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VASCULAR ANOMALIES IN CHILDREN  
VASKULARNE ANOMALIJE KOD DECE

**Correspondence to:**

**Aleksandar Vlahović, M.D., Ph.D.**

Institute for Mother and Child Health  
Care of Republic Serbia "Dr Vukan  
Čupić" Department of Plastic surgery and  
Burns, Radoja Dakića str. 6-8,  
11070 New Belgrade  
Home address:  
Borivoja Stevanovića 10 v,  
11050 Voždovac, Belgrade, Serbia  
E-mail:aleksandarvlahovic@yahoo.com  
Tel:+ 38 165 811 2615

Aleksandar Vlahović<sup>1</sup>, Maja Miličković<sup>2</sup>,  
Nataša Vlahović<sup>3</sup>

<sup>1</sup> Department of Plastic surgery and Burns, Radoja Dakića str. 6-8,  
11070 New Belgrade

<sup>2</sup> Department of Abdominal surgery, Radoja Dakića str. 6-8, 11070 New  
Belgrade

<sup>3</sup> Department of Physical therapy and rehabilitation, Radoja Dakića str.  
6-8, 11070 New Belgrade

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*Ključne reči*

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*Abstract*

A biological classification of vascular anomalies that correlated clinical features, natural history, and cellular characteristics was proposed by Mulliken and Glowacki in 1982 and in 1996 was accepted by the International Society for the Study of Vascular Anomalies (ISSVA). This classification clearly separating vascular tumors which result from active cell proliferation, from vascular malformations, which are inborn defects in vascular morphogenesis. These two types of lesions have different clinical behavior and require different diagnostic and therapeutic strategies. The most frequent vascular tumor is infantile hemangioma (IH). Vascular malformations can be classified according to the vessels types they are composed as simple and combined malformations. Simple vascular malformations are presented as: a) slow flow: capillary, venous, lymphatic and b) fast flow: arterious malformations. Combined vascular malformations are presented as a combination of simple vascular malformations and they can be slow flow, and fast flow. This classification system has facilitated diagnosis, communication, treatment, and research in this field.

*INTRODUCTION*

Vascular anomalies in children are divided into two types: 1) tumors (most being hemangiomas) and 2) vascular malformations<sup>(1-3)</sup>. Infantile hemangiomas (IHs) have unique characteristics, consisting of a growth phase and an involuting phase<sup>(2-5)</sup>. Unlike hemangiomas, vascular malformations which are structural anomalies derived from arteries, capillaries, veins, lymphatics or a combination, rarely involute and grow in proportion to the child<sup>(2,4,6)</sup>.

*VASCULAR TUMORS*

*a) Infantile hemangiomas*

Infantile hemangiomas (IHs) occur in 4 and 12% of all Caucasian, with female predomination 3:1<sup>(1-4,7,8)</sup>. Pathogenesis still remains unknown<sup>(8-10)</sup>. Glucose transporter protein 1 (GLUT 1) is specific and useful immunohistochemical marker for IHs during all phases of these lesions<sup>(11)</sup>. Most IHs involve the head and neck (up to 60%) and exist as solitary lesions, but up

to 20% of infants may have two or more (Fig.1-A)<sup>(3,4)</sup>. Clinical appearance allows differentiation between focal, indeterminate, segmental and diffuse IHs<sup>(8,10)</sup>. The tumor has an initial growth phase during the first 12 months (proliferative phase), and then it involutes over approximately one to seven years (involuting and an involuted phase)<sup>(2-4,10)</sup>. There are two types of congenital hemangioma that is present and fully grown at birth: noninvoluting congenital hemangioma (NICH) and rapidly involuting congenital hemangioma (RICH)<sup>(6,8,11)</sup>. NICH do not go through a regression phase. RICH goes through a rapid regression phase and may be completely gone by the time the child is 12 to 18 months old<sup>(6,8,11)</sup>. Diffuse neonatal hemangiomatosis (DNH) is a rare disorder characterized by the presence of multiple cutaneous and visceral hemangiomas which appear at birth or shortly thereafter<sup>(12)</sup>. The majority of IHs are uncomplicated and require no treatment (only clinical observation and serial clinic visits accompanied by photo documentation)<sup>(2-4,8,10)</sup>. Intervention is typically required for



Figure 1.

