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Case Number 4
Pre-eclampsia Toxaemia

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Case summary:

Demographic details:

Mrs. KG, female, Żejtun
Referred from: GP

Mrs. KG, a 33 year old primagravida rhesus positive woman was referred to the Emergency Department by her family doctor at 27 weeks gestation. At 25 weeks of gestation, she had been diagnosed with hypertension and was started on labetalol therapy. At 27 weeks of gestation she was admitted in view of persistently raised blood pressure which was not being controlled with Labetalol, generalised (facial, hands and lower limbs) oedema and frequent frontal headaches. The patient also complained of photophobia. Following examination it was found that the patient was suffering from pre-eclampsia toxaemia. Delivery was expedited in view of the developing complications.

Presenting complaint:

Facial, hands and bilateral lower limb oedema: 2 weeks
Frontal headaches: 3 days
Photophobia: 3 days
Raised Blood Pressure

History of presenting complaint:

The patient presented with facial, hand and bilateral lower limb oedema which started 2 weeks before. She reported that facial oedema was worse in the morning but then subsided during the day. Frontal headaches had occurred in the past three days and were worse when lying down. Her blood pressure started to rise during the first trimester, at 15 weeks gestation; this indicated that the patient was suffering from essential hypertension.

Present obstetric history:

Mrs. KG is a primagravida. Her last menstrual period was on the 28th of April 2012, computing her expected date of delivery to the 5th of February 2013. She is known to suffer from polycystic ovarian syndrome.

Mrs. KG did not have any problems during the first trimester, except that at 15 weeks gestation, her blood pressure was found to be 140/80mmHg and she was referred for closer monitoring by the family doctor. The patient was on Folic acid during the first trimester and did not report any vaginal bleeding during the first three months. All routine investigations (complete blood count; Syphilis, Hepatitis B and C, HIV screen, blood glucose) were reported within the normal ranges. Her blood group was A Rhesus positive.

She had no problems during the second trimester except for repeatedly borderline high blood pressure which was being monitored by her family doctor. In the late second trimester at 25 weeks gestation, the

patient presented to the antenatal clinic with significant lower limb oedema. Urine testing revealed a trace of albumin in the urine. Her blood pressure was 160/100mmHg. She was admitted to an obstetric ward for 4 hourly blood pressure charting. Pre-eclampsia toxaemia bloods were taken: complete blood count, urea and electrolytes, serum creatinine, uric acid, liver function tests, coagulation profile, random blood glucose and 24-hour urinary collection to test for proteinuria. The results showed elevated uric acid and proteinuria was greater than 300g/24hrs. An abdominal ultrasound and Doppler umbilical blood flow velocimetry were also done. The abdominal ultrasound reported the fetus to be above the 90th centile indicating macrosomia and the need for closer monitoring.Umbilical artery flow had an aqeduate pulsatility index, resistence index and systolic/diastolic ratio. The fact that the child was above the 90th centile, in itself ensures adequate blood supply to the fetus; should the blood supply have been diminished, the fetus would have been on the lower end of the centile chart. She was discharged on 200mg Labetalol daily and her blood pressure was stable on discharge. She was asked to revisit her family doctor for further blood pressure monitoring.

Past gynaecological history:

Patient had her menarche at 14 years of age, her menses were irregular ranging from 40 to 60 days. She had regular smear tests; her last being in 2011 and reported to be normal. She was never on the oral contraceptive pill or on any other formulation of contraception. She had a history of infertility attributable to polycystic ovarian syndrome, for which she was started on clomiphene. This treatment was successful in her achieving a pregnancy.

Past medical and surgical history:

Past medical history:

Polycystic ovarian syndrome

Past surgical history:

Left axillary cystectomy

Drug history:

Drug	Dosage	Frequency	Type	Reason
Folic acid	5mg	Once daily	Vitamin B9	Prevents neural tube defects. Taken during the first trimester.
Pregnatal		Once daily	Multi-vitamins	Helps to cover any nutritional gaps in the mother's diet. Taken from the second trimester onwards.

