DIAGNOSIS AND MANAGEMENT OF LOW-FLOW VENO-LYMPHATIC VASCULAR MALFORMATIONS

DIAGNOSTIKA A LÉČBA NÍZKOPRŮTOKOVÝCH VENO-LYMFATICKÝCH CÉVNÍCH MALFORMACÍ

review

Wayne F. Yakes, M.D.
Vascular Malformation Center

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Korespondenční adresa:
Wayne F. Yakes, M.D.
Director, Vascular Malformation Center
501 E. Hampden, #4600
Englewood CO 80113 USA

SUMMARY

Wayne F. Yakes, M.D. Diagnosis and management of low-flow veno-lymphatic vascular malformations

Venous malformations pose some of the most difficult challenges in the practice of medicine today. Clinical manifestations of these lesions are extremely protean. Because of the rarity of these lesions, experience in their diagnosis and management by most clinicians is limited. This augments the enormity of the problem and can lead to misdiagnoses, inadequate treatment, high complication rates, and poor patient outcomes. Vascular malformations are best treated in medical centers where patients with these maladies are seen regularly and the team approach is utilized. The occasional embolizer will never gain enough experience to adequately treat these problematic lesions. More importantly, when complications do occur, the morbidity of that complication is worsened because of this lack of experience and absence of an experienced team of physicians. All too frequently the patient will ultimately pay for a physician's initial enthusiasm, inexperience, folly, and lack of necessary clinician backup. A cavalier approach to the management of venous malformations will always lead to significant complications and dismal patient outcomes. These patients should be referred to centers that regularly treat vascular malformations, manage the complications that occur appropriately and in a timely manner, and routinely deal with the dilemmas they present. Only in this fashion can significant experience be gained, improved judgment in managing these lesions develop, and definitive appropriate statements in the treatment of vascular anomalies evolve.

Key words: embolization, ethanol, vascular malformations, veno-lymphatic vascular malformations, venous vascular malformation.

SOUHRN

Wayne F. Yakes, M.D. Diagnostika a léčba nízkoprůtokových veno-lymfatických cévních malformací

Venózní malformace představují v současné medicíně jedny z nejvíce obtížných úkolů terapie. Klinické projevy těchto onemocnění jsou velmi variabilní. Z důvodu vzácnosti těchto lézí jsou zkušenosti s diagnostikou a léčnou u většiny kliniků omezeny. Tento fakt umocňuje závažnost problematiky a může mít za následek chybnou diagnostiku, neadekvátní léčbu, vysoký počet komplikací a pro pacienty špatný výsledek léčby. Cévní malformace jsou nejlépe léčeny v centrech, kde jsou pravidelné zkušenosti s jejich léčbou a kde je v léčbě využívána týmová spolupráce. Pokud intervenční radiolog provádí embolizace jen příležitostně, nemůže nikdy dosáhnout dostatečných zkušeností, aby mohl výkon provést adekvátně a ani řešit nastalé komplikace. Pokud není na pracovišti dostatečná zkušenost s léčbou těchto malformací, měli by být nemocní předáni do péče centra, které se touto terapií zabývá cíleně. Jen tento způsob vede k tomu, aby vznikly týmy s dostatečnou zkušeností v rozhodování o terapii a s jejím prováděním.

Klíčová slova: cévní malformace, embolizace, etanol, vaskulární malformace, veno-lymfatické cévní malformace, venózní malformace.

INTRODUCTION

Vascular anomalies constitute some of the most difficult diagnostic and therapeutic enigmas that can be encountered in the practice of medicine. The clinical presentations are extremely protean and can range from an asymptomatic birthmark to life-threatening hemorrhage. Attributing any of these extremely varied symptoms that a patient may present with to a vascular malformation can be challenging to the most experienced clinician. Compounding this problem is the extreme rarity of these vascular lesions. If a clinician sees one patient every few years, it is extremely difficult to gain a learning curve to diagnose and optimally treat them. Typically, these patients bounce from clinician to clinician only to experience disappointing outcomes, complications, and recurrence or worsening of their presenting symptoms. Vascular malformations include high-flow malformations and low-flow malformations. The high-flow malformations include arteriovenous malformations, congenital arteriovenous fistula, posttraumatic arteriovenous fistula, and acquired arteriovenous fistula. Low-flow lesions include venous malformations, lymphatic malformations, and mixed lesions. This article will be devoted to the diagnosis and management of venous malformations.

Before the advent of magnetic resonance imaging (MR), contrast enhanced computerized axial tomography (CT) scanning, and, very rarely, ultrasound imaging, was employed. Most often, patients were evaluated by arteriography and venography. Later, closed system venography and direct puncture venography were employed to better evaluate these postcapillary abnormal venous spaces (1–2). Currently, MR has proven to be the mainstay in initial diagnosis as well as to assess endovascular therapy at follow-up (3–6). Color Doppler imaging (CDI) is also assuming a large role in the initial diagnosis and later follow-up of venous malformations (7–8).

Venous malformations were initially treated by surgeons. Because of significant blood loss that occurred during surgery, partial surgical resections were the rule. Partial resections could cause an initial good clinical response, however, with time, the patients' presenting symptoms recurred or worsened at follow-up. Further, the venous malformation rarely was limited to a subcutaneous position, and more often than not involved multiple muscular structures as well as involving neurovascular compartments. Thus, direct puncture and ethanol embolotherapy has emerged as a primary mode of therapy in the management of these abnormal slow-flow vascular lesions (9–15). This has led to enhanced care of these problematic patients.

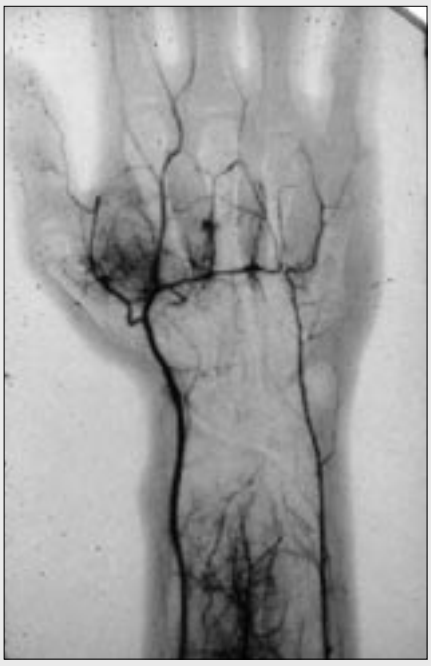
Because the clinical and angiographic manifestations can be extremely varied, venous malformations, and vascular malformations in general, have always been difficult to classify. Moreover, a vast array of descriptive terms has been given to impressive clinical examples in the hopes of distinguishing them as distinct entities or syndromes. This has resulted in confusion in the literature with miscategorizations and, thus, suboptimal treatment of these complex lesions. Some of the confusing terms include congenital arteriovenous aneurysm, interosseous anomaly, cirsoid aneurysm, serpentine aneurysm, capillary telangiectasia, angioma telangiectaticum, angioma arteriala racemosum, angioma simplex, angioma serpingiosum, nevus angiectoides, hemangioma, lymphangioma, hemangiolymphangioma, verrucous hemangioma, capillary hemangioma, cavernous hemangioma, venous angioma naevus flammeus, and the like. Based on the landmark research of Mulliken et al. (16), a rational classification of hemangioma and vascular malformations has evolved that should be incorporated into modern clinical practice. This classification system, based on endothelial cell characteristics, has removed much of the confusion in terminology that is present in the literature today. Once all clinicians understand and utilize this important classification system, ambiguity and confusion will be removed as all clinicians will speak a common language (16–20).

THEORETIC EMBRYOLOGIC ORIGINS

In the embryo, the primitive mesenchyme is nourished by an interlacing system of blood spaces without distinguishable arterial and venous channels. As the embryo matures, the interlacing system of blood spaces becomes more differentiated by partial resorption of the primitive elements and formation of more mature arterial and venous elements within an intervening capillary bed. The classically outlined sequence of events includes: 1. the undifferentiated capillary network stage; 2. the retiform developmental stage characterized by coalescence of the original equipotential capillaries into large interconnecting plexiform vascular spaces without an intervening capillary bed; and 3. the final developmental stage, characterized by the resorption of the primitive vascular elements and the formation of mature arterial, capillary, venous and lymphatic elements. Failure or orderly resorption of arrests in development in these embryologic primitive vascular spaces results in persistence of immature vascular anomalies. Retention of primitive retiform elements is the theoretical origin of congenital venous malformations that are retained in the fetus and are presented at birth (21–24). As Reid has stated, "In view of the common development on each side of the vascular tree, and in view of the enormous constructive and destructive changes necessary before the final pattern of the vascular tree is reached, it is a marvel not that abnormal congenital communications occasionally, or rarely, occur, but that they do not occur more often" (23).

