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VENOUS MALFORMATIONS IN PEDIATRIC PATIENTS: CLINICAL MANIFESTATIONS, DIAGNOSTIC METHODS, AND TREATMENT STRATEGIES

Shaban Memeti[1, 2], Marijan Kamiloski[1, 2], Roza Sokolova[1, 2], Haris Sulejmani[2], Njomza Ljumani Bakiu[1], Violeta Zahovska[4], Gani Ceku[3]

[1] University Clinic of Pediatric Surgery, Skopje, North Macedonia

[2] Faculty of Medicine, S. S. Cyril and Methodius University in Skopje, North Macedonia

[3] Clinic of Pediatric Surgery, University Clinical Centre of Kosovo, Prishtina, Kosovo

[4] University Hospital for Surgical Diseases "St. Naum Ohridski" Skopje, Republic of North Macedonia

Corresponding author: Haris Sulejmani, email address: sulejmani.haris@hotmail.com, mobile phone: +38971986840

ABSTRACT

Introduction: Venous malformations (VMs) are a prevalent type of congenital vascular disorder, affecting nearly 1% of the population. These low-flow vascular anomalies often lead to chronic swelling, pain, and mobility challenges, often interfering with a child's daily life. Their development is mostly caused by genetic abnormalities in the TIE2/TEK and PIK3CA pathways, which cause poor venous remodeling and vascular proliferation. This study aims to assess the clinical manifestations, diagnostic methods, and therapeutic alternatives for pediatric venous malformations, emphasizing the effectiveness of different treatment modalities. Recognizing clinical presentations and understanding treatment outcomes are essential for improving early diagnosis and optimizing patient-centered care strategies.

Materials and methods: Between 2019 and 2023, the Clinic for Pediatric Surgery in Skopje treated 38 pediatric patients with venous abnormalities. Patient demographics, lesion characteristics, and treatment options (including conservative management, sclerotherapy, and surgical intervention) were examined.

Results: The majority of patients (39.5%) received conservative treatment, whereas 23.7% underwent sclerotherapy and 34.2% needed surgical intervention. Sclerotherapy results were evaluated according to lesion size. Treatment was effective for smaller lesions (<5 cm), while bigger or recurring cases required multiple treatment sessions.

Conclusion: The results highlight the importance of early identification and individualized treatment strategies for pediatric venous malformations. Sclerotherapy is the primary therapeutic option for minor to moderate lesions, whereas surgical intervention is designated for symptomatic or refractory patients. A multidisciplinary approach is crucial for enhancing patient outcomes, and future research should focus on the advancement of minimally invasive therapeutic techniques and the exploration of targeted genetic medicines.

Keywords: venous malformations, pediatric vascular anomalies, sclerotherapy, surgical management, congenital vascular disorders, imaging in vascular anomalies

INTRODUCTION

Vascular malformations make up 1% of all pathological disorders in pediatrics. A vascular abnormality refers to abnormal development of capillaries, veins, arteries, and lymphatic vessels. [1] Slow-flow vascular abnormalities with dysplastic venous channels that fail to retract during

embryogenesis cause chronic swelling, discomfort, and functional disability [2]. From isolated cutaneous lesions to large infiltrative abnormalities affecting muscles, joints, and internal organs, VMs vary in clinical presentation [3].

Genetic mutations, particularly in the TIE2/TEK and PIK3CA pathways, play a significant role in the development of venous malformations. These alterations affect endothelial cell function, disrupting normal vascular remodeling and contributing to irregular venous growth. [4]As a result, vascular proliferation may become dysregulated, which, in turn, can facilitate progressive lesion expansion and an elevated risk of thrombosis.[5] In contrast to infantile hemangiomas, which generally experience spontaneous regression, vascular malformations (VMs) endure throughout life and frequently necessitate multimodal treatment approaches, such as sclerotherapy, laser therapy, and surgical excision, contingent upon the size of the lesion and its anatomical involvement [6].