**A**, Superficial IH; **B**, Pyogenic granuloma; **C**, Kaposiform haemangioendothelioma (KHE);  
**D**, Venous malformation (VM); **E**, Capillary malformation (CM);  
**F**, Lymphatic malformation (LM); **G**, Arteriovenous malformation (AVM);  
**H**, Combined vascular malformation – capillary-lymphatic-venous-malformation (CLM)

lesions that may interfere with a vital function such as airway or visual obstruction, ulcerated lesions, or lesions at increased risk for complications, including a poor cosmetic outcome (2-4,8,10,13). Current treatment options are conservative (corticosteroids, interferons, hemiotherapy), laser treatment, and surgical treatment (by lenticular excision, with a linear closure, or by circular excision and „purse-string” closure (2,4,8,10,13-16). Recently propranolol proved itself effective in inducing regression of growing hemangioma (17-19). The use of propranolol in the treatment of IHs was serendipitously discovered in 2008 by Léauté-Labrèze (17). A subgroup of children with IHs exhibits additional associated structural anomalies like in the syndrome called PHACES (Posterior Fossa malformations, Hemangioma, Arterial anomalies, Cardiovascular anomalies, abnormalities of the Eye, Sternal clefting (21).

#### b) Other tumors

*Pyogenic granuloma* is a benign, acquired vascular tumor of the skin and mucous membranes (Fig. 1-B). The treatment options are surgical excision with primary closure or shave excision at the base followed by electrocautery(3,20). *Kaposiform hemangioendothelioma (KHE)* is a vascular tumor associated with the Kasabach-Merritt phenomenon (severe coagulopathy due to platelet trapping and spontaneous bleeding) (Fig. 1-C)(2,3,22). *Hemangiopericytoma, tufted angiomas, spindle cell hemangioendothelioma* are rarely seen vascular tumors (2,3).

#### VASCULAR MALFORMATION

Vascular malformation occurs as a result of errors in embryogenesis(1-4,6). They are histologically normal, but with abnormal architecture(1,6). Typically,

these anomalies are categorized according to the vessels types as simple (capillary, lymphatic, venous and arterial) and combined. Based on a flow-rate, they are classified as slow-flow and fast-flow (1-4,24,27).

#### *Simple vascular malformation*

**Capillary malformations (CM)** (known as “port-wine stain”), occur in 0.1-0.3% of newborns, and can occur in any cutaneous location (Fig. 1-D)(2-4). Over time without treatment, facial CM can become thickened and nodular(2,3). CMs can be confused with the most common vascular birthmark called “nevus flammeus neonatorum”. The latter occurs in 50% of white newborns and is popularly known as “angel kiss” (on the forehead, eyelids, nose, and upper lip) and “stork bite” (on the nuchal area). These irregular macular stains predictably fade and thus represent a minor transient dilatation of dermal vessels. When a CM afflicts the face, the Sturge-Weber syndrome must be suspected. Ipsilateral leptomeningeal and ocular vascular abnormalities may occur(23). Pulsed dye laser is a first treatment option for CMs. Partial excision is the primary treatment for thick, nodular lesions(2-4).

**Venous malformations (VM)** are present at birth, but they are not always evident. These slow-flow anomalies manifest in many forms (Fig. 1- E). They are bluish, soft, and compressible. They can be localized or extensive within an anatomic region.(3,4). Histologically, VM is composed of thin-walled, dilated, sponge-like abnormal channels. Unlike hemangiomas, VMs grow in proportion to the child and do not involute(4). MRI is the most informative imaging modality, but venography may be required preoperatively (26,27). Treatment of VMs is indicated for appearance, pain, or functional problems. The therapeutic mainstays are sclerotherapy and surgical resection. Treatment is multimodal: sclerotherapy or complete surgical extirpation (2-4,26,27). Elastic compression devices aid in pain control, as will aspirin to prevent thrombosis(4,27).

**Lymphatic malformations (LM)** (known as lymphangioma) are present at birth, and larger lesions are sometimes detected on prenatal ultrasound(2-4,25,26). Common sites of occurrence are the face, neck, axilla, chest, buttock, perineum and retroperitoneum/ mediastinum (Fig.1-F)(25,26). LMs are categorized as microcystic, macrocystic or a combination(25). In the head and neck, such bulky lesions may compromise the aerodigestive tract, which may necessitate tracheostomy or feeding devices(3,25,26). Therapy is usually multimodal(25). Surgical resection is infrequently realized due to lesion extent and inevitable incorporation of vital structures(3,26). Sclerotherapy with OK-432 substance (a killed strain of group A *Streptococcus pyogenes*), is only possible with the macrocystic subtype(25). Stocking compression is the mainstay of therapy for extremity lesions(2-4).

