknowledgement

Professor Dr. Kamal Oswal, Department of Radio diagnosis, VIMS Kolkata for help in uterine artery Doppler study.

Conflict of Interest

No financial assistance was taken from any funding organization or pharmaceutical company.

Abbreviations

VIMS - Vivekananda Institute of Medical Sciences; NDI - Notch Depth Index; PI - Pulsatility Index; RI - Resistance Index; SGA - Small For Gestational Age; S/D - Systolic : Diastolic; DSUA - Doppler Sonography of Uterine Artery; ROC - Receiver Operating Characteristics; APA - Adverse Pregnancy Outcome

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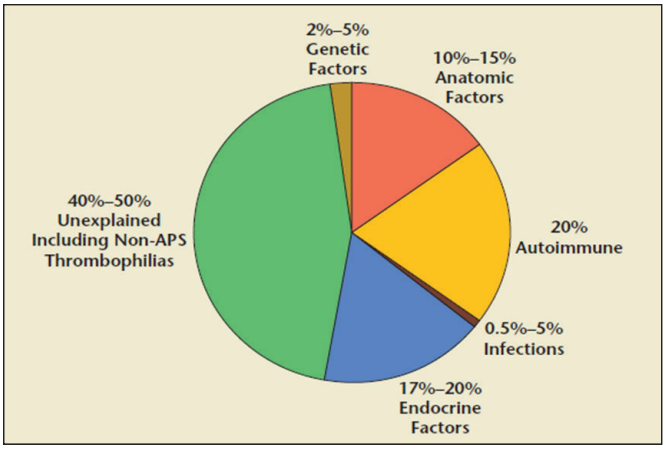
Advances in the Management of Recurrent Pregnancy Loss

Sukumar Barik

Introduction

Pregnancy loss is a common complication in early pregnancy. The prevalence of pregnancy loss ranges from 10 to 15%. Recurrent pregnancy loss (RPL) is less prevalent. RPL affects approximately 1% to 2% of women, when defined as three consecutive pregnancy losses prior to 20 weeks from the last menstrual period.

Aetiology



When to investigate?

Diagnosis of RPL could be considered after the loss of two or more pregnancies particularly in the relatively older age group. At present the recurrent pregnancy loss is the preferred term. This includes early trimester miscarriage, mid trimester miscarriage and intrauterine fetal death.

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As pregnancy loss is a significant negative life event, it should be dealt in a very sensitive manner. The grief experience is intensified because of the repetitive nature of RPL. Several studies revealed that grief reactions are same whether the pregnancy loss is in early pregnancy or in advanced pregnancy.

How far to investigate?

Basic tests:

- Full blood count
- Blood Group and Rhesus factor
- Blood sugar (Fasting and postprandial)
- Thyroid function test and Anti thyroid peroxidase antibody
- Thalassaemia screening
- Rubella IgG

First line tests:
Antiphospholipid antibodies

- Anticardiolipin antibodies IgG and IgM.
- Lupus Anticoagulant.
- β2 glycoprotein I antibodies.

Antinuclear antibodies (ANA)
Assessment of the uterine anatomy

- Transvaginal 3D ultrasound - high sensitivity and specificity; can distinguish between septate uterus, bicornuate uterus.
- Saline infusion sonography - more accurate than Hysterosalpingogram.
- Magnetic resonance imaging - not recommended as first line; can be used where 3D US is not available.

Second line tests:

- Parental Karyotyping - not routinely recommended; could be carried out after individual assessment of risk.
- Genetic analysis of products of conception (POC) - not routinely recommended.
- For genetic analysis of POC - Array-based Comparative Genomic Hybridization (array-CGH).
- Not to screen for hereditary thrombophilia routinely unless in the context of research, or in women with additional risk factors for thrombophilia.
- Assessing sperm DNA fragmentation in couples with RPL can be considered for explanatory purposes.

Managing Antiphospholipid antibody syndrome

Pregnancy is a unique example of Immunological paradox. It contradicts many general rules of immunology. There is unique symbiotic relation between the mother and the fetus. Instead of triggering rejection, it tolerates supports, regulates and nurtures its development.

Antiphospholipid syndrome criteria

Sydney revision of Sapporo criteria 2006

Clinical criteria

1. Vascular thrombosis
2. Pregnancy morbidity:
   (a) Death of normal fetus at or more than 10 weeks period of gestation (POG).
   (b) Premature birth at or less than 34 weeks due to preeclampsia.
   (c) Three or more consecutive miscarriage at less than 10 weeks.
   (d) Placental insufficiency at less than 34 weeks.

Laboratory Criteria

1. Anti cardiolipin antibody – IgG / IgM
2. Lupus anticoagulant
3. Anti beta 2 glycoprotein 1

(Medium to high titer, at least two times; tests done at least 12 weeks apart).

EHSRE recommendations[1]

1. For women who fulfill the laboratory criteria of APS and a history of three or more pregnancy loss, administration with low-dose aspirin (75 to 100 mg/day) starting before conception is suggested. Additionally prophylactive dose of heparin (unfractionated heparin or low molecular weight heparin) starting at date of a positive pregnancy test is also recommended.
2. The Guidance development group suggests offering anticoagulant treatment for women with two pregnancy losses and APS, only in the context of clinical research.

Unexplained RPL

In spite of through investigations, no etiological factors will be found in more than 50% of cases, Last three decades has witnessed the trial of multiples agents for the management of unexplained RPL. At the present time, only two interventions have shown to have some benefit.

1) Progestogen – vaginal micronized progesterone or oral dydrogesterone.
2) Aspirin alone or aspirin and heparin combination.

Recently, several important well designed studies have thrown some lights which will help us to modify our clinical management.

PROMISE Trial (First Trimester PROgesterone Therapy in Women with a History of Unexplained Recurrent MIScarriage). 2

This was a Multi-center, double-blind, randomized, placebo-controlled clinical trial conducted in 36 centers in United Kingdom and 9 centers in Netherlands. Among women with unexplained recurrent miscarriage, this trial wanted to find out whether treatment with progesterone would increase the rates of live births and newborn survival.

Women with recurrent miscarriages were randomly assigned to receive either twice daily vaginal suppositories containing either 400 mg of micronized progesterone or matched placebo. This was started from a time soon after a positive urinary pregnancy

test (and no later than 6 weeks of gestation) through 12 weeks of gestation. Live birth after 24 weeks of gestation was considered as the primary outcome. Eligibility was assessed in 1568 women. 836 of these women who conceived naturally within 1 year and gave consent were included in the trial. They were randomly assigned to receive either progesterone (404 women) or placebo (432 women). The follow-up rate for the primary outcome was satisfactory (98.8%). Analysis of the results showed, the rate of live births was 65.8% in the progesterone group and 63.3% in the placebo group. There were no significant differences in the rate of adverse events between the groups. The study group concluded that progesterone therapy in the first trimester of pregnancy did not result in a significantly higher rate of live births among women with a history of unexplained recurrent miscarriages. So practically, the PROMISE trial failed to show any need for change of practice at current time. However there are several criticisms on this study. Firstly, women with unexplained recurrent miscarriages were randomized to receive vaginal MNP 200mg BID on positive pregnancy test. No Transvaginal ultrasonography was done prior to inclusion to confirm viability. Progesterone was continued only till 12 weeks.