CLASSIFICATION OF HEMANGIOMAS AND VASCULAR MALFORMATIONS

Pediatric hemangioma and vascular malformations have been classified by Mulliken, Glowacki, and coworkers, after research into endothelial cell characteristics, numbers of mast cells present, and endothelial cell *in vitro* characteristics (16–20). It must be emphasized that pediatric hemangiomas are tumors that are usually not present at birth, clinically manifest themselves sometime within the first month of life, and exhibit a rapid growth phase within the first year. More than 90% of these tumors spontaneously regress to near complete resolution by 5 to 7 years of age. Hemangiomas are the most common tumors of infancy and occur with a reported incidence of 1–2.6% (20, 25). Pediatric hemangiomas in the proliferative phase are characterized by rapid growth, signify cant endothelial cell hyperplasia forming syncytial masses, thicke-



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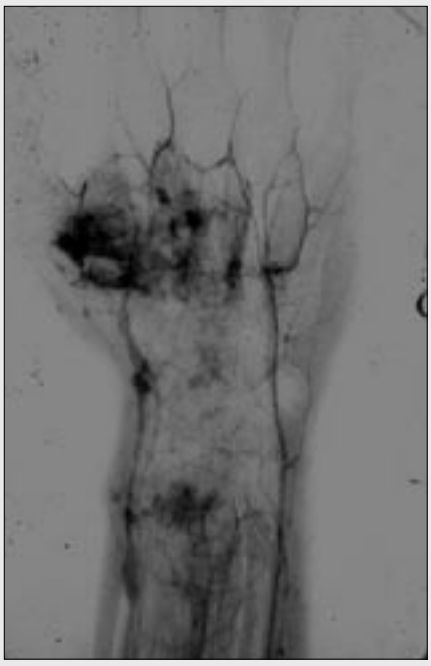

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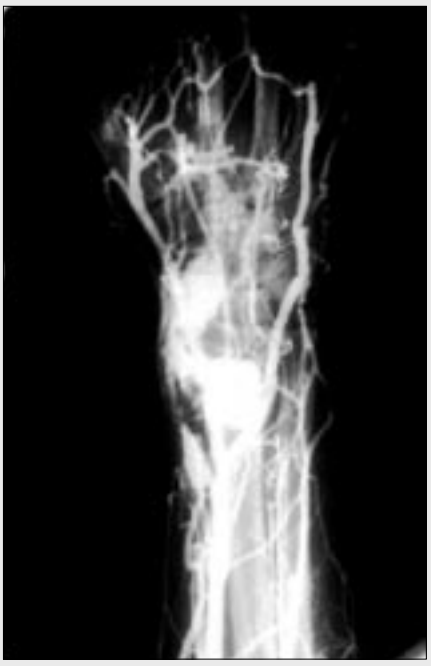

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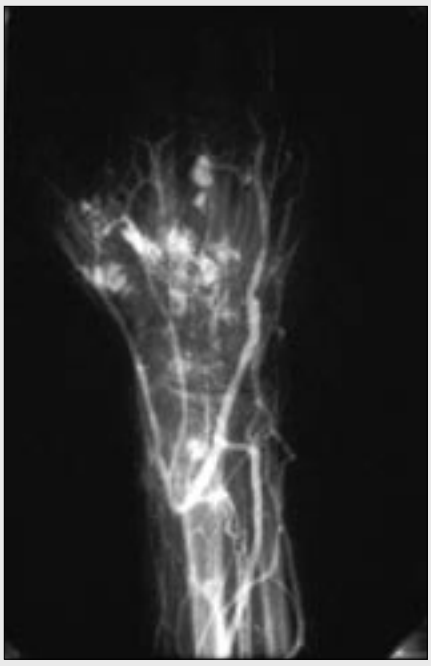

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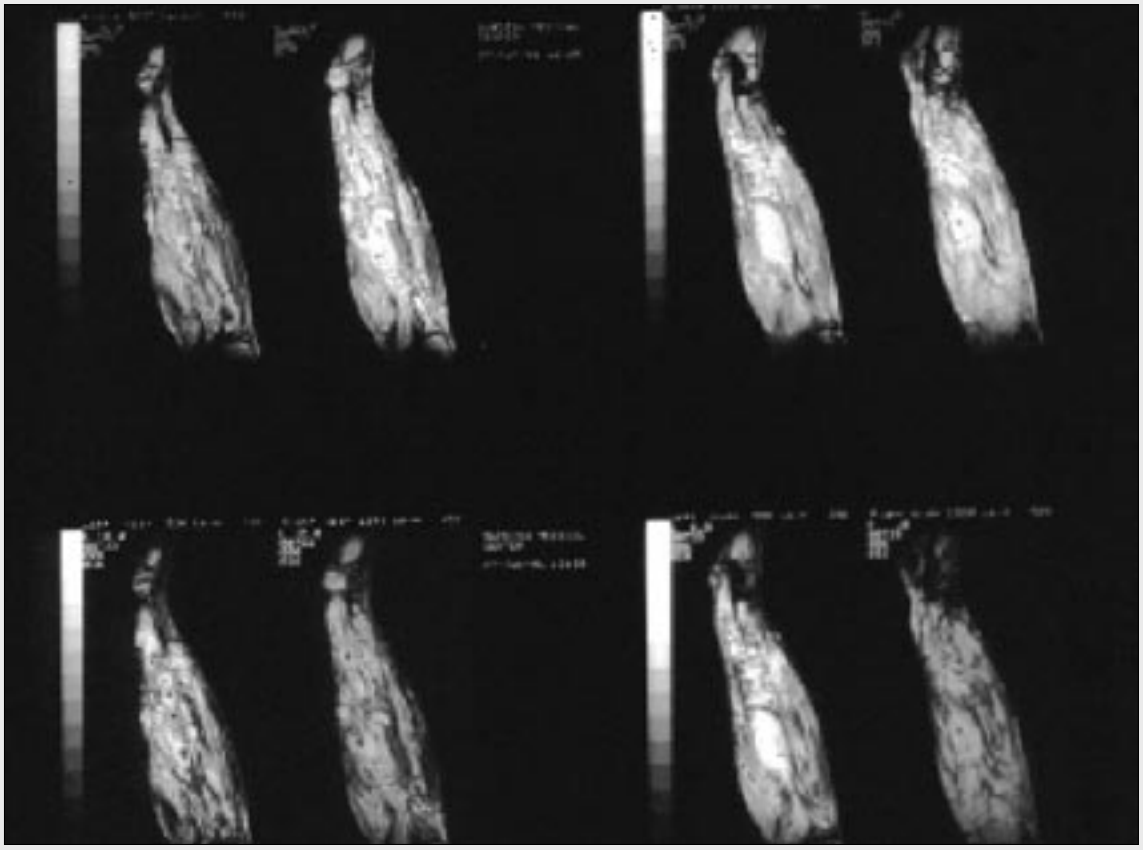
Fig. 1. A – 22 year old male with extensive right forearm, wrist, and hand venous malformation causing weakness in the right forearm and hand with severe pain syndrome. AP right brachial arteriogram. Note normal size of all arteries. Note contrast filling of abnormal vein malformation without AV shunts in the right forearm and hand; B – AP right brachial arteriogram, late phase. Note increase filling with contrast of the abnormal venous malformation spaces in the forearm and hand. No evidence of AV shunting; C – AP venogram right upper extremity. Note contrast filling of abnormal vein malformation in the forearm, wrist, and hand. Venography is superior to arteriography to opacify the lesion with contrast. MR is even more superior than arteriography and venography to visualize vein malformations of the body; D – Lateral right upper extremity venogram. Again, note contrast filling of vein malformation in the forearm flexor compartment, extending into the wrist, and into the hand palmar compartment; E – AP right upper extremity venogram. Note significant absence of the vein malformation previously noted in the forearm, wrist, and hand in image 1C.

Obr. 1. A – 22letý muž s rozsáhlou venózní malformací pravého předloktí zápěstí a ruky, která způsobuje slabost a výraznou bolestivost v postižené oblasti. Předozadní projekce arteriografie pravé paže. Tepny mají normální průsvit, abnormální venózní malformace se plní kontrastní látkou bez známek arterio-venózního zkratu; B – předozadní projekce arteriografie v pozdní fázi. Výrazné naplnění prostorů venózní malformace, bez známek arteriovenózního zkratu; C – předozadní projekce pravé horní končetiny, je dosaženo lepšího naplnění než při arteriografii. MR je ještě vhodnější k zobrazení venózních malformací těla; D – bočná projekce venografie pravé horní končetiny. Kontrastní náplň žilní malformace je přítomna ve flexorovém prostoru předloktí, zasahuje na zápěstí a do palmárního prostoru; E – předozadní projekce venografie pravé horní končetiny, malformace dříve patrná na venografii již není přítomná



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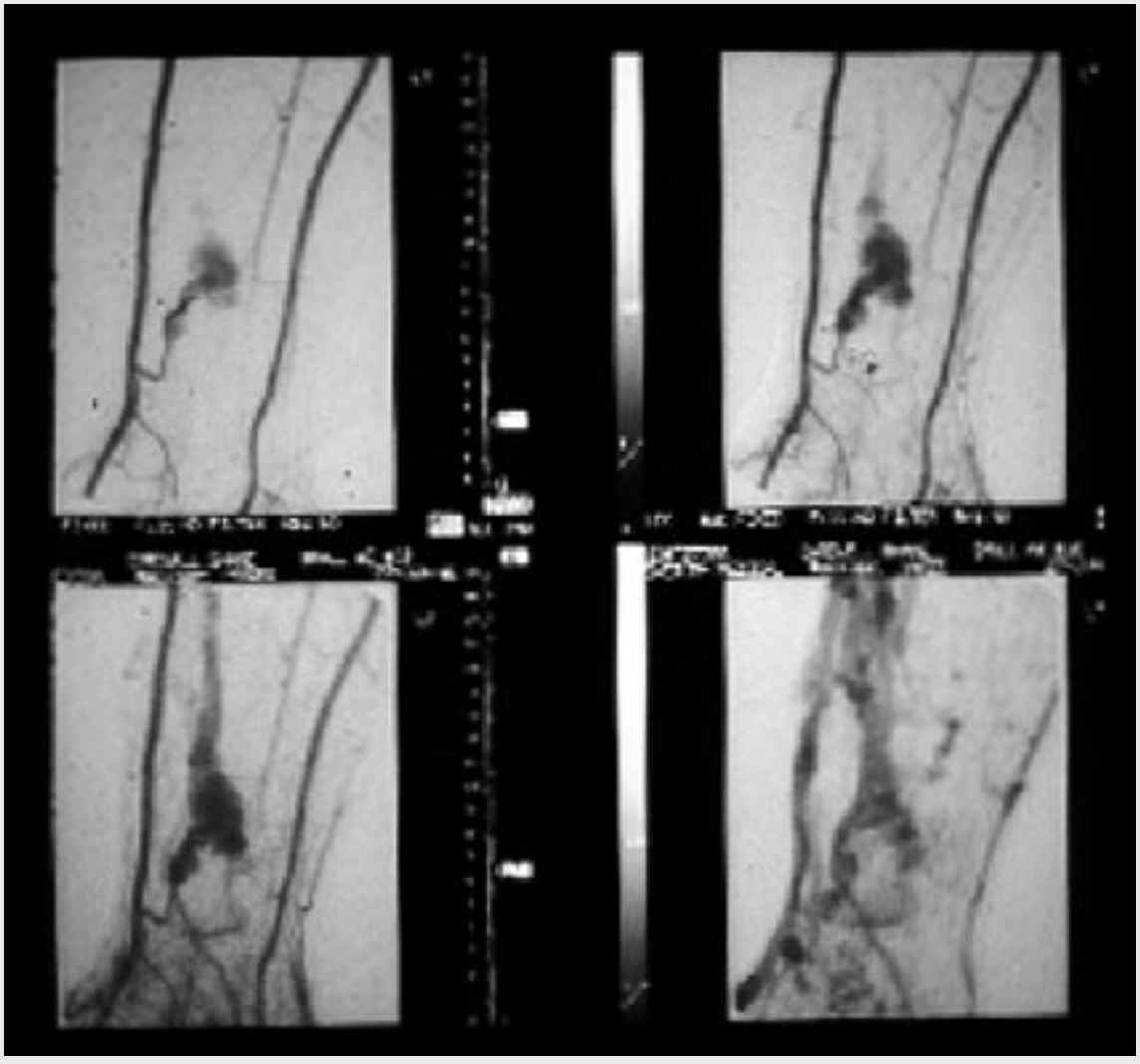

