Original article

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Vascular malformations of the female and male genitalia: type and distribution patterns revealed by magnetic resonance imaging

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Summary

Background. Vascular malformations of the genitalia often go undetected in clinical examination. These vascular malformations can cause a variety of clinical symptoms such as swelling, pain and bleeding.

Aim. To characterize the distribution patterns of genital vascular malformations using magnetic resonance imaging (MRI) and to correlate these patterns with clinical findings in order to guide diagnostic decisions.

Methods. A retrospective analysis of MRIs of the pelvis and legs in 370 patients with vascular malformation was performed to determine the involvement of the internal and external genitalia.

Results. In 71 patients (19%), genital involvement could be identified by MRI. Of these, 11.3% (8 of 71) presented with internal involvement, 36.6% (26 of 71) with external involvement and 52.1% (37 of 71) with both internal and external involvement. Over half (57.1%) of the 49 patients with visible external genital signs detected during a clinical examination had additional internal genital involvement.

Conclusions. Genital involvement is a common finding in patients with vascular malformation of the legs and/or pelvis. Based on our data, we recommend MRI of the legs and pelvic region in patients with externally visible signs of a vascular malformation of the external genitalia in order to exclude additional internal involvement.

Introduction

Vascular malformations are rare, congenital and lifelong diseases caused by mesenchymal and angiogenesis disorders during embryogenic development.[1] Vascular malformations can affect various body parts, such as the head and neck, extremities and pelvis, as well as the genital area.[2–4] Depending on the specific blood flow characteristics, vascular malformations can be differentiated into fast-flow lesions such as arteriovenous malformations (AVMs) and slow-flow lesions such as venous malformations (VMs).[5] According to the classification by the International Society for the Study of Vascular Anomalies (ISSVA), vascular malformations can be subdivided into two subtypes: simple (e.g. isolated VMs) and combined [e.g. venous lymphatic malformation (VLM)].[6] Clinical examination and medical history are the primary diagnostic tools for assessment of vascular malformations.[1] Various imaging techniques such as magnetic resonance imaging (MRI), computed tomography, ultrasonography and angiography can be used to confirm the diagnosis.[7]

In this study, we focused on vascular malformations with genital involvement. This presentation is relatively rare[8–10] but represents an important clinical

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finding as it can cause pain, swelling, bleeding, urinary dysfunction, reduced fertility and pregnancy complications, along with subsequent psychological challenges.[7,11–14] For assessment of the internal genitalia, additional imaging such as MRI has proven valuable.[10,15,16]

The main objective of this retrospective study was to determine the prevalence of internal genital involvement in cases with visible signs of malformation of the external genitalia in order to guide clinicians in further diagnostic decisions. A secondary objective was to assess the types of malformation and the prevalence of genital involvement in patients with vascular malformations in the legs and/or pelvis. We focused on the effect of using MRI to detect genital vascular malformations by comparing the outcomes of MRI with the detection rates achieved by clinical examination (clinical findings) alone.

Methods

The study was reviewed and approved by the ethics committee of Regensburg University (approval no. 18-886-104), and the study was exempt from informed consent.

Study design and participants

This was a cross-sectional, explorative, retrospective study of patients with vascular malformations in the legs and/or pelvis, assessed during the period November 2011 and February 2018 in the tertiary care interdisciplinary Vascular Anomalies Centre (VAC) of the University of Regensburg. The study enrolled 378 patients (130 male, 248 female; mean ± SD age 27.8 ± 17.3 years, range 1.4–63.9 years; 141 patients were aged < 18 years).

Magnetic resonance imaging

At their initial referral, each patient underwent MRI according to a standardized protocol, covering the entire lower body from the pelvis to the feet (independent of the size of the vascular malformation). Standardized MRI was performed on a 3 Tesla MRI scanner (Magnetom Skyra, Siemens Healthineers, Erlangen, Germany) using flexible body coils. The MRI protocol includes a short tau inversion recovery sequence in the axial and coronal planes, a T2-weighted turbo spin echo (TSE) sequence in the axial plane, a T1-weighted TSE sequence in the coronal plane, a time-resolved MR angiography with the contrast agent gadobutrol (Gadovist©; Bayer, Leverkusen, Germany) and a T1-weighted high-resolution three-dimensional gradient echo with spectral fat saturation. The MRI datasets were reviewed by two independent radiologists with extensive experience in imaging of vascular anomalies.