Another study from Delhi has shown interesting results. The study entitled "Oral dydrogesterone treatment during early pregnancy to prevent recurrent pregnancy loss and its role in modulation of cytokine production: a double-blind, randomized, parallel, placebo-controlled trial". The inclusion criteria were: Age 18-35yrs; three or more miscarriages; ultrasonographically confirmed live pregnancy. Dydrogesterone 10mg twice daily till 20 weeks gestation was given in the study group.

This study included 180 patients in each arm. The study results revealed that miscarriage rate 6.9% vs 16.8% (p=0.004). Occurrence of another miscarriage after 3 consecutive abortions was significantly higher (29 of 173; 16.76%) in women with RPL compared with healthy pregnant controls (6 of 174; 3.45%). Risk of occurrence of miscarriage after 3 abortions was 2.4 times higher in the placebo group vs. the treatment group.

This study supports the use of dydrogesterone in women with recurrent miscarriages to improve pregnancy outcome (reduction in miscarriages; improved gestational age and baby weight at delivery).[3]

ESHRE Guidelines for Recurrent Pregnancy Loss (2019)[1]

Recommendation : There is some evidence that oral dydrogesterone initiated when fetal heart action can be confirmed may be effective.

The current Cochrane review on Progestogen for Preventing Miscarriage included twelve trials which included 1,856 women. It was revealed that dosage and duration and routes of progestogen treatment varied across the trials. A possible reduction in the number of miscarriages for women given progestogen supplementation compared to placebo/controls was suggested in the metaanalysis.[4]

PRISM trial (A Randomized Trial of Progesterone in Women with Bleeding in Early Pregnancy) is a RCT, 4153 women under 39 years with early pregnancy bleeding was included. The study was conducted in 48 hospitals in UK. They have excluded non-viable pregnancy, patient with massive bleeding. 2079 received MNP 400mg vaginally twice daily till 16 weeks and 2074 received placebo. The result showed no improvement in birth over 34 weeks (75% vs 72%, RR 1.03, 95% CI 1.00-1.07, p=0.08). In subgroup analysis of women with previous 1/2 miscarriages, 5% increase in live birth with progesterones - 75% vs 70%, (N= 914 vs 886, RR 1.09, 95% CI 1.03-1.15, P=0.003). Interestingly, In women with previous 3 or more miscarriages, increased live birth with progesterone - 72% vs 57% (N= 137 vs 148, RR 1.28, 95% CI 1.08-1.51, P=0.004).[5]

British Journal of Obstetrics and Gynaecology published an article in January 2020 titled" The cost-effectiveness of progesterone in preventing miscarriages in women with early pregnancy bleeding: an economic evaluation based on the PRISM trial". They have concluded that progesterone is associated with a small positive impact and a small additional cost. Both subgroup analyses were more favourable, especially for women who had one or more previous miscarriages. Given available evidence, progesterone is likely to be a cost-effective intervention, particularly for women with previous miscarriage(s).[6]

Key points

- Pregnancy – immunological paradox.
- Immunology of RPL – interesting area of research.
- APS – detection, treatment beneficial.
- Other immunological investigations and treatment – experimental.
- There is no role of progesterone to prevent miscarriage in normal pregnancy.
- Moderate quality evidence of benefit - progesterone use in threatened miscarriage.
- Moderate quality evidence of benefit - progesterone use in unexplained recurrent miscarriage.
- The data with oral dydrogesterone – stronger.

We have made a significant progress in the field of recurrent pregnancy loss but still there is a long way to go.

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Case Report : Obstetrics

Prenatal Ultrasonography and Postnatal Correlation of Arthrogryposis Multiplex Congenita : A Rare Case Report

Tanmay Basak,[1] Swadha Priya Basu,[2] Yeruva Yeshwanth Reddy,[3] Nupur Singh[4]

Abstract

Arthrogryposis Multiplex Congenita is a rare congenital fetal skeletal dysplasia characterized by non-progressive multiple joint contractures affecting one or more areas of body.[1] It is mainly due to fetal akinesia.We are presenting a 22 year old Primigravida lady who came for routine ultrasound examination at 19 weeks of gestation.On ultrasound examination we found multiple joint contractures & gross hypokinesia of fetus and we had a high suspicion of Arthrogryposis Multiplex Congenita. Medical termination of pregnancy done and post-delivery gross specimen and post-delivery radiograph of abortus correlated with ante-natal sonographic findings. So, a diagnosis of Arthrogryposis Multiplex Congenita was made.

Introduction

Arthrogryposis Multiplex Congenita (AMC) is a rare congenital syndrome manifested clinically by widespread non progressive contracture and deformities of multiple joints leading to the limitation of the foetal joint mobility.[2,3] It affects 1 in 3000 individuals with equal gender predisposition.[4] It occurs mainly due to fetal akinesia which may be because of multiple factors like neurogenic or myopathic process, a connective disorder or intrauterine compression.[4,5] The etiologic factor that causes AMC, can generally be observed after autopsy.[6] In AMC patients, beside contracture abnormalities seen especially in distal joints; micrognathia, low-located ears, short neck, smooth-wide nose root and various muscular- skeletal system changes can be observed.[6,7] The deformation, causes fetal morbidity, mortality and economic burden in postnatal period. Proper antenatal Ultrasonography can correctly identify characteristics of AMC in utero6. We report characteristic sonographic features and post natal and pathological corelation of a fetus with suspected AMC.

Case Report

A 22 year old Primigravida lady came to our institution for routine ultrasound scanning at 19 weeks of gestation. There was no significant past medical or surgical history. There was no history of any drug intake. Routine ultrasound was done with curvilinear probe (1-6MHz) and 3D/4D volumev probe (1-6MHz). in E-CUBE 8 USG machine. On ultrasound examination we found single live intrauterine fetus in changing lie with estimated menstrual/ gestational age 19 weeks. The placenta was in fundoanterior position and was

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normal. Fetal heart rate was 146 beats per minute and was regular. Detailed sonographic evaluation of fetal anatomy revealed: overriding of cranial sutures with facial dysmorphia and micrognathia, short neck, narrow thoracic cage, fetal scoliosis and severe fetal hypokinesia. Further evaluation of fetal extrimities demonstrated severe flexion of hips and knees as well as elbows and wrists. The flexion deformities of all extrimities were maintained throughout the realtime examination and no movement of the fetal extrimities was documented. Examinaion of more distal extrimities demonstrated equinovarus clubfeet and clubhands. Amniotic fluid volume was normal and no maternal uterine abnormality were identified.

On patient counselling, parent agreed for termination of pregnancy. Medical Induction was done and a still born female foetus was delivered vaginally with birthweight 470gms. Post-delivery digital radiograph of the foetus was taken.