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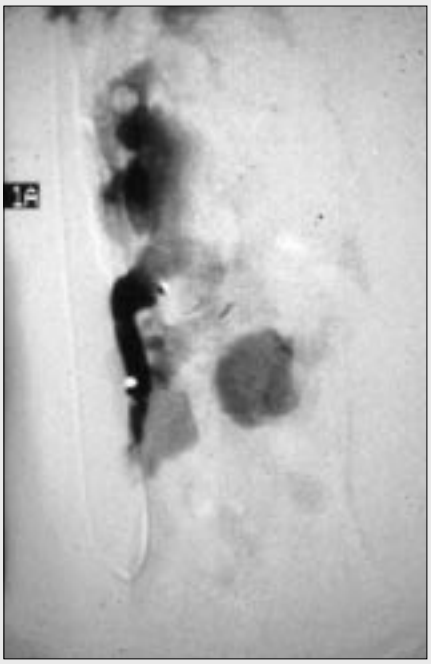

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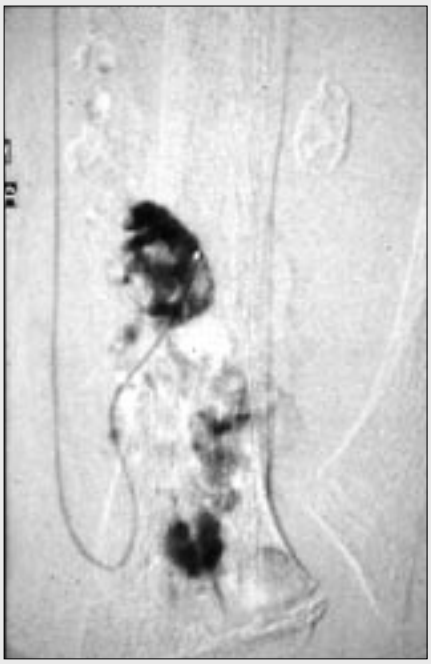

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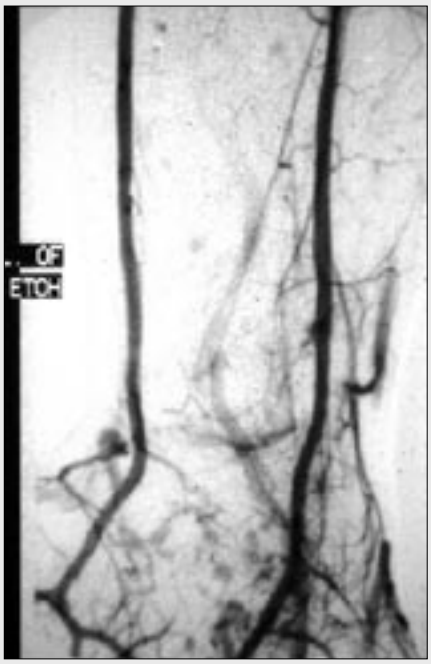

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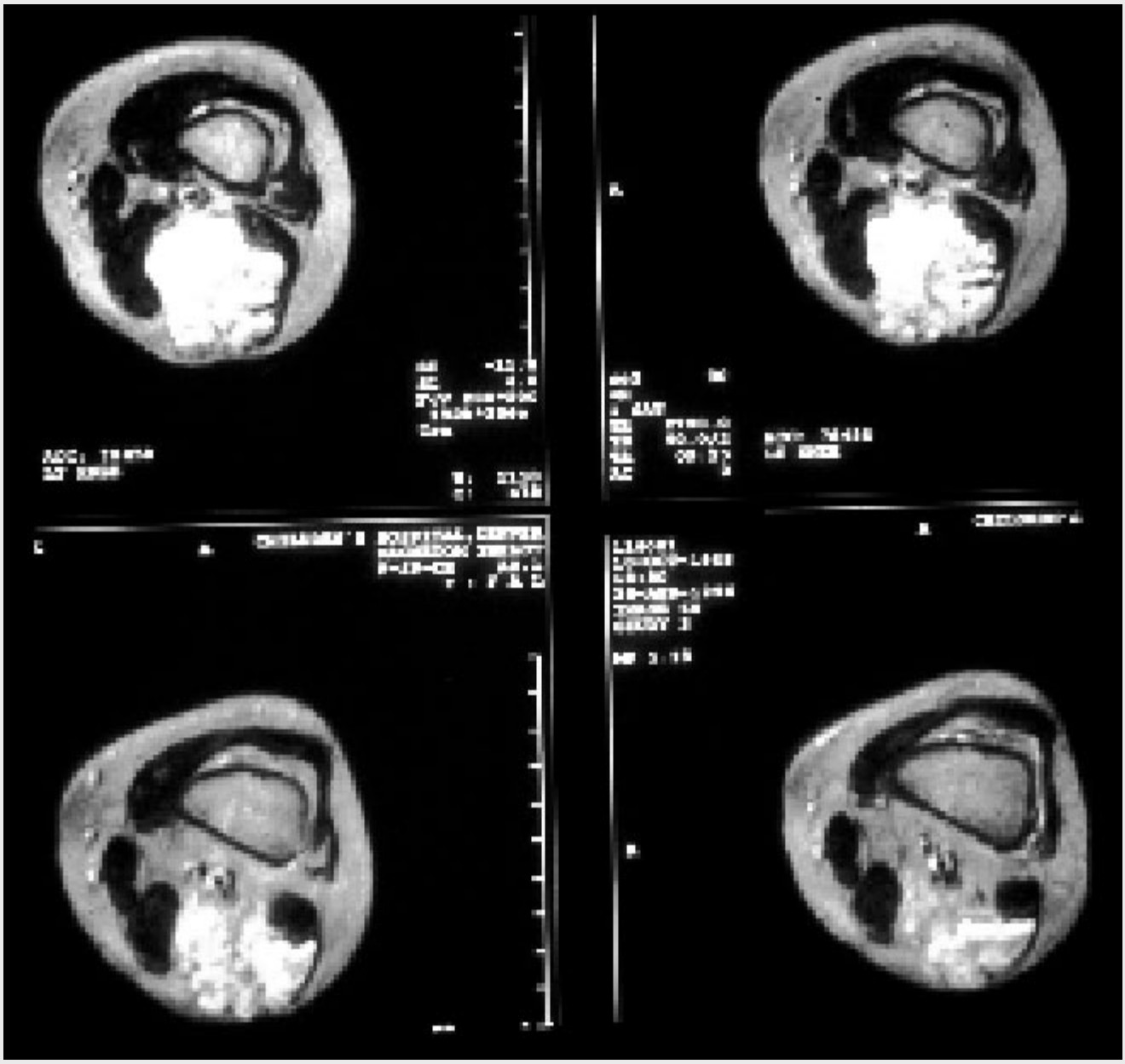
Fig. 2. A – 13 year old male with severe pain in the left forearm and wrist. T-2 weighted MR with fat suppression of the left forearm demonstrating extensive venous malformation throughout the forearm and wrist and evidenced by the bright signal remaining; B – left radial artery arteriogram documenting a direct fistula from the radial artery into the vein malformation masses. This causes increased pain due to the increased arterial pressures within the vein malformation. Concurrent fistulas within venous malformation is a rare phenomenon; C – note microcatheter advanced into the left radial artery branch, contrast injected, and contrast filling within the vein malformation itself. Note no evidence of rapid AV shunting; D – AP left microcatheter arteriogram after injection of 2 ml ethanol. Note thrombosis of the fistula with reflux into the arterial pedicle. No forward contrast flow is noted due to the adjacent thrombosis; E – left brachial arteriogram post embolization of 4 ml ethanol. Note normal filling of all arteries with total absence of radial artery fistula.
Obr. 2. A – 13letý chlapec s výraznou bolestí levého předloktí a zápěstí. T2 vážený obraz magnetické rezonance s potlačením signálu tuku, na levém předloktí se zobrazuje rozsáhlá venózní malformace vyznačující se vysokou intenzitou signálu; B – arteriografie levé radiální tepny zachycuje přímou píštěl mezi radiální arterií a malformací. Píštěl je příčinou bolesti z důvodu přítomnosti arteriálního tlaku v malformaci. Současná přítomnost arteriální píštěle ve venózní malformaci je vzácností; C – mikrokatétr zavedený do větve radiální tepny, po aplikaci kontrastní látky se plní samotná venózní malformace, není přítomný urychlený arteriovenózní zkrat; D – předozadní arteriografie mikrokatétrem po aplikaci 2 ml etanolu, trombóza píštěle zasahuje i do konce přívodní tepénky, kvůli trombóze není přítomen dopřední tok; E – arteriografie levé brachiální tepny po embolizace 4 ml etanolu, normální plnění tepen, chybí píštěl radiální tepny

ned endothelial basement membrane, ready incorporation of tritiated thymidine into the endothelial cells, and the presence of large numbers of mast cells. After this period of rapid expansion in the proliferative phase, hemangiomas stabilize in size and may grow commensurately with the child. Because of the complex nature of hemangioma, the proliferative phase may continue in parts of the tumor as the involution phase starts in other parts of the tumor, but eventually involutive aspects begin to dominate. Involuting hemangiomas show diminished endothelial cellularity and replacement with fibro fatty deposits, exhibit a unilamellar basement membrane, demonstrate no uptake of tritiated thymidine into endothelial cells, and have normal mast cell counts (16–18).

