



## Preeclampsia without hypertension occurring at 17 weeks of amenorrhea; a case report and review of literature

Sindou Sanogo<sup>ID</sup>, Serge Didier Konan, Kouamé Hubert Yao<sup>ID</sup>, Séry Patrick Diopoh, Jean Aka, Randolphe Niava

Department of Nephrology and Internal Medicine, University Hospital of Treichville, Abidjan, Côte d'Ivoire

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### ABSTRACT

In general, the term “preeclampsia” refers to the presence of hypertension associated with proteinuria occurring after 20 weeks of gestation in a previously non-proteinuric and normotensive woman. A 24-year-old woman, known to be non-hypertensive, carried two pregnancies and lost two babies. In 2011, as she was carrying the third (twin) pregnancy at 17 weeks of amenorrhea, she was admitted to the hospital for an 8-kilogram excess weight gain between two antenatal visits spaced 4 weeks apart. The clinical examination revealed 140 mmHg systolic blood pressure and 80 mm Hg diastolic blood pressure. The following days, the systolic blood pressure ranged between 110 and 120 mm Hg. Furthermore, the presence of bilateral and symmetrical pitting edema of the lower limbs was reported. The laboratory assessment upon admission showed the following results, proteinuria; 3.3 g/24 h, total albumin; 1.7 g/dL, total protein; 5.4 g/dL and total calcium was 75 g/L. The test results for HIV serology, HBs antigen and HCV antibodies as well as antinuclear and native anti-DNA antibodies were negative. The treatment consisted of iron, folic acid and calcium supplementation. Cesarean section was scheduled for the 38th week. The immediate aftermath was simple. Formula feeding was recommended for the newborns and ramipril 1.25 mg was initiated in the mother once daily. The evolution was marked by a progressive reduction in proteinuria around 500 mg/24 h six months after delivery, and below 200 mg/24 h one year later. Pre-eclampsia before 20 weeks of gestation is rare. Hypertension, which is its main clinical sign, may be exceptionally absent at this stage.

### Implication for health policy/practice/research/medical education:

We report a case of pre-eclampsia revealed by a pure nephrotic syndrome without associated hypertension, on twin pregnancy discovered at the 17th week of gestation. Correction of hypocalcemia followed by cesarean section resulted in a favorable maternal and fetal evolution.

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### Introduction

In general, the term “pre-eclampsia” refers to the presence of hypertension associated with proteinuria occurring after 20 weeks of gestation in a previously non-proteinuric and normotensive woman (1,2).

For many years, cases of preeclampsia have been observed before 20 weeks of gestation. These were associated with triploidy, trophoblastic disease, or antiphospholipid syndrome (3,4).

Recently, a case of preeclampsia without hypertension was reported at 33 weeks of gestation (5).

We are reporting here a case of gravidic nephropathy with nephrotic syndrome without hypertension, whose diagnosis of pre-eclampsia was made a posteriori.

### Case Presentation

A 24-year-old woman, known to be non-hypertensive, carried two pregnancies and lost two babies in the following conditions:

- The first one at day 2 postpartum, for prolonged fetal distress in 2009,
- The second one at day 15 after cesarean section,

\*Corresponding author: Kouamé Hubert Yao; E-mail: yaohubert@yahoo.fr

for hemorrhage in placenta previa in 2010. During this pregnancy, she experienced excess weight gain (5 kg) at the 16th week of amenorrhea which went unnoticed despite regular antenatal follow-up.

- In 2011, while carrying the third pregnancy at 17 weeks of amenorrhea, she was admitted to the gynecology ward for an 8-kg excess weight gain between 2 antenatal consultations spaced 4 weeks apart. It was indeed a dichorionic (two placentas) diamniotic (two amniotic sacs) twin pregnancy progressively confirmed by obstetric ultrasound.

The clinical examination revealed 140 mm Hg systolic blood pressure and 80 mm Hg diastolic blood pressure. Over the next days, the systolic blood pressure ranged between 110 and 120 mm Hg without antihypertensive treatment. Besides this, the presence of bilateral and symmetrical pitting edema of the lower limbs was reported. The gynecological examination revealed a fundal height at 22 cm, fetal heart sounds and active fetal movements perceived but distant due to abdominal distention. The remaining part of the clinical examination showed no particularities.

