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Management of a Pregnant Woman With Fibromuscular Dysplasia

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Case Introduction

A 39-year-old woman from Morocco presented to the Cardiology Department with high blood pressure, with systolic blood pressure repeatedly measured at 170 mmHg in the office. She was 10-days pregnant. Her treatment included nebivolol 5 mg and barnidipine 10 mg.

Her medical history included migraines, an early miscarriage in 2001, and a second pregnancy with delivery at 27 weeks for preeclampsia in December 2014. At postpartum, she had received amlodipine, and then bisoprolol at another hospital. In September 2015, she had consulted a third hospital for persistent hypertension with moderate to high blood pressure (systolic blood pressure: 170-190 mmHg). Blood pressure was measured at 170/80 mmHg in the office. Cardiac test results were normal. The physician concluded that the patient experienced chronic, rather than pregnancy-related hypertension, and replaced bisoprolol 5 mg with nebivolol 5 mg; barnidipine 10 mg was maintained, and the patient was asked to adhere to the therapeutic regimen. Despite mentioning that the hypertension was likely essential, he ordered an etiological work-up. Renal function was normal (PCr: 58 $\mu\text{mol/l}$; eGFR: 100 ml/min/1.73 m²). Urinary analysis revealed a mildly increased proteinuria of one-half gram per 24 hours. Urinary metanephrines were in the normal range, and the renal duplex study suggested a differential diagnosis of right renal artery stenosis and an arterial loop.

Discussion: Managing the hypertension

Dr. Micali: I would check the urinary sodium to confirm whether the patient is adhering to the hyposodic diet. This is one approach to check and determine whether the patient is consuming salt or not.

Dr. Persu: Yes, I think this is a good point, but this patient is not very adherent, and we had instances where we did not succeed in obtaining 24-hour urine samples. Additionally, this was performed in another hospital. I do not have details, so we must continue without this information.

Dr. Micali: In that case, I would consider a third drug or perhaps a combination to make the treatment easier.

Dr. Persu: I agree.

Dr. Staessen: I am wondering, Alexandre, whether you should have performed other imaging studies in addition to a renal duplex.

Dr. Persu: This was done before we saw her. Yes, I agree that a renal duplex with such an ambiguous result is definitely not sufficient.

Case History (Cont.)

When the patient presented initially to our hospital at the Cardiology Department, she was slightly overweight (BMI: 27.6 kg/m²). We confirmed high blood pressure (left arm: 180/110 mmHg; right arm: 190/105 mmHg). No heart, abdominal, or carotid murmurs were observed, and the examination was otherwise unremarkable. Echocardiography showed no evidence of left ventricular hypertrophy or aortic coarctation.

As the patient was pregnant, the recommendation was to replace the nebivolol and barnidipine, with alpha-methyldopa and nifedipine extended-release; following that, my colleague referred the patient to us.

Dr. Staessen: I am wondering what the rationale is to replace nebivolol and barnidipine with alpha-methyldopa and nifedipine extended-release. I can understand replacing

nebivolol with alpha-methyldopa, because there is considerable experience with alpha-methyldopa in pregnancy. However, nifedipine extended-release is basically a short-acting drug, which is made long-acting by utilizing it in the galenic format. I would have preferred to prescribe amlodipine or a long-acting drug that is considered long-acting per se.

Dr. Persu: I think this is controversial. Indeed, amlodipine is certainly better regarding the duration of action. Though, while there are no good studies with calcium antagonists in pregnancy, there is considerable experience with nifedipine (1), and some groups of obstetricians consider it to be a first-choice drug, so I can understand this choice.

Dr. Dominiczak: There is another potential suggestion. Many obstetricians around Europe and those who deal with these cases would suggest labetalol. Do you want to address this?

Dr. Persu: Yes. This would also be an appropriate second choice after alpha-methyldopa (1). Some studies using first-generation beta-blockers such as atenolol have shown growth restriction (2), and thus some clinicians think it is better to avoid administering beta-blockers old or new at the beginning of a pregnancy. This can be discussed.