Based on prenatal USG findings, we had a high suspicion of Arthrogryposis Multiplex Congenita. Post-delivery gross specimen and post-delivery radiograph of abortus correlated with ante-natal sonographic findings. So, a diagnosis of Arthrogryposis Multiplex Congenita was made.On further work-up, no abnormality found on fetal karyotyping.

Discussion

AMC literally means curving of joints (arthro – joint, gryposis - hooking).

Arthrogryposis Multiplex Congenita (AMC) is a descriptive term characterising the clinical manifestations of joint contracture as flexion of the hips, knees, elbows, adduction of scapulohumeral joint, equinovarus clubfeets, pronated clubhands.[6,7] Exact cause is not known but its complex etiology include fetal akinesia which can be due to fetal or maternal causes such as muscular dystrophia, myasthenia gravis of mother, neurologic (brain, spinal cord and peripheric nerve abnormalities), connective tissue diseases (distrophic displasia, marfan syndrome), the cases causing intrauterine space limitation(twin pregnancy, myomas, uterus abnormalities) can cause AMC by preventing fetal movements.[4,5] In 30% of cases a genetic cause can identified.[8] During early embyrogenesis, joint development is almost always normal. Motion is essential for the normal development of joints and their contiguous structures; lack of fetal movement causes development of the extra connective tissue to develop around the joint. These results in Contractures secondary to fetal akinesia.

For diagnosis family history is essential especially consanguinity. Prenatal history should include exposure to teratogens, maternal illness and documentation of fetal movements.

Prenatal Ultrasound performed at first and second trimester of pregnany can be used to diagnose AMC.

The ultrasound diagnosis of AMC must be suspected when hypokinesia/akinesia, the limitation of foetal joint mobility, the abnormal position or conformation of the limbs are obvious at foetal examination.

Clinically and in terms of ultrasound, 3 subtypes of arthrogryposis multiplex congenita are described.[10–12]

- AMC involving only the limbs (distal arthrogryposis),
- AMC involving the limbs and other regions, and
- AMC involving the limbs and the CNS (Neurological arthrogryposis).

The ultrasound diagnosis of the cases with AMC has been established by identifying the following suggestive and/or characteristic signs[9] (Figures 1-6).

- talipes equinovarus,
- bilateral knee hyperextension,
- fixity of extremities,
- flexion of upper limbs (muscular-joint contracture of the elbow),
- hand clenching (flexion of fingers – overlapping fingers, lack of closing and opening movements in fingers and hands, muscular-joint contracture of radiocarpal joints);
- hypokinesia/foetal akinesia,
- facial dysmorphia
- microcephaly
- narrow thorax
- cystic hygroma
- scoliosis

Considering the prenatal ultrasound and post delivery gross specimen and xray of the abortus , probably this is a case of neurological arthrogryposis.

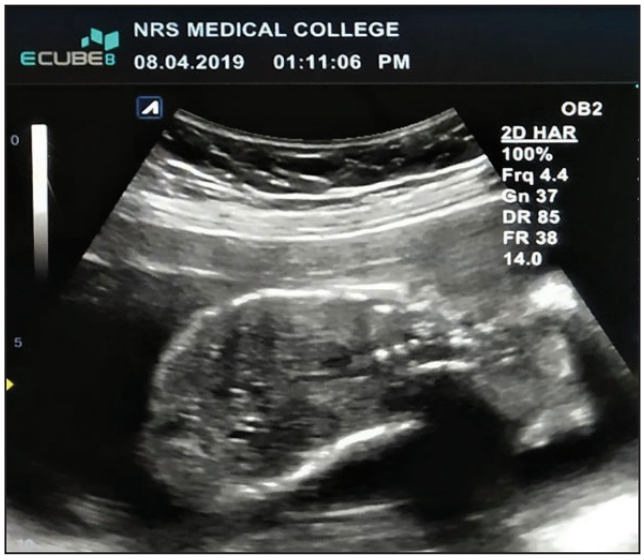


Figure 1: Sagital section of foetus showing narrow thorax

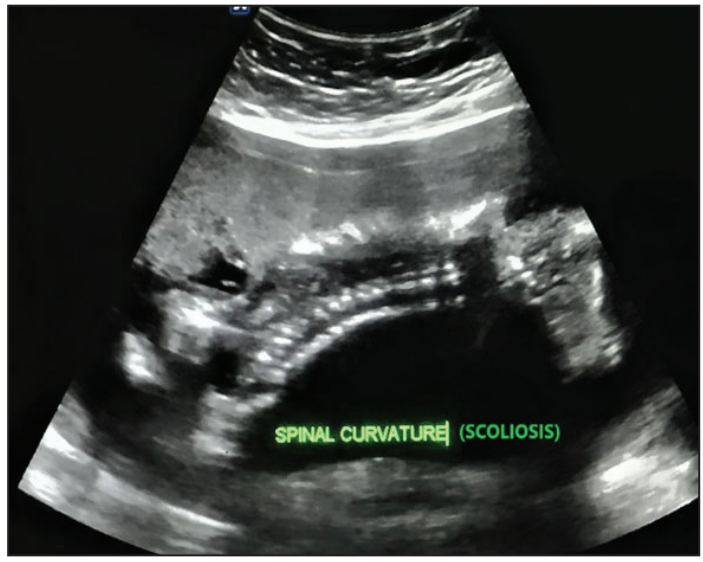
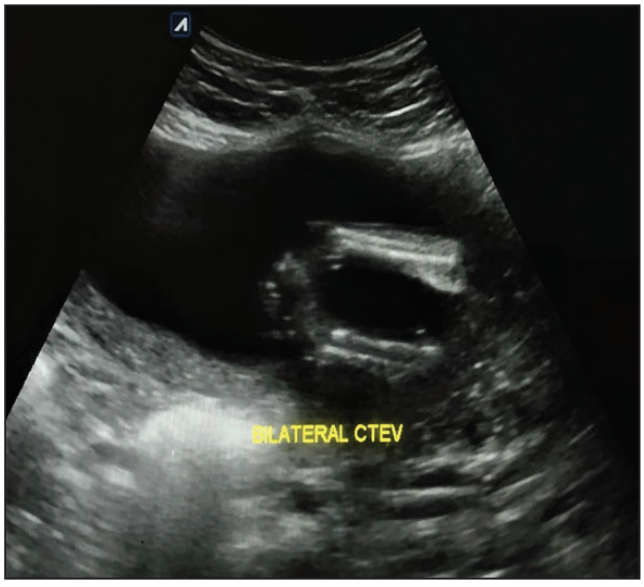