The laboratory assessment upon admission showed the following results, proteinuria; 3.3 g/24 h, total albumin; 1.7 g/dL, total protein; 5.4 g/dL and total calcium was 75 g/L. The tests results for HIV serology as well as antinuclear and native anti-DNA antibodies were negative. The tests results for HBs antigen and anti HCV antibodies were also negative.

Management included regular monitoring of blood pressure and weight gain. No antihypertensive drug was administered. Because of an average weight gain of 4 kg every 15 days, the patient was treated with furosemide at 40 mg once daily and then 80 mg once daily under monitoring of serum potassium that was normal at all controls. This helped to stabilize weight

gain between 1.5-2 kg every 15 days. We also provided iron, folic acid and calcium supplementation. She also received treatment with enoxaparin sodium 4000 IU once daily by subcutaneous injection for one month and then switched to lysine acetylsalicylate 100 mg once daily during meals (discontinued 5 days before cesarean section). The procedure was performed in the 38th week, a segmental transverse cesarean section which enabled the easy extraction of the male twins weighing 2.80 kg for the first one and 2.55 kg for the second one. These newborns were seen by the pediatric neonatologist and were declared healthy. The cesarean section's immediate aftermath was simple. We observed a reversal of transit, a normal diuresis, a progressive spontaneous regression of weight, normal hemodynamics, a good uterine retraction, and soft calves. Formula feeding was recommended for the newborns and ramipril 1.25 mg was initiated in the mother once daily. Furosemide was discontinued.

The evolution was characterized by a progressive reduction in proteinuria around 500 mg/24 h six months after delivery, and below 200 mg/24 h one year later (Table 1).

## Discussion

Pre-eclampsia affects slightly less than 5% of pregnancies in the West (6). In sub-Saharan Africa, the prevalence of pre-eclampsia is around 25% (ranging from 0.93% to 70%) (7). Its incidence tends to increase in developed countries, and is probably in relation to risk factors (8).

The risk factors for pre-eclampsia are varied, including its existence during an earlier pregnancy and pre-existing high blood pressure. There are other maternal risk factors; primiparity (first pregnancy; risk multiplied by three), maternal age greater than 40 years, obesity (multiplies the risk by 1.5 approximately), pre-existing diabetes (multiplies the risk by 3), the presence of antiphospholipid

**Table 1.** Laboratory assessment and management schedule

	Overweight			Cesarean section				Lab Test at M12		
	10/10/ 2011	15/11/ 2011	1/2/ 2012	16/3/ 2012	7/5/ 2012	16/6/ 2012	17/9/ 2012	18/3/ 2013	5/12/ 2013	9/3/ 2015
Creatininemia (mg/dL)		0.6	0.78			0.6		0.6		0.6
Plasma urea (g/L)		0.17	0.21			0.16			0.17	0.17
Albuminemia (g/L)		17	11.8		15.7			35		
Protidemia (g/L)		54	42		53			69		
Hemoglobin (g/dL)		10.5	9.6			12		12	12.2	12
MCV (fl)		86	85			82		89	75.3	
Platelets (10 <sup>3</sup> /mm <sup>3</sup> )		250	301			204		295	300	
Serum calcium (mg/L)		75	74		85	89			90	
Serum glucose (g/L)		0.90	0.69							
Serum uric acid		54	55							
Urine protein (g/24h)		3.3	11.3		8.5	3.75	0.57	0.17	0.16	0.18

MCV; mean corpuscular volume.

antibodies (increases the risk by about 9), the notion of thromboembolic disease, kidney disease, and high altitude (9,10). The risk is increased in case of twin pregnancy with a risk of multiplication by three and in case of primipaternity (first pregnancy of a given couple). This primipaternity evokes a possible reaction mechanism to sperm, supported by other arguments (11). The notion of high blood pressure in the family increases the risk of occurrence by 3. In our patient who was in her third gestation, only twinning was found to be a risk factor for pre-eclampsia.

Nephropathies occurring before 20 weeks of amenorrhea are usually associated with different forms of glomerulopathy such as IgA nephropathy, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis and Fabry disease, but not pre-eclampsia (12,13). The presence of a pregnancy in these conditions may be an aggravating factor for this nephropathy.

Various physiological changes occur during pregnancy with the development of placenta which may be responsible for the most dramatic changes. Indeed, one believes that the placenta secretes various vasoactive substances. Studies have suggested that placental dysfunction could cause hypertensive disorders and kidney disease (14).