Timely diagnosis and proper management of venous malformations in children are critical to preventing complications such as localized intravascular coagulopathy (LIC), persistent pain, and reduced mobility. [7] Due to the complexity of these lesions, a multidisciplinary strategy that includes pediatricians, interventional radiologists, dermatologists, and vascular surgeons is frequently essential to enhance treatment outcomes [8]. This paper explores venous malformations in pediatric patients, with a focus on their underlying pathogenesis, clinical manifestations, diagnostic challenges, and treatment options. These vascular anomalies are frequently mistaken for hemangiomas, which can result in delayed diagnosis and inappropriate management. Enhancing clinical awareness is crucial for facilitating timely and effective interventions.

MATERIALS AND METHODS

From 2019 to 2023, a total of 38 patients with venous malformations were treated at the Clinic for Pediatric Surgery in Skopje. The patients initially reported to the outpatient department with a diagnosis of hemangioma.

Patient histories revealed that all lesions were congenital. Parents observed that the swelling pronounced during crying or physical activity and did not regress over time. Diagnosis was confirmed via ultrasound, while MRI was performed in two children with atypical features to exclude arteriovenous malformations. The cohort comprised 20 males and 18 females, aged between 4 and 14 years, with a mean age of 8.6 years. In 28 individuals, the venous malformation was situated on the extremities (14 with lesions on the upper extremities and 14 on the lower extremities), on the back in 4 patients, and in the neck region in 3 patients. In the remaining three individuals, the lesion was located in different regions (facial, inguinal area, etc.). The primary symptom was discomfort and edema in the afflicted region, reported by nearly all participants. Concerning lesion dimensions, three patients exhibited lesions measuring up to 5 cm, whilst the rest 35 patients had lesions beyond 5 cm. Conservative management was implemented in 15 patients.

RESULTS

The management of venous malformations in this study included a variety of therapeutic approaches, reflecting the diverse clinical presentations and severity of lesions. Conservative treatment was employed in 15 patients (39.5%), whereas sclerotherapy was delivered to 9 individuals (23.7%). Surgical intervention was necessary for 13 patients (34.2%), while only 1 patient (2.6%) had a combination approach utilizing numerous therapy modalities. The majority of patients (63.2%) responded well to non-invasive treatments, including conservative management and sclerotherapy. However, a significant portion (34.2%) required surgery, highlighting the importance of tailoring treatment strategies to lesion severity and patient-specific factors. (Table 1).

Table 1. *Treatment Distribution of Patients with Venous Malformations (N = 38)*

Treatment	Conservative	Sclerotherapy	Operative	Combined
Number of patients	**15**	**9**	**13**	**1**

The images (Figure 1) show several types of venous malformations affecting the upper and lower extremities. The top row shows a localized venous malformation on the palm, which appears as a compressible, bluish subcutaneous mass with well-defined boundaries. The bottom row shows venous malformations on the lower extremities, which are distinguished by large, dilated veins and patchy blue coloring. These findings are consistent with low-flow vascular abnormalities, which can result in edema, discomfort, and functional impairment. Early diagnosis and effective intervention are critical to improving patient outcomes.

Figure 2a shows a venous or lymphatic malformation in the lateral neck before sclerotherapy, presenting as a bluish, swollen lesion without signs of acute inflammation. After treatment, Figure 2b demonstrates a reduction in swelling with post-procedural bruising and mild discoloration, indicating a positive therapeutic response.

