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Hyperhomocysteinemia – A Successful Pregnancy Outcome: A Case Report

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I. Introduction

Spontaneous pregnancy loss , especially when faced with recurrent losses devastates the couple both physically and mentally. Recurrent pregnancy loss is defined as 3 consecutive pregnancy loss prior to 20 weeks[1]. Most common etiologies for spontaneous miscarriages are endocrine abnormalities, autoimmune disorders, uterine anomalies and genetic factors[2]. But even after evaluating these causes , almost 50 % of the cases still remain unexplained[3].

AIMS

To reduce the pregnancy related morbidities due to hyperhomocysteinemia by early identification by prompt evaluation of high risk cases and supplementation of adequate amount of vitamin B6,B9 and B12 in those cases.

OBJECTIVES

To highlight the supplementation of Vit B6,B9 and B12, aspirin prophylaxis and calcium channel blockers in the management of hyperhomocysteinemia with hypertension

II. Background

Homocysteine , a naturally occurring sulphur containing aminoacid, results from demethylation of essential amino acid methionine. Raised levels of homocysteine called as hyperhomocysteinemia , can result from a variety of genetic and environmental factors[4].

III. Case

Presenting the case of 28 year old lady Para-1 Living- 0 came with history of pre eclampsia and abruptio placentae in previous pregnancy with Rh negative pregnancy with intrauterine fetal death.During that pregnancy she had severe oligoamnios from the 20th week of gestation with severe hypertension of 190/120mms of HG .Amniocentesis was done and chromosomal abnormalities of the fetus was excluded.She continued the pregnancy upto 26 th week of gestation and was planned for induction of labour when there was reversal of umbilical arterial blood flow and reversal of a wave in Ductus venosus. Intrauterine fetal death occurred within 4 hours and she delivered a dead fetus weighing 550gram.

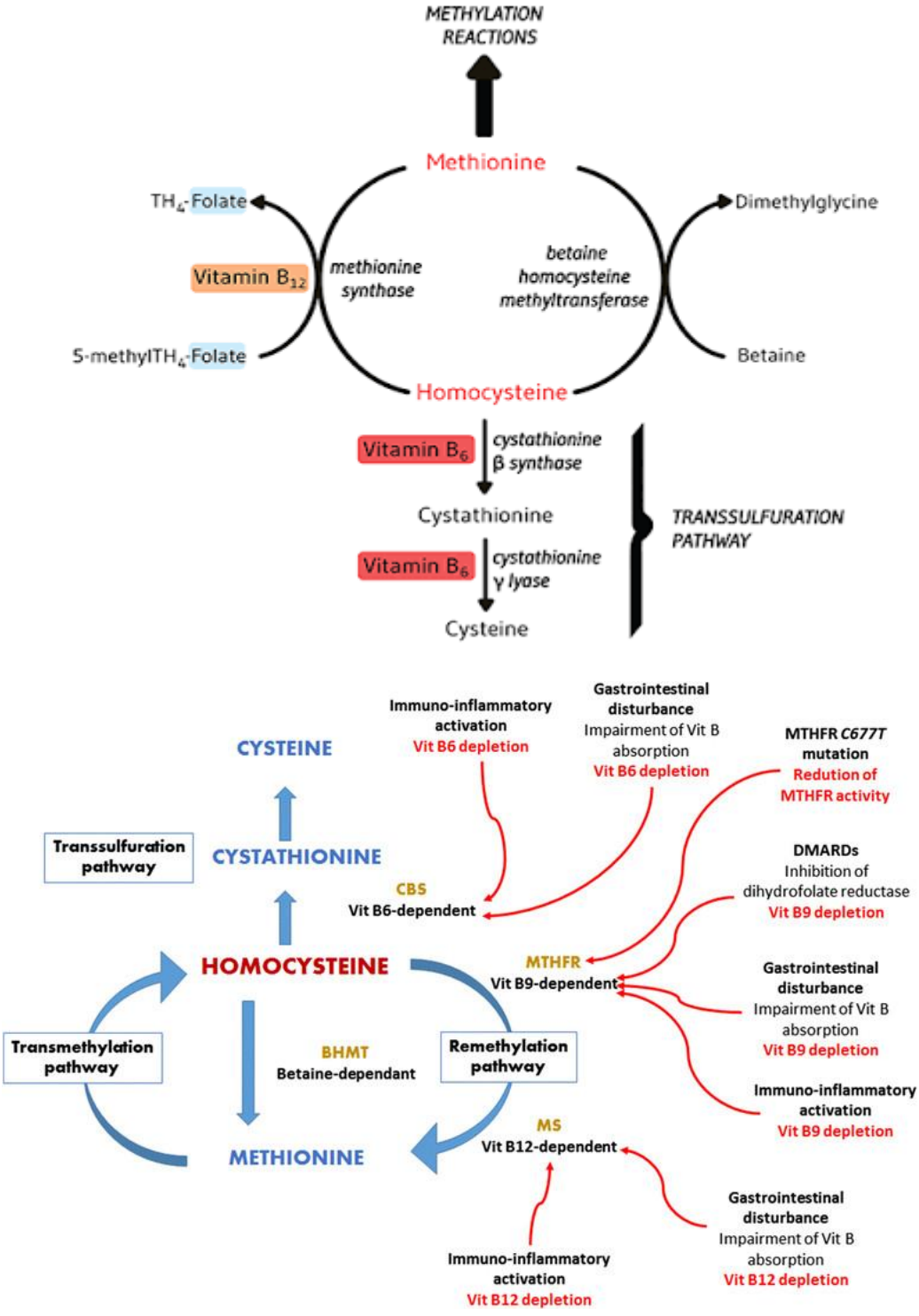
Subsequently she presented with chronic hypertension , which was uncontrolled with beta blockers. Hypercholesterolemia was managed with statins . She was evaluated for the cause of hypertension and intrauterine fetal death ,and,was found to have hyperhomocysteinemia of 18.68 micromoles /l. Thrombophilia and extended thrombophilia and APLA all proved to be within normal criteria. Pre conceptional folic acid was given. She was advised to have planned pregnancy and chronic hypertension was managed with clinidipine . Vit B6, B9 and B12 oral formula was given . Patient was considered as high risk and frequent antenatal examinations were done with regular CTG after 28 weeks. She had abnormal uterine artery doppler studies at 13 weeks of gestation. She was advised to take Aspirin 150mg from 13 weeks of gestation till 36 weeks in view of spontaneous pregnancy loss,early onset preeclampsia in previous pregnancy and abnormal uterine artery Doppler Planned LSCS was done at 37 weeks due to CDMR, delivered a healthy male baby of weight 2.62kg.

