Raging vessels: A case report on a young pregnant overt diabetic patient with cerebral cavernous malformation presenting as pontine hemorrhage and hepatic hemangioma*

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ABSTRACT

Reported is a case of a 29-year old Gravida 5 Para 4(4004), 23 6/7 weeks pregnant, known diabetic with hepatic hemangioma, who previously underwent ligation of ruptured esophageal varices, was admitted for the first time on February 21, 2015 due to left-sided hemiparesis. Identifying the cause of the pontine bleed and its possible association with coexisting medical problems was an arduous process since there are no existing management guidelines. Emergency Caesarean Section with bilateral tubal ligation under general anesthesia was done at 35 weeks AOG and a live baby girl was delivered with an Apgar score of 9,9. Magnetic Resonance Angiography (MRA) of intracranial vessels postpartum revealed a Cavernoma. This case is of particular importance due to the following reasons: 1.) Cerebral Cavernous Malformation (CCM) is a rare disease, 2.) There is scant data associating CCM with pregnancy, 3.) Current literature has not reported CCM with Hepatic Hemangioma in a single patient, 4.) No data has linked it with diabetes mellitus, 5.) There are still no management guidelines of CCM in pregnancy, 6.) A multidisciplinary approach is necessary for optimal maternal and fetal outcomes.

Keywords: Cavernous malformation, cerebrovascular bleed, pontocerebellar haemorrhage, cavernous angioma, liver hemangioma

INTRODUCTION

Vascular anomalies are endothelial malformations and the most common are hemangiomas, lymphatic malformations, capillary malformations (port-wine stains), venous malformations, and arteriovenous malformations.[1] They are divided into congenital or acquired vascular lesions. Congenital malformations include the true arteriovenous malformations (AVMs), venous anomalies, and capillary telangiectasias, while acquired vascular lesions include cavernous angiomas and dural arteriovenous fistulas.[2] Mulliken and Glowacki divided them into vascular tumors, which grows from cellular hyperplasia (including hemangioma) and vascular malformations, which represents a localized defect in vascular morphogenesis (including the capillary, lymphatic, and venous malformations, and the true arteriovenous malformations). Markers of hemangiomas have been shown to coincide with those found in placental tissue[3,4]. Management of vascular anomalies is complex and involves multiple disciplines and therapeutic options and referral to the services of Neurology and Neurosurgery.

Cavernous angiomasor cerebral vascular malformations (CCMs) are tufts of capillary sinusoids that form within the deep hemispheric white matter and brainstem with no normal intervening neural structures. The exact pathophysiology is still unknown, although familial cavernous angiomas have been mapped to several different chromosomal loci: KRIT1 (7q21-q22), CCM2 (7p13), and PDCD10 (3q26.1).[2] CCMs have an incidence rate of 0.47% and is found predominantly in patients aged 30-39 years.[5] In the Philippines, the prevalence rate is 0.49% based on extrapolated statistics.[6] Up to 25% of individuals with CCMs remain asymptomatic throughout their lives, while approximately 50-75% become symptomatic, presenting with seizures, focal neurologic deficits, non-specific headaches, and cerebral hemorrhage.[7] Since CCMs are considered as vascular neoplasms being able to exhibit vascular proliferation and vascular neoangiogenesis, they can modify their morphological and clinical features as a result of hormonal stimulation.[8] Vascular endothelial growth factor (VEGF), basic fibroblast growth factor (b-fgf), and transforming growth factor-a (tgf-a), are known to be all increased in CCMs.[7] Because of this, recent studies have shown that CCMs are more likely to increase in size with higher propensity for hemorhage during pregnancy, since pregnancy is characterized by an increase in the aforementioned hormones to stimulate placenta formation.[9]

Hepatic hemangiomas, are congenital vascular malformations, composed of masses of blood vessels

*Second Place, 2015 Philippine Obstetrical and Gynecological Society (POGS) Residents' Interesting Case Paper Contest, September 28, 2015, 3rd Floor, POGS Building, Quezon City

that are atypical or irregular in arrangement and size.[10] Prevalence in autopsy studies range between 0.4 to 7.4%.[11] Females aged 40-50 years are most frequently affected. Hepatic hemangiomas are divided into 1.) capillary hemangiomas, which are peripheral, small, and multiple, and 2.) cavernous hemangiomas, which are rarer and larger.[12] Like the CCMs, Hepatic hemangiomas can increase in size during pregnancy, since experimental studies show that estrogen augments endothelial cell proliferation, migration, and organization into capillary-like structures.[13] Although liver hemangiomas are generally benign, a rupture of a small hemangioma can lead to serious intra-abdominal hemorrhage and can cause grave complications in pregnancy such as hemorrhagic shock.[14]