Figure 2: Axial skeleton of foetal spine showing scoliosis



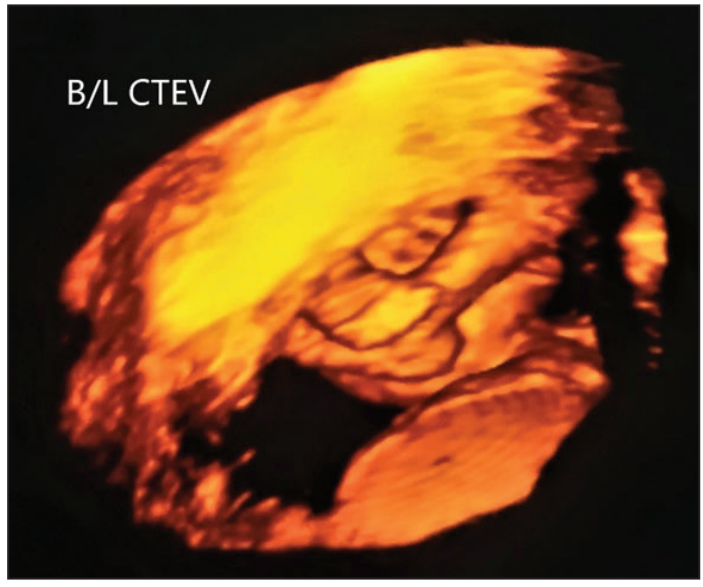
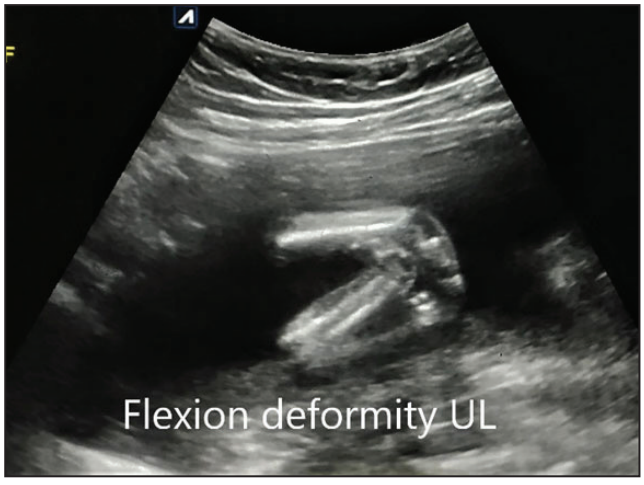


Figure 3 & 4 : 2D (left) and 3D (Right) USG showing fetal bilateral clubfeet



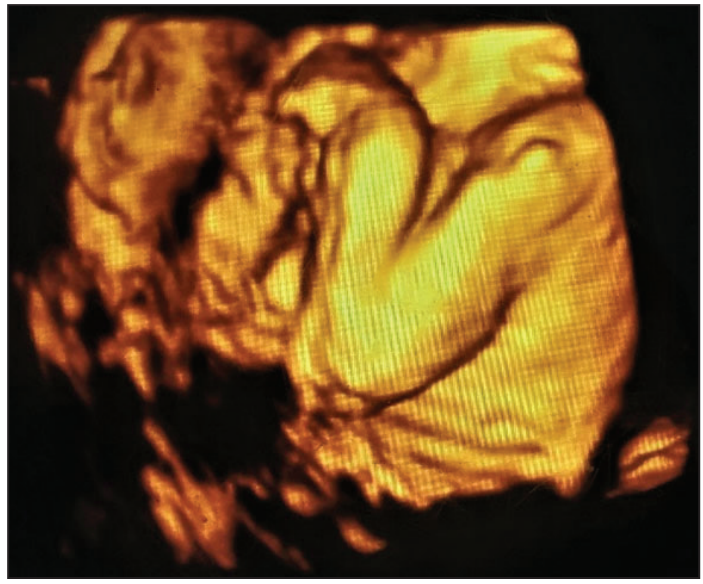


Figure 5 & 6: 2D (left) and 3D (Right) USG showing upper limb flexion deformity

Conclusion

The antenatal ultrasound diagnosis of arthrogryposis is often possible when the examination is done by an expert.It is the diagnostic technique of choice. The ultrasound finding of fetal akinesia is very suspicious. Earlier diagnoses influences the influence for termination of pregnancy.Identifying the etiology of congenital contractures remains uncertain until today and is an important area of research for prenatal diagnosis and pediatric care. Recent research in molecular genetics and immunohistochemistry seems to be useful in clarifying certain etiologies.

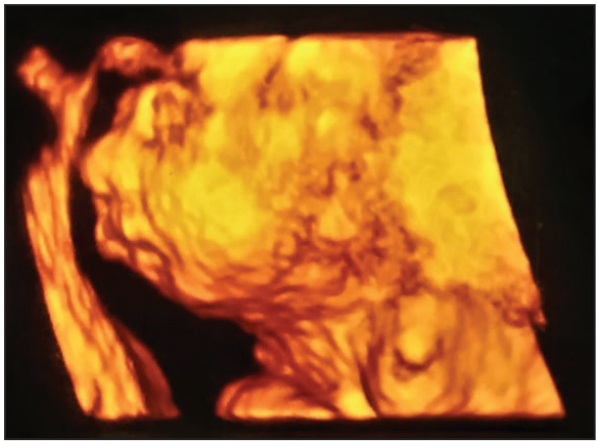


Figure 7: 3D USG showing fetal dysmorphia and micrognathia

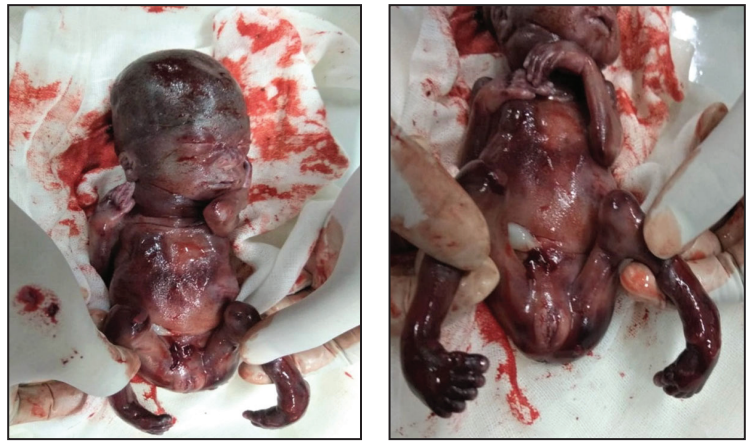


Figure 8 & 9 : Post delivery gros specimen of Stillborn fetus showing flexion deformity of both UL and LL, bilateral clubfeet and narrow thorax.

