Management of a rare case of multiple arteriovenous malformations in the context of neurofibromatosis type 2

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The present article describes a 15-year-old girl with two arteriovenous malformations (AVMs) – on her left labia majora and left thigh – in association with genetically confirmed de-novo neurofibromatosis type 2. This patient’s labia majora AVM was particularly difficult to treat using embolization techniques. She experienced numerous complications including pulmonary edema, venous thromboemboli, severe local area necrosis and a damaged anal sphincter. She required surgical debridement and reconstruction of her suprapubic and perineal regions. The left thigh AVM was later treated using a combination of embolization and surgical resection with no complications. Six years later, she is doing well. To the authors’ knowledge, the present report is the only case of neurofibromatosis type 2 associated with extracranial arteriovenous malformations described in the literature.

Key Words: Arteriovenous malformation; Complications; Embolization; Labia majora; Multiple; Neurofibromatosis type 2; Surgical resection

Arteriovenous malformations (AVMs) comprise only 2.9% of the patient population of the specialized multidisciplinary pediatric Vascular Birthmark Clinic at the Alberta Children’s Hospital (Calgary, Alberta) (1). AVMs are high-flow vascular malformations composed of dysmorphic arterial and venous vessels connected directly to one another without an intervening capillary bed (2). They usually present as a lump, and can be characterized by a bruit, thrill or palpable sensation. AVMs are most commonly found intracranially; if extracranial, they most frequently involve the head and neck, followed by extremity, trunk and visceral regions (3). AVMs occur with equal frequency in males and females. While 40% to 60% are visible at birth, only 30% become clinically apparent in childhood. Certain triggers can cause rapid growth of AVMs such as trauma, clotting, ischemia, embolization, partial resection, and hormonal changes that occur during pregnancy and puberty (4). Extracranial AVMs can present with pain, bleeding and progressive enlargement, with local tissue infiltration and destruction (5,6).

AVMs of the vulva may present as a lump before puberty, but patients usually present after puberty, due to physiological increase in blood flow to the vulva at this time (7). In addition, vascular anomalies of the vulva on their own are exceedingly rare (8). Treatment depends on presentation, location and size (9). Recurrence of AVMs is common, especially with embolization alone (10). AVMs and other vascular malformations are recognized manifestations of neurofibromatosis type 1 (11) but not neurofibromatosis type 2 (NF-2). The present case is unique in that the patient has multiple extracranial AVMs in addition to NF-2.

CASE PRESENTATION

A 15-year-old girl was referred by her family physician to the Vascular Birthmark Clinic at the Alberta Children’s Hospital. Swollen areas on her left labia majora and left lateral thigh had been progressively enlarging over four years. She was not experiencing heavy menstrual periods. On examination, the swelling on her left labia majora was tender, warm, pulsatile and had a palpable thrill (Figure 1). The swelling on her left lateral thigh was minimally tender and nonpulsatile (Figure 2). A Doppler ultrasound, followed by magnetic resonance imaging (MRI), confirmed the diagnosis of AVMs (2 cm × 2 cm × 4 cm labia majora and 2.8 cm × 0.9 cm × 1.5 cm left thigh) (Figures 1 and 2). The labia majora AVM was classified as a Schobinger stage 2 lesion and the lateral thigh AVM a Schobinger stage 1 lesion. The lateral thigh AVM was closely observed for progression (4).

Embolization with and without surgical resection of the labia majora AVM was discussed with the patient and her family. They opted to pursue embolization alone because they were concerned that surgical resection of such an anatomically sensitive area would be potentially disfiguring. A previously obtained magnetic resonance angiography (MRA) image was helpful in planning treatment (Figure 3). The main arterial supply was from the left internal pudendal artery originating from the left internal iliac artery. A second arterial supply was from the extrernal pudendal artery, originating from the femoral artery. Venous drainage was into the superficial pudendal veins, with main drainage into the left common femoral vein. There was also collateral flow into the right common femoral vein.

Under general anesthesia, the patient underwent an angiogram and embolization of the AVM with 100% dehydrated alcohol, approached via the right common femoral artery. Inflating a balloon inside the left common femoral vein with each injection blocked outflow of the alcohol. In the early postoperative period, the patient developed acute respiratory distress; a chest x-ray showed unilateral pulmonary edema and a venous Doppler ultrasound revealed a nonocclusive thrombus of the left common femoral vein. She was managed in the pediatric intensive care unit overnight and started on anticoagulation treatment. The possible etiologies for her pulmonary edema include alcohol-related pulmonary hypertension and subsequent decreased myocardial function, or pulmonary embolus from the femoral vein thrombus. Additionally, she developed a painful ulcer of the mucosal surface of the left labia, which healed with topical cream application over the next two weeks.

