Anesthetic implications for the parturient with hereditary hemorrhagic telangiectasia

Implications anesthésiques chez les parturientes atteintes de télangiectasie hémorragique héréditaire

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Abstract

Purpose To review the effects of hereditary hemorrhagic telangiectasia (HHT) in the parturient and the anesthetic management of such patients during pregnancy and delivery.

Source A literature search (1966–2008) was performed using Medline and EMBASE databases. Bibliographies of retrieved articles were searched for additional sources.

Principal findings Hereditary hemorrhagic telangiectasia affects 1 in 5000–8000 people. It is a genetic condition in which vascular dysplasia affects many organs particularly the pulmonary, cerebral, gastrointestinal, and spinal vasculature. A large proportion of women with HHT have uneventful pregnancies. However, women can present in pregnancy with clinically silent but potentially life-threatening features of the disorder including fatal hemorrhage from ruptured arteriovenous malformations (AVMs), systemic emboli, and high output cardiac failure secondary to arteriovenous shunting. Literature on the anesthetic management of HHT in pregnancy is limited. Both general and regional anesthetic techniques have been successfully performed in these patients, but are reliant on identifying the presence of specific AVMs; avoidance of cardiovascular instability; and prophylaxis against systemic emboli secondary to pulmonary AVM shunting. The presence of spinal AVMs is considered a relative contraindication to regional techniques. As with other systemic AVMs, these can develop and increase in size during pregnancy with implications for the timing of screening and surveillance.

Conclusions An understanding of the presence and potential development of life-threatening AVMs during pregnancy is imperative for anesthesiologists caring for parturients with HHT. Even in the asymptomatic patient, a high index of suspicion should be maintained, screening performed where possible and anesthetic technique adapted accordingly.

Résumé

Objectif Passer en revue les effets de la télangiectasie hémorragique héréditaire (THH) chez les parturientes et la prise en charge de telles patientes pendant leur grossesse et l’accouchement.


Constatations principales La télangiectasie hémorragique héréditaire affecte 1 personne sur 5000 à 8000. Il s’agit d’une condition génétique dans laquelle une dysplasie vasculaire affecte de nombreux organes, et plus particulièrement la vasculature pulmonaire, cérébrale, gastro-intestinale et rachidienne. La plupart des femmes souffrant de THH ont des grossesses sans complications. Toutefois, les femmes peuvent, durant leur grossesse, manifester des caractéristiques de la maladie silencieuses d’un point de vue clinique mais potentiellement fatales, notamment une hémorragie fatale à cause d’une rupture de malformations artério-veineuses (MAV), une embolie systémique, et une insuffisance cardiaque à haut débit provoquée par un shunt artério-veineux. La littérature portant sur la prise en charge anesthésique de la THH
Les embolies systémiques provoquées par une MAV. La présence d’une MAV rachidienne est considérée comme une contre-indication relative au recours à des techniques régionales. Tout comme c’est le cas avec les autres MAV systémiques, elles peuvent se manifester et croître pendant la grossesse, ce qui aura des répercussions sur le délai de dépistage et de surveillance.

Conclusion. Une compréhension de la présence et du développement potentiel de MAV fatales pendant la grossesse est une condition sine qua non pour les anesthésiologistes qui prennent en charge des parturientes souffrant de THH. Même chez une patiente asymptomatique, un indice de suspicion élevé doit être maintenu, un dépistage réalisé où cela est possible et la technique anesthésique adaptée en conséquence.

HHT and anesthesia

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is an inherited condition characterized by multisystem vascular dysplasia and the development of direct arteriovenous communications between arteries and veins that manifests as telangiectasia of skin, mucous membranes, and arteriovenous malformations (AVMs) in the solid organs of the body. Despite increasing understanding of the genetic and pathological features of the disorder, there is no curative treatment. In Europe, the frequency affecting both sexes has been estimated as being between 1 in 5,000 and 1 in 8,000 sufferers.1 Increased frequency occurs in certain populations, including those of Ain (France), Vermont (USA), and Afro-Caribbean populations in the Netherlands Antilles region.2 Sufferers may be asymptomatic, but 90% of people have signs or symptoms by the age of 40. Symptoms range from mild epistaxis to life-threatening hemorrhage or high output cardiac failure secondary to arteriovenous shunting. While many women with HHT have uneventful pregnancies and straightforward deliveries, the hormonal and cardiovascular changes of pregnancy in these women have been associated with disease progression and presentation of severe complications during this period.1,3 In one case series of 111 HHT affected women, 13 suffered life-threatening complications of HHT during pregnancy.3 A number of case reports exist regarding such episodes (Tables 1, 2).

There is limited literature on HHT in pregnancy and the anesthetic management of such patients during pregnancy and delivery. This review describes the current understanding of HHT and its effects on anesthesia during pregnancy and delivery.