Dr. Dominiczak: Labetalol is a mixed alpha-beta, so these concerns may not apply.

Dr. Persu: Indeed, there is no clear evidence that labetalol causes problems during pregnancy, but some clinicians have reservations using it in the first trimester. Overall, there is little evidence on the best antihypertensive treatments in pregnancy (1).

We saw the patient for the first time at the hypertension consultation in January 2016, at which time she had experienced nine weeks of amenorrhea. She complained of nausea and vomiting. At that time, her treatment was mostly unchanged, but acetylsalicylic acid 80 milligram was added. Her blood pressure remained high (seated: 168/111 mmHg; standing: 166/112 mmHg); she was poorly adherent to the treatment because she could not tolerate it well, she said. Additionally, vomiting made it challenging.

At that time, she also informed us that she underwent an abdominal CT angiography at another hospital when she was at the beginning of her pregnancy, but was not aware of it.

Then, we decided to examine the recently performed CT study and to perform a 24-hour ABPM, and schedule another appointment within 3 weeks, because it was difficult to convince the patient to take any medications; and we wanted to follow up and see if she was truly hypertensive and determine the severity of hypertension.

Dr. Rossi: Alexandre, one reason for replacing a beta-blocker with alpha-methyldopa could be to plan the measurement of renin, because with a beta-blocker, renin would be zero.

Dr. Persu: That is true and a good point. However, I think that the main reason for prescribing alpha-methyldopa was that, in current practice in Belgium, it remains the first choice in pregnancy.

Dr. Rossi: In addition to that, it is very surprising to learn that in spite of nine weeks of amenorrhea, they did a CT scan. We do not do this unless they are negative for pregnancy.

Dr. Persu: The CT scan was performed several weeks before the first consultation in our centre. The patient was probably not aware that she was pregnant. Also, the fact that examinations were performed at several different hospitals increases the risk of such occurrences.

Dr. Rossi: Yes, but at least at my institution, the radiologists would not perform any X-ray if they can't exclude pregnancy.

Dr. Persu: We have the same policy in our hospital. They would not accept it.

Dr. Dominiczak: This is a very important learning point. I think that we are going to put this in the paper: every woman of child-bearing age is pregnant until proven otherwise. That is what I was taught as a junior doctor.

Dr. Persu: In our hospital, even without evidence of pregnancy, we would not have performed it without a pregnancy test. That is true.

Dr. Micali: The patient is pregnant. She still has very high blood pressure. You could increase the alpha-methyldopa dose, and consider hospitalizing the patient, taking into account the fact that she is not taking the medication.

Dr. Persu: I think you could. However, this patient was difficult to manage. This is a real-life case. She would not accept medication or hospitalization easily. You may consider either quick 24-hour ambulatory monitoring or hospitalization for monitoring. We chose the first option.

Dr. Bursztyn: I do not think that, with repeated high blood pressure as in this patient, ambulatory monitoring is going to be of any help.

Dr. Persu: I agree that we were very sure she was hypertensive. However, ABPM might still be useful for grading the severity of hypertension, and also to convince her that antihypertensive treatment was truly required.

Kidney Images

The images can be observed. We see the abdominal CT angiography, which will be followed by better images later. Currently, this is the one we can examine. You can see irregularities in the mid-distal right renal artery. Additionally, we do not have all images from this hospital, but we know that the right kidney was slightly reduced in size with delayed concentration (?) of contrast.

Another point mentioned was that this patient has no celiac trunk. She has a separate emergence of the splenic and hepatic arteries, and stenosis of the hepatic artery. This does not change her follow-up now, but I am interested in how the audience would interpret these images.

Dr. Williams: She is young, and she has multiple stenotic lesions, which are irregular. Thus, she has FMD (fibromuscular dysplasia). It is likely she has FMD in multiple vascular beds.

My question is, if the film was examined a few weeks prior, was any action taken then? The tragedy is, of course, this is one of the easiest conditions to treat.