Vascular malformations, which include venous malformations, are vascular lesions that are present at birth and grow commensurately with the child. Vascular malformations demonstrate no endotheolial cell proliferation, contain large vascular channels line by flat endothelium, have a unilamellar basement membrane, do not incorporate tritiated thymidine into endothelial cells, and have normal mast cell counts. They may be formed from any combination of primitive arterial, capillary, venous, or lymphatic elements with or without direct arteriovenous (AV) shunts. Vascular malformations are true structural anomalies resulting from errors in vascular morphogenesis. Trauma, surgery, or hormonal influences caused by birth control pills, puberty, and pregnancy may cause vascular malformations to enlarge and become more symptomatic (20–26).

Vascular malformations are categorized into arterial, capillary, venous, or lymphatic vascular elements that are malformed. The term "hemangioma" should be solely reserved for the previously described pediatric tumor, which is usually not present at birth, becomes manifest within the first month of life, and exhibits a rapid proliferative phase followed by an involutive phase. The older terms describing adult conditions such as "cavernous hemangioma," "hepatic hemangioma," "extremity hemangioma," vertebral body hemangioma," "venous angioma," "intramuscular hemangioma," etc., should be replaced with the term "venous malformation." Being that hemangioma is universally absent by age 10 years, it, therefore, cannot exist in the adult patient. Therefore, we should exclude all terms such as "hepatic hemangioma," "vertebral body hemangioma," "cavernous hemangioma," etc., to describe lesions that exist in the adult population. These lesions are truly malformed veins and should be stated as such in our literature.

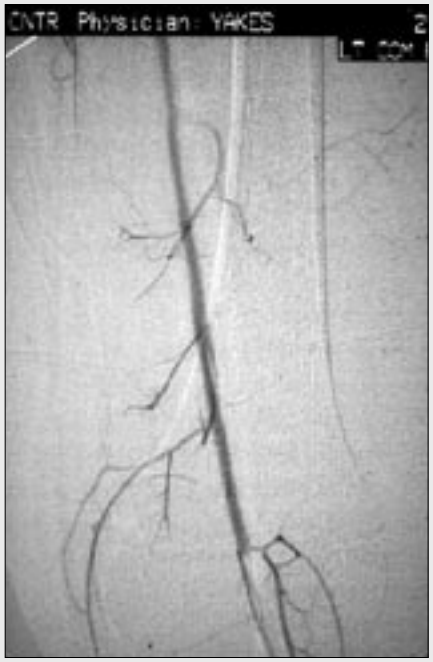
Other rare types of congenital hemangioma include RICH (Rapidly Involuting Congenital Hemangioma) and NICH (Non-Involuting Congenital Hemangioma) occur. Kapasi-Form Hemangioendothelioma is another rare lesion confused with pediatric hemangioma. When it infiltrates the liver



▲ Obr. 3A

of a neonate, it causes life-threatening high-output cardiac failure. When it infiltrates the trunk it causes the Kasabach--Merritt Syndrome of platelet consumptive coagulopathy.

Eponyms have further clouded and confused the nomenclature of hemangiomas and vascular malformations in the literature. Maffuci's syndrome (Kast syndrome) has been defined as a condition whereby the patient has multiple enchondromas and coexisting hemangiomatosis (27). The term "hemangiomatosis" should be replaced with "venous malformations." The Riley-Smith syndrome is characterized by macrocephaly, pseudopapilladema, and multiple hemangiomas (28). The term "hemangioma" should be replaced with "venous malformation." The Riley-Smith syndrome, the Proteus syndrome (29), and Bannayan's syndrome (30, 31) are probably a spectrum of similar congenital vascular anomalies. Gorham syndrome, Gorham-Stout syndrome, and Trinquoste syndrome are similar entities describing an osteolysis (disappearing bone disease) caused by an underlying hemangiomatosis (32). The term "hemangiomatosis" should be replaced by "intraosseous vascular malformation." Another confusing group of eponyms (Klippel-Trenaunay syndrome, Parkes-Weber syndrome, Klippel--Trenaunay-Weber syndrome, Klippel-Trenaunay-Weber-Rubashov syndrome, giant limb of Robertson, naevus vasculosus osteophyperrtrophycus, naevus verrucous hypertrophycans, osteohypertrophic naevus flammeus, angioosteohypertrophy syndrome) all describe a congenital entity characterized by unilateral limb hypertrophy; cutaneous port wine stains; lymphatic malformations; a normal, hypoplastic, or atretic deep venous system; occasional extension of the vascular malformation into the trunk; a retained embryonic lower extremity lateral venous anomaly (Servelle's vein); and increased subcutaneous fat in the affected limb. The lower extremity is more commonly affected than the upper extremity. There may be the coexistence of multiple arteriovenous fistulas as well (33, 34).



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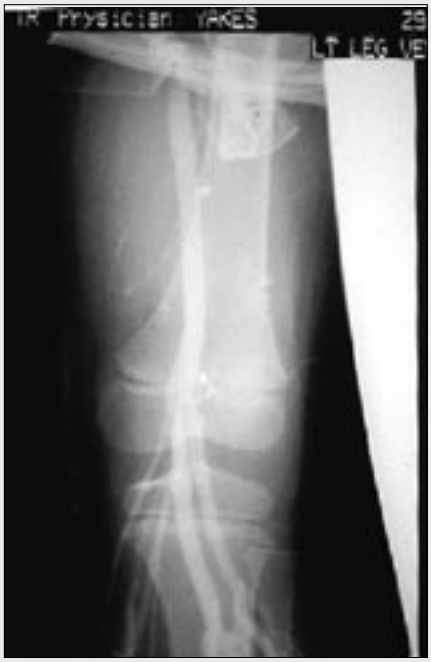

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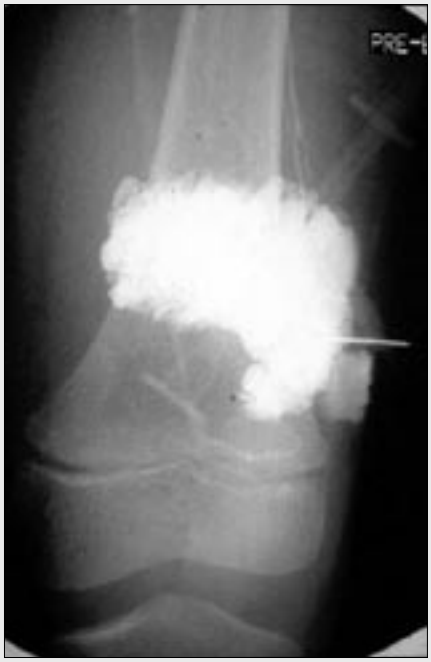

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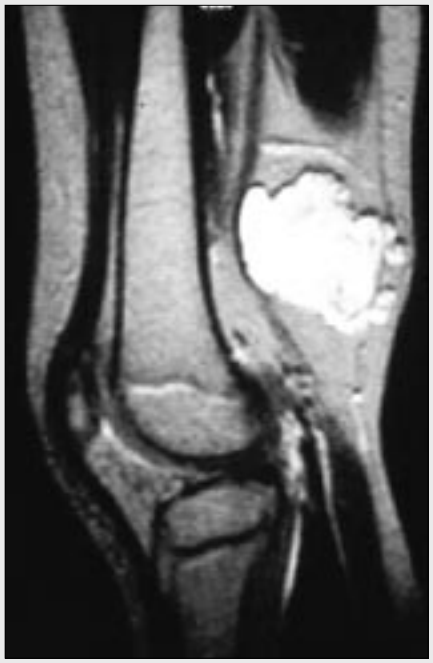

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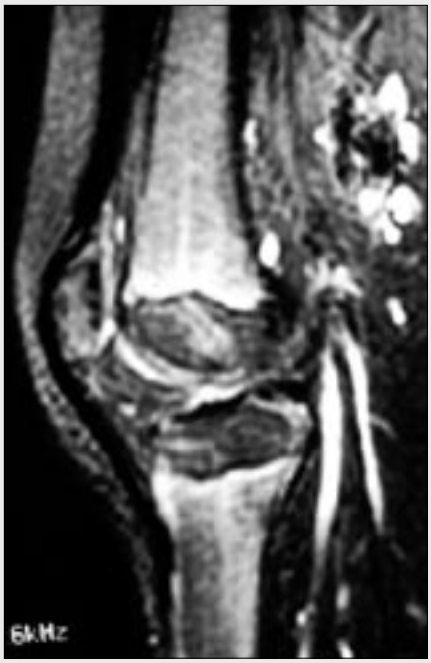

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Fig. 3. A – 7 year old female with painful growing mass in the left distal posterior thigh. Axial MR T-2 weighted images with fat suppression demonstrate the extensiveness of this lesion in the posterior hamstring muscles noted by the bright signal. The patient had surgery seven months prior to remove the lesion, but significant regrowth to the lesion growing larger than preoperative size is noted on this MR. The patient is now referred for endovascular ethanol therapy; B – left common femoral arteriogram demonstrating no vascularity to the venous malformation. No AV shunting present; C – AP left lower extremity venogram. No contrast filling of the vein malformation noted on this study. Venous malformation lesions are usually not seen or poorly opacified on venographic contrast studies. MR is the gold standard with T-2 weighted fat suppression or STIR imaging; D – direct puncture into the lesion with a needle and contrast injection fully fills a large component of the vein malformation noted on MR. From this volume of contrast, the amount of ethanol to fill this compartment can be calculated; E – sagittal STIR MR image of the distal left thigh prior to percutaneous ethanol treatment. Note the bright signal within the vein malformation lesion. Note the mass effect on the sciatic nerve, popliteal vein, and popliteal artery; F – sagittal T-2 fat suppressed distal left thigh image. Note significant reduction in the malformation as evidenced by the large area of decreased signal. Compared to image 3e.