An English language literature search was performed using Medline and EMBASE databases from 1966 to 2008 using the following keywords and terms: “hereditary hemorrhagic telangiectasia”, “HHT”, “Osler-Weber-Rendu”, “pregnancy”, “obstetric”, “anesthesia”, “arteriovenous malformation”, “general anesthesia”, “spinal anesthesia”, and “epidural anesthesia”. Bibliographies of retrieved articles were reviewed for additional sources.

HHT: etiology and diagnosis

Inherited as an autosomal dominant trait, HHT has been linked to mutations in two different genes (endoglin ENG 9q33-34 and activin receptor-like kinase ALK-1 12q11-14) classified as subtype HHT1 or HHT2.2 Both encode receptor proteins in the transforming growth factor β (TGF-β) superfamily (which is involved in cell proliferation, differentiation, adhesion, and migration) and are highly expressed on vascular endothelial cells.3 At least one other gene is thought to be involved.4 Although the specific mutation influences the extremely variable phenotypic presentation of the disease, the diversity of clinical presentations within a family suggests that other epigenetic factors or modifying genes have a role.5

Historically, the disorder was described as a clinical triad of recurrent epistaxis, mucocutaneous telangiectasia, and a positive family history. International consensus criteria (the Curacao criteria) for diagnosis have now been formulated.6 Of four diagnostic features (recurrent epistaxis, multiple telangiectases, visceral lesions, and a positive family history), the presence of three or more confers a definite diagnosis of HHT. In the majority of people, recurrent epistaxis is the earliest presenting feature of the disease and may cause significant anemia. Pulmonary and other solid organ AVMs tend to become apparent from puberty. Mucocutaneous and gastrointestinal telangiectasia also develop with increasing age and may lead to chronic anemia.1

Potentially life-threatening AVMs are most commonly recognized within the pulmonary, hepatic, and cerebral circulations. However, they may develop in any system and have been described in the spinal, coronary, renal, splenic, ocular, uterine, and vaginal circulatory systems.5,7

Management of patients with HHT includes screening for AVMs, correction of vascular anomalies, where possible, and management of complications as they occur. Such management is usually undertaken at specialist units where screening-surveillance recommendations have been published, particularly when pregnancy is being considered or confirmed.1,3,8 Many women with HHT are well-informed
Table 1 Case reports of HHT in parturients: mode of delivery known

| Location   | Reference                        | Patient information          | Clinical presentation                                                                 | Management                  | When          | Gestation and mode of delivery | Anesthesia   | Comments on maternal outcome                                                                 | Infant outcome |
|------------|----------------------------------|------------------------------|--------------------------------------------------------------------------------------|-----------------------------|---------------|-------------------------------|--------------|---------------------------------------------------------------------------------------------|----------------|-------------------------------------------------|
| Pulmonary  | Swinburne et al.                  | 21 yo, 3rd trimester, known HHT | Worsening hypoxemia                                                                  | Surgical resection          | Post-partum  | 35/40; Em LSCS                | –            | Limited exercise tolerance                                                               | Live infant   |
| Pulmonary  | Gammon et al.                     | 27 yo, 2nd trimester         | Hemorrhax, hypoxemia (ruptured AVM)                                                  | Embotherapy                 | At presentation | 30/40; NVD                  | –            | Reduced shunt fraction (7%)  Well                                                          | Live infant   |
| Pulmonary  | Waring et al.                     | 27 yo, G3P2, 2nd trimester, known HHT | Dyspnea, hypoxemia, hemorhorax (ruptured AVM). Complicated by rheumatic heart disease | Embotherapy                 | At presentation | 32/40; NVD                  | Epidural     | Severe mitral regurgitation diagnosed 6 wk post-embotherapy. Post-delivery congestive heart failure resolved. | Live infant   |
| Pulmonary  | Laroche et al.                   | 37 yo, G3P0, 3rd trimester, known HHT | Hemorhorax (ruptured AVM)                                                            | Emergency RLL lobectomy     | At presentation | 37/40; LSCS                  | –            | Well at 3 yr follow up.                                                                     | Live infant   |
| Pulmonary  | Ference et al.                    | 3rd trimester                | Hemorrhax (ruptured AVM)                                                             | Multiple thoracocentesis   | At delivery    | NVD                           | –            | No further complication                                                                  | Live infant   |
| Pulmonary  | Ference et al.                    | Not recorded                  | Hemothypsis (ruptured AVM)                                                           | Embotherapy                 | Post-delivery Em LSCS | –                             | –            | No further complication                                                                  | Live infant   |
| Pulmonary  | Shovlin et al.                   | 27 yo, 2 months postpartum, known HHT | Dyspnea, cyanosis, Deterioration postpartum                                          | Embotherapy at pre-conception diagnosis, Nil required during pregnancy. | N/A            | 38/40; forceps delivery        | –            | Postpartum decreased exercise tolerance and recurrence of PAVMs, too small for embolotherapy. | –             |
| Pulmonary  | Shovlin et al.                   | 16 yo, G1P0, 5 months postpartum, known HHT | Planned follow up                                                                    | Embotherapy at pre-conception diagnosis, Nil required during pregnancy. | N/A            | Premature labor 33/40, forceps delivery          | –            | Deterioration in R-L shunt, arterial oxygenation and exercise capacity.          | –             |
| Pulmonary  | Shovlin et al.                   | 17 yo, G1P0, known HHT        | Previous lung resection at 9 years of age. No treatment reported during pregnancy.    |                              | N/A            | LSCS                          | –            | Miscarriages at 19 and 20 years old. Tubal ligation at 21 years. Severe cyanosis at 29 years, 11 PAVMs embolized with modest improvement in oxygenation. | –             |
| Pulmonary  | Freixinet et al.                  | 24 yo, 2nd trimester          | Hemorrhax, hypoxemia (ruptured AVM)                                                  | Surgical resection          | At presentation | 27/40; LSCS during thoracotomy | GA           | Discharged without sequelae.                                                                | Live infant   |
| Pulmonary  | Adegboyega et al.                 | 33 yo, G3P2, 3rd trimester    | Intrapulmonary hemorrhage and hemorrhax (ruptured AVM)                               | Conservative management     | NA            | El LSCS                      | –            | Well until fatal hemothorax 13 years later.                                               | –             |
| Pulmonary  | Jakobi et al.                     | 28 yo, G1P0, 1st trimester, known HHT | DVT, clubbing and hypoxemia                                                          | Embotherapy                 | Post miscarriage | 25/40; miscarriage            | N/A          | Good condition second pregnancy, term vaginal delivery                                   | Miscarriage 25/40 |

