Mycotic aneurysm in pregnancy: A case report*

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ABSTRACT

Reported is a case of a 20-year old G2P1 (1001) Pregnancy Uterine 22 weeks age of gestation (AOG), who suffered three episodes of aneurysmal rupture over a period of almost 8 weeks, the last being fatal occurring on the 27th week AOG, despite aggressive antimicrobial treatment, insertion of ventriculo-peritoneal shunt and clinically improving neurologic status. The patient succumbed to subarachnoid hemorrhage resulting from the third aneurysmal rupture. Mycotic aneurysm is a serious and catastrophic clinical condition, more so in a pregnant patient wherein management options are limited in order to preserve pregnancy.

This report will discuss the first documented case in the Philippines of mycotic aneurysm in pregnancy secondary to a valvular heart disease, to increase awareness on such cases for timely diagnosis and management.

Keywords: Endocarditis, Mycotic Aneurysm, Pregnancy

INTRODUCTION

Aneurysm is a rare complication in pregnancy with no existing definitive treatment guideline. The term mycotic aneurysm was first coined by Osler in 1885 to describe aortic aneurysms resembling "fungal growths" in a man with endocarditis.[1] The term is now used to describe infectious arterial aneurysms in general. Due to their friable walls, patients are predisposed to spontaneous rupture which results in intracranial hemorrhage causing significant morbidity and mortality as high as 60–90% in earlier case studies, and 12–32% in more recent literature reviews.[2]

This report will discuss a case of intracranial mycotic aneurysm in pregnancy with a history of valvular heart disease. The incidence of associated mycotic aneurysms in patients with infective endocarditis has been reported to be 2-10%. Frazee et al. reported an incidence of mycotic cerebral aneurysms of 4% in all patients with intracranial aneurysms and 3% of all patients with infective endocarditis. However, the incidence of infective endocarditis in pregnancy has been reported to be 1 in 8000 deliveries (0.0125%). Cox et al. reported it to be 1 in 16 500 (0.006%).[3]

CASE REPORT

A 20-year old, G2P1 (1001) presented at the emergency room due to decreased sensorium and left-sided weakness. Patient was on her 23nd week of gestation, asymptomatic, until thirteen days prior to admission when the patient developed headache, vomiting and undocumented fever. Upon consult and subsequent admission in a local hospital, the patient had one episode of seizure followed by progressive left-sided weakness. Plain cranial computed tomography (CT) scan revealed an acute intraparenchymal hemorrhage involving the right frontal lobe. Patient was given Ampicillin 2g and Mannitol 150mL however, status continued to deteriorate and patient was referred to our institution for further management.

At the emergency room, the patient was seen by Neurology service whose primary impression was ruptured arteriovenous malformation. She had a Glasgow Coma Scale (GCS) of 13 (E4V3M6), drowsy, with spontaneous eye opening, minimal verbal output but was able to follow commands. Patient was tachycardic at 113 beats per minute (bpm) but the rest of the vital signs were unremarkable. Cardiac examination revealed an adynamic precordium however a murmur was noted upon auscultation. Focusing on the abdomen, fundic height was 20 cm, with fetal heart rate of 150 bpm. Neurologic examination revealed presence of nuchal rigidity and hemiparesis, with a manual muscle testing grade of 0/5 and 4/5 on the left and right extremities, respectively. Deep tendon reflexes of both lower extremities were noted to be +1, while both upper extremities were graded +2. Sensory function of all dermatomes and cranial nerves were intact.

On further evaluation, medical history revealed that the patient was diagnosed with an undocumented heart condition at five years of age however no further consult

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and management was done. In 2015, during the patient's first pregnancy, a 2d-echo done for cardiac clearance revealed a valvular heart disease probably rheumatic. The first pregnancy was carried to term and was delivered via normal spontaneous delivery with no post-partum complications. The rest of the patient's medical history were non-contributory. Patient was referred to Obstetrics service for co-management and was admitted as a case of Ruptured Arteriovenous Malformation, Gravidocardiac secondary to Rheumatic Heard Disease, rule out Preeclampsia.

Repeat cranial CT scan revealed a decrease in the parenchymal hemorrhage and presence of subfalcine herniation. Pelvic ultrasound revealed a viable pregnancy with a gestational age that coincides with the last menstrual period (LMP). With a resolving hematoma 13 days post-ictus, patient was managed conservatively with Mannitol 150cc, Dexamethasone 4mg/tab and Nimodipine 30mg/tab. CT Angiography showed non-significant decrease in the parenchymal hemorrhage and multiple saccular aneurysms were identified. At this time, Neurology service was considering a Mycotic Aneurysm secondary to Rheumatic Heart Disease. The patient underwent a series of diagnostics (Table 1), all of which revealed unremarkable findings. With normal laboratory results and no episodes of blood pressure elevation, Preeclampsia was ruled out.