Obr. 3. A – 7letá dívka s bolestivou rostoucí rezistencí vzadu na distálním stehnu. Axiální MR T2 vážený obraz s potlačením signálu tuku ukazuje rozsáhlost léze dorzálních svalů s vysokou signální intenzitou. Nemocná prodělala před několika měsíci nesekční chirurgický výkon, ale dochází k novému nárůstu léze do velikosti větší než před operací. Nemocná je nyní poslána k endovaskulární terapii etanolem; B – arteriografie společné stehenní tepny bez arteriálního zásobení malformace a bez známek arteriovenózního zkratu; C – předozadní venogram dolní končetiny, není přítomná náplň žil. Venózní malformace se obvykle špatně opacifikují při prováděné venografii, zlatým standardem je proto T2 vážený obraz MR s potlačením signálu tuku nebo STIR; D – přímou punkcí útvaru se naplní po aplikaci kontrastní látky celý rozsáhlý objem malformace patrný na MR. Podle množství kontrastní látky je možné spočítat objem alkoholu k pozdější aplikaci; E – sagitální STIRM MR obraz distálního stehna před perkutánní léčbou etanolem. V malformaci je vysoký signál, je přítomen tlak na n. ischiadicus a na podkolenní tepnu i žílu; F – sagitální T2 vážený MR obraz s potlačením signálu tuku distálního stehna, zřetelné zmenšení velikosti malformace společně se snížením signálu v porovnání s obrazem 3A

Another unusual circumstance is severe epistaxis that can occur in patients with Hereditary Hemorrhagic Telangiectasia (HHT). HHT is an autosomal dominant disease characterized by dermal, mucosal, and visceral telangiectasias, pulmonary arterial venous fistulae, and cerebral arteriovenous malformations. The most common manifestation of HHT is recurrent epistaxis occurring in 90% of patients with a mortality rate of up to 4%. In this patient group, severe epistaxis occurs spontaneously and is easily provoked by bending over, sneezing, running, dry mucus membranes, or emotional stress (44–49).

Recurrent familial epistaxis was first recognized by Babbington in 1865. Later, descriptions were written by Legg in 1876, Chari in 1887, and Chauffadin in 1896 who confused this disorder with hemophilia. Rendu distinguished it from hemophilia in 1896. Osler in 1901 published his classic description of the disease entitled, "On a Familial Form of Recurring Epistaxis with Multiple Telangiectasia of the Skin and Mucous Membranes". Weber described a family with recurring epistaxis in 1907. This disease was therefore commonly referred to an Osler-Weber-Rendu disease. Hanes suggested the name Hereditary Hemorrhagic Telangiectasia in 1909.

Because of the concurrent strong history of pulmonary arterial venous fistulae, blood gas determination should be performed in these patients. They can suffer from decreased oxygen saturation and relative hypoxemia. Further, thromboembolic complications, the so-called "paradoxical emboli", can occur in these patients and they are at increased risk for neurologic insult if pulmonary AVF are greater than 3mm in diameter. Further, arteriography should be performed to evaluate for the presence of cerebral arteriovenous malformations (AVMs). Cerebral AVMs have the significant incidence of subarachnoid hemorrhage with resultant neurological deficits and death. Intestinal malformations can cause gastrointestinal bleeding.

These examples are but a few of the confusing terms used in the literature and in clinical practice. Utilizing this modern classification system, the current confusion can be eliminated and all clinicians can finally speak the same language. Accurate terminology will lead to precise identification of clinical entities and to enhanced patient care. The remainder of this chapter will utilize this modern classification system originated by Mulliken, Glowacki, and coworkers (33, 34).

CONCEPTS IN PATIENT MANAGEMENT

Vascular malformations are congenital lesions that are present at birth, whether or not evident clinically. They do grow commensurately with the child. A thorough clinical exam and history can usually establish the diagnosis of hemangioma or vascular malformation. Hemangiomas are usually not present at birth and initially have a bright scarlet skin lesion that gradually deepens as the mass enlarges. Vascular malformations have a persistent color, usually more bluish, depending on the dominant arterial, capillary, venous, or lymphatic component present. Evaluating for skeletal abnormalities, abnormal veins, arterial abnormalities, pulsatility or nonpulsatility of a lesion, if the lesion swells when dependent and flattens when elevated, disparity of limb size, if reflex bradycardia occurs (Nicoladoni-Branham test), neurologic evaluation, and a good history can frequently diagnose a hemangioma or categorize a vascular malformation.

ULTRASOUND EVALUATION

Color Doppler imaging has proven to be an excellent diagnostic tool in the initial evaluations of patients with venous malformations. It can accurately determine if a high-flow or low-flow lesion is present. CDI with spectral analysis gives very accurate information to categorize a high-flow or low--flow malformation. A high-flow malformation has in-flow arteries that typically demonstrate high velocity and a low--resistance waveform. Low-flow malformations demonstrate normal arterial flow volumes as well as normal high arterial resistance in the arteries that supply the locale in which the venous malformation is present. Lower resistance waveforms may be present in the intramuscular type of venous malformations. CDI further characterizes the venous malformation as demonstrating slow to stagnant flow within the malformation itself.

Low-flow malformations vary widely in appearance on B-mode imaging depending upon the relative proportions of dilated postcapillary channels in the vessel wall. A vessel wall may appear relatively echogenic. If the luminal components predominate there may be multiple cystic spaces or even isolated dilated varices. There is a continuous spectrum in different areas of the venous malformation that may have different sonographic characteristics. Likewise, the degree of compressibility varies depending upon the composition of the venous malformation. If luminal components predominate the lesion may be almost completely compressible. Echogenic venous malformations in which the wall components predominate (with smaller luminal elements) are generally less compressible. On B-mode imaging very slow to stagnant flow is identified. Flow is frequently too slow to demonstrate without augmentation on even the most sensitive settings with the best color Doppler equipment. We have found "autoaugmentation" to be the most effective means of demonstrating flow within venous malformations. Compression of the venous malformation followed by sudden release of the compression resulting in refilling of the malformation with more rapid than normal flow from the surrounding uncompressed areas does cause a Doppler shift. The fact that arteries in the area of the malformation have normal high--resistance velocities correlates well with the fact that this is not an arterial abnormality but truly a postcapillary venous lesion.

CDI can be useful in monitoring the treatment of malformations. CDI can confirm thrombosis within the malformation as demonstrated by noncompressibility. Being that vein malformations and lymphatic malformations eventually connect to normal deep and superficial venous structures, a follow-up extremity deep venous assessment is crucial prior to discharge. In treating a venous malformation of the extremity, deep vein thrombosis (DVT) is a potential complication. On post-operative day number 1, all patients undergo deep-vein noninvasive venous assessment to determine the presence or absence or deep-vein thrombosis. This is an important complication to evaluate early rather than having to deal with the sequelae that can occur as the DVT worsens.

MR EVALUATION

MR allows imaging of high-flow and low-flow malformations and can distinguish accurately between these two entities. Further, anatomic relationships of adjacent organs, nerves, muscles, tendons, and other tissues are readily discernible in exquisite detail. Venous malformations and lymphatic malformations typically have high signal intensity on long TR/TE sequences whereas high-flow lesions usually demonstrate a signal void on most sequences. These flow voids are felt to be predominantly due to time of flight phenomenon with turbulence-related dephasing also contributing to signal loss. Venous malformations have several characteristics that have been previously described that include a serpentine pattern with internal striations or septations and associated focal muscle atrophy. Venous and lymphatic malformations have a characteristic signal intensity that is greater than skeletal muscle on both T1-and T2-weighted images. Pathologically these findings have correlated with fibro fatty septae between endothelial cell lined vascular channels.

The high signal intensity seen on spin echo sequences with long TR/TE has been attributed to stagnant flow in these abnormal vascular spaces. In areas where tissue fat is prominent, we will frequently perform fast spin echo T2 sequences with fat suppression to aid in delineating the true extent of the venous malformation. MR STIR imaging sequences also demonstrate the lesion to advantage. Our series not only has confirmed the typical features described, but we have also determined other characteristics with diagnostic and therapeutic implications. Other characteristics that we have noted are propensity for discontinuous multifocal involvement of several foci of venous malformation, a tendency for orientation along the long axis of affected extremities, a tendency to follow neurovascular distributions in the extremities, occasional extension of malformation into the tendon sheaths, and associated enlargement of subcutaneous fat. These additional characteristics may prove helpful in the differential diagnosis of problematic cases. Further, the fact that venous malformations frequently follow neurovascular distributions and the fact that there may be enlargement of subcutaneous fat again points to the developmental congenital tissue dysplasia as opposed to a dysplasia related to blood vessels alone.

MR exquisitely delineates the full extent of venous malformation and is vastly superior to arteriography or venography in its evaluation. In an anatomic site such as the head and neck area in which closed system venography and direct puncture venography can be difficult, MR is very informative and completely defines the extent of a lesion and its involvement with specific tissues. At follow-up MR is outstanding to evaluate the efficacy of therapy. As portions of venous malformation are ablated, they lose the typical increased signal seen on T2-weighted images. This is very important in that MR will be important to determine residual areas of venous malformation that still require therapy. MR can then direct therapy toward these specific anatomic sites (3).