Sclerotherapy patients were classified according to the extent of their lesions and the method of treatment, which offered a perspective on the efficacy of this therapeutic approach. Sclerotherapy was administered as a monotherapy to three patients in Group I, who had venous malformations that were less than 5 cm in size. The results were exceptional, indicating that this intervention is particularly effective for minor lesions. In Group II, three patients with venous malformations more than 5 cm in size underwent sclerotherapy as monotherapy. However, the results were classified as satisfactory, suggesting a slightly lower success rate than that of smaller lesions. Group III was composed of four patients who underwent repetitive sclerotherapy sessions over a three- to four-month period. The outcomes were still classified as good, despite the necessity of this approach in these cases. This underscores the fact that larger or more complex malformations may necessitate multiple treatment cycles to achieve optimal results. (Table 2)

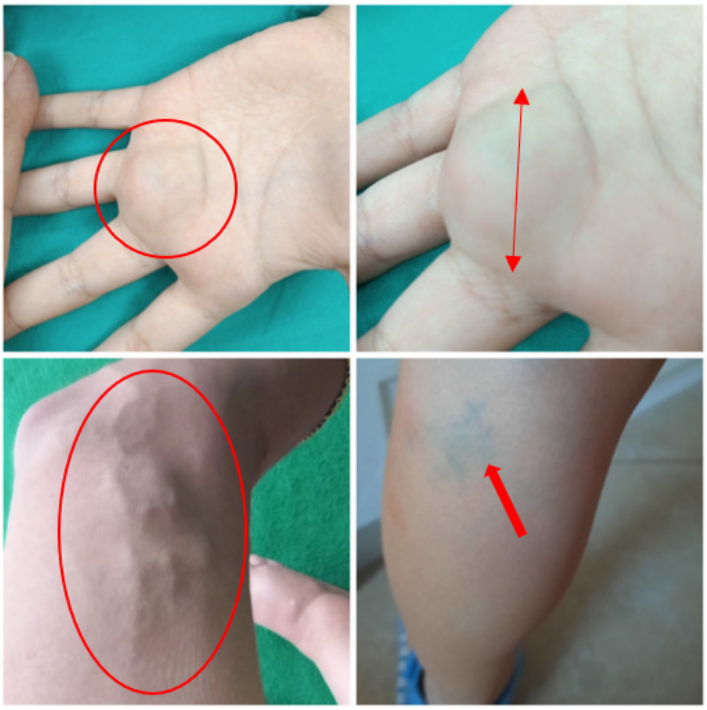

Figure 1. *Clinical Presentation of Venous Malformations in Pediatric Patients*

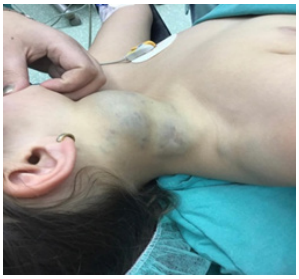

Figure 2a/2b. *Pre- and post-sclerotherapy changes in a venous malformation.*

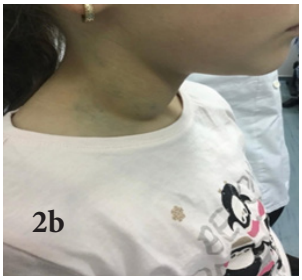

Table 2. *Sclerotherapy Treatment Categories and Patient Outcomes*

Category	Treatment	Patients	Results
Group I: Venous malformations (< 5 cm in size)	Sclerotherapy as monotherapy	3	Excellent
Group II: Venous malformations (> 5 cm in size)	Sclerotherapy as monotherapy	3	Good
Group III: Sclerotherapy - repetitive after 3 to 4 months	Sclerotherapy as monotherapy - repetitive after 3 to 4 months	4	Good

These findings indicate that while conservative and minimally invasive treatments were generally effective throughout the study period (2019-2023), a considerable number of patients still required surgical management, especially for larger or symptomatic lesions.

Figure 3 illustrates the distribution of treatment approaches among 38 patients, specifically the proportion of conservative, sclerotherapy, operative, and combined treatments. Furthermore, Figure 4 illustrates the efficacy of sclerotherapy in relation to various lesion sizes, emphasizing the necessity of repeat procedures in specific instances and the influence of lesion size on treatment outcomes.