Two months later, the patient was investigated for the development of severe intermittent headaches, which started after the embolization episode. The family was concerned with the possibility of intracranial AVMs. MRI of the brain did not reveal an AVM but did reveal multiple schwannomas of the left third, right sixth and ninth, and bilateral fifth and eighth cranial nerves. A clinical diagnosis of NF-2 was made. She had no family history of NF-2. She saw multiple specialists and the genetics team confirmed a de novo mutation. The multidisciplinary team had not previously encountered a patient with the combined diagnoses of AVMs and NF-2. To date, no specific treatment has been required for the intracranial schwannomas other than yearly evaluation.

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Eight months after the embolization, the pulsation and swelling in the area of the labia majora AVM was returning and the lateral thigh AVM was also increasing in size. It was decided to proceed with a second embolization procedure for the labia majora AVM. Repeat angiogram showed that the labia majora AVM had decreased in size from the original presentation, but was still supplied by a branch of the left internal pudendal artery, as well as a new feeding branch from the right superficial femoral artery. Repeat embolization with alcohol was completed over two sessions 48 h apart. The first approach was to embolize the left internal pudendal artery; the second approach was to obstruct the new branch from the right superficial femoral artery using microcoils in addition to the alcohol. She was anticoagulated for seven days. Unfortunately, she developed extensive ischemic changes of the surrounding areas of her mons pubis, perineum and perianal area. These ischemic changes were initially managed conservatively and eventually progressed to full thickness necrosis, which completely demarcated by two weeks postprocedure (Figure 4).

Surgical debridement and reconstruction was required. Operative findings included full-thickness necrosis of the mons pubis with thrombosis of subcutaneous veins and necrosis of fat. The left buttck had full thickness necrosis extending into the anal canal. Undermining and advancement of local tissue achieved closure of the debrided areas. Intraoperatively, pediatric general surgery was consulted due to the lack of anal sphincter tone.

She was kept on bed rest with a foley catheter in place and serial compression devices on her legs. Complications developed including rectal incontinence, urinary tract infection, partial dehiscence of her wounds and an extensive left femoral vein thrombus that extended to the left external iliac vein, despite her previous anticoagulation. Her thrombophilia screen was negative. She required anticoagulation for many months postoperatively.

Two weeks later, the patient returned to the operating room for a second debridement, definitive closure of the abdominal wall with an abdominoplasty type flap and closure of the perineum with rotation flaps. The lower abdominal flap was elevated and advanced distally. A quilting type suture was used in the deep tissue to relax tension on the closure. The result was a W-type scar above the external genitalia. She was in hospital for 35 days.

The patient was followed by multiple specialists over the ensuing two years for both her initial diagnoses and her new complications post-treatment. However, she slowly improved and returned to her normal activities due to an unrelenting attitude and dedication to

![Figure 1](image1.png)

**Figure 1** Left panel Arteriovenous malformation of left labia majora. Enlarged area in red circle is pulsatile, warm and tender. Right panel Magnetic resonance imaging (T1 axial) with gadolinium: lobulated mass is confined to the left labia, consisting largely of dilated vascular structures with no appreciable soft tissue component. Nidus measures approximately $2 \text{ cm} \times 2 \text{ cm} \times 4 \text{ cm}$. Large flow voids are apparent, consistent with a high-flow vascular malformation

![Figure 2](image2.png)

**Figure 2** Left panel Arteriovenous malformation of left lateral thigh. Enlarged area in red circle is minimally tender and non pulsatile. Right panel Magnetic resonance imaging (T1 axial) with gadolinium: ill-defined lesion in the deep superficial fascia and superficial aspect of left vastus lateralis muscle; no mass effect – measures $2.5 \text{ cm} \times 1.3 \text{ cm} \times 2.9 \text{ cm}$

![Figure 3](image3.png)

**Figure 3** Pelvic magnetic resonance angiography. The left labia majora arteriovenous malformation is in the red circle. The main arterial supply is from the left internal pudendal artery (pudendal a), originating from the left internal iliac artery (iliac a). Venous drainage is into the superficial external pudendal veins, which empty into the left common femoral vein

![Figure 4](image4.png)

**Figure 4** Complications of embolization. Patient seen in the operating room two weeks after her second embolization procedure. The areas of cutaneous necrosis have demarcated on the mons pubis. The open area is also apparent on the left buttck and extends into the perianal area. The upper horizontal green line marks the typical level of an abdominoplasty incision. The lower oblique green lines mark the inguinal folds
A rare case of multiple AVMs

Two years after her previous operation, she underwent further reduction of the left labia majora and revision of the lower abdominal scar. The left thigh AVM nidus was also excised at the same time due to its symptomatic nature and continued progression. This excision was performed 24 h after embolization with alcohol, with no complications. At the time of this operation, there was no sign of recurrence of the left labia majora AVM. MRA performed 12 months postoperatively demonstrated almost total regression of the labial AVM (Figure 5).