Lomax et al.
<table>
<thead>
<tr>
<th>Location</th>
<th>Reference</th>
<th>Patient information</th>
<th>Clinical presentation</th>
<th>Management</th>
<th>When</th>
<th>Gestation and mode of delivery</th>
<th>Anesthesia</th>
<th>Comments on maternal outcome</th>
<th>Infant outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Jakobi et al. (^a)</td>
<td>19 yo, G1P0, 2nd trimester</td>
<td>Hemothorax (TIA and PAVM missed at 20 weeks)</td>
<td>Surgical resection</td>
<td>26/40 gestation</td>
<td>40/40; NVD</td>
<td>–</td>
<td>Hysteresia improved for remainder of pregnancy. Postpartum embolotherapy of other PAVMs</td>
<td>Fetal growth retardation</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Sugiyama et al. (^a)</td>
<td>29 yo, G1P2, postpartum, known HHT</td>
<td>Known PAVMs pre-conception, but asymptomatic until dyspnea post-delivery. Hepatic shunt noted.</td>
<td>Transcatheter embolization</td>
<td>At presentation</td>
<td>36/40; LSCS</td>
<td>–</td>
<td>Clinically improved</td>
<td>IUGR</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Livneh et al. (^a)</td>
<td>28 yo, G2P1, 2nd trimester, known HHT</td>
<td>Dyspnea, edema secondary to high output heart failure</td>
<td>Diuretics and supportive treatment</td>
<td>Presentation to delivery</td>
<td>NVD</td>
<td>–</td>
<td>Signs and symptoms of heart failure regressed completely at 4 mth postpartum.</td>
<td>–</td>
</tr>
<tr>
<td>Gastric and hepatic</td>
<td>Hillert et al. (^a)</td>
<td>39 yo, G2P?, 3rd trimester, known HHT</td>
<td>Abdominal pain and gastrointestinal bleeding (ruptured AVM)</td>
<td>Bilroth I resection of stomach, embolization of hepatic artery, liver transplantation</td>
<td>Postpartum</td>
<td>29/40; LSCS</td>
<td>–</td>
<td>Well at 1 yr follow up.</td>
<td>–</td>
</tr>
<tr>
<td>Uterine, vaginal, cervical, spinal, and cutaneous</td>
<td>Dahlgren et al. (^a)</td>
<td>29 yo, G?P0, 2nd trimester, known HHT</td>
<td>Known high risk. New uterine, vaginal, cervix and SAVMs</td>
<td>Conservative management</td>
<td>N/A</td>
<td>36/40; LSCS</td>
<td>GA</td>
<td>Uneventful</td>
<td>Live infant</td>
</tr>
</tbody>
</table>

AVM Arteriovenous malformation, DVT deep venous thrombosis, HHT Hereditary hemorrhagic telangiectasia, LSCS Lower segment Cesarean delivery, NVD Normal vaginal delivery, RLL right lower lobectomy, TIA transient ischemic attack

\(^a\)English Abstract available only

\(^b\)Case series of 161 pregnancies in 47 women. Only the 11 cases with complications included in Tables 1 and 2
### Table 2 Case reports of HHT complications in parturients; mode of delivery not known