Diabetes mellitus (DM) is a metabolic disorder of 2 types: Type 1 DM is the result of complete or near-total insulin deficiency, while Type 2 DM is characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production.[2] DM can be pregestational or overt, or Gestational Diabetes Mellitus (GDM), which is characterized by elevation of glucose levels responsible for a several adverse perinatal outcomes including hyperglycemia, fetal hypoglycemia, requirement of neonatal intensive care and neonatal mortality.[15] Recent literature has shown that endothelial cells in patients with GDM cause an increase in VEGF to regulate the vascular tone and angiogenesis in the placenta.[16]

This case report explores the origins of the three pathologies that are rarely encountered together in obstetrical practice. Recognition of disparate symptomatology is important for properly managing these patients.

CASE REPORT

E.R., a 29-year old female, G5P4 (4004), from Payatas, Quezon City, was brought to the emergency room on February 21, 2015 at 23 weeks and 6 days AOG with chief complaint of left-sided hemiparesis.

Past medical history revealed that the patient was diagnosed with diabetes mellitus Type 1 at the age of 23, non-compliant with metformin, later shifted to Insulin glargine (long acting) and Insulin glulisine (rapid acting) in 2012. She underwent Open Cholecystectomy in this institution in 2009. She was hospitalized 4 times in 2012 for severe anemia due to upper gastrointestinal bleeding secondary to bleeding esophageal varices, and received multiple blood transfusions. In the last admission that year she underwent ligation of bleeding esophageal varices, with the finding of a hepatic hemangioma as the cause of the portal hypertension.

Family history showed presence of hypertension stage II of her father and diabetes mellitus type 2 in anuncle. There are no neurologic, psychiatric nor hematologic disorders.

Gynecologic, menstrual, and sexual history were unremarkable. She had 4 uncomplicated pregnancies carried to term and delivered via normal spontaneous delivery by a midwife at a lying-in in 2004, 2006, 2007, and 2008, the weights of all babies were unrecalled. No prenatal check-up was done for her present pregnancy. Personal and social history showed that she is an occasional alcoholic beverage drinker and a 7- pack year smoker.

History of present illness showed that one day prior to admission, patient suddenly had left-sided hemiparesis associated with slurring of speech and gait instability. Review of systems showed left-sided weakness. There was no blurring of vision, dizziness, palpitation, and fever.

Upon admission, blood pressure was 100/70, with cardiac rate of 92 beats per minute, respiratory rate of 22 cycles per minute, temperature of 37.3 ^{0}C, and a body mass index of 30.14kg/m^2. Heart and chest findings were normal. Fundic height was 23 cm, with fetal heart tones of 140 bpm, with no uterine contractions. There was no ascites nor caput medusa. Liver span was normal at 11 cm, while the Traube's space was slightly obliterated. The cervix was closed and uneffaced. Mental status examination showed that patient was well-groomed, weak-looking, with left facial asymmetry. She spoke in sentences with slurred speech, euthymic, with appropriate affect with no disorder in thought perception, process, and content. She was oriented to time, place, and person. Her remote, immediate, and recent memory were intact. Neurologic examination showed that she had a deficit in cranial nerves V and VII, with decreased sensory in the left hemifacial area, left facial asymmetry and a shallow left nasolabial fold. The rest of the cranial nerves were intact. Motor examination showed 5/5 strength in the right upper and lower extremities, while her left upper and lower extremities only scored 4/5. There was no spasticity, rigidity nor atrophy; there was pronator drift on the left upper extremity. Sensory perception was 100% on the right upper and lower extremities while left extremities only scored 70%. Deep tendon reflexes were all normal at 2+; Babinski, Brudzinski, and Kernig's test were negative. Upon cerebellar examination, vertical upward gaze-evoked nystagmus on both eyes, withdysmetria on finger to nose test on the left extremity.

Admitting diagnosis was G5P4 (4004) Pregnancy Uterine 23 weeks and 6 days AOG by LMP, Cerebrovascular Accident; Overt Diabetes Mellitus, unknown control; status post Open Cholecystectomy (2009), status post Ligation of Bleeding Esophageal Varices (2012).