Anti D IgG of 300mcg was given postpartum.She received postpartum thromboprophylaxis . She was advised to continue homocysteine oral formula and clinidipine postpartum.

IV. Conclusion

This case warrants the evaluation of hyperhomocysteinemia levels in young patient with early onset pre eclampsia, chronic hypertension, spontaneous pregnancy loss, intrauterine fetal death and fetal growth restriction.Supplementation of vitamin B6,B9 and B12 during pregnancy may improve the maternal and fetal outcome

HOMOCYSTEINE METABOLISM



CAUSES OF HYPERHOMOCYSTEINEMIA[5]

1. Genetic defects

- CBS , MS deficiency
- MTHFR deficiency- C667T mutation

2. Nutritional deficiency

- Vitamin B6,B9 and B12

3. Other cofactors

- CKD, hypothyroidism, psoariasis , SLE
- Drugs- methotrexate, phenytoin, theophylline, niacin, carbamazepine, immunosuppressants
- Alcohol, coffee , smoking

CLINICAL OUTCOMES IN PREGNANCY

- **Approximately 2-3 fold increased risk for**

Pregnancy induced hypertension
Abruptio placentae
Intrauterine growth restriction[6]

- **Cobalamine deficiency causes**

HELLP syndrome
Abruptio placentae
IUGR
IUFD[7]

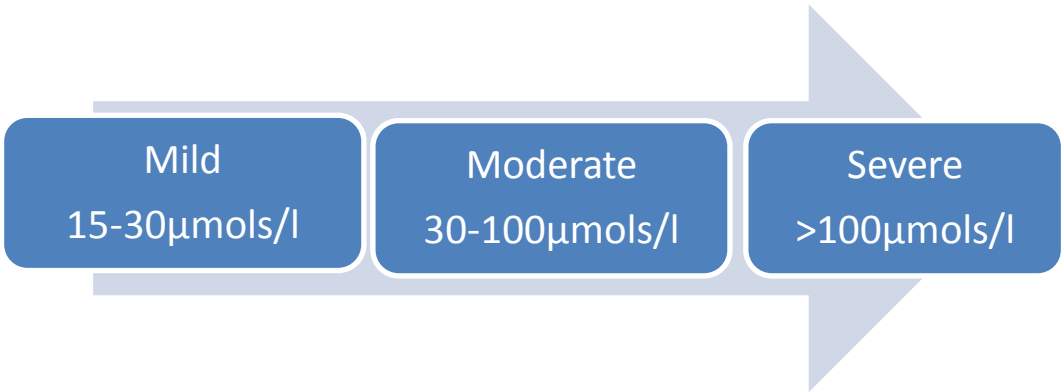
- **Pyridoxal -5-phosphate deficiency causes**

Increased risk for pregnancy induced hypertension- 4 fold [6]

DIAGNOSIS

Patient should be overnight fasting and take morning sample of blood in EDTA bulb. The sample should be centrifuged immediately or should keep on wet ice till centrifugation.

ELEVATED HOMOCYSTEINE LEVELS[8]



Homocysteine levels in pregnancy decreases due to

- Hemodilution.
- Raised GFR
- Hormonal changes of pregnancy
- Increased fetal uptake[9]

In pregnancy- fasting threshold >12µmoles/l (hyperhomocysteinemia)[9]

V. Discussion

Hyperhomocysteinemia has emerged as a strong risk factor for many diseases but its role in RPL has been confirmed recently[10]. It not only hampers chances of pregnancy but also interferes with successful pregnancy outcome. Hyperhomocysteinemia in pregnant women has been associated with various placental pathologies like RPL, Abruption, pre eclampsia, fetal growth restriction and still birth[11].The mechanism of blood vessel alteration is still not known perfectly. Homocysteine causes endothelial dysfunction by various mechanisms like NO inhibition and increasing contractile prostanoids[12]. The probable mechanism by which it

affects pregnancy and implantation is by inhibition of trophoblast function and cell death[13]. In a prospective study conducted in a tertiary care centre in Bangalore by Indrani Mukhopadhyay et al , 100 cases were assessed and 32%of RPL patients had hyperhomocysteinemia[14].

In another study conducted by Nisha Bhatia et al ,out of 50 RPL cases 19 were found to have hyperhomocysteinemia, of that 14 patients developed hypertensive disorders in pregnancy during their antenatal period[10].

Hence we can infer that plasma homocysteine measured in early pregnancy may be a positive predictor of pregnancy complications and timely intervention can prevent development of these complications. Serum homocysteine measurement should be included in routine work up for RPL. Treatment of hyperhomocysteinemia with vitamin B6,B9 and B12 decreases homocysteine levels significantly

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