Vascular malformation categorization

Assignment of malformation type was based on clinical diagnosis, which included evaluation of clinical examination, medical history records, and MRI scans of the legs and pelvis. Using the ISSVA classification, specific MRI features were assessed and patients were categorized into four cohorts: AVM, VM, LM and combined malformation (Table 1).[6] For combined vascular malformations, the genital malformation type was assessed separately from any malformations in extragenital regions of the pelvis and/or legs.

Magnetic resonance imaging assessment and correlation with clinical symptoms

To determine the prevalence of genital involvement in our study population, we used the MRI scans to assess the morphology of the external genitalia (female: labia majora and labia minora; male: penis and scrotum) and internal genitalia (female: vagina, uterus, ovary and cervix; male: testis, prostate and seminal vesicle). We also identified the distribution patterns and categorized the genital malformations into three groups: internal, external, or both external and internal (Fig. 1, lower half).

Table 1 Clinical diagnosis of genital involvement.

	Patients with:	
Clinical diagnosis[a]	Vascular malformation, *n*	Genital involvement, *n* (%)
All patients	370	71 (19.2)
Simple malformations		
Arteriovenous	61	6 (9.9)
Venous	167	22 (13.2)
Lymphatic	13	4 (30.8)
Combined malformations		
All	129	39 (30.2)
Capillary venous lymphatic	55	24 (43.6)
Venous lymphatic	20	6 (30.0)
Capillary venous	49	9 (18.4)
Capillary lymphatic	5	0 (0)

[a]Malformation types were verified by the patient's results (including medical history, clinical examination, magnetic resonance imaging).

To explore the prevalence of internal genital involvement in cases with external visible genital malformation signs, the medical records of patients with genital involvement in the MRI were accessed. We reviewed the clinical findings noted during the clinical examination and any associated genital symptoms. External involvement often produces visible symptoms such as soft tissue swelling, skin discoloration or dysplastic veins, and bleeding or lymphorrhoea.[2,3,6] These symptoms can often be noticed upon clinical examination and are described as 'visible malformation signs' for this study (see Fig. 2 as an example for visible malformation signs). Concomitant symptoms, such as pain and discomfort, as well as pregnancy-associated changes in symptoms, were also assessed. We correlated these clinical findings with the MRI findings to determine the prevalence of internal genital involvement in cases with visible signs on the external genitalia (Table 2).

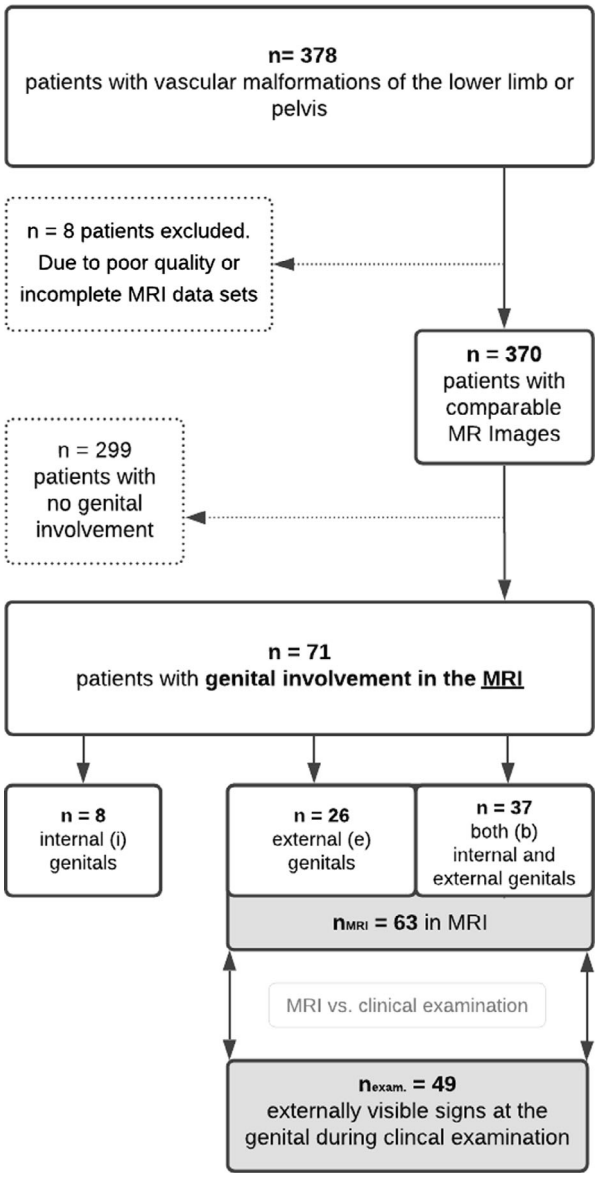

Figure 1 Subject flow diagram: inclusion and exclusion criteria are provided in the upper half, while the bottom half shows the differentiation of the patients into the three subcohorts, based on internal, external, or both external and internal genital involvement. MRI, magnetic resonance imaging.