Complete blood count, blood chemistries, coagulation studies showed normal results. Random blood

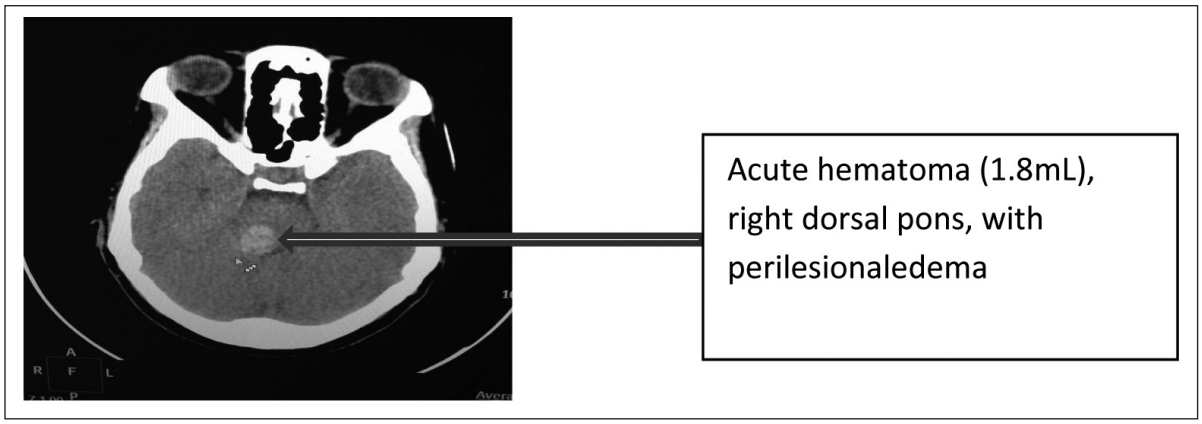

Figure 1. Cranial CT Scan

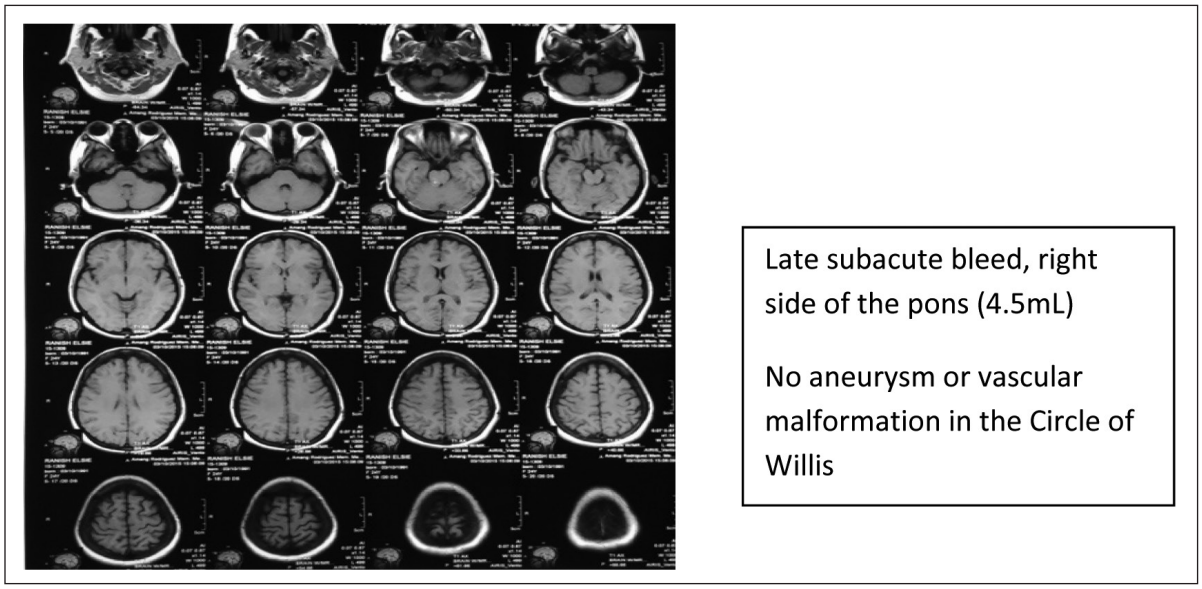

Figure 2. Cranial MRI

glucose, fasting blood sugar, and HbA1c were all elevated at 202mg/dl, 180mg/dl and 6.67%, respectively. Plain cranial CT scan (Figure 1) showed ahematoma of 1.8 cc in the right dorsal pons with perilesionaledema. 12-L ECG and Chest X-ray were normal. Pelvic ultrasound showed a single live intrauterine pregnancy in cephalic presentation with composite age of 23 weeks and 4 days, with good cardiac and somatic activities, placenta anterior grade 1, and adequate amniotic fluid volumeof 13 cm.