Dr. Persu: One of the messages of this case is that, in these patients who go from one doctor to another, there is a major risk of loss of information, dilution of responsibility, and so on.

Dr. Burszty: I am not completely sure about the diagnosis. There are other diseases in young women that may cause obstructive stenosis. For instance, Takayasu arteritis is one pathology. I would, if this was not initially done, have examined the peripheral pulses.

Dr. Persu: Peripheral pulses were present, she has no inflammatory syndrome, and later, you will see images that are much more typical. For the hepatic artery lesion, we cannot be sure, but, in the context of renal artery irregularities, I agree with Dr Williams that it is probably from FMD as well.

Dr. Williams: In Takayasu arteritis, you do not usually see beading of the artery. You might observe stenosis, but you will not see beading; she had multiple beads along the renal artery, which is very characteristic of renal FMD.

Images (cont.)

Another image shows that the hepatic stenosis was quite severe. I would like to make the point that this might be an anatomical variant. However, such variants seem to be very rare. Therefore, an FMD-related lesion is a more likely explanation.

At the next consultation, blood pressure was a little lower (seated: 167/102 mmHg; standing: 153/99 mmHg). Daytime and nighttime mean ambulatory blood pressure were 159/106 mmHg and 144/86 mmHg, respectively. As indicated by a colleague, the hypertension was confirmed, but a little less severe than expected. Renal function was normal (PCr: 64 $\mu\text{mol/l}$; eGFR: 103 ml/min/1.73 m²) and proteinuria was moderately increased (1 g/24 h).

Discussion: Proteinuria?

Dr. Dominiczak: She is 12 weeks pregnant, which is less than 20 weeks. It cannot be preeclampsia.

Dr. Persu: Indeed. She already had baseline proteinuria to some extent.

Dr. Dominiczak: This is chronic hypertension of pregnancy that is worsening and heading towards preeclampsia, super-imposed on pregnancy-related hypertension.

Dr. Rossi: First, it would be very important to know what her blood pressure was before pregnancy, and if she previously had proteinuria, and, second, it would be important to know the resistive indexes inside both kidneys, because that would provide an idea of the impact of the kidney stenosis.

Dr. Persu: The few measurements we observed before pregnancy suggest grade 2 to 3 hypertension, so she likely suffers from preexisting, chronic hypertension. She already had 500-milligram 24-hour proteinuria before pregnancy as revealed by analysis of a single sample. Finally, the resistive indexes were normal in both the kidneys.

Dr. Bursztyn: Normally, you have no proteinuria in renovascular hypertension, unless there is an occlusion. The increasing proteinuria by the gram or perhaps grams suggests imminent occlusion.

Dr. Waisman: In the first trimester of pregnancy, if proteinuria and hypertension are present, molar pregnancy should be considered.

Dr. Persu: This is a good point, but it was not confirmed. It was not molar in this case.

Dr. Tsanova: When you have proteinuria and hypertension in a young woman before pregnancy, we must always consider chronic glomerulonephritis or other chronic renal disease. Although renal function is normal, this may be the beginning of such a disease. Often, we do not think about the urine and urine sediments, and whether something else is present.

Dr. Persu: This may be; however, it is difficult to accept that a patient has two relatively uncommon diseases simultaneously. Many young patients with severe hypertension can have some degree of proteinuria, which will increase during pregnancy. This is my view.

Therapy discussion as pregnancy progresses

We added labetalol and ensured that she took the other medications. We had planned to see her soon after this. We told her that, after delivery, we should consider confirming the diagnosis of FMD by renal angiography and performing renal angioplasty. Additionally, a more extended vascular work-up was needed.

Dr. Amar: Alexandre, she has very severe hypertension with severe renal artery stenosis. At some point, without ACE inhibitor treatment, her hypertension would never be controlled during pregnancy and as she cannot be treated with ACE inhibitors (1), thus termination of pregnancy should be discussed?