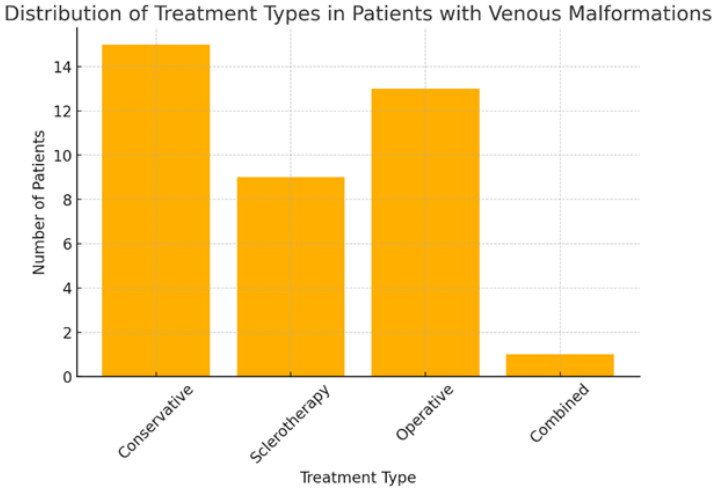

Figure 3. *Distribution of Treatment Types in Patients with Venous Malformations*

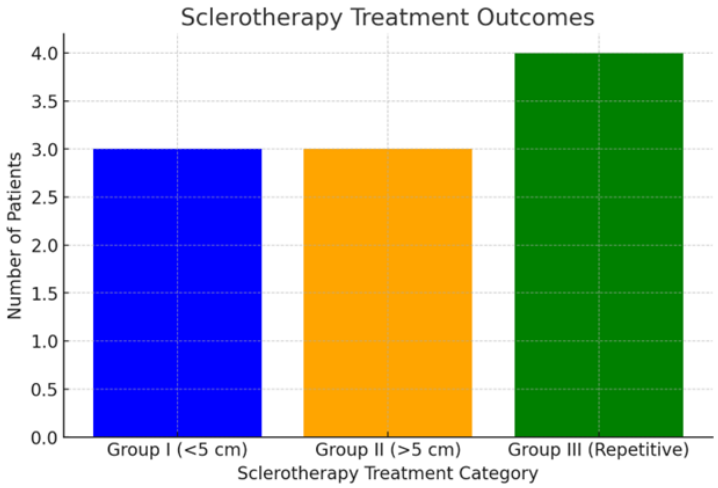

Figure 4. *Sclerotherapy Treatment Outcomes*

DISCUSSION

The management of venous malformations in this study, covering the period from 2019 to 2023, included a variety of therapeutic approaches, highlighting the varied clinical presentations and lesion severity.

The introduction of imaging techniques, including Doppler ultrasonography, magnetic resonance imaging (MRI), and computed tomography (CT), has markedly enhanced the precision of vascular malformation diagnosis and lesion characterization [9]. Doppler ultrasound is the primary diagnostic modality, demonstrating compressible, hypoechoic venous channels with diminished flow, while MRI offers comprehensive anatomical details and is crucial for evaluating deep or severe lesions [10]. The application of contrast-enhanced MRI has shown advantageous in distinguishing VMs from other vascular abnormalities, facilitating treatment planning [3].