If pre-eclampsia is a common situation after 20 weeks of gestation, some cases of earlier onset have been reported. In some cases, it has been associated with the partial mole and triploidy, where authors have reported that the increase in paternal genetic material associated with diandric triploid placenta may support the role of immunologic factors in the development of preeclampsia (15-18). Another case of pre-eclampsia complicated with HELLP (hemolysis, elevated liver enzyme levels, and low platelet levels), syndrome in association with antiphospholipid syndrome has been reported (19).

All these associated factors justify through investigations in case of early pre-eclampsia. No etiological factor is rarely found as is the case in the observation made by Toshiyuki et al (20). In their observation, an autoimmune etiology was suspected in the female patient, based on her past history of hyperthyroidism and the presence of thyroid peroxidase antibodies, but none of the other known autoimmune antibodies was found (20). In our case, since the etiological assessment of the nephrotic syndrome was incomplete, for economic reasons, we cannot state that the etiological factor was absent.

The clinical expression of pre-eclampsia is, above all, a rise in blood pressure that should be confirmed twice (21). In our case, a blood pressure surge was observed only once. Recently, Koizumi et al reported a case of pre-eclampsia without hypertension that was discovered at 33 weeks of gestation, in a context of pure nephrotic syndrome. The renal biopsy that was performed after delivery revealed lesions suggestive of glomerular

endotheliosis, despite the absence of hypertension. This made it possible to make the final diagnosis of pre-eclampsia (5). Pre-eclampsia thus expresses itself in the form of pure nephrotic syndrome (22), as observed in our study. In our female patient case, the renal biopsy could not be performed. However, the regression of proteinuria after delivery by caesarean section enabled us to make the final diagnosis of pre-eclampsia a posteriori.

The management of pre-eclampsia is done in a hospital environment with close maternal and fetal supervision. Only the birth of the child enables to stop the secretion of the placenta and the progression of pre-eclampsia towards its neurological, hepatic and renal complications. Before 34 weeks of amenorrhea, it is advisable to perform fetal lung maturation with corticosteroids. In case of serious complications, emergency fetal extraction may be indicated for maternal rescue. While waiting for a compatible term of childbirth between the child's life and that of the mother, she can receive antihypertensive medications under medical supervision in a hospital environment. In our case, no antihypertensive treatment was instituted. Intravenous magnesium sulfate helps to reduce the occurrence of eclampsia (23). In women at risk, administering small doses of aspirin to them may reduce the risk of pre-eclampsia. For this type of treatment to be effective, it must begin before 16 weeks of pregnancy. Hence the importance of identifying high-risk pregnancies at their beginning. Guidelines for the prevention of pre-eclampsia in various countries recommend the administration of low doses of aspirin for all high-risk pregnancies in the first trimester or at least before the 16th week (24). In addition, calcium is recommended for women on low-calcium diet or with calcium deficiency for the prevention of pre-eclampsia (25,26). While diuretics had been discontinued as anti-hypertensives in pregnancy due to decreased plasma volume and the risk of worsening chronic fetal distress (27), we used it in our patient to stabilize excessive weight. This did not cause fetal hypertrophy in the twins.

The outcomes of pre-eclampsia may be the occurrence of complications that may be life-threatening for the patient. In fact, death due to eclampsia occurs in 0.1% to 10% of cases according to the series (7). It is a major cause of maternal mortality in developing countries (28). When it occurs before 20 weeks of amenorrhea, the fetal prognosis is almost always poor. In our case, the absence of arterial hypertension and calcium supplementation could explain the good maternal and fetal prognosis.

## Conclusion

Pre-eclampsia rarely occurs before 20 weeks of gestation. Hypertension which is its major clinical sign may be exceptionally absent at this stage. Surveillance in pregnant women should take all clinical parameters, including excess weight gain, into consideration. Its presence must

justify an in-depth assessment to optimize treatment and care.

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### Authors' contribution

KHY has made a substantial contribution to conception and design, analysis and interpretation of data. SS has also been involved in drafting the manuscript and revising it critically for important intellectual content. KSD and DSP have collected data. JA and RN have revised the manuscript critically for important intellectual content.

### Conflict of interests

The authors declare no conflict of interest.

### Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. In addition, informed consent has been obtained from the patient for publication of this case report.

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