CHARACTERIZATION OF THE VEIN ANOMALY

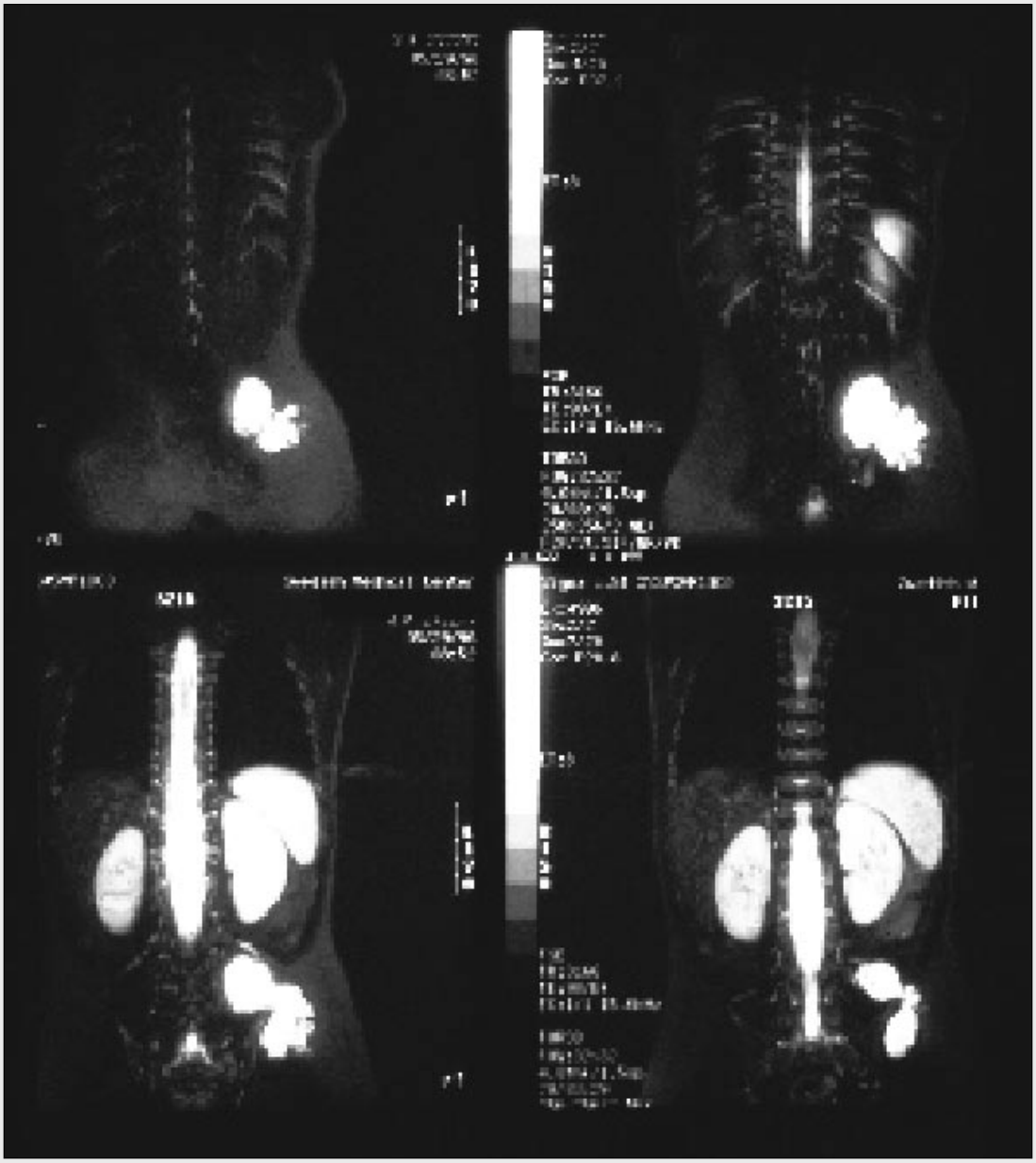
Vein anomalies may occur anywhere in the body but are most often seen in the superior vena cava (SVC), inferior vena cava (IVC), portal vein, and peripheral veins. The SVC may be duplicated, left-sided, or demonstrate anomalous systemic venous return. The IVC may be duplicated, left-sided, have continuation into the azygos and hemiazygos veins or be atretic. The portal vein may be duplicated, have congenital porto--systemic connection or may be atretic. Peripheral veins may be atretic, hypoplastic, duplicated, demonstrate avalvulosis or demonstrate vein aneurysms.

Venous malformations are congenital lesions arising from abnormal vein morphogenesis. On plain x-ray films calcified phleboliths may be present. In-flow arteries are of normal size because there is a normal intervening capillary bed. In the late arterial phase contrast pooling in the postcapillary dilated abnormal venous structures occurs because of slow stagnant flow within the malformation. Vein malformations are usually incompletely opacified by arteriography alone. Closed system venography and direct puncture venography better demonstrate the extent of the abnormal vascular spaces (1, 2). Again, CDI and MR are excellent noninvasive imaging modalities that can document the presence of a slow-flow malformation and distinguish it from a high-flow malformation. Further, the relationship to adjacent anatomic structures are easily demonstrated

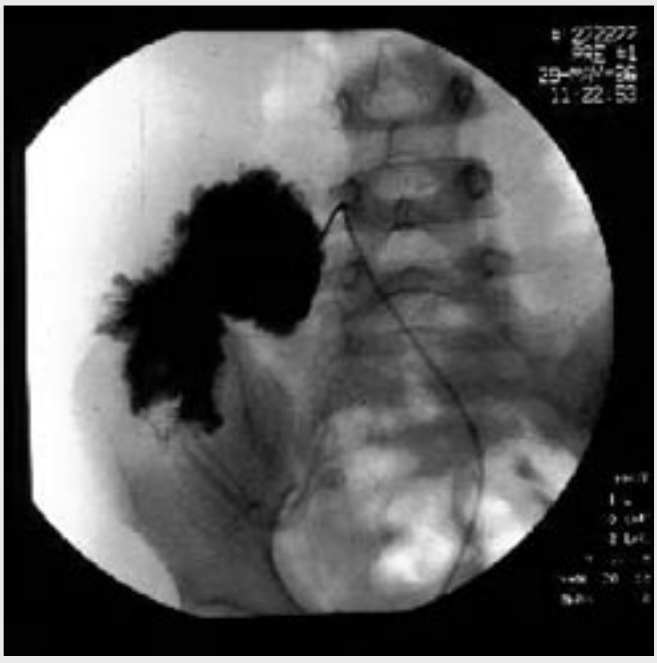
VEIN MALFORMATION TYPES

Venous malformations may be asymptomatic, cosmetically deforming, cause pain, induce neuropathy, ulcerate, hemorrhage, induce changes of abnormal bone growth, cause pathologic fractures, cause a platelet consumptive coagulopathy, and have mixed venous-lymphatic components. Because of the sophistication of CDI and MR to noninvasively diagnose the presence of venous malformation and distinguish it from other types of malformations, venography and arteriography are required only when therapy is indicated. Arteriography usually is normal; however, an occult congenital arteriovenous fistula may be present in mixed lesions and needs to be documented prior to therapy. After careful scrutiny of all baseline studies an appropriate treatment plan can be presented to the patient and the referring clinician.

Intramuscular venous malformations, previously incorrectly termed "intramuscular hemangioma," comprise a rarer subgroup of venous malformations (35, 36). These venous malformations are largely contained within the muscle and may extend into the surrounding tissues. Although histologically identical, intramuscular venous malformations have a different clinical presentation than the typical venous malformation. The age at presentation in this subgroup of patients is usually 20–30 years but it may be earlier or later. These lesions most commonly occur in the extremities and all patients present with a growing palpable mass with or without pain. Arteriographically, intramuscular venous malformation frequently has hypertrophied arterial in-flow with a dense tissue stain. Arteriovenous shunting is noticeably absent. It is this increased arterial flow that can make the diagnosis somewhat confusing. However, MR evaluation will be conclusive in that intramuscular venous malformation exhibits the same MR characteristics as traditional malformations. Intramuscular venous malformations do exhibit increased signal on long TR/TE imaging sequences.



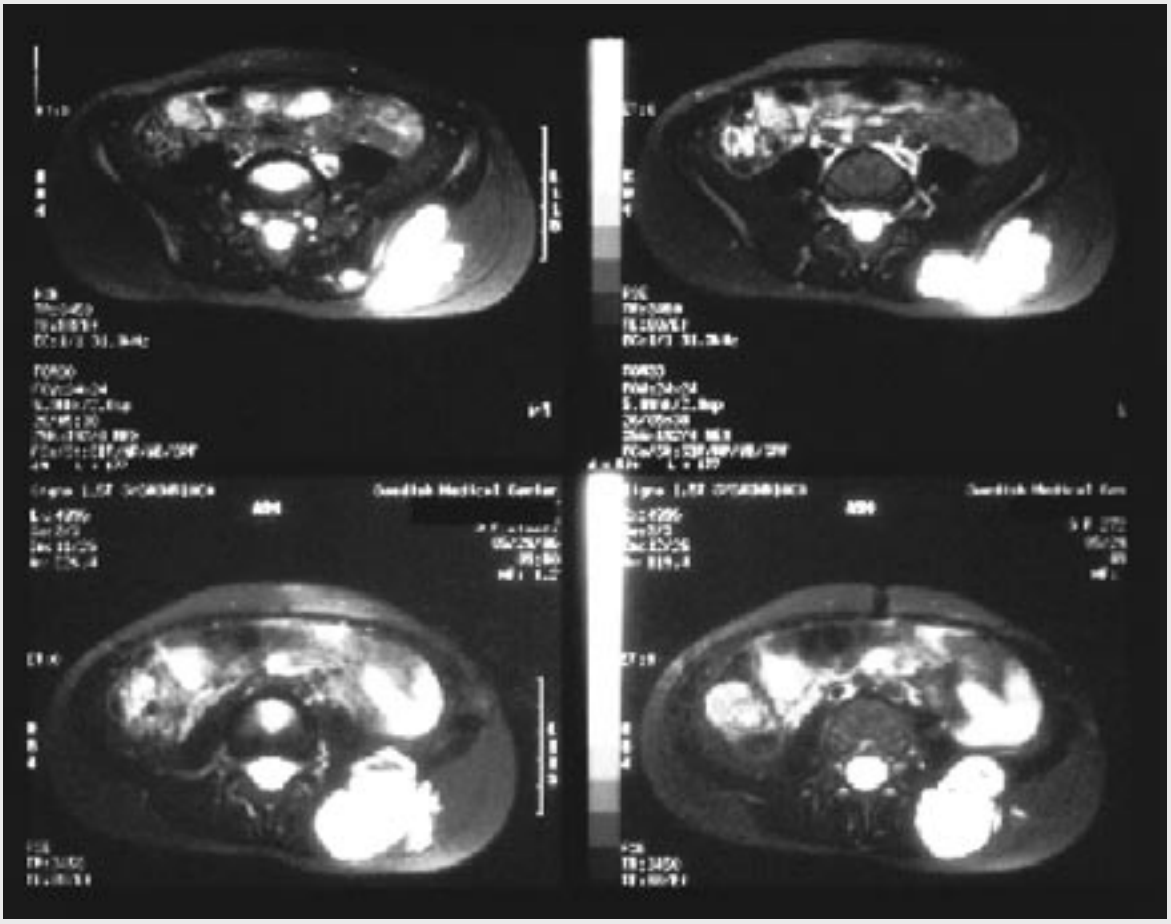
▲ Obr. 4A



◀ Obr. 4B

Fig. 4. A – 5 year old female with painful growing mass in the left lower back and buttock area. Coronal T-2 fat suppressed image of lower back. Note bright signal of vein malformation in the left paraspinal area extending to the left buttock region; B – direct puncture contrast injection into the lesion with the patient in the prone position. Note the similarity of the contrast image compared to the MR image in 4A; C – axial T-2 fat suppressed image of the lower back prior to percutaneous ethanol treatment. Note the bright signal in the images of the lesion; D – axial T-2 fat suppressed images of the lower back six months after percutaneous ethanol therapy. Note remarkable absence of the vein malformation due to ethanol treatment. The patient no longer has any pain syndrome. The patient will be followed over the years with MR imaging.