<table>
<thead>
<tr>
<th>Location of AVM</th>
<th>Presentation</th>
<th>Patient information</th>
<th>Management</th>
<th>Outcomes</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Hemothorax (ruptured PAVM)</td>
<td>2nd trimester</td>
<td>Bed rest and thoracostomy tube</td>
<td>No further complications, live infant</td>
<td>Ference et al. 20</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>28 yo, G3P0, presented 2 mth after miscarriage</td>
<td>Embolotherapy</td>
<td>Improved arterial oxygenation and decreased shunt, uneventful pregnancy following year</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Pulmonary hemorrhage (ruptured PAVM)</td>
<td>G1P0</td>
<td>Not recorded</td>
<td>Fatal</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Minor hemoptysis during second trimester, pulmonary hemorrhage near term (ruptured AVM)</td>
<td>19 yo, G1P0, 2nd trimester</td>
<td>Not recorded</td>
<td>Fatal</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Syncopal episodes, dyspnea</td>
<td>17 yo, G1P0, 2nd trimester</td>
<td>Embolotherapy postpartum</td>
<td>Not recorded</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>20 yo, G1P0, 2nd trimester, known HHT</td>
<td>Not recorded</td>
<td>1 yr postpartum was hypoxemic and 2 PAVMs diagnosed</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Hemothorax (ruptured PAVM)</td>
<td>24 yo, 2nd trimester, known HHT</td>
<td>Embolotherapy</td>
<td>Normalized shunt fraction and no recurrence at follow up, live infant</td>
<td>Bevelaqua et al. 18</td>
<td></td>
</tr>
<tr>
<td>CNS or respiratory</td>
<td>CVA peripartum</td>
<td>GIP?</td>
<td>Pre CVA noted to be cyanosed ?untreated PAVMs</td>
<td>Fatal</td>
<td>Shovlin et al. b14</td>
</tr>
<tr>
<td>CVA ?mechanism</td>
<td>G3P2, 2nd trimester</td>
<td>Treatment of PAVMs refused, cyanosis since childhood</td>
<td>Not recorded</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>Transient hemiparesis 6 mth postpartum</td>
<td>G1P1</td>
<td>Not recorded</td>
<td>Full recovery and two subsequent uneventful pregnancies</td>
<td>Shovlin et al. b14</td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>Intracranial hematoma</td>
<td>24 yo</td>
<td>Not recorded</td>
<td>Not recorded</td>
<td>Gillard et al. a56</td>
</tr>
<tr>
<td>Successive lobar intracerebral hematomas</td>
<td>3rd trimester, known HHT</td>
<td>Not recorded</td>
<td>Not recorded</td>
<td>Neau et al. a57</td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>Right upper quadrant pain; probable hepatobiliary necrosis</td>
<td>33 yo</td>
<td>Pain settled spontaneously.</td>
<td>5 yr later presented with cardiac and liver failure secondary to hepatic AVMs requiring liver transplant. Diagnosis HHT made.</td>
<td>Bauer et al. a58</td>
</tr>
<tr>
<td></td>
<td>Gangrenous cholecystitis</td>
<td>31 yo, 2nd trimester</td>
<td>Cholecystectomy</td>
<td>Biliary necrosis, worsening liver function requiring liver transplantation several months post-delivery</td>
<td>McInroy et al. a59</td>
</tr>
<tr>
<td>Dyspnea, edema secondary to high output heart failure</td>
<td>32 yo, G2P1, 2nd trimester</td>
<td>Not recorded</td>
<td>Signs and symptoms mostly regressed at 4 mth postpartum</td>
<td>Livneh et al. a60</td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>Hemorrhage from root of tongue</td>
<td>Not recorded</td>
<td>Not recorded</td>
<td>Marusov et al. a60</td>
<td></td>
</tr>
</tbody>
</table>

AVM Arteriovenous malformations, CNS Central nervous system, CVA Cerebrovascular accident, G Gravida, P Parity, HHT Hereditary hemorrhagic telangiectasia, LSCS Lower segment Cesarean delivery, NVD Normal vaginal delivery, PAVM Pulmonary arteriovenous malformations

a English Abstract available only

b Case series of 161 pregnancies in 47 women. Only the 11 cases with complications included in Tables 1 and 2
of the risks associated in pregnancy from patient group internet sites, including www.telangiectasia.co.uk and www.hht.org.3

HHT: specific manifestations and pregnancy

Enlargements of arteriovenous malformations may occur during pregnancy and are best described in the case of pulmonary AVMs (PAVMs).1,9–12 The effect of pregnancy on vascular malformations is thought to be due to increased circulating blood volume, cardiac output, venous congestion secondary to the gravid uterus, and/or hormonal effects on the vasculature, with most changes occurring in the second and third trimesters.9,11,13–15 It has been hypothesized that the increased estrogen and progesterone levels of pregnancy increase TGF-β, accentuating the abnormal growth and enlargement of the vasculature.14