The patient was immediately referred to the services of Perinatology, Neurology, Neurosurgery, Endocrinology, Gastroenterology, Anesthesiology, Ophthalmology and Pediatrics. Neurology service recommended neuroprotection parameters by maintaining capillary blood glucose (CBG) levels at 110-180 mg/dl, Mean Arterial Pressure at 110-120 mmHg, or Systolic BP of 140 mmHg, temperature at 36-37 degrees Celsius, and O2 saturation at 97%. Patient was given mannitol and citicholine. Patient was started on a diabetic diet with 1800 kcal/kg/day. Insulin isophane and Insulin regular (Humulin 70/30) was started, and dosage had tobe frequently adjusted because of poor glucose control. Ophthalmologic findings were normal. A Cranial MRI (Figure 2) was done to rule out neoplastic versus vascular cause of the neurologic lesion, which revealed a T1 and T2 hyperintense signal in the right side of the pons, indicating a subacute bleed, with a volume of 4.5 cc and was negative for aneurysm or vascular malformation in the Circle of Willis.

A multidisciplinary conference was done at the 25th week AOG. With both aneurysm and vascular malformation eliminated through cranial imaging, it was difficult to address the pontine bleed, since the involved vessels were not yet identified. Since both MRI and CT scan results were inconclusive, Magnetic Resonance Angiography (MRA) of the carotid and vertebral arteries (4-vessel angiogram) was contemplated. During this time, the patient was clinically improving with a stable neurologic status. With Neurosurgery's position that no surgical intervention was necessary, it was decided that the MRA be done postpartum. Close monitoring was done daily by checking for the development of decerebrate posturing, bilateral pinpoint pupils, loss of conjugate horizontal movements

with retained vertical movements and accommodation, and medial deviation of the eyes. Fetal heart tones were monitored every 4 hours while fetal well-being was monitored by twice weekly Biophysical Profile.

Glucose levels fluctuated requiring constant adjustments of Humulin 70/30 dosing. Metformin 500mg/tab 1 tab once a day was added. Long term plan was to carry the pregnancy as close to 38-39 weeks for as long as the mother was stable, since it is well established that fetal lung maturity occurs later in pregnancies of diabetic patients. The following would be the indications for immediate delivery: progression of the neurologic deficit, altered consciousness, and fetal compromise. The mode of delivery would be cesarean section under general anesthesia, as labor pains could aggravate the pontine bleed.

Because of the previous history of upper gastrointestinal bleed, hepatobiliary ultrasound was done to document other gastrointestinal anomalies. It showed a normal-sized liver, with heterogenous parenchymal echopattern and smooth margins; multiple hyperechoic nodules were again seen in the posterosuperior and anteroinferior segments of the right lobe; with no discrete calcifications; the portal vein and its tributaries were unremarkable. Splenomegaly was also noted. Impression was Liver Hemangioma. (Figure 3)

Patient underwent rehabilitation to improve strength and function of her left extremities. Patient was noted to be improving daily with less dysarthria, and was slowly regaining strength of her left upper extremity. Fair glucose control was achieved with Humulin 70/30, 58u am and 38u pm. Metformin was discontinued.

An ultrasound done during this time showed a fetus appropriate for gestational age and a normal Biophysical Profile. She was instructed to strictly do CBG monitoring 30 minutes premeals and 2 hours postprandial and Insulin administration. Discharge diagnosis was G5P4 (4004) Pregnancy Uterine 31 weeks 5 days AOG by Early Ultrasound (23 weeks) Cerebrovascular Hemorrhage, Pons, probably secondary to a Vascular Malformation; Overt Diabetes Mellitus, controlled; Hepatic Hemangioma; Status Post Open Cholecystectomy (2009); Status Post Ligation for Bleeding Esophageal Varices (2012).

Twice weekly BPS was done with a result of 8/8. CBG values were normal. However, on her prenatal check-up at 35 5/7 weeks AOG, patient complained of labor pains and vaginal spotting. Internal examination showed a 1 cm dilated cervix, 60% effaced, station -2, intact bag of water, with moderate to strong uterine contractions. An emergency caesarean section with bilateral tubal ligation