Family history:

Her mother is known to suffer from essential hypertension. Two of her aunts are known to suffer from type 2 diabetes mellitus.

Social history:

She is married and lives with her husband. She works as a teacher. She does not smoke or drink alcohol and does not exercise regularly.

Systemic inquiry:

- General Health: looks oedematous
- Cardiovascular System: nil to note
- Respiratory System: shortness of breath on exertion
- Gastrointestinal System: nil to note
- Genitourinary System: nil to note
- Central Nervous System: frontal headaches, photophobia
- Musculoskeletal System: nil to note
- Endocrine System: nil to note
- Others: nil to note

Current therapy:

Labetalol 100mg BD – to lower the patient's blood pressure.

Discussion of results of general and specific examinations:

At 27 weeks of gestation: On inspection, the patient looked ill and severely oedematous; involving the face, both hands and both lower limbs up to the knees. The patient's blood pressure was found to be 152/83mmHg and her pulse was 110 beats/min regular.

Blood pressure and pulse monitoring were carried out 4 hourly in order to check if the patient was worsening or getting better. Her blood pressure readings were quite labile and were not adequately controlled with therapy.

On auscultation, the chest was clear. There was adequate air entry on both sides of the chest. No bibasal crackles were heard which would have been a sign of pulmonary oedema – a complication of pre-eclampsia toxaemia.

On abdominal examination, the abdomen was distended compatible with pregnancy. The foetus was palpable in a longitudinal lie and the presentation was cephalic. The fetal heart rate was audible and of normal rate. The abdomen was soft and non-tender. No pain was elicited in the right upper quadrant. Right upper quadrant pain is a sign of impending eclampsia due to capsular pain from the liver.

From the neurological examination, the patient was noted to have hyper-reflexia which was most marked in the knee jerk on both sides. There was also one tap of clonus. Together with the symptoms of photophobia and frontal headaches, symptomatology pointed to central nervous system involvement.

Differential diagnosis:

- Pre-eclampsia toxaemia
- Pregnancy-induced hypertension with a urinary tract infection
- Nephrotic Syndrome

Diagnostic procedures:

Laboratory exams:

Test: Complete blood count.
Justification for test: To look for anaemia (haemolysis) and thrombocytopenia (platelet count <100x10^9/L), both signs of haematological disturbances, part of pre-eclampsia[5].
Result: At diagnosis (25^{+2} weeks gestation): Hb – 12.5g/dL, Platelets – 332x10^9/L
Pre-operative (29^{+2} weeks gestation): Hb – 12.3g/dL, Platelets – 338x10^9/L
Post-operative: Hb – 11.2g/dL (low), Platelets – 380x10^9/L
Conclusion: Both the haemoglobin level and the platelet count were normal throughout her pregnancy hence demonstrating a lack of haematological disturbances due to pre-eclampsia.

Test: Uric acid
Justification for test: In women with pre-eclampsia, serum uric acid is elevated (mean: 6.2 +/- 1.4mg/dl)[8], however it has been shown to be a weak predictor of pre-eclampsia and severe hypertension[9]. It may be a predictor of renal tubular dysfunction, but is not a specific marker[10].
Result: At diagnosis (25^{+2} weeks gestation): 257umol/L
Pre-operative (29^{+2} weeks gestation): 348umol/L (high)
Post-operative: 446umol/L (high)
Conclusion: An elevation of the patient's uric acid level in the serum at 29^{+2} weeks gestation could be an indicator decreased renal perfusion or increased uric acid production by the poorly perfused tissue[12], hence a demonstration of multisystem involvement in pre-eclampsia. This also shows a progression to the worse in our patient, despite the treatment given, and hence could have contributed to the decision to carry out an elective cesarean section so early on in pregnancy. Since the pre-eclamptic state does not resolve immediately after the birth of the child (up to 6 weeks post-partum), the level of serum uric acid was persistently high even post-operatively.