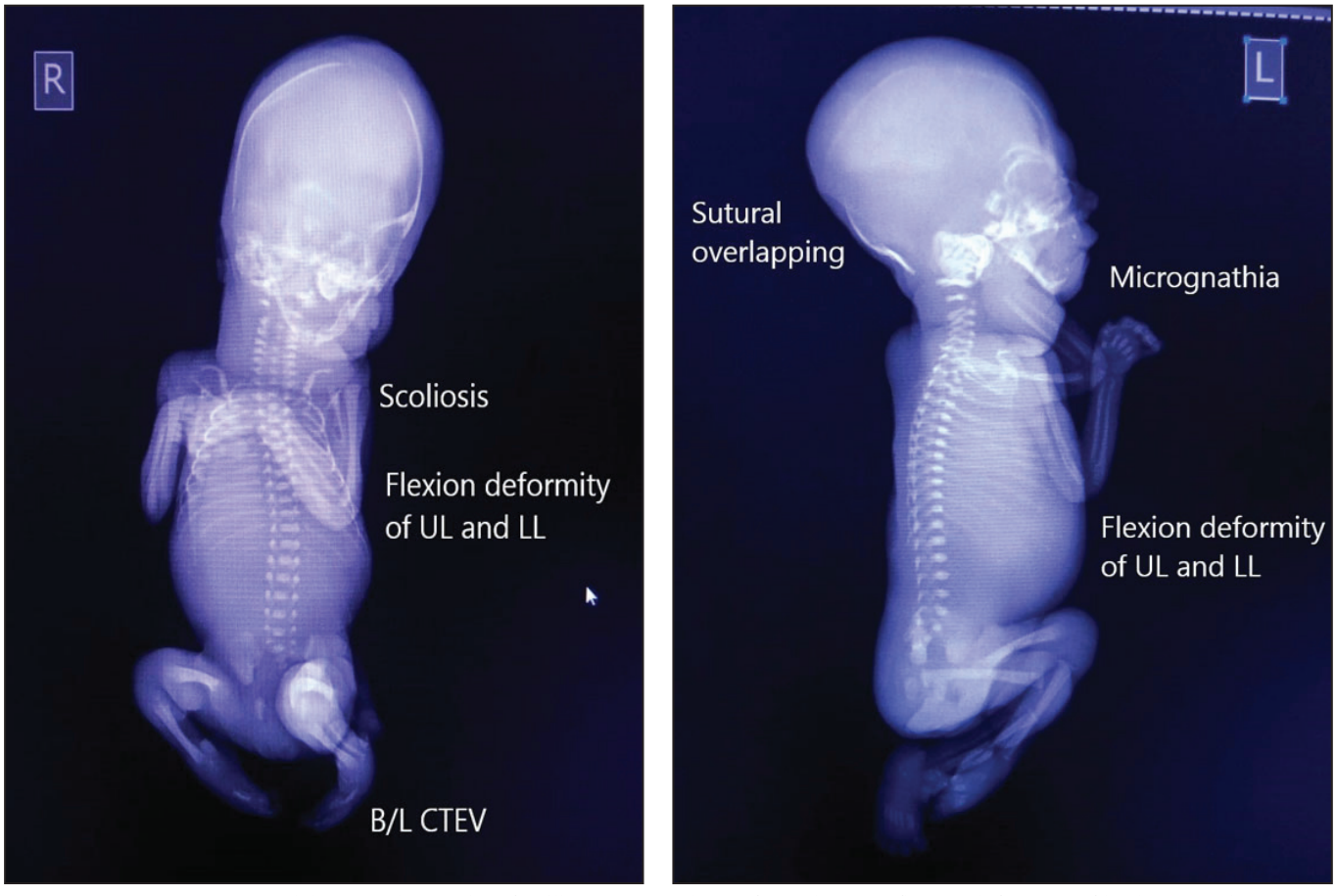


Figure 11 & 12 : Post delivery radiographs of stillborn (AP and Lat) fetus showing flexion deformity of both UL and LL, micrognathia, skull deformity, bilateral clubfeet and scoliosis.

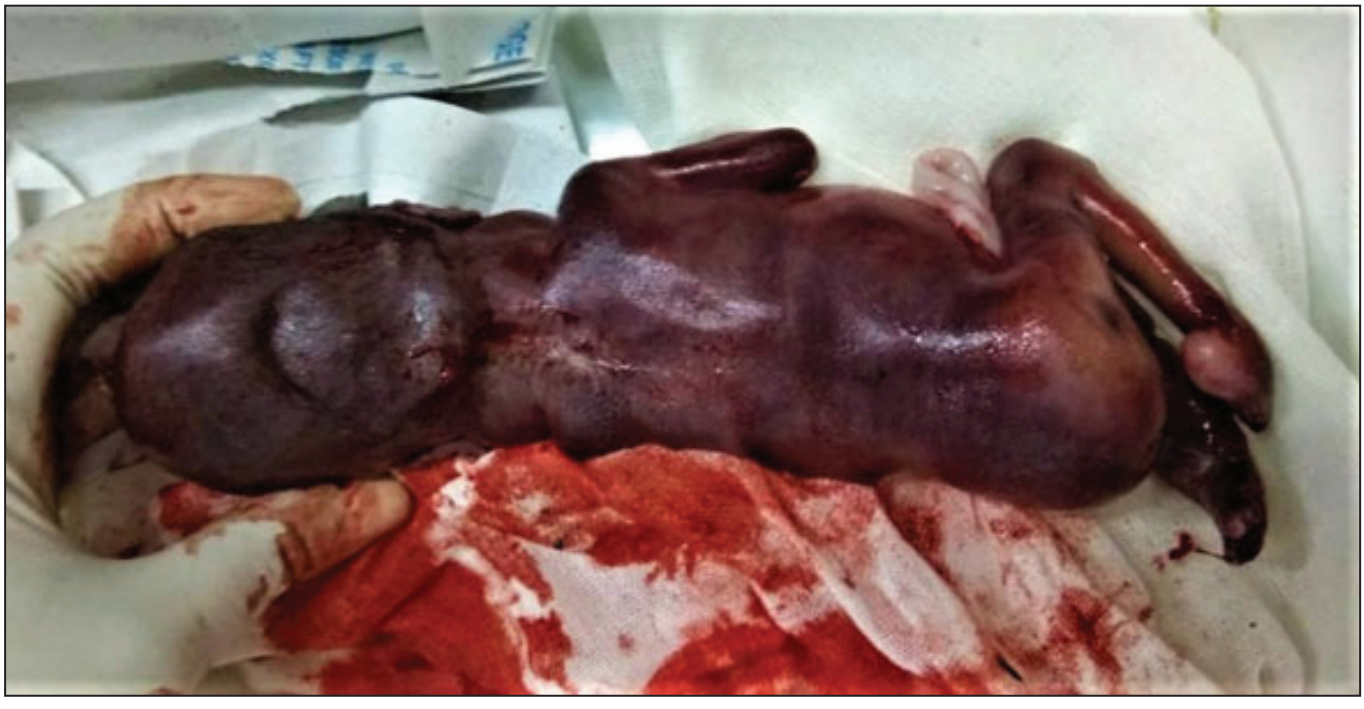


Figure 10 : Post delivery gros specimen of Stillborn fetus showing skull deformity & scoliosis.

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Original Article - Gynecology

Killer of Mothers in Early Pregnancy – Ectopic Pregnancy - Case Series in Rural Medical College

Sima Biswas

Abstract

Aim: To evaluate the importance of early diagnosis & intervention of ectopic pregnancy.

Methods: Case series of 4 patients who presented to our institution with various presentation -asymptomatic to haemodynamicaly unstable over last 6 months, they were clinically suspected & early surgical intervention was taken .Review of literature was done .Clinical presentation & different aspects of ectopic pregnancy is discussed.