Results

Magnetic resonance imaging scans

After analysing the MRIs of the 378 patients, 8 patients were excluded (5 had incomplete MRI acquisition, 3 had motion artefacts). Of the remaining 370 patients, 71 (19%) had signs of vascular malformations affecting the genitalia on their MRI scans (Fig. 1, upper half). Table 1 shows the different malformation types seen in the 370 patients and the percentages of participants with genital involvement for each malformation type. In our study population, we did not find any patients with simple capillary malformation, as this can usually be diagnosed without application of MRI.[17]

Categorization of vascular malformations

After identifying the 71 patients with genital involvement, the type of vascular malformation was verified by MRI (Table 2). In combined malformations, local genital findings can differ from those of other anatomical locations. For example, the capillary portion of a combined capillary VLM may involve only the distal leg, whereas the lymphatic and venous part of the malformation can be located in the genital area. This explains the apparent discrepancy in group sizes between Tables 1 and 2.

Correlation between results of clinical examination and magnetic resonance imaging

Table 2 provides the percentages of patients with internal, external, and both internal and external genital involvement as detected via MRI. Isolated internal involvement was detected in 8 patients (11%) and was most frequent in the AVM group; there were no cases in the VLM group. There were 26 patients (37%) with vascular malformation of the external genitals without involvement of internal genital structures, while 37

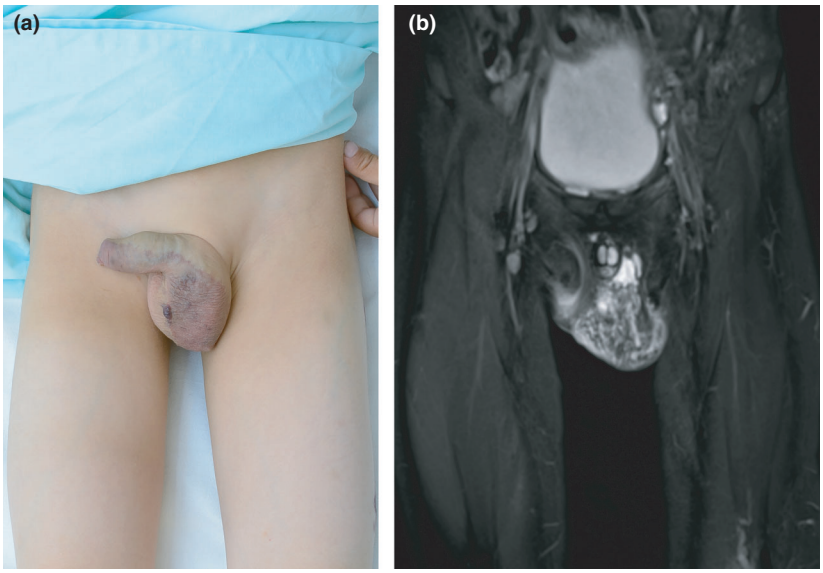

Figure 2 (a, b) Patient with capillary–venous–lymphatic malformation: (a) clinical image of the pelvis and thighs. (b) contrast-enhanced T1-weighted magnetic resonance image of the same area (coronal view), showing venous portions in scrotum and penis with prostate and seminal vesicle involvement, and capillary portions at the skin level of the scrotum and penis.

patients (52%) had involvement of both the external and internal genitalia.

Upon clinical examination (without the use of MRI), external genital involvement could be identified visually in 49 of the 71 patients (69%) noting symptoms such as bleeding, swelling, skin discoloration, dysplastic veins and lymphorrhoea (Table 2). By contrast, MRI scans assisted in the identification of 63 patients (total patient numbers for external and 'both' groups in Table 1 and bottom half of Fig. 1) with vascular malformation lesions on their external genitalia. Thus, even where there was external genital malformation, 22% of cases remained undetected by clinical examination (an example of a case with discrete external involvement and massive involvement of internal structures is shown in Fig. 3).