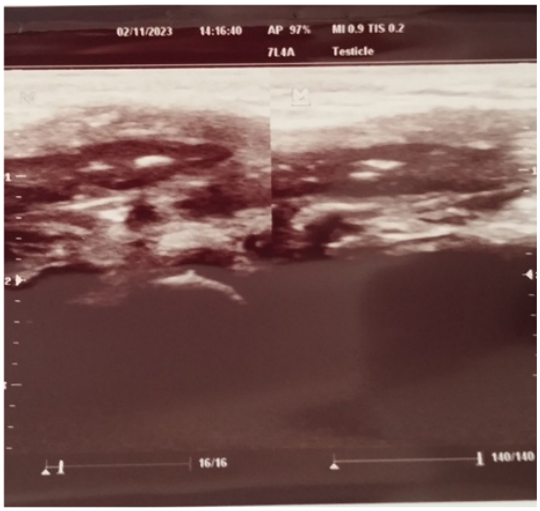

Figure 4. *Ultrasound Imaging of a Testicular Venous Malformation*

The grayscale B-mode ultrasound scan shows heterogeneous hypoechoic and hyperechoic areas, indicating the presence of a venous malformation. The image (Figure 4) shows dilated venous channels with irregular architecture, characteristic of low-flow vascular malformations. While this imaging modality offers detailed anatomical insights, Doppler ultrasound is crucial for assessing slow venous flow and differentiating the lesion from other vascular anomalies. Further evaluation using contrast-enhanced imaging may be required to determine the level of involvement and optimize treatment plans.

Therapeutic strategies for venous malformations have progressed throughout time, with sclerotherapy becoming the primary treatment modality. Sclerosing drugs, including ethanol, polidocanol, and sodium tetradecyl sulfate, cause endothelial injury and fibrosis, resulting in lesion reduction [6]. The selection of sclerosing agent is based upon the lesion's location, dimensions, and the patient's tolerance. Bleomycin sclerotherapy has been especially efficacious in managing large and infiltrative vascular malformations, owing to its reduced risk of tissue necrosis relative to ethanol-based treatments [5]. Recent studies indicate that the combination of sclerotherapy and laser treatment can improve outcomes in superficial vascular malformations.

Surgical resection is typically designated for well-defined, symptomatic lesions that do not respond to conservative treatments or sclerotherapy [10]. Nonetheless, total excision is frequently difficult, especially for diffuse or infiltrative vascular malformations, as inadequate resection may result in recurrence and worsen symptoms [8]. In some instances, surgical intervention is coupled with preoperative sclerotherapy to diminish lesion size and mitigate surgical complications [6].

Extensive venous malformations increase the risk of localized intravascular coagulopathy (LIC), leading to recurring blood clot formation and potential bleeding complications. [5] The management of LIC entails anticoagulation utilizing low-molecular-weight heparin (LMWH) and, in certain instances, fibrinolytic treatment, especially for individuals experiencing recurrent thrombosis [7]. Furthermore, it is imperative to watch for indications of disseminated intravascular coagulation (DIC), especially in individuals presenting with extensive, symptomatic lesions [5].

Despite progress in diagnostic and therapeutic techniques, the long-term care of pediatric vascular malformations remains complex. Consistent follow-up is essential to evaluate lesion advancement, determine therapy effectiveness, and address consequences [9]. Our findings emphasize the importance of a multidisciplinary approach in optimizing patient care. Future research should focus on refining minimally invasive therapies and exploring targeted genetic treatments to enhance outcomes [4]. Considering the influence of venous

malformations on quality of life, a patient-centered, multidisciplinary strategy is essential for enhancing outcomes in affected children [1].

CONCLUSION

Venous malformations are complex vascular anomalies that require early and correct diagnosis to avoid consequences such as localized intravascular coagulopathy (LIC), chronic pain, and functional loss. This study emphasizes the various clinical manifestations of pediatric VMs and the significance of a multimodal therapy approach. Sclerotherapy is highly effective for treating small to moderate venous malformations, especially when used alone for lesions <5 cm. However, larger or more complex lesions frequently require numerous therapy cycles or surgical intervention, emphasizing the importance of personalized patient management. Since venous malformations can progress over time, long-term follow-up is crucial to monitor treatment effectiveness, prevent complications, and improve functional outcomes. Future developments should concentrate on improving minimally invasive therapeutic approaches, expanding pharmacological therapy options, and investigating genetic-based targeted medicines to improve venous malformation care. A multidisciplinary collaboration among pediatricians, vascular surgeons, and interventional radiologists is crucial for providing comprehensive, patient-centered care and optimizing outcomes in the management of pediatric venous malformations.