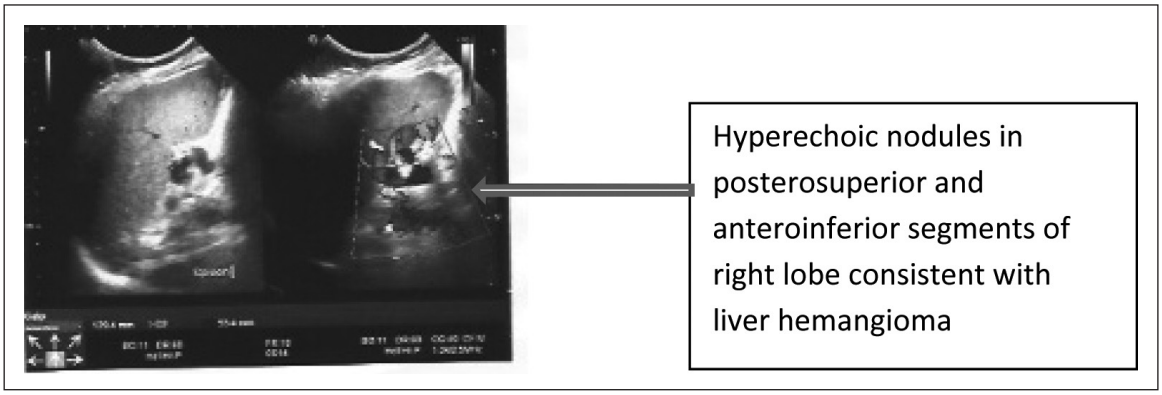

Figure 3. Hepatobiliary Ultrasound

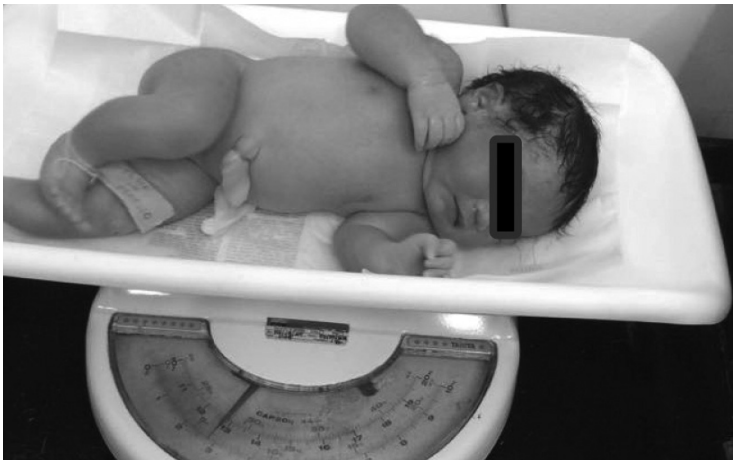

Figure 4. Delivery of a live baby girl, Apgar Score of 9,9, BW 2900g

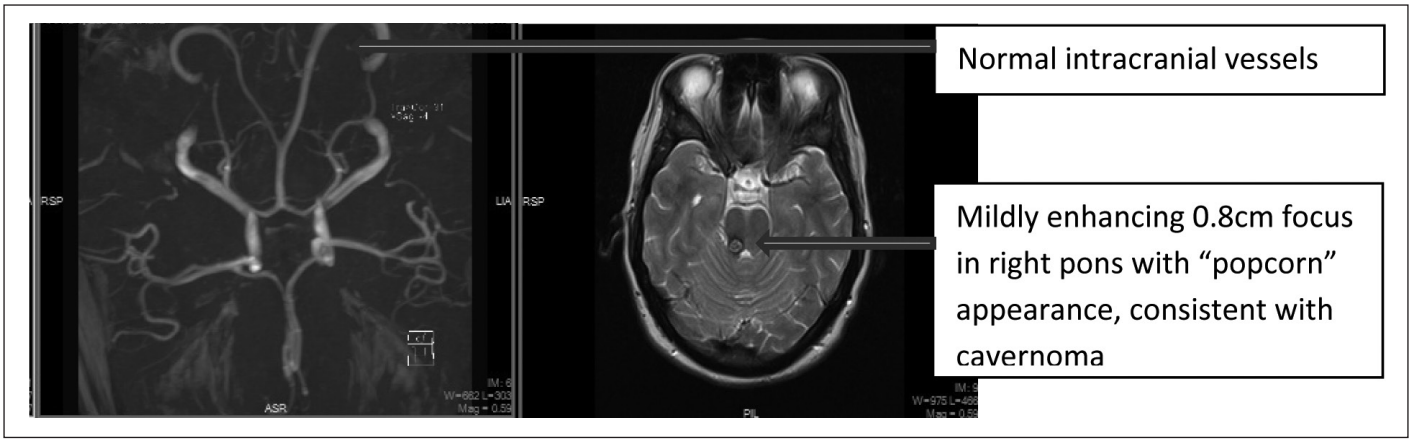

Figure 5. Cranial MRI with Contrast and MRA of Intracranial Vessels

under general anesthesia was done and she delivered to a live baby girl, Apgar score 9,9, birth weight of 2900 kg, pediatric aging of 39 weeks (Figure 4). Seizure precautions were observed throughout the procedure. The neonate's CBG was normal at 88 mg/dl. The patient was discharged improved. Three weeks post-partum, a cranial MRI with contrast and MRA of the intracranial vessels showed a mixed round T1/T2W intensity signal focus with some enhancement, measuring 0.8 cm in diameter seen in the right pons, demonstrating a "popcorn" appearance with a rim of signal loss due to hemosiderin and was signed out as a Cavernoma (Figure 5). The patient is regularly following-up with the services of neurology, endocrinology, and gastroenterology. Neurology services is still monitoring the patient by regularly assessing the neurologic exam and is still contemplating on doing MRA with contrast of the great vessels to document any other vascular anomalies. MRI every 1-2 years will be done if she remains neurologically stable. Endocrinology advised to continue insulin and to monitor the cbg, while gastroenterology advised the patient to come back if she presented with any signs of gastrointestinal bleeding or abdominal pain.

DISCUSSION

In a pregnant patient with a significant history of portal hypertension from liver hemangioma with concomitant overt diabetes mellitus, several questions must be answered in order to manage the patient properly. First, are the signs and symptoms restricted to the nervous system, or do they arise in the context of a systemic illness, taking into consideration her co-morbidities? Since the neurologic deficit is a result of a pontine bleed, which vessels are involved? What should be done if the bleeding persists? Does she need immediate surgical intervention? How should the pregnancy be managed to ensure optimal outcomes for both mother and baby?

The patient presented with the clinical features of stroke in the young with a rapid onset of the neurologic deficit, pointing to a possible vascular event. Hemorrhage rather than ischemia was favored since patient did not have a history of transient remission or regression, a component of the latter. Toxic and metabolic processes were excluded since there was no evolution of the symptoms. An Infectious process was not entertained because of absence of fever, neck rigidity, nor altered level of consciousness, as well as the absence of the Brudzinski sign. There was no history of drug or neurotoxin use that could cause the hemiparesis, cranial V and VII deficit, and dysarthria.

The initial imaging only revealed pontinehemorrhage, ruling out malformation. The location is consistent with the "crossed" weakness of the limbs and isolated cranial nerve abnormalities (CN V and VII), which point to a lesion in the brainstem. Cranial MRA postpartum revealed a Cavernoma or Cerebral Cavernous Malformation, ruling out other vascular anomalies such as Arteriovenous Malformation and Moyamoya disease.