Obr. 4. A – 5letá dívka s bolestivou rostoucí expanzí vlevo v bederní a hýžďové oblasti. Koronární T2 vážený MR obraz s potlačením signálu tuku, vysoký signál intenzity vlevo paraspinálně zasahující do hýžďové oblasti; B – přímá punkce s aplikací kontrastní látky v poloze na břiše, obraz je obdobou MR zobrazení; C – axiální T2 vážený MR obraz s potlačením signálu tuku před perkutánní aplikací etanolu s vysokou signální intenzitou malformace; D – axiální T2 vážený MR obraz s potlačením signálu tuku šest měsíců po perkutánní terapii etanolem, malformace není již přítomna, nemocná je bez známek bolesti, v budoucnosti bude provedena další kontrola pomocí magnetické rezonance



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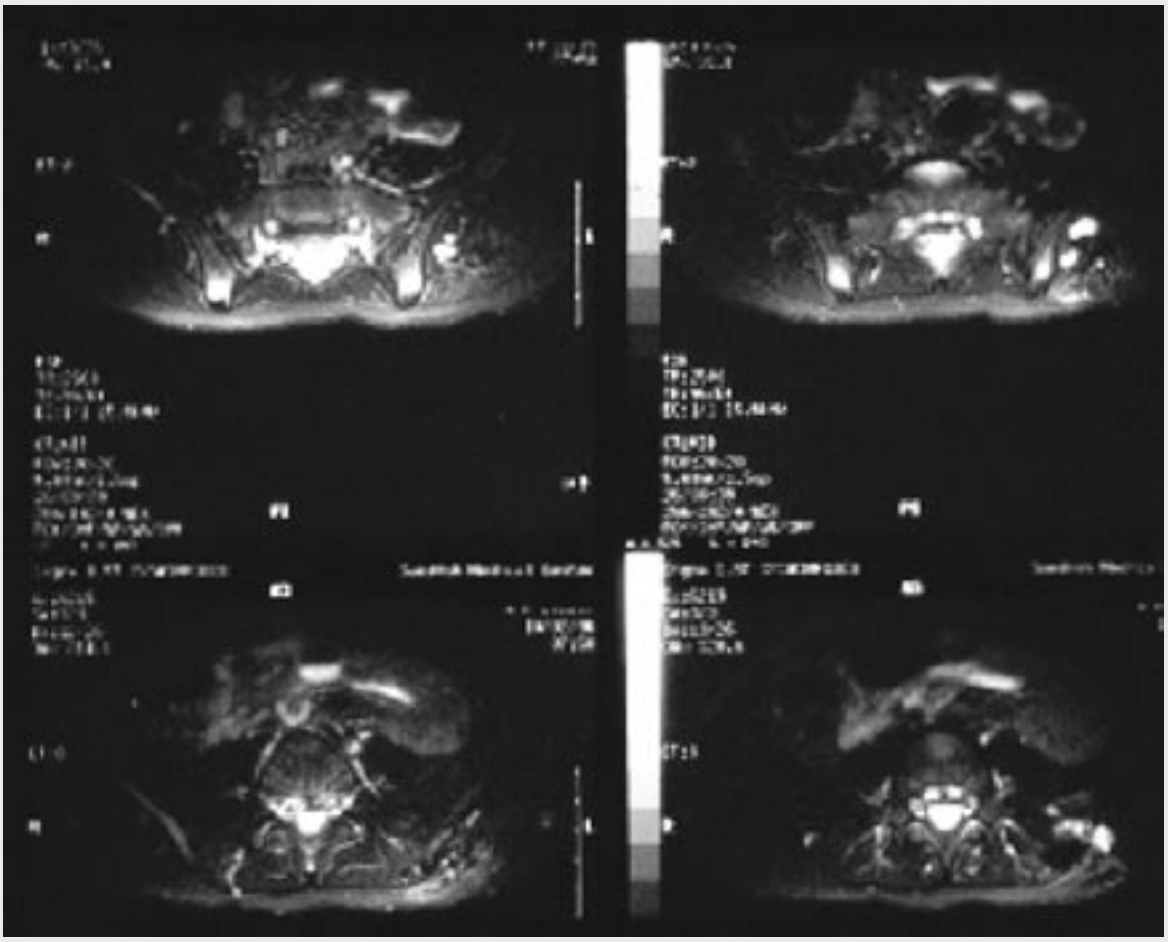


Obr. 4D

Intramuscular venous malformations respond to percutaneous ethanol therapy the same as traditional venous malformations. Because of this type of malformation's ability to be contained solely within a single muscle, if that muscle can be sacrificed without compromising function, then resection of that muscle can lead to cure of the venous malformation. In this setting arterial embolization with polyvinyl alcohol particles is a useful preoperative surgical adjunctive procedure to minimize the blood loss at surgery. In those lesions whereby removal of that muscle or muscle group will lead to significant functional impairment, direct puncture ethanol therapy is an excellent alternative. At follow-up after therapy MR is essential and will define those treated areas (loss of signal of T2) and residual malformation requiring treatment (increased T2 signal).

Vertebral body hemangiomas are not hemangiomas. They are truly venous malformations that involve bone. These lesions are relatively common abnormalities and have been found in 10.7% of spines at autopsy and in 14.2% of people over the age of 60 years. Many patients are asymptomatic and have been incidentally discovered on routine plane films of the chest or abdomen. However, when venous malformation of the vertebral body grows into the epidural space to compress the spinal cord, slow progressive myopathy can result. Epidural hemorrhage and compression is extremely uncommon. Treatments for patients who have symptomatic vertebral body venous malformations include surgery, radiation therapy, and transarterial particulate embolization (38–40).

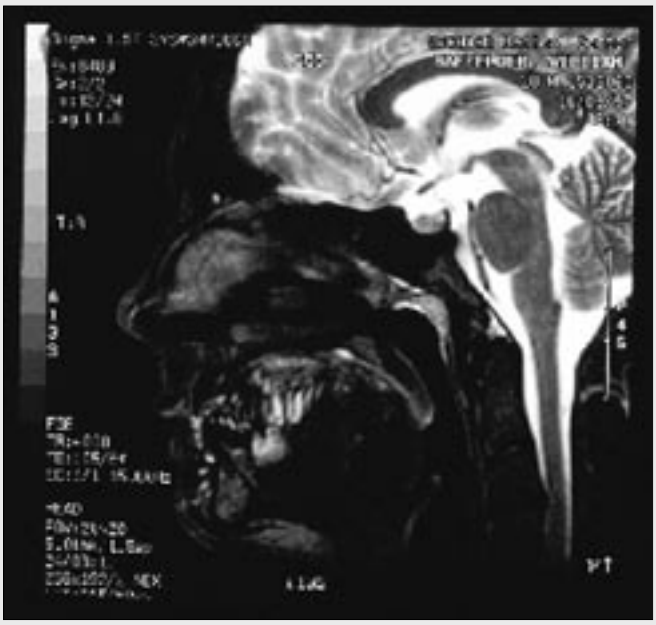
Surgery is often associated with profuse hemorrhage resulting in incomplete resections. Radiotherapy is moderately effective, however, its main drawback is not only that the effects on the venous malformation are delayed, but there is a risk of radionecrosis of the spinal cord. Transarterial particulate embolization decreases the arterial inflow because the particles lodge proximal to the capillary bed. The venous malformation itself remains untreated. Risks of transarterial particulate embolization also include spinal cord infarction when prominent radiculomedullary branches arise from the artery that supplies the abnormal vertebral body and spinal cord. Recently there has been the development of direct intravertebral injection of methylmethacrylate. It does occupy space and create a permanent and noncompressible cast within the vertebral body; however, it does not destroy the venous malformation. Further, if the venous malformation extends into the epidural space the injection of this acrylic substance can aggravate cord compression by forming a rock inside of the pliable vascular structure.

Direct percutaneous intralesional injection of ethanol is an extremely attractive alternative to the management of vertebral body venous malformations. Just as peripheral venous malformations of the body respond to ethanol direct intralesional treatment, so does venous malformation within vertebral bodies. Direct injection of ethanol is safer than transarterial embolization because it thromboses the venous malformation itself and does not affect the inflow artery which may have prominent radiculomedullary arterial branches to the spinal cord. Further, ethanol can completely eradicate the venous malformation and preserve the bone trabecular support for vertebral stability. This would then obviate any surgical approach to promote stabilization of the vertebral body. We have found this technique to be extremely attractive to treat vertebral body hemangiomas as well as vertebral body aneurysmal bone cyst which, in essence, are almost the same entity. Other investigators have reported excellent success with intralesional injection of ethanol (42). In those venous malformations that do extend to the epidural space compressing the spinal cord, ethanol injections will eradicate the hemangioma and cause it to regress from the epidural space. Ethanol is very attractive because it averts vertebral body corpectomy operative blood loss, lengthy convalescence postoperatively, does not cause radionecrosis of the spinal cord as can happen with radiosurgery, and preserves the inflow artery to the vertebral body and spinal cord supply and can be repeated as necessary to totally obliterate any residual portions of the venous malformation. We prefer the transpedicular approach and this is championed by other investigators as well (42).