Patient's status gradually improved as manifested by improving MMT scores, a GCS of 14 (E4V4M6) and no further decrease in sensorium.

Twenty-four days post ictus, the patient was again noted to be drowsy with GCS of 11 (E4V1M6) and decreased MMT scores. Repeat CT scan revealed a decrease in the previously noted hyperdensity. However, a new hyperdensity was noted due to an acute rebleed. Communicating hydrocephalus was seen necessitating a ventriculo-peritoneal shunt insertion to which the patient initially responded favorably. Neurosurgery suggested that the patient be started on Ampicillin 2g for the management of mycotic aneurysm. On the 25th week of gestation, a multidisciplinary meeting was held and it was agreed upon by the services of Obstetrics, Neurology and Neurosurgery that this is a case of Mycotic Aneurysm due to: occurrence at a young age, multiplicity, history of a valvular heart disease, and febrile episodes prior to neurologic symptoms. Neurosurgery opted for conservative management because the hematoma was resolving and clipping and coiling were not ideal at that time. The Infectious Diseases service discussed that in the absence of positive cultures, Vancomycin (Category C) plus Piperacillin-Tazobactam (Category B) are the antibiotics of choice but since the patient is pregnant, they opted to step down and give Ampicillin-Sulbactam (Category B) instead, for 4-6 weeks. Lastly, all the services agreed that the patient may be discharged if improvement continues. Remote from delivery, no aggressive measures were contemplated with regards to the pregnancy.

Forty days post-ictus, repeat CT scan revealed an almost complete resorption of the bleed. Patient was noted to be GCS 15, with motor strength of 5/5 on the right extremities and 4/5 on left extremities, with good fetal heart tones and no signs of preterm labor. Patient was then cleared for possible discharge. At 51 days post-ictus, patient had sudden onset of severe headache, weakness of the left extremities with motor strength of 1/5, and absent eye opening with isocoric pupils. An acute rebleed was considered. Cranial CT scan was not done due to the patient's unstable status. Furthermore, fetal heart tones were no longer appreciated. Patient expired and was signed out as a case of G2P1 (1001) Pregnancy Uterine at 27 weeks and 2 days AOG by ultrasound, Transtentorial Herniation secondary to Intracerebral Hemorrhage secondary to Ruptured Mycotic Aneurysm, Valvular Heart Disease.

CASE DISCUSSION

An aneurysm is an abnormal focal dilation of the artery which may become secondarily infected due to bacteremia or septic embolization, as in the case of mycotic aneurysm. Cerebral mycotic aneurysms represent less than 5% of all intracerebral aneurysms.[8] Although some authors use the term "mycotic" to describe infected aneurysm regardless of etiology, this report limits use of the term to those aneurysms that develop when material originating in the heart causes arterial wall infection and subsequently dilation.[4]

Aneurysms may be classified into true aneurysms which involve all three layers of the arterial wall, or false aneurysms which is a collection of blood which leaked out of the artery but still confined within the tissue. In the index patient, a history of valvular heart disease increases the risk of developing an infected aneurysm, and endocarditis is identified as the likely etiology in 17 to 29 % of cases.[4] Mycotic aneurysms most commonly develop in the cerebral vessels typically at arterial bifurcations. Septic embolism from the heart can occlude the vasa vasorum of the vessel or the vessel lumen leading to vascular wall infection and mycotic aneurysm formation. Because of its embolic nature, mycotic aneurysms are often multiple, but they can also be solitary.

Mycotic aneurysm should be suspected in any patient with endocarditis who has neurological symptoms that are not explained by systemic illness. In a case series of 28 documented mycotic aneurysms by Burst et. al., 8 patients had a known valvular heart disease and 27 had infective

Table 1. Laboratories

Complete Blood Count					
	3/20/17	**3/23/17**	**3/30/17**	**4/5/17**	**4/6/17**
Hemoglobin	111	104	100	102	86
Hematocrit	0.35	0.32	0.29	0.28	0.25
WBC	10.1	12.2	10.1	8.7	10.1
Platelet Count	386	329	319	292	237

Coagulation Studies			
	3/20/17	**4/5/17**	**4/6/17**
Protime (PT)	11.6	11.2	13.0
PT % activity	130	142	100
PT INR	0.87	0.83	1.00
PT N Control	13.0	13.0	13.0
Activated Plasma Thromboplastin Time (APTT)	20.0	22.9	30.6
APTT N control	32.7	32.5	30.9