Test: Urea and Electrolytes
Justification for test: To look for renal dysfunction; serum creatinine >90µmol/L[5].
Result: At diagnosis (25^{+2} weeks gestation): creatinine – 53umol/L, urea-3mmol/L; electrolytes within range
Pre-operative (29^{+2} weeks gestation): creatinine – 66umol/L, urea – 3.4mmol/L; electrolytes – within range
Post-operative: creatinine – 76umol/L, urea – 4.7mmol/L; electrolytes – within range
Conclusion: Despite the elevation of uric acid levels in the serum, serum creatinine, urea and electrolyte levels were continuously within the normal range. Being good predictors of renal function, such results indicate very little kidney damage if any, as indicated previously from the elevated uric acid levels.

Test: Liver function tests
Justification for test: To look for elevated liver enzymes, which would indicate liver malfunction as part of the multisystem effects seen in pre-eclampsia: ALT >32 IU/L, AST >30 IU/L 5.
Result: At diagnosis (25^{+2} weeks gestation): ALT – 12 IU/L, ALP – 85 IU/L
Pre-operative (29^{+2} weeks gestation): ALT – 15 IU/L, ALP – 109 IU/L (high)
Post-operative: ALT – 22 IU/L, ALP – 77 IU/L
Conclusion: Normal aminotransferase levels show lack of liver involvement in the patient's condition. It is also an indicator for HELLP syndrome.

Test: APTT/INR

Justification for test: These tests are only done if liver function tests and platelet count are abnormal. They may be abnormal in consumptive coagulopathies and disseminated intravascular coagulation, both known complications of severe pre-eclampsia[10].

Result: At diagnosis (25^{+2} weeks gestation): APTT – 29.9s (high), INR – 0.87 (low)
Pre-operative (29^{+2} weeks gestation): APTT – 26.7s; INR – 0.86 (low)
Post-operative: APTT – 28.3s, INR – 0.87 (low)

Conclusion: APTT and INR values were borderline, and hence the results are not significant of an underlying coagulopathy.

Test: Thyroid function tests

Justification for test: Abnormal TSH levels could be associated with pre-eclampsia. A U.S. study found a rise in TSH levels in pre-eclamptic females, when compared to normotensive patients. The findings suggest that there is the possibility of developing hypothyroidism during pre-eclampsia, but more so 20 years after birth of the child[11]. Thyroid function tests in pregnancy need to be carefully interpreted since can be due to serum and functional physiological changes.

Result: Post-operative: TSH – 1.95mIU/L, free T4 – 11.6pmol/L

Conclusion: Thyroid function was found to be normal.

Test: Urinalysis, microscopy and culture

Justification for test: Urinalysis may be used as a screen for proteinuria[10]. Microscopy is used to detect the presence of cells and casts in the urine which could be a beneficial diagnostic tool, while culture is indicated for screening for a possible urinary tract infection.

Result: Pre-operative (29^{+2} weeks gestation): proteins – 150mg/dL (very high); erythrocytes – 0-5/mm^3, leukocytes – 0-5/mm^3, casts-absent, MC and S – Acinetobacter baumannii cultivated.
Post-operative: proteins – 25mg/dL (high); erythrocytes – negative, leukocytes – negative, casts - absent.

Conclusion: The increased glomerular permeability characteristic of pre-eclampsia was the cause of the significant proteinuria the patient experienced[12]. An increasing proteinuria and worsening blood pressure recordings indicate a declining condition and hence point towards the choice to deliver the child.

Instrumental exams:

Test: Cardiotocography

Justification for test: It is a screening test to monitor foetal well-being. It shows acute cardiac changes in the foetus reflecting placental flow. It indicates acute hypoxia and foetuses in danger of developing hypoxia[15].

