Bevacizumab in Pediatric Neuro-Oncology

By Mariah Bashir, MD and Karen Moeller, MD

Bevacizumab and Brain Tumors

Multiple trials and series have been done recently to elucidate the value of bevacizumab in pediatric recurrent high-grade gliomas with disappointing results thus far. Wolff et al reported 2 of 12 patients with recurrent diffuse intrinsic pontine gliomas having a response to protocols containing bevacizumab which was not different from the response rate to other treatments. In a series from Narayana et al, 12 patients with recurrent or progressive high-grade gliomas were treated with bevacizumab and irinotecan: 11 patients experienced relapse and 10 patients succumbed to disease progression. A phase II Pediatric Brain Tumor Consortium followed 15 patients treated with Bevacizumab and CPT-11 with recurrent malignant gliomas and 16 patients with diffuse brainstem gliomas; this study found no sustained responses in either group, and median time to progression for all patients enrolled was 127 days for malignant glioma and 71 days for diffuse brainstem glioma. Parekh et al also showed a similar suboptimal response rate in their series of pediatric patients treated for recurrent malignant glioma. The substantial inferior response rates in children in comparison with adults in high-grade glioma populations is speculated to be due to biological differences in the tumors themselves between these two patient groups.

Experience with bevacizumab in the treatment of recurrent or refractory medulloblastoma is limited but somewhat more encouraging. Aguilera et al presented two cases of relapsed or refractory medulloblastoma treated with bevacizumab and irinotecan with the addition of temozolamide in one patient. They found progression-free survival of 18 and 30 months, with one patient continuing on therapy for 35 months with stable disease.

Based on experience to date, bevacizumab is currently not considered first-line therapy for pediatric brain tumors; rather, it is used in patients with recurrent or refractory tumors that are not responding to standard treatments, typically in combination with other chemotherapy agents. Research is ongoing, however, in efforts to explore its effectiveness as a first line agent in pediatric brain tumor patients.

Bevacizumab and Radiation Necrosis

Bevacizumab has been shown to be useful in the treatment of radiation necrosis. Its effectiveness in this setting has been hypothesized to be secondary to reduced vascular permeability and decreased edema. It has been applied to pontine gliomas previously treated with radiation therapy, where necrosis occurs frequently and is thought to be related to a combination of radiation therapy and the biology of the tumor itself. Steroids, currently the first line treatment for radiation necrosis, substantially reduce edema but are associated with numerous side effects, especially when taken at large doses for prolonged periods, with morbidity not infrequently precluding its use. Bevacizumab, as a single agent, has a less severe side effect profile, and can be used in patients not tolerating steroid treatment. It can also be tried in patients in whom the radiation necrosis is not responding to steroid protocols.

Imaging

Imaging findings in patients on treatment with bevacizumab are remarkably predictable in both tumor and radiation necrosis patients. Typically there is some reduction in the overall mass size and moderate decreased enhancement within the lesion. Perilesional edema is also reduced.

Bevacizumab continued on page 2
Conclusion

In summary, use of bevacizumab in pediatric Neuro-Oncology is currently confined to patients with brain tumors that are refractory to established protocols. Used as a first line agent has been disappointing in early studies although research is ongoing. In treating brain tumors it is routinely used in combination with at least one other chemotherapeutic agent. It may be useful on its own in the treatment of radiation necrosis in patients not responding to or not tolerating steroid treatment. Imaging changes are predictable during bevacizumab treatment characterized by a decreased lesion size, reduced enhancement and decreased perilesional edema.

Further Reading


Side Effects

Side effects from bevacizumab are typically less severe compared with other chemotherapy agents. The most common adverse effect is hypertension. Other side effects include menorrhagia and irregular menses, proteinuria, nephritic syndrome, posterior reversible encephalopathy syndrome, and headache sometimes associated with nausea and vomiting. More rare side effects include lymphopenia, hemorrhage, and poor wound healing.
RADIOLOGICAL DIAGNOSIS OF VASCULAR ANOMALIES IN THE HEAD AND NECK: CONVENTIONAL CONTRAST ENHANCED MRI AND DYNAMIC MRA IMAGING FEATURES

(No potential conflict of interest relevant to this article was reported.)

By Aylin Tekes, MD and Eman Alqahtani, MD
Johns Hopkins Hospital

Introduction

Vascular anomalies (VAs) have been confusing to most physicians due to overlapping clinical and imaging findings between different types of anomalies. Rarity of the VAs, lack of experience and multidisciplinary approach contribute to the chaos that goes on in diagnosis and management.

Historically, VAs were named based on location, fluid content or discoloration on the skin resulting in redundant, ambiguous and misleading terms. Nomenclature of VAs has evolved from “angiomas” or “vascular birthmarks” and the term “hemangioma” has incorrectly served as a generic word to describe most of this VAs. A recent publication in 2009 outlined that the term “hemangioma” was used incorrectly in 71.3% of publications that year.

Accurate diagnosis and “common language” between different disciplines requires consistent use of correct terminology for each vascular anomaly. Current classification system that was approved by International Society for the Study of Vascular Anomalies (ISSVA) in 1996 stems from the biological behaviour based classification system, introduced by Drs. Mulliken and Glowacki in 1982.

In this first biological classification vascular anomalies were divided into two major groups: vascular tumors (with cellular proliferation and hyperplasia) and vascular malformations (focal defects of vascular morphogenesis). Vascular malformations (V-Ms) were subdivided further into malformations consisting of capillary, venous, arterial, lymphatic, or fistulous networks.