Blood Chemistry								
	3/20/17	**3/23/17**	**3/25/17**	**3/27/17**	**3/30/17**	**4/5/17**	**4/6/17**	**4/13/17**
Glucose	4.79							
Na	137	138		134	135	137	138	
K	3.73	3.17		3.87	3.86	4.15	2.78	
Cl	104	102				104	106	
Ca	2.14							
Mg	0.79							
SGOT	100	71						
SGPT	189	181						
LDH	330							
BUN	4.70	1.40			1.90	1.50		
Creatinine	36.76	34.45			29.67	18.97		
ESR			30					130
CRP			18					

Urinalysis			
3/20/17			
Dark Yellow	Slightly Turbid	pH 6	1SG 1.03
(-) Sugar	+1 Albumin	WBC 5-10	RBC 15-20

Gram Stain and Culture Studies	
Blood Gram Stain/Culture Stain Right Arm	Few growth of contaminants
Blood Gram Stain/Culture Stain Left Arm	No growth after 5 days of incubation
Urine Gram Stain	WBC 3-6/OIO Gram Negative Bacilli
Urine Culture Stain	No growth after 2 days incubation
Sputum Gram Stain/Culture Stain	Gram Negative Bacilli

Table 2. Serial Pelvic Ultrasound

Pelvic Ultrasound		
March 21, 2017	**March 28, 2017**	**April 11, 2017**
Single, live, intrauterine pregnancy 23 weeks and 5 days Breech EFW 494 g Placenta fundal, gr. 1 AFI 7.60 cm Oligohydramnios for AOG (5th percentile at 95mm)	Single, live, intrauterine pregnancy 23 weeks and 5 days Cephalic EFW 590 g Placenta anterior AFI 11.39	Single, live, intrauterine pregnancy 24 weeks and 6 days Breech EFW 729 g Placenta anterofundal, gr. 2 AFI 12.63 cm

Table 3. Previous Imaging Procedures

2d Echocardiogram
October 16, 2015
Valvular heart disease, probably rheumatic
Dilated mitral valve annulus with severe mitral regurgitation
Eccentric left ventricular hypertrophyy with normal wall motion, contractility and systolic function
Normal right ventricular dimension with normal wall motion and systolic function
Normal right atrium, main pulmonary artery and aortic root
Normal mean pulmonary artery pressure

Plain Cranial CT Scan
March 10, 2017
Acute Intraparenchymal hemorrhage (approximately 47.8 cc) involving the right frontal lobe with associated intraventricular extension, perilesional edema, mild obstructive hydrocephalus and mild right to left subfalcine herniation. Consider small subacute hematoma within the right posterior parietal lobe with minimal perilesional edema

endocarditis.[1] Lee et. al., stated that mycotic aneurysms can develop from hematogenous spread of infectious microemboli into the vasa vasorum of a normal-caliber artery or a preexisting aneurysm.[9] In the index patient, a history of a valvular heart disease may have resulted in a hematogenous spread of an embolus from the heart. Mycotic cerebral aneurysms can cause headache, seizures, or focal neurologic symptoms but many are asymptomatic until aneurysmal rupture and hemorrhage occur. The index patient initially presented with a seizure episode followed by left sided weakness.

The suspicion of a mycotic aneurysm should be supported by laboratory results and imaging and CT angiography is the most useful for its diagnosis.[5] Findings on CT angiography suggestive of a mycotic aneurysm include the following [4]:

- Saccular, eccentric aneurysm or multilobulated aneurysm
- Soft tissue inflammation or mass around a vessel
- Aneurysm with intramural air
- Perivascular fluid collection

The wide availability of computerized tomographic (CT) scanning has revolutionized the management of intracranial hemorrhage in pregnancy. It is safe for both mother and fetus. A CT scan will accurately demonstrate the bleeding and its extent. In a study by Sun and Slivka, a 29-year-old woman on her 30th week of gestation, who presented with headache and seizure episoxodes, was diagnosed with mycotic aneurysm through a series of imaging studies such as CT scan,

magnetic resonance angiogram and catheter digital subtraction angiography. The patient met the following criteria for mycotic aneurysm – angiographic features, multiplicity, distal location, and young age. According to Sun and Slivka, CT angiography is as sensitive as digital subtraction angiography in detecting the aneurysm. Lee et. al., stated that CT angiography is the current imaging modality of choice for the evaluation of suspected mycotic aneurysms. In a study by Kannoth, new generation CT angiograms have a sensitivity of 90-98% with specificity of 100%. In the index patient, initial imaging modality used was plain cranial CT scan due to financial constraints. CT angiography was done once and revealed a mass effect due to the presence of subfalcine herniation. Also noted were multiple saccular aneurysms on the right middle cerebral artery, posterior cerebral artery, right anterior cerebral artery and another whose exact location cannot be ascertained. This multiplicity suggests mycotic aneurysm.