Pulmonary features of HHT

Up to 48% of patients with HHT are thought to have PAVMs.16 Pulmonary AVMs are usually multiple in the HHT patient; they may not be clinically evident and are often small and easily missed on routine radiographic examination.17 Presenting symptoms may include chest pain and dyspnea, but the majority of patients are asymptomatic.1,11 Patients may demonstrate clubbing, cyanosis, polycythemia, dyspnea, and bruits on chest examination; though none of these signs are universally present, and a shunt of at least 20% is said to be required for chronic hypoxia-induced clubbing and cyanosis.11,18 Due to the PAVMs typically being located in the lower lobes, postural changes in the degree of shunt in the supine position characteristically show an improvement in oxygenation (as measured by pulse oximetry or arterial gas sampling) over those in the sitting position.9,10 Despite an enlarging PAVM during pregnancy, oxygen saturation may even be higher than pre-pregnancy levels due to the gravid uterus decreasing the blood flow to the lower lung when supine.9

Pulmonary AVMs have been widely investigated in association with HHT and as independent entities. Another risk, aside from the increased risk of rupture presenting with massive hemoptysis and/or hemothorax, includes significant right to left shunt resulting in hypoxemia, heart failure, and the potential passage of emboli across the shunt into the systemic circulation causing complications, such as stroke and cerebral or systemic abscesses.8,18–20 In Shovlin’s series of 262 pregnancies, 1% were associated with a major PAVM bleed, 1.2% were associated with stroke (though not all HHT related), and 1% were associated with maternal death. A prior diagnosis of HHT or PAVM was associated with improved survival in the event of a major complication in pregnancy.3 Indeed, it is recommended that all HHT-affected women should be screened for PAVMs.3 In many cases, the most useful diagnostic imaging modality is helical computed tomography (CT); more invasive pulmonary angiography is reserved for the treatment of PAVMs. Most of the teratogenic effects of ionizing radiation tend to occur during the first 8–11 weeks of gestation.21 However, it is possible to protect the fetus with appropriate shielding. The dose of radiation is estimated as being less than half the maximum recommended occupational exposure for a pregnant worker.15,18 Due to the potentially fatal complications occurring during pregnancy, any woman of reproductive age diagnosed with a PAVM should be offered treatment.12

It may be appropriate to attempt closure of the PAVM either with surgery or, more commonly, with angiographic embolization techniques, which have been undertaken in pregnant patients in their second and third trimesters when interventional radiology carries a lower teratogenic risk.15,21 Nevertheless, more disease may be identified than can be treated. In such cases, management aims to minimize the risk of cerebral embolic events1 by including the administration of prophylactic antibiotics during delivery and paying meticulous attention to avoiding air bubbles and, thus, paradoxical air embolism during intravenous injection. For this reason, a loss of resistance to saline has been recommended for placing an epidural rather than a loss of resistance to air technique.22

It is important to be aware that new PAVMs may develop despite previous negative screening. Further investigation should be considered in any pregnant woman with HHT who has not had recent PAVM screening. Hemoptysis in a pregnant woman with HHT, which cannot be accounted for by epistaxis, should be considered a medical emergency. Some authors would advocate ongoing surveillance of women with known, suspected, or previously treated PAVMs during pregnancy with a variety of investigations, including regular radiographic imaging, blood gas analysis, postural pulse oximetry, and echocardiography.5,10,23 At least three cases of recanalization of previously treated PAVMs have been described in pregnancy.10,11,21 In cases of ruptured PAVMs, recurrent bleeding, large PAVMs, and failed embolization, thoracotomy and lung resection is the remaining option; such cases are described at 26 and 29 weeks’ gestation followed by deliveries at term.19,24

Systemic and pulmonary hypertension have both been described in non-pregnant HHT patients, and the presence of AVMs may reduce the impact of pulmonary hypertension by providing a low-resistance alternate pathway. This should be taken into account if the shunt is reduced by embolotherapy, as may happen during pregnancy. Pulmonary hypertension may be secondary to the increased
cardiac output occurring with systemic AVMs or intrinsic to the pulmonary vasculature; however, it is rarely severe.2

Cerebral AVMs

Ten percent of patients with HHT have cerebral AVMs (CAVMs) which can present with headache, seizures, focal neurology, or cerebral hemorrhage.1 Cerebral AVMs may be found anywhere in the vasculature of the central nervous system. Patients less frequently exhibit cerebral telangiectasia, aneurysms, and cavernous angiomas.1 Magnetic resonance imaging (MRI) is the most sensitive non-invasive detection tool, and, compared to computerized tomography or angiography, it reduces the radiation risks to the fetus. However, it has been suggested that it is prudent to avoid its use in the first trimester.25 Even with MRI, a proportion of CAVMs may not be detected. In addition, the investigation is contraindicated in patients with non-MRI compatible coils in their pulmonary circulation.1 Routine screening is not undertaken in the United Kingdom unless there are neurological signs, symptoms, or a family history of cerebral hemorrhage; therefore, the presence of CAVMs is often unknown during pregnancy and delivery.3 However, most of the central nervous system-related complications of HHT probably arise via pulmonary AVMs.17