Results: We discuss a wide spectrum of ectopic pregnancy with various clinical presentations, none of them presented with classical signs & symptoms. One of the case presented with only vomiting with ultrasonography finding of 11 weeks unruptured pregnancy in isthmus of right fallopian tube. This is very rare finding that such advanced unruptured ectopic pregnancy without any prior symptoms. In one case we found ruptured ectopic with expelled out fetus in abdominal cavity, following injudicious self intake of MTP kit, fetus was of crown rump length of approximately 10 weeks – this is also rare case. Two cases presented with features mimicking perforation of gut & peptic ulcer disease respectively that were atypical presentation. Early surgical intervention was done & treated accordingly depending upon the site of involvement.

Conclusion: Patients of ectopic pregnancy may present with varied presentation. Early conformation of pregnancy and early registration is very important in spite of absence of any risk factors or symptoms. Since it has varied presentation, high degree of clinical suspicion is required for early diagnosis & management, especially for unruptured ectopic pregnancy. Overall patient's education regarding sign, symptoms of ectopic pregnancy & potential of safe abortion method by trained person is required for reduction of maternal morbidity & mortality.

Introduction: Ectopic pregnancy is a potential life threatening condition if early diagnosis is missed.[1] The presentation may vary widely from being asymptomatic to haemodynamically compromised.[2] Incidence of ectopic pregnancy is 2%,[3,4] Incidence increased over past decade due to increased risk & early diagnosis. Combined approach of TVS & serum hcg estimation is gold standard for conformation & management. Ectopic pregnancy occur when implantation of fertilized ovum occur outside the uterine cavity. Most common site is ampulla of fallopian tube, others are isthmus, infundibulum,

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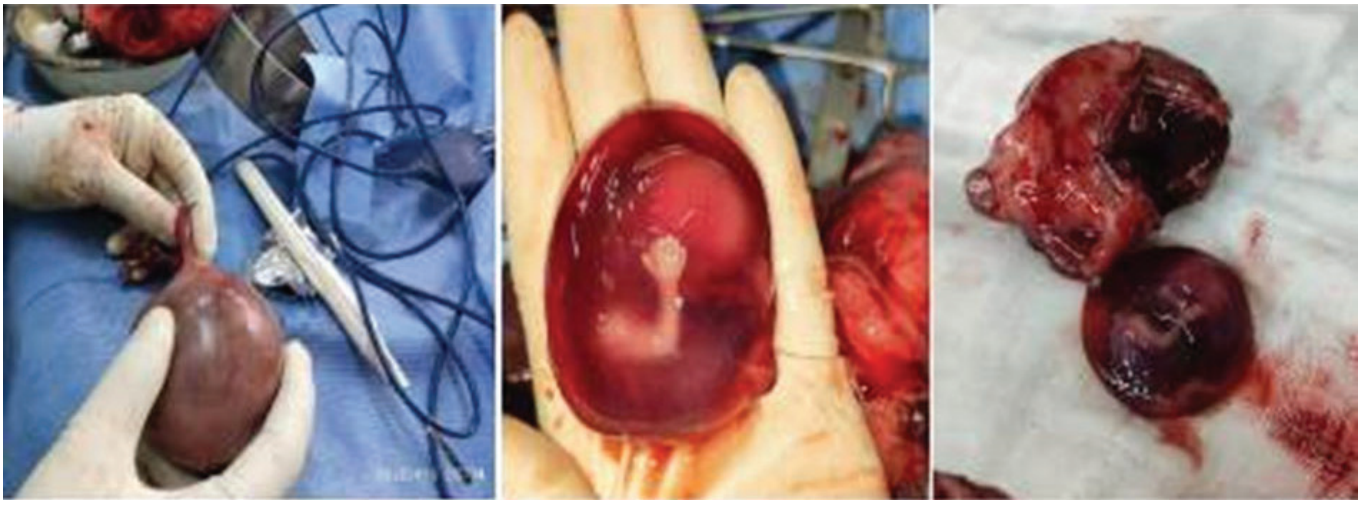


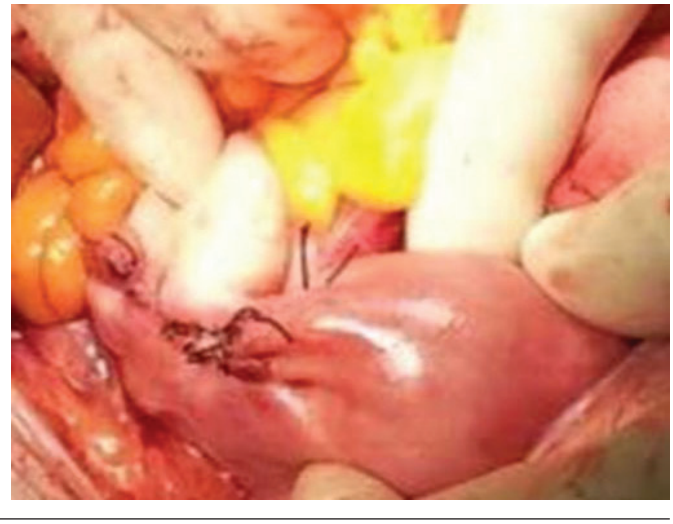
ovary, abdomen, cervix, caesarean section scar.[5,6] There are various risk factors like previous history of tubal surgery, ectopic pregnancy, IUCD insertion, tubectomy, pelvic inflammatory disease. It has different mode of presentation – asymptomatic to unconsciousness. Since various atypical presentations, clinical knowledge needs to be applied for early diagnosis and urgent intervention. Diagnosis done by clinical features, ultrasound, hcg doubling time (66 % raise over 48 hrs.). Ectopic pregnancy can be managed by different methods like medical, surgical, or expectant management depending upon the age, reproductive history & condition of contralateral fallopian tube. Here we discuss a wide spectrum ectopic cases which highlights atypical presentation, atypical finding (unruptured 11 wks. gestational fetus with intact placenta) & use of unsafe method of abortion.

Case no 1: Unruptured large ectopic pregnancy in isthmus of fallopian tube without any significant symptoms.

19 yrs. old nulliparous lady presented in emergency with complain of vomiting for 3 times within 1 hour. She had history of amenorrhea for 3 months, her urine pregnancy test was clearly positive in emergency. On admission her pulse, BP was normal, she was haemodynamically stable. Her abdominal examination revealed only slightly bulky uterus. On vaginal examination a mass was felt through the right fornices which was separated from uterus. There was no cervical motion tenderness. On searching a usg report, done 1 wk before was found from patient party which revealed : single gestational sac with collapsed fetus in right adnexa, gestational age 11 wks., no cardiac activity or vascularity noted in fetus, placenta was fundal anterior. Pt was prepared for exploratory laparotomy. On laparotomy unruptured soft mass was found in isthmus of right fallopian tube. Intra-abdominally there was no evidence of rupture. Right sided partial salpingectomy was done. Cut section of mass reveled well–defined placenta with intact gestational sac of crown ramp length 42.5 mm which corresponds approximately 11 to 12 wks.

Case 2: Ectopic pregnancy presented as uterine perforation following D & E.