**Arteriovenous malformations (AVM)** is distinctive from other vascular malformations due to its high flow, expressed outwardly by a palpable thrill, audible bruit and general warmth and redness (Fig.1-G)(3,4,27). Schobinger proposed a four stages clinical system in 1990, according to clinical manifestations and present complications(4,27). Ideal initial imaging is via ultrasonography and color Doppler, with MRI to evaluate extent of malformation(26). Treatment options are embolization and surgical resection(3,27).

### COMBINED VASCULAR MALFORMATIONS

#### *Slow flow combined vascular malformations*

They can be different according to vessel type combination (capillary, lymphatic, venous).

**Klippel-Trenaunay syndrome** is a well-worn eponym for capillary-lymphatic-venous malformation (CLVM) that is associated with soft tissue/skeletal hypertrophy, usually of one or more limbs (Fig. 1-H) (2,3). The disorder is thought to be sporadic; it is obvious at birth(3). **Proteus syndrome** is a sporadic and progressive vascular, skeletal, and soft tissue condition (2). The major diagnostic features include verrucous (linear) nevus, lipomas and lipomatosis, macrocephaly (calvarial hyperostosis), asymmetric limbs with partial gigantism of the hands and feet or both, and curious cerebiform plantar thickening (“moccasin” feet) (2,3). **Maffucci syndrome** denotes the coexistence of exophytic vascular anomalies with bony exostoses and enchondromas(2,-4).

#### *Fast flow combined vascular malformations*

These anomalies are less common than slow-flow combined disorders. The abbreviations for capillary-arteriovenous fistulas (CAVFs) and capillary-arteriovenous malformation (CAVM) correspond to the old eponym **Parkes-Weber syndrome**(2-4). The vascular anomaly is obvious at birth. The involved limb is covered by a geographic pink, macular stain and is enlarged symmetrically(2,3).

### CONCLUSION

This new classification system has facilitated diagnosis, communication, treatment, and research in this field. Most large pediatric centers now have a vascular anomalies team which includes plastic or pediatric surgeons, pediatric dermatologists, radiologist, anesthesiologist, ENT specialist, ophthalmologists, physical therapy specialist etc. These multifaceted teams can help provide all the essential medical and surgical options.

## Apstrakt

Biološka klasifikacija vaskularnih anomalija koja povezuje kliničku prezentaciju, prirodni tok i ćelijske karakteristike predložena je od strane Malikena i Glovacke 1982. godine, a prihvaćena je 1996. godine od strane Međunarodnog Udruženja za Proučavanje Vaskularnih Anomalija (MUPVA). Ova klasifikacija jasno odvaja vaskularne tumore, koji nastaju aktivnom ćelijskom proliferacijom, od vaskularnih malformacija, koje su urođeni defekt u vaskularnoj morfogenezi. Ove dve vrste promena imaju različito kliničko ponašanje i zahtevaju različite dijagnostičke i terapijske procedure. Najčešći vaskularni tumor je dečji hemangiom (DH). Vaskularnemalformacije se klasifikuju, na osnovu vrste krvnog suda od kog su sastavljene, na jednostavne i kombinovane. Jednostavne vaskularne malformacije mogu biti: a) sporoprotodne: kapilarne, venske, limfatične malformacije, i b) brzoprotodne: arterijske malformacije. Kombinovane vaskularne malformacije nastaju kombinacijom jednostavnih vaskularnih malformacija i mogu biti sporoprotodne i brzoprotodne. Ovaj sistem klasifikacije olakšao je dijagnozu, komunikaciju, lečenje i istraživanje u ovoj oblasti.