Whether pregnancy increases the size of CAVMs in HHT or the likelihood of bleeding is an area of some controversy due to limited data, even in CAVMs in non-HHT women.1,25–34 It was initially thought that there was a significant risk of bleeding associated with rapid changes in cardiac output in any woman with CAVMs, for example, during the first trimester, labor, and delivery, but a retrospective analysis of 451 women found that the 3.5% risk of primary hemorrhage from a CAVM of any etiology during pregnancy did not differ significantly from the annual bleeding rate in a non-gravid patient.29,31 No relationship with parity or trimester has been found.35

In the event of any CAVM rupture during pregnancy, the risk of recurrent bleeding is unknown, but estimates have been as high as 27–30%, particularly during labor, delivery, and subsequent deliveries.32,36 Furthermore, bleeding from a CAVM during pregnancy carries a higher maternal mortality (28%) than in the non-gravid patient.32 There are descriptions in the literature of the successful treatment of both ruptured and unruptured CAVMs of varying etiologies during pregnancy that were subsequently followed by successful delivery at term.25,31–34

Spinal AVMs

Spinal AVMs (SAVMs) affect up to 1% of patients with HHT.3 Rupture of SAVMs is uncommon, and most patients present with a gradual onset of symptoms ranging from neck or back pain, to nerve root pain, to focal sensory and motor neurology, to disturbance of defecation and micturition.37

Pregnancy exacerbates symptoms, and reports of SAVM regression postpartum have been reported.37,38 The neurological deficits can result from a change in the arteriovenous (A-V) pressure gradient, with the increased venous pressure decreasing spinal blood flow. This, in combination with reflex intramedullary vasodilatation, increases tissue pressure and hence edema, with worsening ischemic damage to the cord.37 Therefore, much attention is focused on avoiding the increases in venous pressure which occur with uterine contractions and valsalva maneuvers.39

Gastrointestinal AVMs

Fifteen percent of HHT patients are affected by gastrointestinal telangiectasia, particularly in the stomach and proximal duodenum, causing iron deficiency anemia. Hepatic AVMs (HAVMs) may occur in up to 30% of HHT patients, and are more prevalent in women.1,5 Up to 50% of HAVMs are thought to be clinically silent, but they can cause a large left to right shunt and present with high output heart failure, portal hypertension, portosystemic encephalopathy, or biliary disease.5,40 Hereditary hemorrhagic telangiectasia may cause liver fibrosis and cirrhosis.41 This has been attributed to increased sinusoidal blood flow, resulting in deposition of fibrous tissue and nodule formation in the liver. An alternative hypothesis is the presence of nodular transformation and hyperplasia leading to “pseudo-cirrhosis”.42

It is thought that there is enlargement of HAVMs during pregnancy similar to that occurring in other organ systems.1,4,44 Two case reports have been published of women presenting with hepatic AVMs and bile duct ischemia during pregnancy. Although some cases resolve post delivery, in at least one case, transplantation was required postpartum because of progressive liver dysfunction due to the advanced stage of HHT in the liver.43

Other systems

AVMs have also been identified in HHT patients in the coronary circulation, the ophthalmic system, and the spleen;5 however, no reports have identified these AVMs as being associated with pregnancy. Although there are reports of vaginal AVMs in the pregnancies of non-HHT women, even if a vaginal delivery is planned, there are no recommendations for screening of the pelvis for HHT.44 However, screening for HHT would appear prudent.
HHT and the obstetric anesthesiologist

All HHT pregnancies should be considered of significant risk. The specific manifestations of the disease that are identified in any one patient will influence the choice of obstetric analgesic or anesthetic technique, and further investigation to exclude secondary clinical disease may also be indicated. The two areas of greatest concern in planning anesthetic techniques are the respiratory and nervous systems, and these are considered below.

Respiratory system

Epistaxis affects 90% of patients with HHT by the age of 21 years. Opinions differ over whether pregnancy affects the severity of epistaxis, but it is rarely the presenting feature of the disorder in pregnancy. Mucocutaneous telangiectasia has been described on the lips, gums, tongue, palate, epiglottis, as well as in the larynx, trachea, and bronchi. They are unlikely to cause significant problems other than the potential for increased bleeding from oropharyngeal trauma, such as may occur at laryngoscopy and endotracheal tube manipulation during general anesthesia for Cesarean delivery. Avoidance of blind intubation techniques is advisable.