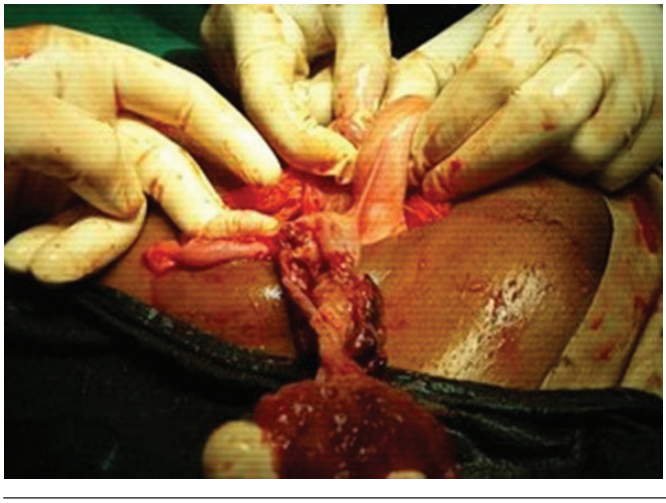
27 yrs 3rd gravida mother admitted in the department with complain of severe diffuse abdominal pain. She had history of one & half month amenorrhea & dilatation, evacuation just 24 hrs before her admission. There was no evidence of USG conformation of pregnancy. Her urine pregnancy test was faintly positive. On examination she had sever pallor (urgent Hb report was 6.5 gm.%), BP was 90/60 mm hg, pulse 122 bpm. Abdominal examination reveled distended abdomen with severe tenderness, muscle guarding and

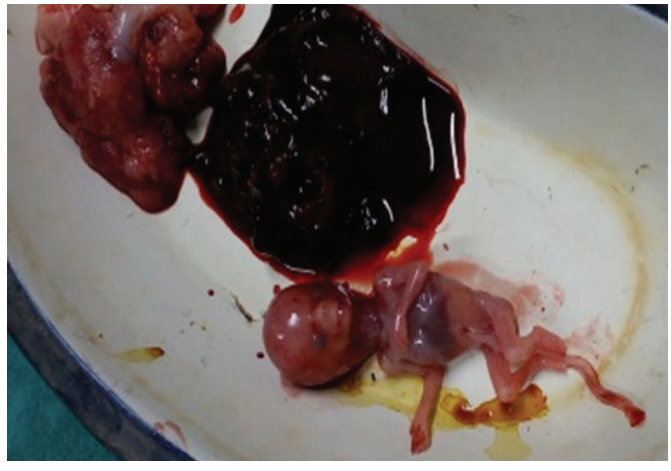


rigidity. On diagnostic paracentesis hemoperitonium found. There was mild vaginal bleeding, sever cervical motion tenderness and fullness of left fornices on vaginal examination. On exploratory laparotomy hemoperitonium (approximately 2 litters) with left sided ruptured cornual ectopic pregnancy was found. Repair of cornual area combined with bilateral tubal ligation was performed with proper hemostasis. Patient was haemodynamicaly unstable even after operation and was shifted to CCU; she was transfused 3 units blood and ultimately discharged in stable condition. Ectopic pregnancy was confirmed by histopathological examination.

Case 3: Ruptured ectopic pregnancy following self intake of MTP kit.

25 yrs 4th gravida patient presented with complain of abdominal pain & mild irregular bleeding per vagina. Date of LMP was not known to patient but history of about 3 month's amenorrhea. On enquiry she gave history of self intake of abortificient two times in a month and last one was 5 days before of admission. There was no USG documentation of pregnancy. Her urine pregnancy test was faintly positive on admission. She was hemodynamicaly unstable – had pallor (urgent Hb report 5 gm.%), pulse 128 bpm, BP 90 /50 mm hg. Tenderness and muscle guarding was present on abdominal examination. Diagnostic paracentesis revealed hemoperitonium. On per vaginal examination fullness of left fornices and cervical motion tenderness was found. Exploratory laparotomy done which showed hemoperitonium (approximately 2.5 lit.) with ruptured ectopic pregnancy with attached placenta in right fallopian tube and expelled out fetus of approx. 10 wks. in abdominal cavity. Right sided partial salpingectomy with contralateral

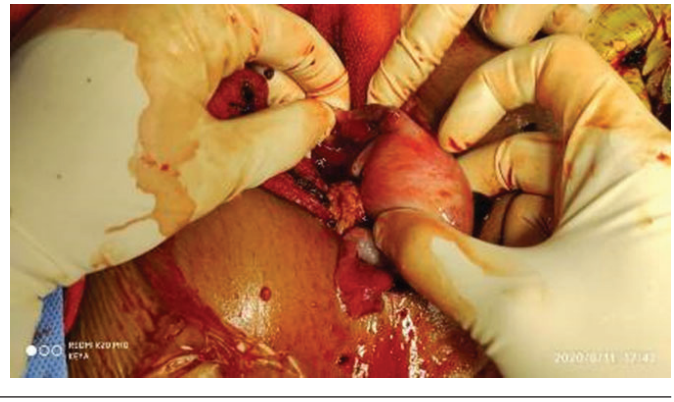




tubectomy was done. Patient was shifted to CCU, 5 units' blood transfusion done. She was discharged in stable condition. Conformation of ectopic pregnancy was done by histopathological examination.

Case 4: Ruptured ectopic pregnancy presented with upper abdominal pain mimicking peptic ulcer disease.

20 years old nulliparous patient presented in emergency with diffuse upper abdominal pain and acidity for 3 days. Pain was gradually increasing in nature. She had history of delayed menstruation of 16 days. There was no tachycardia, no pallor, BP was normal. On abdominal examination there was diffuse tenderness without any muscle guarding or rigidity. Per vaginal examination revealed no diffinit mass or tenderness in fornices, uterus was just bulky. Ultrasonography was done which showed right sided adnexal mass with empty uterine cavity. So patient was prepared for exploratory laparotomy which revealed hemoperitonium (approximately 1 lit.) and ruptured ectopic pregnancy in isthmus of left fallopian tube. Left sided partial salpingectomy done. 2 units blood transfusion was done and discharged in stable condition. Confirmation of ectopic pregnancy was done with histopathological examination.



Discussion

Ectopic pregnancy affects approx. 2% of gestation.[3] Fallopian tube is the commonest site of involvement and others includes ovaries, abdomen, caesarean section scar, and cervix. Ectopic pregnancy may be initially missed in diagnosis and remains a significant contributor to pregnancy related death and decreased fertility.[7] In general ectopic pregnancy causes largest morbidity and mortality in earlier pregnancy.[8] Approximately 5% of all maternal deaths are directly related to ectopic pregnancy and half of those cases not being evaluated for diagnosis.[1] Classical presenting symptoms include lower quadrant abdominal pain, vaginal bleeding and short period of amenorrhea,[7] but half of patient present atypically and may asymptomatic at earlier gestation.[3,7] In case of ruptured ectopic pregnancy severe abdominal pain and bulged vaginal fornices may found but unruptured ectopic pregnancy can be confused with normal intrauterine pregnancy.[9] So it has varied presentation and high degree of clinical suspicion is required for early diagnosis and management, especially for unruptured ectopic pregnancy. Early intervention carries better prognosis.[3] Ectopic pregnancy not only causes future pain and impaired fertility, it can also acutely causes intraperitoneal bleeding, anemia, potential necessitating of blood transfusion.[4,10] Transvaginal sonography along with serum hcg estimation is gold standard diagnostic approach. Serum hcg level > 2000 IU / l with no intrauterine pregnancy in TVS is treated as extra uterine pregnancy.