Result: At diagnosis (25^{+2} weeks gestation): Baseline rate: 150bpm, Variability: >5 beats per minute, accelerations: present and concordant with uterine contractions, decelerations: nil.
Pre-operative (29^{+2} weeks gestation): Baseline rate: 140bpm, variability: >5 beats per minute, accelerations; present and concordant with uterine contractions, decelerations: nil.

Conclusion: The cardiotocograms done were normal. According to the NICE guidelines, the four categories of variables: baseline rate, variability, accelerations and decelerations fall within the reassuring ranges[13].

Test: Doppler ultrasound

Justification for test: It is used to evaluate the feto-placental unit in order to assess placental insufficiency – a known complication of pre-eclampsia. If the placenta is functioning well, the blood flows easily. If there is placental insufficiency, there would be resistance to blood flow. In extreme cases where the resistance is too high, there may be periods

of reverse blood flow from the fetus to the umbilical blood vessels. Umbilical cord flow together with symptomatology can indicate the severity of the disease.

Result: At diagnosis (25^{+2} weeks gestation): pulsatility index, resistance index and systolic/diastolic ratio were within the normal ranges.
Pre-operative (29^{+2} weeks gestation): pulsatility index, resistance index and systolic/diastolic ratio were within the normal ranges.

Conclusion: The ultrasounds indicated that the foetus was receiving an adequate blood supply.

Test: 24-hour urinary collection

Justification for test: It is a quantitative method to measure proteinuria[1]. This test was done to confirm the diagnosis of pre-eclampsia[3].

Result: At diagnosis (25^{+2} weeks gestation): 211.2mg/24hr (high)
Pre-operative (29^{+2} weeks gestation): 1257mg/24hr (very high)

Conclusion: Both results indicate that there was significant proteinuria in concordance with the diagnosis.

Test: Oral glucose tolerance test

Justification for test: On Doppler ultrasound the foetus was found to be greater than the 90th centile indicating macrosomia. This may be caused by diabetes mellitus[4]. The patient also had a history of polycystic ovarian syndrome which may be associated with the development of diabetes [2].

Result: At 28 weeks gestation: Fasting blood glucose: 4.1mmol/L; at 1hr: 8.88mmol/L; at 2hr: 7.88mmol/L.

Conclusion: The results obtained were within the normal ranges except the 2 hour glucose which is slightly above the higher limit of normal (7.8mmol/L) which indicates impaired glucose tolerance[14].

Therapy:

In view of her uncontrolled hypertension and symptoms, the patient was started on the following drug regime:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Labetalol	100mg	BD	Alpha/Beta blocker	Lowers high blood pressure
Nifedipine	20mg	BD	Calcium channel blocker	Lowers high blood pressure
Hydralazine	10mg	QDS	Vascular smooth muscle relaxant	Lowers high blood pressure

At 29^{+2} weeks of gestation: Despite the change introduced in her drug therapy the patient's condition remained uncontrolled. Her condition continued to worsen. Her blood pressure was found to be 180/110mmHg. On inspection, she had facial, hand and lower limb oedema. She had bibasal crackles on chest auscultation – a sign of pulmonary oedema. On urinalysis there was 3 + protein and macroscopic haematuria. The patient was catheterised and a urinometer was attached in order to measure urine output accurately. A decision was taken to perform a lower segment Caesarian section due to worsening blood pressure and the developing complications. Pre-operatively, pre-eclampsia toxaemia bloods were taken. Blood was cross-matched and grouped and saved. She was administered two doses of dexamethasone 12mg via intramuscular route at 12hrs apart to try and stimulate foetal pulmonary type 1 pneumocyte conversion to type 2 pneumocyte for surfactant release. She was also started on low molecular weight heparin since pre-eclampsia is associated with a high risk of thrombotic events. The patient was started on continuous cardiotocographic monitoring, in order to monitor foetal well-being. She was continued on Labetalol and Nifedipine whilst Hydralazine (PO) was added to her drug regime.

Surgery:

Emergency lower segment Caesarian section was done at 29^{+2} weeks gestation, under epidural anaesthesia. It was remarked that both ovaries were polycystic and the Fallopian tubes were normal.