This discrepancy between clinical and MRI findings varied by sex, with 33 of female cases detected by clinical examination vs. 36 detected by MRI, compared with 16 vs. 27, respectively, for male cases.

Of the 49 patients who were found to have visible signs of malformation on the external genitalia during the clinical examination, 28 (57%) had additional internal genital involvement revealed by MRI. Distinct sex differences were observed for the occurrence of visible clinical signs on the external genitalia: the records of 33 of the 40 female patients (82.5%) and 16 of the 31 male patients (51.6%) described at least one of the predefined visible signs. Swelling and skin discoloration were found more often in female than in male patients (swelling: 60% vs. 22.6%; discoloration: 52.5% vs. 29%, respectively).

Of the 48 patients in the VM group (detected by MRI), 32 (67%) had external genital malformations that could be identified by means of clinical examination, with swelling being the most common sign, whereas 44 participants (92%) who had malformations identified by MRI also had external genital involvement that was seen on the MRI images (i.e. the MRI identified an additional 12 patients with external genital involvement that was missed by clinical examination). The proportion of patients with the lowest occurrence of externally visible signs was the AVM subgroup (16.7%). All patients in the VLM group and 87.5% in the LM group showed visible signs, with the most common findings being dysplastic veins (66.7%) and lymphorrhoea (62.5%), respectively.

Pain was the most pronounced concomitant symptom of malformations (45 of 71 patients, 63.4%). Another concomitant manifestation was worsening of symptoms such as swelling and bleeding during pregnancy, which was identified in five women in the VM group.

Discussion

In this study, we determined the prevalence of genital involvement in a relatively broad population of patients with vascular malformation of the legs and/or pelvic regions. Without considering malformation type or patient sex, 19% of the participants had malformation involvement in the external and/or internal genitalia. Vogel *et al.*, who investigated vascular anomalies in the external genitalia of female children, reported

Table 2 Magnetic resonance imaging and clinical findings.

Local malformation type	MRI findings			Clinical findings and concomitant symptoms			
				Visible signs[b,c] (n = 49)		Pain (n = 45)[c]	
	Total (n = 71)[a]	Female (n = 40)	Male (n = 31)	Female (n = 33)	Male (n = 16)	Female (n = 30)	Male (n = 15)
AVM, *n* (%)	6 (8.5)	2 [5][d]	4 [13][d]	1	0	2	2
Internal	3		3				1
External	1	1		1		1	
Both	2	1	1			1	1
VM, *n* (%)	48 (67.6)	32 [80]	16 [52]	26	6	26	6
Internal	4	4				3	
External	19	13	6	12	2	11	1
Both	25	15	10	14	4	12	5
LM, *n* (%)	8 (11.3)	2 [5]	6 [19]	2	5		3
Internal	1		1				1
External	5	1	4	1	4		1
Both	2	1	1	1	1		1
VLM, *n* (%)	9 (12.7)	4 [10]	5 [16]	4	5	2	4
Internal							
External	1		1		1		1
Both	8	4	4	4	4	2	3

AVM, arteriovenous malformation; LM, lymphatic malformation; MRI, magnetic resonance imaging; VLM, venous lymphatic malformation; VM venous malformation. [a]MRI verified malformation types in patients with genital involvement (n = 71). [b]Visible signs during clinical examination were defined as swellings, bleeding, skin discolorations, dysplastic veins, lymphorrhoea or thrombophlebitis. [c]For each investigated malformation type, the total numbers of male and female patients with visually detected and painful genital malformations (results of clinical examination) are listed. [d]Values in square brackets indicate the relative frequency of gender-specific distributions.

that 1.9% (60 of 3186) of their participants had vascular malformation of the genitals.[8] This discrepancy between that study and ours may be explained by different inclusion criteria. The previous study included all types of vascular anomalies (vascular malformations and vascular tumours) and enrolled patients who displayed vascular anomalies anywhere in the body, not just the pelvis and/or legs.