Dr. Persu: We will discuss this later, but we did not consider this option because, as you will see, we ultimately succeeded in achieving better, albeit suboptimal, blood pressure control. However, in some cases, I agree that this can be a major issue.

At this time, she is probably more compliant with taking her medication, and has had amenorrhea for 15 weeks. Her high blood pressure is less severe with an estimated home blood pressure of 140/90 mmHg, which is not optimal, but certainly acceptable in pregnancy (1). However, this result was obtained with a therapeutic regimen including most medications recommended in first-line treatment of hypertensive women.

We now can see the development. She had mild hypertension (office seated blood pressure: 150/100 mmHg, 144/86 mmHg, and 156/93 mmHg at 3 different consultations, respectively). We ordered another ABPM, but she did not comply. We requested 24-hour urine, which was difficult to obtain, but eventually achieved at 31 weeks of pregnancy. Proteinuria was 0.67 g/24 h, and thus did not increase.

The obstetricians assessed her three days later and documented a proteinuria increase to almost 1 g/24 hour. Her blood pressure remained at 148/100 mmHg.

Dr. Persu: She is now at 31 weeks of pregnancy and she has proteinuria of 1 g/24 h. What would you have advised?

Dr. Bursztyn: I would advise to take no action. At this point, the high blood pressure is not placing her at risk. In any case, the prognosis of pregnancy is not primarily determined by blood pressure levels. I believe that the improvement in blood pressure, may also be dependent on the progression of pregnancy, with the normally acquired resistance to angiotensin II.

Dr. Staessen: If there would have been no side effects, why not up titrate alpha-methyldopa to the maximum dose of 2 grams?

Dr. Persu: This was not what our obstetric colleagues have done. Additionally, in fact, the blood pressure was acceptable. I think they were concerned by the association with proteinuria and considered it to be preeclampsia.

Dr. Kahan: I come from a country with a strong tradition of using beta-blockers in cardiovascular diseases, and we use beta-blockers commonly in pregnancy. It is not easy to draw generalized conclusions from the previously mentioned single small study on atenolol(1). In contrast, the extensive experience with some other beta blockers such as metoprolol, bisoprolol (and labetalol) during pregnancy suggests that those are reasonably safe.

Labetalol should be used in high doses to benefit from the alpha-blocking properties. I would have started with a much higher dose. You can use up to 800 milligrams three times daily. Indeed, you may increase alpha-methyldopa, but I would certainly increase the labetalol dose to achieve some alpha-blocking effects, because you show here that a low-dose, providing unspecific beta-blockade only, had little effect on blood pressure.

Dr. Persu: Indeed, we still had good options to improve blood pressure, but, as already mentioned, the obstetricians were not as concerned about blood pressure. They stated,

"She is now 31 weeks pregnant, and hypertensive with proteinuria and preeclampsia, we can proceed to delivery." However, this reasoning does not convince me, between others because proteinuria was already present and in the same range before pregnancy.

Dr. Dominiczak: We had three opinions. That is not what happened in the real-world scenario. In real life, they delivered the baby.

Delivery

The patient gave birth to a girl of 1550 g. The pediatricians suspected Down syndrome, which had unfortunately not been detected during the pre-natal period but was eventually confirmed by karyotypic analysis.

Other considerations

The American FMD Registry (3) data suggest that hypertension and migraine are very often associated with FMD. This patient had migraine, which was an additional valuable, though not specific clue. In a young lady with this presentation and suspicion of renal artery stenosis or arterial loop, it is believed that people should have been much more aggressive to make a timely diagnosis before pregnancy; however, that is only an opinion.