Cerebral cavernous malformation (CCM) is a form of vascular anomaly that occurs in 0.1 to 0.5% of individuals, which can be inherited via autosomal dominant pattern in 20% of cases, while some cases occur sporadically.[18] Gaultet. al[19] reported that 25% of CCM patients remain asymptomatic throughout their lifetime, 9% become symptomatic before age 10, 19% after age 40. The 29-year old patient presented belongs to 62-72% of CCM patients who are between 10 to 40 years old.[7] Presentations vary, as most experience seizures in 40-70%, while 35-50% have focal neurologic deficit, and 41% have cerebral hemorrhage.[19] In this case, patient presented with both neurologic deficit and cerebral hemorrhage based on imaging. The reported annual incidence of brainstem hemorrhage is 2.5 to 5%, and is even higher in patients with malformation more than 0.5 cm, those who are less than 35 years old and those with associated venous anomalies.[20] Patient is at high risk of developing brainstem

bleed since she fulfilled all criteria.

The pathogenesis of CCM has still has to be identified, but Haasdijk, et. al[21] suggests that during the formation of the primary vascular plexus, a perturbed relationship between adhesion and migration of endothelial precursor cells develop. Loss of function of one of the CCM proteins in endothelial cells which bridge molecules between junctional and cytoplasmic proteins leads to a decrease in adhesion.

Another theory is that CCMs and other vascular malformations undergo morphological changes during pregnancy due to the increase in vascular endothelial growth factor and basic fibroblast growth factor which stimulate placenta formation.[22] There is evidence that the said growth factors can induce angiogenesis and increase the size of CCMs, thereby increasing the rate of hemorrhage.[23]

Kleaveland et.al.[24] reported three genes that have been associated with the development of CCMs. First is KRIT1 (CCM1) located on chromosome 7q11.2-21, involved in 39% of cases, mutation of which is associated with hyperkeratotic cutaneous capillary-venous malformation. Second is MGC4607 (Malcavernin or CCM2) located on chromosome 7p13. Sirvente et al reported that its mutation is less prone to cutaneous vascular malformation.[25] This patient might have the mutation in the third gene, PDCD10 (CCM3) located on chromosome 3q26.1, which is involved in 21% of cases, since this gene is associated with venous malformation. However, molecular studies and genetic testing which are not locally available are needed for documentation. It is also important to note the probability of clinical penetrance in patients with CCM since it is an autosomal dominant disorder. Patients with mutation in CCM1 have 88% clinical penetrance, while those involving CCM2 have 100%, and those with CCM3 have 63%.[26] To estimate the genetic risk, a three-generation genogram is needed, which must specify the presence of seizure, focal neurologic deficit, cerebral hemorrhage, and recurrent headaches.[27] MRI must also be done since family history of CCM can only be confirmed through it.