Six years after she initially presented, she continues to attend the pediatric Vascular Birthmark Clinic. There has been no further recurrence of the labia majora AVM or the left thigh AVM. She is satisfied with her cosmetic outcome (Figure 6). She experiences little to no rectal incontinence, and is no longer on anticoagulation. Her headaches are manageable and she continues to be followed yearly by neurosurgery with MRIs of her brain. A gynecologist and a colorectal specialist also follow her.

DISCUSSION

Given the multimodality management of AVMs, surgical planning should be performed in a multidisciplinary setting (1,12) such as the Alberta Children’s Hospital Vascular Birthmark Clinic. Treatment must be individualized because of the variable presentation, location and size of AVMs (9). The Schoenbinger classification may be used as a guideline: stage 1 lesions are quiescent, and may be followed closely or excised electively; stage 2 lesions are expansive, and generally require combined embolization and surgical resection; stage 3 lesions are destructive, and require technically more challenging embolization and surgical resection than stage 2 lesions; and stage 4 lesions result in cardiac failure (4).

Vascular anomalies of the vulva are exceedingly rare and those that are reported are usually venous malformations (7,8). In a review involving 646 women with anomalies of the female lower genital tract, only five venous malformations of the vulva and no AVMs were noted (8). AVMs of the vulva are rarely encountered and particularly challenging due to the complex local anatomy. Vulva AVMs require treatment before the onset of menarche because of the potential for massive hemorrhage (13). However, our patient’s age at presentation was postmenarche. Combined embolization and surgical resection is the most successful treatment for well-localized stage 1 or 2 AVMs (3). In young patients, complete resection is often impossible or would result in severe disfigurement. Embolization and sclerotherapy may be used to control symptoms and to limit the extent of the AVM. The risk of solely using interventional radiology techniques is that there may be only transient improvement of the AVM due to new vessel recruitment (10,14,15). Embolization can be performed using coils or glue, either accessing the malformation from proximal arterial or retrograde venous approaches. Sclerotherapy involves direct puncture of the nidus during local arterial and venous occlusion (3). Local and systemic effects of alcohol embolization include possible necrosis of skin, nerve, fat and muscle, hemoglobinuria, thrombosis of deep veins, distant embolism and cardiac arrest. Our patient developed many of these complications. In retrospect, initially using a combined approach of surgical resection 24 h to 48 h postembolization may have elicited better results for our patient in terms of fewer complications, less chance of recurrence and better cosmesis.

The numerical incidence of multiple extracranial AVMs occurring in a single patient has not been reported in the literature and, thus, is believed to be extremely rare. When patients have been reported with multiple AVMs, it tends to be in the context of a hereditary entity such as hereditary hemorrhagic telangiectasia, Wyburn-Mason syndrome, Rendu-Osler-Weber syndrome or a strong family history of vascular malformations (16,17). Our patient presented with multiple extracranial AVMs in the context of a de-novo NF-2 mutation. AVMs and other vascular malformations are recognized manifestations of...
neurofibromatosis type 1 (11) but not NF-2. NF-2 is an autosomal-dominant multiple neoplasia syndrome occurring in one in 25,000 live births, with nearly 100% penetrance by 60 years of age (18). To our knowledge, this is the first association of AVMs and NF-2 reported in the literature; a possible biological basis between NF-2 and AVMs remains to be explored.

This patient will require continued multidisciplinary follow-up and she is being transitioned to adult care providers. The pediatric Vascular Birthmark clinic will help with this transition. Some patients teach one a great deal about management of diagnoses, about dealing with complications and about how to help that next patient. She has been one of these patients. Our current protocol for management of symptomatic AVMs includes multidisciplinary assessment (plastic surgery, interventional radiology, pediatrics and any other pertinent specialty), diagnostic imaging with ultrasound, MRI, MRA and, occasionally, computed tomography angiography, discussion of treatment options with the family and, if appropriate, we favour combined embolization followed 24 h to 48 h hours later by surgical resection rather than embolization alone.

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