I will now discuss the arguments regarding an increased risk of pregnancy in patients with FMD. In fact, to my knowledge, there is only one study (4) on the prognosis of pregnancies in patients who had subsequent intervention for renal artery stenosis, either atherosclerotic or due to FMD. The authors obtained data on pregnancy only in a minority, as this was long before renal artery angioplasty was performed. Interestingly, half of patients with FMD had a history of preeclampsia, compared to only 20% of patients with atherosclerotic renal artery stenosis; however, 20% is already high. Preeclampsia remained associated with FMD in a multivariable model adjusting for smoking status, age at time of revascularization, and estimated glomerular filtration rate (odds ratio 9.51, $P = 0.017$). If we compare this with the literature, in the famous paper by Sibai, in healthy nulliparous women, the prevalence of preeclampsia is 2% to 7% (5), while it reaches 22% in women with chronic hypertension (6); here, we see a much higher prevalence. Patients with FMD may be at a higher risk of preeclampsia, but this study (4) has many potential biases. For the aforementioned reasons, I am not convinced that our patient had preeclampsia. Still, this was a good opportunity to make a comment on this.

Additionally, Dr. Amar mentioned that there may be some cases of FMD in pregnancy, especially unifocal FMD, which are so severe that RAS inhibitor use cannot be avoided, and thus some professionals advise that termination of pregnancy should be considered. In such cases, we may even consider angioplasty with minimum contrast. This must be discussed on a case-by-case basis. Besides, here, as indicated by Dr. Kahan and others, we still had medical therapeutic options.

Dr. Amar: Regarding angioplasty during pregnancy, we had a discussion and concluded that, in order to avoid difficulties for the baby, the procedure must be less than 10 minutes long. We did not do this and I would be interested to know if anyone has any experience.

Dr. Micali: Yes, in certain sites in Buenos Aires, we sometimes perform angioplasty in pregnant patients. We do it in a very short procedure with protection for the baby. So far, we have not had any negative results.

Dr. Parsa: Pregnant women respond well to simple balloon angioplasty. Stenting is not needed in patients with FMD, so we can do it after 16 weeks of gestation. This is safe for the baby.

Dr. Persu: Yes, that is also an important point, as renal artery stenting is normally not required and even contra-indicated in patients with FMD-related renal artery stenosis (7).

Dr. Rossi: This does not appear to be FMD. The CT images of the hepatic artery, renal proximal ostial renal artery stenosis, and the renal CT angiogram were not typical for FMD.

A classification was proposed by Harrison and MacCormack in 1964 at the time when they performed surgery on these arteries. They divided them into four different classes. One class was perimedial fibrodysplasia, which is a different disease, and very difficult to treat with angioplasty because they do not respond very well and there is a high risk of rupture of the artery and stenosis recurrence.

I do not think that, at this point in the case, angioplasty was at stake. The goal was to look after this woman through her pregnancy and delivery of the baby, and then reconsider the treatment afterward.

Dr. Persu: In this case, I agree with you. In much more difficult cases, angioplasty during pregnancy could be considered. The second point is that the initial images were not high quality. I will present better images, but the renal lesions were clearly located in the middle and distal, not proximal, artery, which fits with the diagnosis of FMD (7). I agree that the hepatic artery stenosis *per se* is not pathognomonic. The clear diagnosis will be shown later.

Dr. Tagetti: I am wondering if there were some ultrasound signs of fetal suffering, for example, if the baby was small for gestational age.

Dr. Persu: No. Thank you.

Case Resolution

Before looking at the images, we will return to the patient. We saw her postpartum. She was anxious because her baby had a confirmed diagnosis of Down syndrome. She once again ceased the antihypertensive treatment for nausea. Blood pressure was once again found to be increased (seated office blood pressure: 170/100 mmHg; standing: 152/106 mmHg), while it had improved before cesarean section. As she was not breastfeeding, in order to improve drug adherence, we prescribed a fixed dose combination of amlodipine and perindopril, 5 mg each daily. We discussed with her about the need to schedule a renal arteriography in order to confirm the diagnosis of renal artery FMD followed by renal artery revascularization.

First, we performed an abdominal CT-angiography, and the higher quality images show a clear string-of-beads (Figure 1a). We also confirmed the hepatic stenosis (Figure 1b). According to the multi-centre ARCADIA study led by Pierre Francois Plouin (8), we know that, if patients with FMD are evaluated on a systematic basis, FMD of more than one vascular bed is discovered in half of the cases.