Abbreviations

VMs – Venous Malformations

LIC – Localized Intravascular Coagulopathy

DIC – Disseminated Intravascular Coagulation

MRI – Magnetic Resonance Imaging

CT – Computed Tomography

LMWH – Low-Molecular-Weight Heparin

Ethical Approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of the Clinic for Pediatric Surgery, Skopje. The data collection and analysis followed the institution's guidelines for research on human subjects.

Informed Consent

Written informed consent was obtained from the legal guardians of all pediatric patients included in this study. Patients' data were anonymized to ensure confidentiality.

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study.

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Резиме

ВЕНСКИ МАЛФОРМАЦИИ КАЈ ПЕДИЈАТРИСКИ ПАЦИЕНТИ: КЛИНИЧКИ МАНИФЕСТАЦИИ, ДИЈАГНОСТИЧКИ МЕТОДИ И СТРАТЕГИИ НА ЛЕКУВАЊЕ

Шабан Мемети[1, 2], Маријан Камилоски[1, 2], Роза Соколова[1, 2], Харис Сулејмани[2], Њомза Љумани Бакиу[1], Виолета Заховска[4], Гани Чеку[3]

[1] Универзитетска клиника за детска хирургија, Скопје, РС Македонија

[2] Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[3] Клиника за детска хирургија, Универзитетски клинички центар на Косово, Приштина, Косово

[4] Универзитетска клиника за хируршки болести „Св. Наум Охридски“, Скопје, РС Македонија

Вовед: Венските малформации (ВМ) претставуваат честа вродена васкуларна аномалија, која зафаќа речиси 1 % од популацијата. Овие васкуларни аномалии со низок проток често резултираат со хронични отоци, болка и ограничена подвижност, што значително влијае врз квалитетот на животот кај децата. Најчесто овие малформации настануваат како резултат на генетски промени во TIE2/TEK и PIK3CA сигналните патишта, предизвикувајќи неправилно формирање на венскиот систем и прекумерно растење на крвните садови. Целта на оваа студија е да ги анализира клиничките манифестации, дијагностичките методи и терапевтските опции кај педијатриските венски малформации, со акцент на ефикасноста на различните методи на лекување. Раното препознавање на клиничката презентација и подоброто разбирање на резултатите од третманот се клучни за рана дијагноза и подобрување на индивидуализираните пристапи во лекувањето.

Материјали и методи: Во периодот од 2019 до 2023 година на Клиниката за детска хирургија во Скопје беа третирани 38 педијатриски пациенти со венски малформации. Анализирани беа демографските податоци, карактеристиките на малформациите и користените методи на лекување (конзервативен третман, склеротерапија и хируршка интервенција).

Резултати: Најголем дел од пациентите (39,5 %) биле лекувани конзервативно, додека 23,7 % биле третирани со склеротерапија, а 34,2 % имале потреба од хируршка интервенција. Ефикасноста на склеротерапијата беше оценувана според големината на малформацијата, при што помалите лезии (< 5 cm) покажаа добри резултати, додека поголемите или повторувачките лезии бараа повеќекратни третмани.

Заклучок: Резултатите ја потенцираат важноста на раното откривање и индивидуализиран пристап во лекувањето на педијатриските венски малформации. Склеротерапијата останува прв избор за помали и умерени лезии, додека хируршката интервенција е резервирана за пациенти со симптоматски и тешки случаи. Мултидисциплинарниот пристап е неопходен за подобрување на резултатите од третманот. Идните истражувања би требало да бидат насочени кон развој на минимално инвазивни техники и испитување на целните генетски терапии.

Клучни зборови: венски малформации, педијатриски васкуларни аномалии, склеротерапија, хируршки третман, вродени васкуларни нарушувања, имиџинг во васкуларни аномалии