Magnetic resonance imaging is still the best tool as it localizes the lesion, evaluates the presence or absence of venous anomalies, and timing of bleeding in case of hemorrhage.[28] Gadolinium-enhanced imaging is more useful, however, it is associated with adverse effects on the fetus and is generally avoided in pregnancy unless there is a clear essential indication to do so, such as planning for surgery. Since the patient was neurologically stable and did not require surgery, MRA was deferred until postpartum.

The indication for surgery will depend on the clinical course of the patient and MRI characteristics (localization, size, or new hemorrhage) of the CCM lesion. Surgery for deep-seated or brainstem lesions has a morbidity rate of 30-70% and mortality rate of 2%.[29] Hasegawa, et. al.[30] reported that stereotactic surgery is indicated for brainstem lesions, however radiation-induced necrosis could be as high as 27% whereas a report by Pham, et al[29] showed that stereotactic surgery (such as gamma-knife surgery) for CCM lesions is still controversial. With limited information regarding treatment strategy, management is often decided based on the previous reports of the same case. A study by Yamada, et al[31] considered the presence or absence of the history of hemorrhage and the age of gestation in determining pregnancy termination. Surgery was indicated for those <31 weeks AOG (inducing abortion or fetal death) and is often delayed for those more than 32 weeks AOG. However, the decision must still be based on religious or individual views. The patient presented had a history of ligation of bleeding esophageal varices and was first seen with a neurologic deficit at the 23rd week of pregnancy. Since therapeutic abortion is not practiced in this country, pregnancy was allowed to continue until term provided that the mother was stable and fetal well-being was closely monitored.

Data regarding medical management is still inconsistent and includes Simvastatin (by inhibiting RhoA), Fasudil (by inhibiting RhoA effect or protein ROCK), and adenosine monophosphate elevating drugs which, according to Borikova, et. Al[32] stabilize CCM lesions by improving vascular integrity. Wilhelm, et. al.[33] suggested that Sorafenib, which is an antiangiogenic drug, prevents progression of CCM lesions by targeting VEGF receptors. There is no data yet regarding medical management for CCM in pregnancy.

Gault, et al.[19] recommended that a caesarean section must be considered in patients with large lesions or recent symptomatic hemorrhage, but normal delivery is not contraindicated in patients with small lesions and without recent clinical signs of hemorrhage. Yamada, et. al[31] stated that to avoid excessive blood pressure elevation, caesarean delivery or painless delivery should be done as a rule. In other studies,[34] obstetricians choose caesarean delivery to avoid the hemodynamic changes during vaginal delivery. A caesarean section was done in this patient considering a recent pontinehemorrhage and to adhere to the parameters for neuroprotection.

As for the timing of delivery, Yamada[31] stated that early induction of labor may be considered at 32 weeks when the weight of the fetus would be 2000 g. This was not followed in this case as we were also dealing with Diabetes Mellitus, which delays fetal lung maturity, especially in those with poor glycemic control (>110mg/dl), regardless of the class of diabetes.[35]

In general, there is no anesthetic regimen that has been shown to confer “cerebral protection” in this type

of patient. General anesthesia was used in this particular case to reduce the risk of encountering an "aberrant" blood vessel, reduce the risk of increase in intracanial pressure, and herniation. The choice of anesthesia must be individualized and must maintain euvolemia, normotension, isotonicity, and normoglycemia.[36]

For clinical monitoring of CCM postpartum, an MRI every 1-2 years is suggested, provided that the patient's neurologic status does not exacerbate. But if a new neurologic lesion should arise or if present status aggravates, MRI must be repeated immediately.[21]

The prognosis of CCM patients after surgery is generally favorable, however, long term prognosis is still not known. The patient was informed that the re-bleed after first bleeding episode is about 3.1-4.5 %.[37,38] Plan for this patient was to regularly do neurologic examination and monitor with MRI every 1-2 years if she remains neurologically stable. Also, MRA with contrast of the great vessels was also contemplated to detect any other vascular anomalies.