Using the Kannoth Diagnostic Criteria[6] (see Box 1), the patient scored a total of 3 for (1) the presence of multiple aneurysms on angiography, (2) an age of less than 45 years and (3) the presence of an intraparenchymal hemorrhage on CT scan. The patient had undocumented febrile episodes prior to onset of neurologic symptoms however, it did not last for more than 7 days. The patient also had a history of valvular heart disease but recent endocarditis was not confirmed.

In a case report by El Gawly, a 31-year old pregnant woman on her 39th week of gestation was admitted due to severe frontal headache, photophobia, vomiting and neck pain.[7] Provisional diagnosis was subarachnoid hemorrhage. A live male infant was eventually delivered. Cerebral angiography revealed suspected multiple aneurysms and was managed with craniotomy and clipping of the aneurysm. The postoperative period was eventful and the patient made a complete recovery.

In mycotic aneurysm, the choice of antibiotics should be guided by the most likely infecting organism based on cultures. The optimal duration of antibiotic therapy is uncertain but ideally at least 6 weeks of antimicrobial therapy is administered. In this patient, Ampicillin-Sulbactam was given despite negative culture studies.

Ruptured mycotic aneurysms especially if with mass effect, are generally managed surgically. However, due to the improving clinical status, a ventriculo-peritoneal shunt was done instead to which the patient initially responded favorably. Despite aggressive antimicrobial therapy and a seemingly improving neurologic status, multiple aneurysms persisted. Unfortunately for this patient, the third episode of rupture resulted in a fatal subarachnoid hemorrhage. Remote from term, delivery was not a consideration. Moreover, there is an expected rise back to or above the normal maternal blood pressure in the post partum period and this hemodynamic change can increase the risk of aneurysm rupture. In a study by Barbarite et al, 78% of ruptured aneurysms occurred during the 3rd trimester, compared to only 8% and 11% in the 1st and 2nd trimester respectively.[10] In mycotic aneurysm, vessel walls are more friable and a higher incidence of rebleed is expected.

The normal hemodynamic changes in pregnancy include increase in cardiac output, plasma volume and redistribution of cardiac output between various organs. There is also increase in the levels of estrogen, progesterone, vascular endothelial growth factor and relaxin, and increased wall tension from intraparenchymal artery hypoplasia. Vascular stress is therefore increased during pregnancy. The occurrence of aneurysm affects pregnancy in terms of management. Whether ruptured or unruptured, calcium channel blockers are given for 3 weeks to prevent vasospasm and to maintain a low normal blood pressure to reduce vascular stress. This may result to decreased venous return leading to decreased uteroplacental blood flow.

Box 1 Proposed characteristics included under the supportive criteria for a diagnosis of infectious aneurysm (IA)*

- A. Presence/recent history† of a predisposing infection
(1) Infective endocarditis
(2) Meningitis
(3) Orbital cellulits
(4) Cavernous sinus thrombophlebitis
  - $A_{sum} = 1+2+3+4$.
  - A Category score = 1, if $A_{sum} \geq 1$, 0 if <1
- B. Angiographic features
(1) Multiplicity
(2) Distal location
(3) Fusiform shape
(4) Change in size or appearance of new aneurysm on follow-up angiogram
  - $B_{sum} = 1+2+3+4$
  - B Category score = 1, if $B_{sum} \geq 1$, 0 if <1
- C. Other contributory features
(1) Age less than 45 y
(2) Fever/recent history of fever ⩾7 days
(3) Recent lumbar puncture
(4) Intraparenchymal haemorrhage in CT/MRI Scan
  - $C_{sum} = 1+2+3+4$
  - C Category score = 1, if $C_{sum} \geq 1$, 0 if <1
- Total score $= A_{sum}+B_{sum}+C_{sum}$

*Assign 1 point for each positive response.
†Recent history = within past 8 weeks.