Diagnosis:

The patient was diagnosed with pre-eclampsia toxaemia; defined as an elevation of blood pressure above 140/90, with proteinuria or oedema of the hands, feet and face[4]. It predominantly affects primagravida females[5] and is more common at increasing gestational age[4]. The patient was preganant with her first child, and had various other risk factors for developing this condition; including: polycystic ovarian syndrome and a family history of essential hypertension[6]. After previously being diagnosed with hypertension and started on treatment, at 27 weeks of gestation, she presented to her family doctor with generalised oedema, and frontal headaches. She later developed photophobia and also complained of shortness of breath. On examination however, no basal crackles were heard, which would have hinted the presence of pulmonary oedema. She did have hyperreflexia on examination – which is a sign of cerebral irritation, a blood pressure 152/83 mmHg, and proteinuria on urine dipstick and in the 24hr urine collection test. Pre-eclampsia is diagnosed when hypertension with blood pressure ≥140/90 and proteinuria; defined as ≥300mg/day in a single specimen or ≥ 1+ on urine dipstick, are detected for the first time after 20 weeks' gestation. Being a multi-organ disease, the diagnosis of pre-eclampsia becomes more certain if symptoms and signs associated with organ system malfunction are diagnosed in addition to the hypertension and proteinuria[7]. Such symptoms and signs include:

Symptoms:
- Persistent severe headache
- Persistent epigastric pain
- Disturbances in vision
- Vomiting
- Severe swelling of the face, hands and feet, of sudden onset

Signs:
- Hyperreflexia (Neurological disturbance)
- Serum Creatinine concentration ≥110mmol/L (Renal insufficiency)
- Thrombocytopenia; platelet count $\leq 100 \times 10^9$/L (Haematological disturbance)
- Disseminated intravascular coagulation (Haematological disturbance)
- Elevated liver enzymes (Liver disease)

Many of the above mentioned signs and symptoms were present in this patient, hence pointing towards the diagnosis of pre-eclampsia toxaemia. Thus the patient was admitted for closer monitoring of her condition and the investigations listed previously were conducted. From the results of the investigations, the diagnosis of pre-eclampsia was confirmed.

Final treatment and follow ups:

Severe pre-eclamptic hypertension is a risk factor for placental abruption and fetal growth restriction, while risking hepatic rupture and development of eclampsia in the mother[12]. Thus, after all measures were taken to control her condition and delay birth as much as possible, an elective C-section was performed in view of severe Pre-eclampsia toxemia and the maternal complications.

She had been on labetalol and nifedipine treatment, despite which, her hypertension continued to worsen. Pre-operatively her blood pressure varied between 145/85 – 170/90mmHg. She also developed bibasal

crackles; a sign of pulmonary oedema, and haematuria; a sign of renal tubular damage. Thus she was given corticosteroid therapy, in hope for improving fetal lung maturation, and started on 40mg clexane prophylactically. The epidural procedure was commenced and 4g of magnesium sulfate in 100mLs of normal saline was administered to the patient pre-operatively (to reduce the risk of convulsions in the presence of hyper-reflexia and increased cerebral excitability) and the C-section was performed, to prevent an eclamptic episode. Delivery by C-section was preferred since child was pre-term. A female infant weighing 1180 grams was born. She had an Apgar score of 6 and 8 at 1 and 5 minutes respectively. The infant was intubated and transferred to the neonatal paediatric intensive care unit.

The risk of development of eclampsia or continuation of the pre-eclamptic state does not resolve immediately after delivery of the child[7]. Thus the patient was kept on labetalol treatment post-partum, as indicated in the NICE guidelines[9]. The patient was also given oxygen via nasal prongs. In addition, she was put on an intravenous infusion of magnesium sulfate (2mL/hr) therapy, which was continued for 24 hrs, and was kept on a slow intravenous infusion of saline. The mother was also monitored for signs of toxaemia, including; hypotension, respiratory depression, oliguria and loss of reflexes. Her blood pressure was monitored every four hours, Pre-eclamptic Toxaemia (PET) blood tests were once again taken post-operatively, and fluid balance was continuously monitored. Patient was sent home after 8 days in view of blood pressure 130/80 mmHg, stable blood tests and improving clinical picture of her condition.