## REFERENCES

- Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg* 1982; 69, 3: 412-422.
- Fishman SJ, Mulliken JB. Vascular anomalies. *Ped Clin N Am* 1998; 45, 6: 1455-1477.
- Mulliken JB, Fishman SJ, Burrows P. Vascular anomalies. *Curr Prob Surg* 2000; 37, 8: 520-584.
- Gamper TJ, Morgan RF. Vascular anomalies. *Plast Reconstr Surg* 2002; 110: 572-86.
- Hassanein AH, Mulliken JB, Fishman SJ, Greene AK. Evaluation of terminology for vascular anomalies in current literature. *Plast Reconstr Surg* 2011; 127, 3: 347-351.
- Cohen MM. Vascular update: morphogenesis, tumors, malformations, and molecular dimensions. *Am J Med Genet Part A* 2006; 140A: 2013-2038.
- North PE, Waner M, Mizeracki A, Mihm MC. GLUT 1: a newly discovered immunohistochemical marker for juvenile hemangiomas. *Hum Pathol* 2000; 31, 1:11-22.
- Bruckner AL, Frieden IJ. Infantile hemangiomas. *J Am Acad Dermatol* 2006; 55, 4: 671-682.
- Bauland CG, van Steensel MA, Steijnen PM, Rieu PNMA, Spauwen PHM. The pathogenesis of hemangiomas:review. *Plast Reconstr Surg* 2006; 117, 2: 29-35.
- Haggstrom AN, Drolet BA, Baselga E, Chamlin SL, Garzon MC, et al. Prospective study of infantile hemangiomas: Clinical characteristics predicting complications and treatment. *Pediatr* 2006; 118, 3: 882-87.
- Mulliken JB, Enjolras O. Congenital hemangiomas and infantile hemangioma: missing links. *J Am Acad Dermatol* 2004; 50, 6: 875-882.
- Vlahovic A, Simic R, Djokic D, Ceran C. Diffuse neonatal hemangiomatosis treatment with cyclophosphamide a case report. *J Pediatr Hematol Oncol* 2009; 31,11:858-860.
- Frieden IJ, Haggstrom AN, Drolet BA et al. Infantile hemangiomas: current knowledge, future directions. Proceedings of a research workshop on infantile hemangiomas. *Ped Dermatol* 2005; 22, 5: 383-406.
- Bauland CG, Smit JM, Ketelaars R, Rieu PNMA, Spauwen PHM. Management of hemangiomas of infancy: a retrospective analysis and treatment protocol. *Scand J Plast Reconstr Surg Hand Surg*. 2008;42:86-91.
- Waner M, Buckmiller L, Suen JY. Surgical management of hemangiomas of the head and neck. *Oper Tech Otolaryngol Head Neck Surg* 2002; 13, 1:77-84.
- Vlahovic A, Simic R, Kravljanc Dj. Circular excision and purse string suture technique in the management of facial hemangiomas. *Int J Pediatr Otolaryngol* 2007;71:1311-1315.
- Leaute-Labreze C, Dumas de la Roque E, Hubiche T, Boralevi F. Propranolol for severe hemangiomas of infancy, *N Engl J Med* 2008; 358: 2649-2651.
- Waner M, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: risk and recommendations. *Pediatr Dermatol* 2009; 26, 5: 610-614.
- de Graaf M, Breur JMPJ, Raphael MF, Vos M, Breugnot CC, Pasmans SGMA. Adverse effects of propranolol when used in the treatment of hemangiomas: a case series of 28 infants. *J Am Acad Dermatol* 2011; 65, 2:320-327.
- Pagliari KA, Cohen BA. Pyogenic granuloma in children. *Pediatr Dermatol* 2004; 21, 1: 10-13.
- Metry DW, Garzon MC, Drolet BA, Frommelt P, Haggstrom A et al. PHACE syndrome: current knowledge, future directions. *Pediatr Dermatol*. 2009; 26, 4: 381-398.
- Enjolras O, Wassef M, Mazoyer E, Frieden IJ, Rieu PN et al. Infants with Kasabach-Merritt syndrome do not have "true" hemangiomas. *J Pediatr* 1997; 130, 4: 631-640.
- Thomas-Sohl KA, Vaslow DF, Maria BL. Sturge-Weber syndrome: a review. *Pediatr Neurol* 2004;30, 5:303-310.
- Zhou Q, Zheng JW, Mai HM, Luo QF, Fan XD et al. Treatment guidelines of lymphatic malformations of the head and neck. *Or Oncol* 2011; 47: 1105-1109.
- Edwards PD, Rahbar R, Ferraro FN, Burrows PE, Mulliken JB. Lingual malformation of the lingual base and oral floor. *Plast Reconstr Surg* 2005; 115, 7: 1906-1915.
- Burrows EP, Laor T et al. Diagnostic imaging in the evaluation of vascular birthmarks. *Dermatol Clin* 1998; 16(3):455-88.
- Upton J, Coombs CJ, Mulliken JB et al. vascular malformations of the upper limb: a review of 270 patients. *J Hand Surg* 1999; 63(2):155-59.