Typically tubal ectopic pregnancies in the isthmus ruptured within the first few weeks of gestation, ampullary pregnancy being slightly more expandable, cornue and abdomen may allow for further gestational development due to ability to distend.[3] One of our presented case described as unruptured ectopic pregnancy in isthmus of about 11 weeks. with no significant signs, symptoms of ectopic. Our 2 cases had diagnostic dilemma – one presented with features mimicking uterine perforation, one with features of peptic ulcer disease. Other case indicates injudicious use of MTP kit herself followed by ruptured ectopic pregnancy with expelled out fetus.

Caitlin Gauvin, Melissa Amberger et all reported cornual ectopic pregnancy with exposed fetus of 17wks [USG findings].[11] They also reported ruptured ampullary ectopic of 11wks 1 day gestation.[11] On 2015 D Goswami, N Agrawl et all reported a non-ruptured twin tubal ectopic pregnancy with fetal crown rump length of 2 cm.[12] Pinkee Saxena, Poonam Laul reported a case of ruptured twin tubal ectopic in left ampulla of size 6* 6 cm.[13]

All of this reported cases were ruptured ectopic pregnancy with advance gestation like our case No 3. None of these are like our case of unruptured ectopic of 11wks gestation with intact placenta without any prior symptoms. A Funamizu, A Fukui et al. reported a case of bilateral tubal ectopic pregnancy with unruptured gestational sac of 4 cm[14] like our case No 1.

Agarwal Shubhra, Kaur Satwant et al. reported a case of ruptured ampullary ectopic pregnancy due to injudicious use of MTP kit like our ruptured ectopic in ampulla with expelled out fetus following self intake of MTP kits.[15]

Ectopic pregnancy can be managed medically and surgically. Surgery may be laparotomy or laparoscopy depending on expertise, facility of laparoscopy and patient's hemodynamic conditions. Our two cases were hemodynamically unstable so exploratory laparotomy was performed. Another two cases, though was stable but due to lack of laparoscopic facility we opted for laparotomy.

Conclusion

This is a case series of ectopic pregnancy with varied presentation and management in modern obstetrics with aim of improving fertility outcomes. These case series highlights the importance of early confirmation of pregnancy and early registration inspite of absence of any risk factors or symptoms. It also revealed the importance of patient's education regarding signs and symptoms of ectopic pregnancy and also perception of safe abortion method by trained person. This series also emphasizes the overall importance of early and consistent prenatal care for quick detection of ectopic pregnancy and reduction of maternal morbidity as well as mortality.

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Case Report - Gynecology

When Common Presents as Uncommon

Kavita Bansal,[1] Juhi Sisodia[2]

Abstract

Cutaneous tuberculosis is a rare form of extra-pulmonary tuberculosis. It comprises of nearly 2% of all cases of extra-pulmonary tuberculosis. Main causative agent is Mycobacterium tuberculosis. Its clinical presentation is variable. Differential diagnosis of cutaneous tuberculosis should be considered in any case of atypical presentation of skin lesion.

Key Words – cutaneous tuberculosis, ulcer, mycobacterium, granulomatous infiltrates.

Introduction

One of the oldest disease known to mankind is Tuberculosis. TB is primarily a disease of lungs, but systemic dissemination of bacilli from primary foci is well known. One such site is skin, causing cutaneous tuberculosis. It can manifest as an inflammatory disorder of skin with no other systemic symptoms. A high index of suspicion can help in early diagnosis and treatment.

Case Report

Here is an interesting case of cutaneous TB, which was incidentally diagnosed after a surgery. A 52 year old woman from low socio-economic status underwent total abdominal hysterectomy at our hospital, for post-menopausal bleeding. Preoperative investigations were normal. There was no significant per-operative finding. Patient was discharged on day 3 of surgery. On day 7 she came back to hospital with c/o discharge from abdominal wound site. She was admitted for conservative management.

There was discoloration of skin around abdominal incision site with sero-purulent discharge, which did not respond to routine antibiotics and dressing. The skin at one point of incision site appeared like an eaten up ulcer with rolled-in margins. The floor was covered with unhealthy tissue.

Apart from above symptoms, there was no other symptoms like fever, cough or chills.

Due to unusual appearance of wound, tissue biopsy from wound edge was taken and sent for histopathological examination and mycobacterial culture. Histopathological examination showed multiple neutrophilic micro abscess in epidermis. Granulomatous infiltrates were seen in dermis. Zeihl-Nelson stain showed acid fast bacilli. Chest x-ray was clear and sputum culture was negative.

Patient was started on ATT. Dramatic response was seen within 10 days of ATT. Good resolution of cutaneous lesion with healthy granulation tissue started appearing. Resuturing was done after 1 month.

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Discussion

Tuberculosis is a major health problem in India. Cutaneous TB is usually caused by Mycobacterium tuberculosis and Mycobacterium bovis, sometimes by Calmette-Guerin bacilli. Mycobacterium tuberculosis is a rod shaped unencapsulated bacillus. It stains red by fuchsin and is not discoloured by acid because the cell wall is rich in complex lipids. Hence it is an acid fast bacillus. It is an aerobic bacillus. It is a facultative intracellular bacillus, that is, it can live both inside and outside phagocytic cell.

Affection by this bacilli depends on host's immunity. Infection can be by exogenous or endogenous route. When there is direct inoculation of bacilli into skin of susceptible host, it is called exogenous infection. When the primary focus is somewhere else and there is hematogenous or lymphatic dissemination to skin, it is called endogenous infection. Skin as primary focus is rare. Primary focus is usually lungs. Cutaneous TB comprises of nearly 2% of all extra pulmonary TB cases.

Malnutrition and low socio-economic status are predisposing factors for cutaneous TB.

Clinical presentations of cutaneous TB are diverse. It can be in the form of inflammatory papules, verrucous plaques, chronic ulcers, tuberculous chancre, tuberculids or scrofuloderma.

Lab diagnosis - 1) Tuberculin skin test has low sensitivity and specificity. 2) Immunological test-interferon gamma release assay. 3) Histopathology of skin biopsy shows granulomatous infiltrates. 4) Staining and culture - most common staining technique is Ziehl-Nelson. Microscopic examination of acid fast bacillus is done. Culture of bacillus is gold standard method for its identification. 5) PCR assays, genotyping, RFLP are recent advances in diagnosis of cutaneous TB.

Conclusion

Differential diagnosis of cutaneous TB should be considered in any case with non-healing skin lesion and atypical presentation of ulcer. Hence a high index of suspicion helps in prompt diagnosis and treatment.

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