Hemangioma is the most common benign tumor of the liver, the most common type being the cavernous hemangioma. Cavernous Liver Hemangiomas are composed of widely dilated nonanastomotic vascular spaces lined by flat endothelial cells. It usually has no clinical significance, however, Takahashi, et, al.[39] reported that a giant cavernous hemagioma caused secondary Portal Hypertension, probably due to obstruction of the extra-hepatic portal vein due to pressure of the tumor. Hekomoglu, et. al.[40] also reported a cavernous hemangioma associated with arterioportal and portosystemic shunts, causing portal hypertension. Dynamic contrast-enhanced CT scan with triple phase CT with delayed imaging is the best diagnostic tool for cavernous hemangiomas, however, it was not performed in this patient due to insufficient funds. Ultrasonography was done instead, showing hyperechoic nodules with smooth and clear borders, consistent with hemangioma.[41] Small hemangiomas (<4cm) can be managed by observation and should be followed up by periodic radiologic examination, while spontaneous or traumatic rupture, intratumoral bleeding, and consumptive coagulopathy (in Kassabach-Merrit Syndrome) are absolute indications for surgery.[41]

In normal pregnancy, a physiological insulin resistance is necessary to provide glucose to the growing fetus. This normal adaptation, however, does not occur in certain conditions, thus creating insulin resistance, the pathology of diabetes mellitus. One out of 10 pregnant women is affected by Gestational diabetes mellitus worldwide. It is associated with multiple adverse maternal outcomes including hypertensive disorders, hemorrhage, infections, and obstructed labor; while perinatal outcomes include neonatal hypoglycaemia, premature delivery, shoulder dystocia or birth injury, the need for intensive neonatal care, hyperbilirubinemia, hypocalcemia, and birth weight above the 90th percentile. Hyperglycemia generates an adaptive response in the fetus to control the glucose level, by having hyperinsulinemia. Other adaptive responses by the fetus include elevation of glucose consumption by the placenta, and feto-placental blood flow. Escudero, et. al[15] reported that due to the lack of innervation in the placenta, the vascular tone is controlled by the release of vasoactive molecules from the endothelium. These vasoactive molecules also regulate endothelial proliferation and migration, affecting angiogenesis. The placenta in a patient with diabetes mellitus is characterized by hypervascularization and elevation in the pro-angiogenic signals such as Vascular Endothelial Growth Factor (VEGF). It is noteworthy that VEGF is also elevated in vascular malformations such as CCM. The presence of both conditions where VEGF levels are elevated could have potentiated a worsening of this patient's clinical condition.

How she was able to have uncomplicated pregnancies prior to this pregnancy remains unresolved, but the most probable answer is that an even more uncontrolled blood glucose elevation which happened in 2009 may have triggered an elevation of vascular endothelial growth factor leading to exacerbation of a maybe previously present ccm and hemangioma. An analytical research should be done in order to establish the relationship of the three diseases.

SUMMARY AND CONCLUSION

Although it is currently believed that pregnancy could increase the levels of endothelial growth factors such as vascular endothelial growth factor that could predispose the patient to have an increased risk of developing vascular anomalies, a disease such as Cerebral Cavernous Malformation is still rarely encountered and reported in pregnancy. Its occurrence with another vascular malformation, Hepatic Hemangioma, and Diabetes Mellitus, makes this case even rarer, and therefore, making diagnosis and management more difficult and complex. The paucity of management strategies restricts the clinician in making therapeutic options that will ensure optimal outcomes for both mother and baby. That is why a collaborative effort among obstetricians, perinatologists, neurologists, neurosurgeons, internists, pediatricians and radiologists in devising a therapeutic plan was integral from the time of cinching the diagnosis, tackling individual clinical problems and addressing the interweaving developments as the disease unfolded and decisions had to be made. Cases such as this clearly demonstrates that the core of Obstetrics is decision-making.

RECOMMENDATIONS:

1. In a young pregnant patient presenting with cerebrovascular bleed, it is important to obtain a thorough clinical history, complete physical and neurologic examination and diagnostic tests. Management is still individualized and is done with the help of other services.
2. Contraception is also recommended for patients who have completed their family size. Bilateral tubal ligation or a progestin-only method such as an implant or a metabolically neutral method such as an IUD may be used in cases of CCM with concomitant Diabetes Mellitus.
3. Monitoringof patients should be done every 1-2 years with MRI for patients with CCM that is not enlarging, and with regular follow-up with Neurology and Endocrinology. However symptomatic patients require close follow-up and must be assessed whether or not surgical intervention is needed.

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