In the presence of pulmonary AVMs in pregnancy, the risks associated with anesthesia mainly relate to the management of significant shunt and/or heart failure and the anticipation of potential systemic embolism across the AVM. Antibiotic prophylaxis is recommended for vaginal and operative delivery to avoid septic embolism causing systemic infection, particularly cerebral abscesses. Management of general or regional anesthesia should aim to minimize right to left shunting by reducing pulmonary vascular resistance and maintaining systemic vascular resistance. Indeed, a (non-pregnant) patient with known bilateral PAVMs and HHT underwent general anesthesia with worsening hypoxemia, which was attributed to either an increase in pulmonary vascular resistance due to positive pressure ventilation or possibly to a decrease in cardiac output (also as a result of positive pressure ventilation) leading to mixed venous desaturation and subsequent arterial desaturation. Epidural analgesia has been used in labor and subsequent anesthesia for tubal ligation in a patient with HHT, PAVMs, and mitral regurgitation. Epidural management was chosen primarily because of the valvular heart disease, but the authors speculated that it may have reduced surges in cardiac output and consequent distension of the PAVMs. The risk of epidural hematoma from a spinal AVM was outweighed by the risks posed by the cardiovascular disease. Occasionally anesthesia for Cesarean delivery has been provided as a result of the need for emergency management of PAVM complications, as in one report describing a woman with HHT at 27 weeks of pregnancy who developed a hemothorax secondary to PAVM rupture. During surgical resection of the PAVMs, the woman suffered from hypovolemic shock, which necessitated an emergency lower segment Cesarean delivery resulting in a good outcome for both mother and baby.

Nervous system

A number of reports and reviews exist regarding the management of pregnant women with cerebral AVMs outside the context of HHT. While it is likely that the same issues apply to women with HHT and cerebral AVMs, evidence is lacking.

Operative or vaginal delivery has been used for non-HHT women with treated and untreated cerebral AVMs. In patients with high operative risk, inoperable lesions, or low-risk presenting in advanced pregnancy or labor, a conservative approach is taken with regard to the CAVM. Although there is a trend towards Cesarean delivery in these women, some reports claim that this affords no definite advantage over vaginal delivery. However, elective Cesarean delivery does allow for planning and for relevant expertise to be readily available.

Both general anesthesia and regional techniques have been described in pregnant women with ruptured and unruptured CAVMs. It is known that the rise in arterial pressure during a valsalva manoeuvre is mirrored by an increase in cerebrospinal fluid (CSF) pressure. However, when released, CSF pressure decreases more quickly than arterial pressure, and this is thought to be the point where the AVM wall is potentially under the most stress. This cardiovascular instability with labor and valsalva manoeuvres can be managed with regional techniques including epidurals, or pudendal blocks if spinal AVMs are suspected. Successful vaginal delivery with epidural analgesia has been described in a 21-year-old woman at 39 weeks’ gestation with a ruptured CAVM that was incompletely resected. A combined spinal-epidural technique was rejected because identification of epidural malfunction would be delayed, and there were concerns regarding the maintenance of maternal cardiovascular stability and the risk of a post-dural puncture headache confusing the neurological picture. The rationale behind the use of epidurals for operative delivery lies in the good quality analgesia both peri- and post-operatively, the avoidance of cardiovascular stresses, and the ability to monitor the neurological condition of the awake patient; however, attention to anti-emesis is mandatory to avoid unnecessary increases in intracranial pressure. Yih reports the management of a 37-year-old non-HHT woman presenting at 32 weeks’ gestation with a recurrent bleed
from a previously ruptured CAVM. Using intravenous labetalol and sublingual nifedipine, a healthy female was delivered by Cesarean delivery under epidural anesthesia with both central venous and invasive arterial blood pressure monitoring. An epidural was selected over a single-shot spinal to minimize the risk of sudden hypotension. Incremental doses of epidural lignocaine were given to gain adequate anesthesia, and cardiovascular stability was maintained, even on administration of the 5 U of oxytocin. A further rise in cardiac output is caused by oxytocic drugs, but their judicious use, rather than avoidance (with the risk of uterine atony), has been advocated—again, precautions may be needed to avoid vomiting, particularly if ergometrine is required. However, in the presence of raised intracranial pressure, it has been argued that epidural injection may exacerbate this and, therefore, it should be avoided.

Both general and regional techniques require meticulous control of blood pressure to avoid alterations in intracranial pressure, and invasive monitoring should be considered on an individual basis. However, balancing the low risks associated with placing an arterial line, it would appear prudent to use invasive arterial monitoring particularly when cardiovascular instability is expected, such as during induction and emergence from general anesthesia and in establishing regional and particularly spinal anesthesia for Cesarean delivery. Specific disease variants, such as the presence of a large AVM, untreated or ruptured AVM would also indicate the need for invasive monitoring.