The main objective of our study was to determine the probability that patients with a vascular malformation of the external genitalia detected using clinical findings such as swelling or skin discoloration would have additional internal genital involvement. Our findings indicated that 57% of patients (37 of 63) with externally visible malformation signs had additional internal genital involvement. A study from 2017

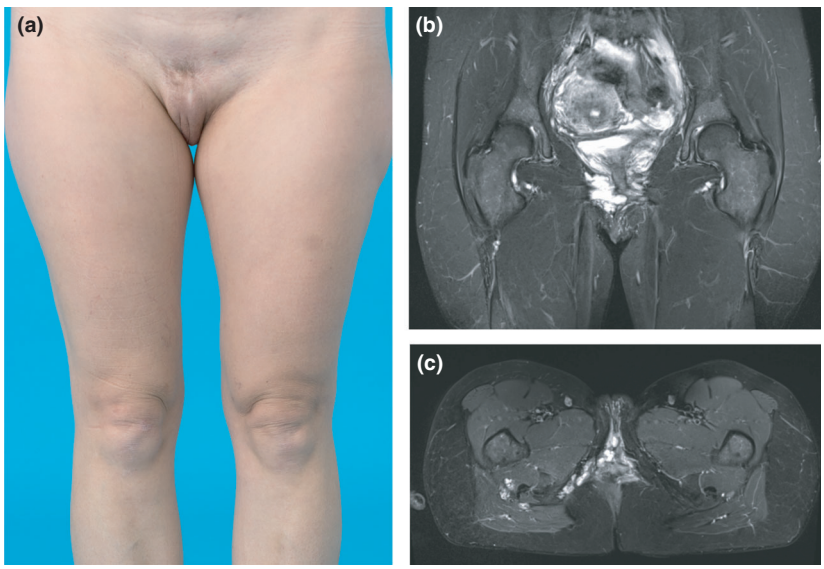

Figure 3 (a–c) Venous malformation: (a) clinical image of the pelvis and legs; (b,c) contrast-enhanced T1-weighted magnetic resonance image in (b) coronal view and (c) axial view of the same area, showing discrete external involvement of the right labia and extensive internal involvement (vagina, cervix, uterus, right ovary).

determined the frequency of an additional internal vascular anomaly in cases of focal genital venous malformations to be 45% (10 of 22 patients).[18] Despite different inclusion criteria regarding malformation types, our results confirm that approximately 50% of external genital cases also have internal involvement. This suggests that in cases of vascular malformation of the external genitalia, a small externally visible finding is often combined with a larger internal lesion, which can cause substantial health concerns if undetected.

The fact that external genital involvement was undetected in 22% of the cases by clinical examination supports the need for MRI in these cases. Possible reasons why some vascular malformation with external involvement were not identified during clinical examination may include patient reluctance to report local symptoms or a relatively deep malformation that involves the subcutaneous external genitalia and may not be sufficiently close to the skin to be noticeable.

Consequently, our findings confirm the importance of using additional imaging in the detection and treatment of vascular malformations. In these cases, MRI should be the technique of choice as it provides excellent soft-tissue contrast and high spatial resolution, and allows for tracking of flow patterns using a contrast agent with high specificity and sensitivity.[4,10,15,16,19]

In the current study, five patients with VM reported worsening of symptoms during pregnancy, which supports other studies that focused on female genitalia[3,9] and should be considered in the clinical care of women of childbearing age.

There are some limitations of our study that should be considered. First, we used a retrospective study design, which may result in less accurate patient reports compared with a prospective study. Another limitation is the heterogeneity of our study population. Other studies have focused on one entity such as VM or included only one sex.[3,9,18] Conversely, the heterogeneity of our study may also be a strength, as it may represent a more realistic patient population comparable to that seen in everyday clinical practice. It also enabled us to generate a relatively large sample size in this specific field compared with previous studies (which had 60,[7] 56,[8] 22[9] and 8[18] patients).

Conclusion

Our study showed a strong association between vascular malformation of the legs and/or pelvis and genitalia in both males and females. More importantly, we showed that additional involvement of internal genital structures is a common finding in patients with visible malformation lesions of the external genitalia. This highlights the importance of using MRI in malformation diagnostics as it increases the chance of identifying additional internal genital involvement. In several cases MRI also detected discrete, visually inconspicuous malformations of the external genitalia. Based on our findings, we recommend that whenever there is a suspicion of vascular malformation of the genital area or the legs, MRI of the pelvic region and legs should be performed at least once in the patient's lifetime.

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What's already known about this topic?

- Vascular malformations can involve the genitalia in rare cases.
- Involvement of the external genitalia is mostly detectable via clinical examination, whereas internal genital involvement needs further diagnostic tools.
- MRI is the gold standard technique to understand the underlying pathology of the vessel architecture and flow characteristics.

What does this study add?

- Visible external genital involvement can be seen as tip of the iceberg, as around 50% of cases with visible vascular malformation signs at the external genitalia are also affected by additional internal genital involvement.
- MRI can detect cases with internal genital involvement even if there are no or only very subtle external signs.

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