In parallel with the discussion on arteriography, we performed CT-angiography of the head and neck to search for cervico-cephalic FMD lesions; this CT was normal. The Willis polygon can be seen here, but details will not be discussed. Her 24-hour ABPM post-pregnancy can be observed. The mean daytime and nighttime blood pressure were 161/102 and 133/85 mmHg, respectively, which indicate moderate hypertension. Once again, we could not obtain a 24-hour urinary specimen.

At the medical visit, the patient had once again stopped her medication. In the meantime, her daughter was hospitalized. The office seated blood pressure was measured at 173/99 mmHg. We advised barnidipine 10 mg because she did not tolerate the fixed dose combination; we then ordered the arteriography.

The patient was admitted for arteriography, but she left the hospital before it was performed, because her baby died that day, apparently of an infectious complication.

We thus reprogrammed the arteriography. In the meantime, with single-dose monotherapy, her blood pressure had improved greatly (147/83 mmHg and 139/80 mmHg), which was probably because she was no longer pregnant.

Now, the arteriography can be seen. This is the early arteriography. You can see a clear string of beads in the 2 last centimeters of the right renal artery (Figure 2a). These lesions probably existed for a long time. Indeed, at a later phase after injection, you can also see an impressive collateral circulation (Figure 2b). Despite this, there was some degree of hypoperfusion of the ipsilateral kidney; the other kidney had slightly increased in size.

We performed angioplasty without stenting, as recommended in FMD treatment (7), and though you see still some beads, the technical results were quite good (Figure 2c); thus, the interventional radiologist was satisfied. We were, too, because, in the meantime, the patient once again stopped her medication, and, despite stopping her medication, her blood pressure was almost normal at 136/88 mmHg.

Then, she left for Morocco for several months and we could not convince her to stay any longer under medical observation. However, we succeeded in obtaining another ABPM, which confirms blood pressure improvement despite some peaks (mean daytime blood pressure: 138/91 mmHg; mean nighttime blood pressure: 120/73 mmHg). Her blood pressure was not normal, but only mildly or borderline elevated. We also scheduled a renal duplex, but this had to be postponed until she returns.

Additional points should be raised, but I would like to hear your comments on the progress so far.

Dr. Touyz: I would like to go back to the migraines. Could you tell us about what happened to the migraines during her pregnancy, and also what the relationship is between the migraines and the FMD?

Dr. Persu: Initially, we were quite skeptical about the association of FMD and migraine, because FMD is most often encountered in young ladies who often experience migraine, even in the absence of FMD, but, nowadays, the U.S. Registry shows quite convincing evidence that FMD is often associated with typical migraines (3).

A more indirect argument is that the first susceptibility *locus* associated with FMD, corresponding to an intronic variant in the phosphatase and actin regulator 1 gene (*PHACTR1*) is also associated with migraines (9). During pregnancy, the patient fortunately had no major complaints of migraine.

Dr. Barigou: I see that this clinical case raises more than a case of FMD in a woman. It raises the complex question of hypertension in pregnant women. Because, if the possibility of secondary hypertension had been considered before pregnancy, there should have been a good work-up, and simply applying the recommendations may have led to an earlier diagnosis.

This case does not simply illustrate the diagnosis and management of FMD, but the fact that, after a pregnancy-related hypertension, a complete secondary hypertension work-up is required.

Dr. Persu: I agree. At least, screening for FMD-related renal artery stenosis is appropriate.

Dr. Deinum: What would have happened if your CT scan would not have shown this image of FMD? FMD is not detected by CT scanning at our hospital, but instead by angiography. Would you have discarded the diagnosis of FMD?

Dr. Persu: It is a difficult case. The patient had severe hypertension. She was not easily accepting drug treatment. It is important to be sure. Additionally, in our renal denervation trials, we diagnosed distal FMD in two patients by arteriography only, as it had remained undetected by CT. I would have also pursued arteriography, as you would have. Additionally, there was doubt, as this turbulence at the renal duplex seemed to be indicative of something else.