There are two published cases of paralysis and cord compression after regional anesthesia for delivery due to SAVMs. Most anesthesiologists would consider confirmed SAVMs as a contraindication to the use of spinal and epidural anesthesia, even if positioned at a distant vertebral level. Reticence to perform regional techniques is due to the potential for direct trauma to an AVM with the potential for epidural hematoma and the risk of CSF loss and resulting tension placed on the wall of an SAVM by deliberate or accidental dural puncture. Furthermore, changes in cord hemodynamics by large SAVMs can cause widespread enlargement of the epidural veins, increasing the chance of trauma. Additional potential mechanisms of harm include increases in epidural pressure secondary to epidural injection and epidural- or spinal-induced hypotension (with or without use of vasopressors), which may further compromise spinal cord perfusion. It has been suggested that even distant SAVMs may cause a change in venous drainage locally at the site of injection, thus altering the A-V gradient. Conversely, some argue that the increase in pressure following epidural injection is only transient, and in the rare situation of a patient who has sustained a spinal injury from a distant SAVM bleed, there may even be some benefits of an epidural in managing autonomic hyperreflexia perioperatively, thus avoiding the need to use suxamethonium with the risk of associated hyperkalemia.

The successful management of a patient with a cervical SAVM undergoing Cesarean delivery using spinal anesthesia has been described. This technique avoids the risk of hemodynamic instability associated with airway manipulation under general anesthesia where spinal cord perfusion is already vulnerable. However, the associated risk of marked hypotension with regional anesthesia can result in increased venous pressure from vomiting. “Steal” secondary to vasodilatation below the level of block, along with vasopressor use, may further alter spinal cord blood flow. Alternatively, a combined spinal-epidural anesthesia has been used for Cesarean delivery in a non-HHT pregnant woman with a SAVM at T10. This technique enables low volumes of anesthetic to be injected epidurally while limiting the increases in epidural pressure and providing a gradual onset block with minimal blood pressure changes, thus reducing the need to use vasoactive agents.

One case report of a pregnant woman with HHT describes the use of regional analgesia for labor pain without complication; it is not stated whether there was prior imaging of her spinal circulation. If there has been no diagnosis of spinal AVM, then some authors have recommended an MRI in order to exclude such pathology and to enable the patient to have regional anesthesia or analgesia. However, when considering the potential development and growth of pre-existing lesions during pregnancy, the optimum time for this is unclear.

Overall, issues regarding the nervous system that are of primary concern to the obstetric anesthesiologist include a high index of suspicion for undiagnosed manifestations of the disorder as well as management of known manifestations of the condition. Decisions regarding anesthetic technique depend on the identification, evolution, and treatment of CAVMs as well as the presence or absence of spinal AVMs. Even in the patient with relatively mild disease, consideration needs to be given to the unrecognized development or progression of arteriovenous malformations. Although not commented on in the literature, it would appear prudent to undertake and document a neurological examination for these women, though circumstances may preclude this prior to the provision of regional anesthesia and analgesia.

**Conclusion**

From this review of the literature, it is clear that most women with HHT have uneventful pregnancies and safe deliveries. However, due to the deterioration of pre-conception AVMs and the development of new AVMs, a small
proportion will present with clinically silent but potentially life threatening complications of the disorder. These are most commonly located in the pulmonary vasculature, followed in frequency by the cerebral, gastrointestinal, and spinal circulations. The complex and varied clinical features of this disorder cause particular problems during pregnancy due to the cardiovascular and hormonally induced enlargement of certain AVMs with concurrent risks of rupture, shunt-induced high cardiac output failure, and systemic embolism. Uncertainty remains regarding the optimum screening and surveillance of these patients during pregnancy. However, all HHT pregnancies should be considered as high-risk.

Since PAVMs occur in up to 48% of HHT patients, these women are screened for them and treatment is considered, particularly before conception. Where possible, symptomatic patients in pregnancy are treated, and sudden dyspnea or hemoptysis should be treated as a medical emergency. Antibiotic prophylaxis should be provided during delivery to reduce the risk of infected systemic emboli.

Up to 10% of HHT patients may have CAVMs. Compared to North America, pre-conception cerebral MRI is not routinely performed in the UK unless patients are asymptomatic. Routine screening for SAVMs (affects 1%) is not performed in either region. Thus, unless CAVMs have been excluded, prolonged second stages of labor should be avoided. The avoidance of cardiovascular instability associated with labor and delivery favor a regional anesthetic technique for vaginal or operative delivery; however, this option is complicated by the small but potentially devastating risk of trauma to SAVMs. Early imaging for SAVMs would seem logical and possible with appropriate fetal shielding, but the optimum timing to identify newly developed malformations during pregnancy is unclear.

Ultimately, before balancing the risks of imaging, intervention, and mode of delivery, each individual patient should be evaluated by a multidisciplinary team for the presence (from previous screening) and further development of old and new AVMs during pregnancy. This facilitates more informed decision-making regarding general and regional techniques for the safe anesthetic management of labor and delivery.

Conflicts of interest  None declared.

References


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