After discharge from hospital, patient was advised to have her blood pressure checked at least every 1-2 days for up to two weeks after discharge. Antihypertensive therapy should be adjusted by her doctor according to her blood pressure readings. The patient was offered a post-natal review 6 weeks after birth, to check her blood pressure readings, and whether or not she is still on antihypertensive therapy, which would then be an indiction for further investigations and management[9].

Fact Box 4:

Title: Pre-eclampsia toxaemia

This is a multi-system disorder which manifests as hypertension and proteinuria after 20 weeks of gestation. The disease originates from the placenta and is cured by delivery. There is blood vessel endothelial damage with a maternal inflammatory response which leads to vasospasm, increased capillary permeability and clotting dysfunction which account for hypertension, proteinuria, reduced placental blood flow and reduced cerebral perfusion resulting in eclampsia.

Risk factors:

- Nulliparity
- Previous history
- Family history
- Older maternal age
- Chronic hypertension
- Diabetes
- Twin pregnancies
- Autoimmune disease
- Renal disease
- Obesity

Symptoms: Usually asymptomatic.
At a late stage:

- Headaches
- Drowsiness
- Visual disturbances
- Nausea and vomiting
- Epigastric pain

Signs:

- Hypertension
- Gross and non-postural oedema
- Epigastric tenderness
- Proteinuria on urinalysis
- Hyperreflexia
- Clonus

Prevention:

All pregnant women, should have regular blood pressure and urinalysis checks. Low dose aspirin (75mg) starting from 16 weeks reduces the risk of pre-eclampsia and is recommended in women at risk.

References:

1. http://emedicine.medscape.com/article/1476919-overview#aw2aab6c14 – accessed on 29th December 2012.
2. http://www.diabetes.org/living-with-diabetes/women/polycystic-ovarian-syndrome.html - accessed on 29th December 2012.
3. Impey L, Child T. Obstetrics and Gynaecology. 2012:12:172-181.
4. http://hcp.obgyn.net/ultrasound/content/article/1760982/1898011 - accessed on 2nd January 2013

5. Williams D, Craft N. Easily Missed? Pre eclampsia. BMJ 2012; 345:e4437
6. NHS. Antenatal Care. NICE Clinical Guideline 62. 2010; 1.9.2; 35
7. Duley L, Meher S, Abalos E. Management of Pre eclampsia. BMJ 2006; 332(7539): 463-468.
8. Lim KH, Friedman SA, Ecker JL et al. The clinical utilityof serum uric acid measurements in hypertensive diseases of preganancy. Am Obstet Gynecol 1988; 178(5): 1067-71.
9. NICE Clinical Guideline: Hypertension in Pregnancy: the management of hypertensive disorders during pregnancy. Royal College of Obstetricians and Gynaecologists 2011; 112-113.
10. Manaj A, Rrugia A, Manoku N. The impact of pre eclampsia in pregnancy. J Prenat Med 2011; 5(1): 19-22
11. Hendrick B. Preeclampsia linked to reduced thyroid function. WebMD, LCC 2009
12. Longo SA, Dola CP, Pridjian G. Preeclampsia and Eclampsia revisited. South Med J 2003; 96(9)
13. NICE Clinical Guideline: The use of electronic fetal monitoring: the use and interpretiation of cardiotocography in intrapartum fetal surveillance. May 2011:8-9.
14. http://www.medicinenet.com/glucose_tolerance_test/page2.htm - accessed on 9th January 2013.
15. Grivel RM, Alfirevic Z, Gyte GML et al. Antenatal Cardiotocography for foetal assessment (Review). The Cochrane Collaboration 2010; 2-4.