MANAGEMENT CONSIDERATIONS

Because of the significant pain that always occurs with the placement of ethanol intravascularly during a procedure, general anesthesia is a requirement. As we have evolved in our monitoring of patients during the procedure, patients with large diffuse venous malformations, as opposed to small-localized lesions, may additionally undergo Swan-Ganz line and arterial line monitoring. Pulmonary pressures are constantly monitored during the injection of absolute ethanol (98% dehydrated alcohol injection USP, Abbott Laboratories, North Chicago, IL) into the venous malformation and immediately in the postinjection period. If one injects no more ethanol than 0.1 ml/kg (ideal body weight) every 10 minutes, then Swan-Ganz monitoring may be obviated. Decadron (dexamethasone sodium phosphate USP, Merck & Co., Inc., West Point, PA) is given intravenously to all patients prior to the procedure. Adults are usually given 10 mg intravenously and children from 3 to 10 mg depending on body weight. The area of the malformation that is to be treated is prepped with Betadine scrub and draped in sterile fashion. Real-time CDI and fluoroscopy imaging techniques are utilized to gain percutaneous access, delineate the intravascular extent of the malformation, and deliver the appropriate ethanol volume for therapy. Direct access needles are utilized to enter the abnormal vascular spaces. Direct puncture venograms are then performed to access the adequacy of position prior to ethanol injection. Further, the venogram is very helpful to delineate any venous outflow from the malformation that connects to the normal deep venous system. As has been stated previously, deep-vein thrombosis is an unwanted potential complication of the procedure.

Ethanol endovascular therapy is directed against abnormal malformed venous elements, not the normal deep or superficial venous systems. Venous malformations usually demonstrate stagnant flow within the abnormal vascular spaces. If venous occlusion is necessary to prevent unwanted outflow into normal venous structures, extrinsic tourniquets, pneumatic blood pressure cuffs, and manual digital compression can be utilized to limit the flow into the normal deep and superficial venous system. The amount of ethanol utilized is equal to the flow-volume characteristics of the malformation compartment being treated. No predetermined ethanol volumes are considered. The total maximum volumes of ethanol used in



▲ Obr. 5A

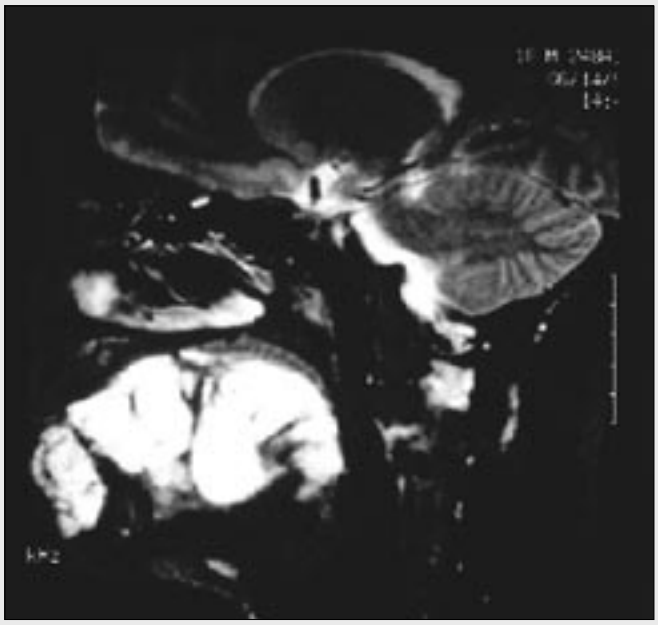


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Fig. 5. ***A – 17 year old male with significant malocculsion of the maxilla and mandible due to gross enlargement of the tongue because of massive infiltration with vein malformation. Sagittal MR T-2 with fat suppression performed in the facial area. Note massive infiltration of the tongue with venous malformation. Note extensive vein malformation involvement of the lower lip and chin also evidenced by the bright signal; B – sagittal MR T-2 with fat suppression image. Note dramatic decrease in signal with reduction in size of the tongue, lower lip, and chin area after serial direct puncture ethanol treatments.***

Obr. 5. ***A – 17letý mladík s významnou poruchou skusu kvůli rozsáhlému zvětšení jazyka masivní infiltrací venózní malformací. Sagitální T2 vážený MR obraz obličeje s potlačením signálu tuku, dobře zřetelná infiltrace jazyka malformací s vysokou signální intenzitou přesahuje na dolní ret a na bradu; B – sagitální T2 vážený MR obraz obličeje s potlačením signálu tuku, signál i objem výrazně poklesl po sérii přímé aplikace etanolu jak v oblasti jazyka, tak i v dolním rtu a na bradě***

treating vein malformations should not exceed 1 ml/kg body weight total dose. Pre-and-postprocedure direct puncture venograms document the level of thrombosis in the portion of the venous malformation being treated. Ultrasound can also document thrombosis with compression techniques. Usually multiple sites are treated in the same procedure.

Postprocedure the patients are revived from general anesthesia and sent to the recovery room for initial observation. After the patient is stable, they are sent to the routine hospital ward, and discharaged three hours observation. Medical management on the ward consists of Decadron therapy intravenously according to body weight (1 mg/25 kg every 6–8 hours intravenously), intravenous fluids (lactated Ringer's or D5 1/4 NS with 20 mEq KCI), Inaspine (Droperidol injection, Janssen Pharmaceuticals, Inc., Titusville, NJ) given intravenously prn to control postoperative nausea, oral, or intramuscular (IM) Toradol (Ketorolac tromethamine, Syntex Laboratories, Inc., Palo Alto, CA) therapy according to body weight in adult patients is very helpful to control any pain and swelling. Various oral and IV pain medications are not usually required. Discharge medications include a Medrol Dose Pack (Methyprednisolone tables USP, Upjohn Co., Kalamazoo, MI) after discharge to aid in the resolution of swelling.

All patients will exhibit focal swelling in the area of malformation treated postprocedure. Most patients will resolve the majority of the swelling by 2 weeks. In those patients with lower extremity and foot malformations, swelling may last longer due to the fact that the leg and foot are not only dependent organs but are weight-bearing structures as well. Usually after 4 weeks, all swelling is resolved and the patient, being at the new baseline, is ready for follow-up therapy as indicated.

After serial therapy, MR is essential to document the reduction in the mass of venous malformation. Decrease in presenting symptoms, which is usually pain, also correlates well with the amount of malformation treated. In those patients who present with a pain syndrome, serial devascularization of the malformation will usually completely obliterate or at least dramatically reduce the amount of pain the patient suffers. At our institution, patients with residual pain undergo neurostimulation with the Synaptic 2000 (Synaptic Corp., RFP Inc., Aurora, CO) pain-control device. This unique noninvasive device has proven very helpful in controlling residual pain of patients. Not only has the Synaptic 2000 device reduced the need for oral narcotic medications in patients presenting with pain, but it has also obviated treatment by controlling the pain to such a level that further endovascular therapy was not warranted. Additional applications have been noted with this device with regard to nerve injury recovery, microrevascularization stimulation in ischemic tissues, decreased swelling postprocedure, and tissue healing postinjury; and other indications are being evaluated at this time as well. We are in our early experience with this device.

Not all patients require total obliteration of their malformation to achieve a symptomatic improvement. Permanent partial ablations frequently result in resolution of clinical symptoms. At long-term follow-up in our patients, symptomatic clinical "cures" were present despite the fact that residual malformation remained as documented by MR.

A complication rate of 3% has been observed in all anatomic locations. Complications from ethanol endovascular therapy of venous malformation include minor skin blisters, bruising, skin necrosis, minor tongue necrosis, superficial infection/cellulitis, transient pain, muscle contracture, deep vein thrombosis, pulmonary embolus, sensory nerve injury, motor nerve injury, transient pain, maxilla bone injury, and cardiopulmonary collapse. We have had two deaths in our series directly attributable to ethanol endovascular therapy in venous malformations. The patient suffered from cardiopulmonary collapse and failed all resuscitative efforts. The patient's death was caused by cerebral anoxia, resulting in brain death.

All tissue injuries undergo the usual wound-healing process. Those patients with skin injuries undergo routine wound care and in those patients who become infected or develop cellulitis, antibiotics are an additional requirement. In the vast majority of cases, the infections have been related to skin flora such as *Staphylococcus aureus*. In one patient with a small area of buttock skin necrosis, *E. coli* has cultured from the wound. Routine wound care usually heals the area of necrosis. Skin grafting is rarely indicated.

In malformations involving the musculature, an uncommon complication of contracture may occur as the malformation scars and shrinks within the muscle. We have found that routine physical therapy begun early in those patients with intramuscular involvement will usually obviate or at least minimize this problem. Very rarely deep-vein thrombosis may occur and, depending on the level of thrombosis, standard heparin and coumadin therapy is utilized. In those patients who have a sensory or a motor nerve injury, it is usually a transient phenomenon despite the fact that nerves usually parallel arteries. Nerve injuries can, nonetheless, occur. Again, neurostimulation therapy with the Synaptic 2000 has hastened the recovery of sensory and motor nerves in selected patients.

In patients who have extensive venous malformations, especially those whereby an entire extremity is involved or a large truncal lesion, coagulation and laboratory evaluations are mandatory. Evaluations of fibrinogen, platelets, PT, PTT, INR, bleeding times, and D-Dimers should be evaluated. In those patients with extensive malformations, they may have a chronic disseminated intravascular coagulopathy state. This can be evidenced by abnormal bleeding times, low fibrinogen levels, low platelet levels, and positive D-Dimers. If such a patient with extensive venous malformation may require surgery for whatever reason, hematologic work-up may save a disaster. With treatment of the malformation there can be improvement in these hematologic parameters. This could be considered a variant of the Kasabach-Merritt syndrome. However, this is not a pediatric hemangioma causing the problem, this is a venous malformation. With ethanol treatment of venous malformations in patients with chronic DIC, extensive treatment can cause fibrinogen levels and platelets levels to drop. A hematology consultation may be required in this subgroup of patients.

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