Box 1. Kannoth Diagnostic Criteria [6]

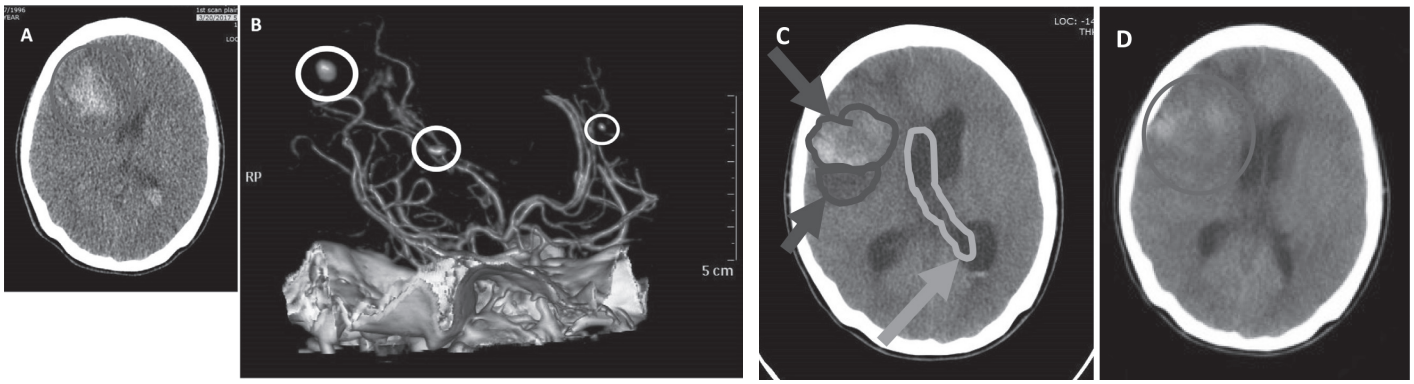

Figure 1. (A) Plain Cranial CT Scan on day of admission showed Parenchymal hemorrhage (14cc) involving the right frontal lobe with intraventricular extension, and resultant mild subfalcine herniation. (B) Sixteen days post-ictus, CT angiography revealed an acute to subacute parenchymal hemorrhage measuring approximately 13cc involving the right frontal lobe with intraventricular extension; multiple saccular aneurysms were noted. (C) Follow-up CT scan showed decrease in density and amount of the previously noted hyperdensity due to evolution of the hematoma in the right frontal lobe, now measuring approximately 9.33cc by CT volumetry. A new hyperdensity was noted posteroinferiorly in relation to the aforementioned hematoma, measuring approximately 8.0cc. (D) There is almost complete resorption of bleed in right frontal lobe and right ventricle, and marked decrease in the size of ventricles.

SUMMARY/CONCLUSION

Mycotic aneurysm in pregnancy is a rare and fatal complication with no widely accepted treatment guideline. This distinct group of intracranial aneurysms stands out from other types of aneurysms due to its infectious etiology, incidence in relatively young patients and multiplicity. It usually occurs in the setting of an infective endocarditis and in this case, the patient was diagnosed with a valvular heat disease but was not monitored accordingly. This patient was managed medically with antibiotics and insertion of a ventriculo-peritoneal shunt. However, these attempts were unsuccessful in preventing another episode of rupture.

The specific management of an infected aneurysm must be individualized and is dependent on the characteristics of the aneurysm. Administration of antibiotics should be given for 4-6 weeks to achieve optimum effect. While a four-vessel angiogram would be ideal to diagnose an aneurysm accurately, the advent of CT angiography has provided an opportunity to monitor the patient non-invasively.

Though there were documented cases of successfully managed mycotic aneurysms, this patient was given limited options due to the attempt of preserving the pregnancy until delivery is acceptable. The patient succumbed after 40 hospital days.

Limitations of this case include (1) insufficient history taking of early signs of aneurysm, (2) inadequate work-up of the patient's valvular heart disease and (3) financial constraints that hindered timely management from its onset

In reviewing the management done to this patient and current literature regarding mycotic aneurysm in pregnancy, we recommend the following measures to manage similar cases especially in a low-resource setting.

In a gravidocardiac patient who presents with neurologic symptoms, we advise that the patient undergo (1) CT angiogram without delay to confirm the presence of aneurysm and its characteristics, (2) 2D echocardiogram to confirm the presence of heart disease and (3) culture studies to identify the infecting organism.

Our primary strategy is to manage the patient conservatively with antibiotics. Serial cranial CT angiogram is advised every 2-3 weeks to monitor the progress of aneurysm. Fetal growth monitoring every 2-4 weeks, congenital anomaly scan and antepartum fetal surveillance are likewise recommended for fetal status monitoring. Delivery should be done as close to term as possible. Early termination is only advisable if with favorable fetal survival dependent on the institution, or if non-reassuring fetal status is noted and patient is already nearing term. Delivery must be coordinated with Neurosurgery as immediate neurosurgical procedure may be necessary if maternal status suddenly. Likewise, overall management must be carefully planned with the help of neurologists, internists, anesthesiologists and pediatricians. ■

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