Dr. Dominiczak: With repeat CT scan after the pregnancy, would you have preferred to skip that for an arteriography?

Dr. Persu: We may have considered this. We might have considered arteriography from the start.

Dr. Micali: Did you examine for drug consumption of cocaine, amphetamines, or other substances? This is an unreliable patient; she was pregnant and not taking medication. We perhaps should have assessed this.

Dr. Persu: Yes, I agree. I might be naïve. This is a very religious patient, so I do not think so; however, it is possible.

Dr. Micali: It is possible, but not a guarantee.

Dr. Persu: In her case, non-adherence was more a problem of awareness and understanding the medical aspects than of other considerations.

Dr. Sharabi: It is nice to see the beads when you make the diagnosis of FMD, but, at least in our experience, we came across very few patients with a single lesion, and no explanation other than FMD. The absence of beads does not rule out FMD. I am trying to say that, in some cases, you might remain with a single lesion, even if you do arteriography.

Dr. Persu: Yes. If a single stenotic lesion is present, in the absence of string-of-beads, it is much more difficult. If only the hepatic artery lesion or an isolated renal artery stenosis was present, then the diagnosis of focal FMD may have been considered, but without absolute certainty.

Key issues that need to be kept in mind for this patient:

Did this patient have true preeclampsia? We can likely say she did not, but this patient's FMD might lead to a higher risk for preeclampsia. Should we consider renal PTA during pregnancy? Not in this case, but possibly in other more complicated cases, but this is speculative. We should definitely include more detailed data on pregnancies in the registries of patients with FMD (3,10).

So far, it was not discussed if recommending lifelong acetylsalicylic treatment is appropriate in patients with FMD. American medical professionals do this, because they assume turbulence may lead to an increased risk of thrombosis (11). European professionals are less prone to do it, at least in the absence of cervico-cephalic FMD lesions, as there is no evidence of benefit. This patient should benefit from an indefinite follow-up (7), as renal artery lesions may recur and she could develop FMD lesions in other vascular beds. She may also wish to become pregnant again. In this case, my hope is that her blood pressure normalizes, and then management will be easier.

Some more theoretical concerns and practical messages I would like to share or to discuss with you follow here.

First, general messages on the risk associated with “medical shopping” and poor drug adherence, as well as the need for increased awareness of FMD by the radiologists, because if “irregularities” or “loops” are described, many physicians may be tempted to not take action, because in their mind these terms do not refer to a disease. In contrast, if the protocol states “compatible with multifocal FMD”, this needs to be accounted for.

Second, I am strongly in favor of aggressive or at least state-of-the-art screening for FMD in hypertensive women of childbearing age. I know that Dr. Rossi is strongly in favor of searching

for pheochromocytoma in these circumstances, but, even more, in my modest opinion, the possibility of FMD should be assessed in these women because it is much more frequent than we thought previously. According to studies in renal donor candidates, the prevalence of renal artery FMD in the population could be 3% to 6% (12). Additionally, we tend not to assess this condition often enough in non-Caucasians. In particular, most hypertensive patients of African descent probably have essential, low-renin hypertension. Still, some could have FMD. Additionally, as mentioned earlier, multisite FMD is frequent (8) and all main arterial sites should be evaluated for lesions.

There are also some potential risks of pregnancy. Patients with FMD may develop resistant hypertension during pregnancy, and are also at risk of aneurysm and dissection; admittedly however, the risks specifically associated with pregnancy are not well-explored. Finally, in young hypertensive women with renal artery FMD, angioplasty without stenting often cures hypertension or at least substantially improves blood pressure (7). These were the key messages, which can now be discussed.

Dr. Kahan: How come the Down syndrome was missed when this woman was screened? If Down syndrome had been detected early in the pregnancy, would that have changed the management of this patient? She already has one child.

Dr. Persu: I have no detail on this. I am not an expert. In some cases, it can be missed by triple test and echography. If it had been identified, this would have led to a complex ethical discussion.

Dr. Persu: The patient wished to keep her child and do the best for her; she was very committed, and she likely would have declined the termination of pregnancy as well.

Dr. Burszty: I would like to make a comment on the combination of alpha-methyldopa and labetalol, which does not seem practical. There is no utility in reducing sympathetic outflow centrally and then attempting to block it peripherally. Physicians use this combination out of therapeutic frustration because of the limited treatment options during pregnancy.

Dr. Dominiczak: So, you state that you would rather administer a large dose of labetalol or alpha-methyldopa. Thank you.

Dr. Rossi: I would like to challenge you on the treatment beyond the first trimester. A renin-dependent form of hypertension is actually present. What is your feeling about using an ACE inhibitor or an AT-1 receptor blocker after the organogenesis is complete?

Dr. Persu: While first-trimester exposure to ACE inhibitors may lead to an increased risk of congenital malformations, second- and third-trimester exposure is associated with oligohydramnios, anuria and renal failure (1). Thus, it might be difficult to justify. Furthermore, I am convinced that this patient could be successfully treated using a standard antihypertensive regimen for pregnant women if she adheres to the treatment. We showed this.

Dr. Dominiczak: Could I help in answering this question? In 20 years of overseeing a medical obstetric clinic in Glasgow, I administered an ACE inhibitor once to a patient with Takayasu arthritis who was in critical health; it is very difficult and almost impossible to persuade obstetricians to administer ACE inhibitors because of contraindicating guidelines. It involves more than teratogenicity. There are also urinary abnormalities reported in animal studies (1). They do not want to consider it in any case.

Dr. Aparicio: This is a very short question. Do you think that what is observed at the hepatic artery is a unifocal FMD or an anatomical variant?

Dr. Persu: I do not know for sure, but when a patient has typical FMD in one vascular bed, I think the other atypical manifestations observed are likely due to FMD as well.

Dr. Dominiczak: This is a very good case. We are very grateful for the presentation and the fantastic discussion. We have not yet answered all questions.

I would like to remind you that, both in Europe and the United States, new guidelines are being proposed, and it is very important that we consider the following: female sex, young age, and severe hypertension, and completion of a work-up for secondary hypertension. As mentioned, many problems could have been prevented, had we confirmed the diagnosis before she became pregnant for the third.

Summary

We discussed the case of a young hypertensive woman. The diagnosis of multifocal FMD of the right renal artery was first suspected during her third pregnancy. A worsening of hypertension during pregnancy combined with poor drug adherence made blood pressure control difficult. A cesarean section was performed at 31 weeks gestation, considering the association of suboptimal control of blood pressure and proteinuria, despite the fact that the latter was present from the beginning, and probably reflected the severity of hypertension rather than superimposed preeclampsia. After delivery, renal artery angioplasty led to an almost complete normalization of blood pressure. Vascular screening did not disclose other arterial lesions, with the exception of hepatic artery stenosis. FMD is less rare than previously thought. In young patients with recently diagnosed hypertension, renal artery angioplasty often cures hypertension or at least substantially improves blood pressure. The risk of pregnancy in patients with FMD may be higher than that in healthy normotensive or even hypertensive women, both for the mother and the child. Therefore, all hypertensive women of childbearing age should be screened for renal artery FMD using state-of-the art imaging methods such as CT-angiography or, if contra-indicated, MR-angiography.

Figure legends

Figure 1: Abdominal CT-angiography. (a) “String-of-beads” of the distal part of the right renal artery suggestive of multifocal FMD; (b) separate emergence of the splenic and hepatic arteries from the aorta with stenosis of hepatic artery, possibly representing unifocal FMD.

Figure 2: Right renal artery selective angiography. (a) Severe stenosis of the two last centimeters of the right renal artery, with a “string-of-beads” aspect that was highly suggestive of

multifocal FMD; (b) collateral circulation (later phase of injection); (c) right renal artery after balloon angioplasty with satisfactory results and persistence of only a few beads.

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