Soft tissue vascular anomalies can present anywhere in the body from head to toe, head and neck being the most common site. Most VAs can be diagnosed and classified according to physical exam and history, however radiological evaluation is needed to provide diagnosis in challenging cases, define the full anatomical detail of the VA, help target areas that need treatment, and monitor treatment response. Accurate classification is crucial since morbidity and treatment differs significantly between different groups of vascular anomalies.

In this article, we will review the magnetic resonance imaging (MRI) features of VAs based on conventional MRI and dynamic contrast enhanced Magnetic Resonance Angiography (DCE-MRA) that help achieve accurate diagnosis.

MR Imaging Protocol

MRI is the most suitable imaging modality for the soft tissue vascular anomalies in the head and neck in children with lack of ionizing radiation and excellent soft tissue contrast, and multiplanar imaging capabilities.

We perform fat saturated/suppressed T2 Weighted (T2-W) imaging in all three orthogonal planes. Fat suppression/saturation is crucial, since almost all vascular anomalies present with increased T2 signal. This is followed by an axial pre-contrast T1 Weighted (T1-W) image.

Upon administration of contrast, dynamic contrast enhanced MRA (DCE-MRA) is performed followed by post contrast T1-W imaging with fat saturation in all three orthogonal planes.

DCE-MRA is a 3D gradient echo (GRE) time-resolved MRA technique used to dynamically assess the timing of contrast enhancement and define the arterial feeders and venous drainage of a vascular anomaly. Timing/phase (arterial, capillary, venous or none) of enhancement provides great information in classification of vascular anomalies.

Spatial resolution of DCE-MRA is relatively low compared to conventional 3-D MRA techniques however image quality and spatial resolution of the data can be further enhanced with the use of blood-pool MR contrast agents, which reversibly binds to serum albumin (binding fraction of approximately 90%).

Advantages over traditional contrast agents include higher intravascular concentration of contrast over a longer time period of time and increased relaxivity, giving better signal (SNR) and contrast to noise ratios (CNR) for imaging. In addition, children have a much faster circulation time than adults, and lower doses are used and injection times are longer, resulting in higher contrast dilution. Blood-pool contrast agents can be administered at an approximately 3-fold lower dose than diffusible contrast agents while achieving an SNR gain. Both, arterial and venous enhancement persists over a prolonged time, making contrast timing less critical: bolus tracking is not required. These are highly advantageous points that make them preferable in the evaluation of vascular anomalies in children.

VASCULAR ANOMALIES

Vascular Tumors

Infantile Hemangiomas (IH)

IHs make up to at least 90% of all vascular tumors. IHs are the most common vascular tumors of infancy, more common in white caucasian infants with the highest incidence in preterm infants weighing less than 1,000 g. IH often are inapparent at birth and most appear in the first 6 weeks of life with a typical triphasic evolution: proliferation, plateau and involution. Approximately 80% of IH reach their maximum size between 3-5 months of age. IH are positive for immunohistochemical markers such as GLUT-1 that help differentiation from congenital hemangiomas and vascular malformations. Morphologically, IH can be divided as focal, segmental and indeterminate. Segmental hemangiomas are important to recognize since it can be part of PHACE syndrome: posterior fossa malformation, hemangiomas, arterial anomalies, coarctation of the aorta, and eye abnormalities.

The evolutionary phase of the...
hemangioma determines the imaging features. IH is a well-defined, focal, soft tissue mass. Although infiltration of more than one tissue plane/adjacent organ may be observed, they generally present as a mass enlarging from a center in a single tissue plane.

MR imaging reveals a T2 bright, T1 isointense mass with homogenous avid contrast enhancement. Best diagnostic clue is a soft tissue mass that shows homogenous contrast enhancement that starts in the “arterial” phase in the DCE-MRA (Fig 1 on pg. 6).

In T2-W imaging arterial feeder can be depicted as serpiginous flow void. Typically, no perilesional edema is observed. The term “phlebolith” refers to “calcification in a vein”, thus it is commonly seen in venous malformations, not hemangiomas. Presence of calcification in a vascular soft tissue mass should raise the possibility of congenital vascular hemangiomas, or hemangioendotheliomas, not an IH.

During the involution phase, areas of fibro-fatty transformation can be recognized within the mass, which may reveal itself as areas of non-enhancing tissue. Approximately 40% of IH in the head neck region involute with fat replacement (Fig 2 on pg. 6).

Although imaging is not required for the majority of IHs, MRI can be performed to confirm the diagnosis in atypical cases, or to determine anatomical extent for deep lesions. In addition imaging might be required in excluding other lesions such as uncommon congenital vascular tumors, soft-tissue malignancies such as rhabdomyosarcomas, congenital lesions such as nasal gliomas or hemangiomas.

Vascular Malformations

V-Ms are believed to represent developmental dysmorphogenesis in angiogenesis and vasculogenesis between 4th and 10th weeks of intrauterine life. Molecular discoveries indicate genes expressed in endothelial cells and involved in receptor signalling [12]. They are present at birth although may not become visible till childhood, or rarely till adulthood.

V-Ms grow commensurately with the child, and exacerbations may follow after trauma, infection or hormonal changes. Typically, they do not regress spontaneously, unlike IH. Isolated forms of V-Ms are far more common than mixed types (involving more than one vessel type such as capillary-lymphovenous). Mixed/complex types of vascular malformations can be seen in the setting of syndromes, such as Klippel-Trenaunay, Parkes-Weber, Blue Rubber Bleb Nevus, or Maffucci.

V-Ms are classified based on the flow-rate and involved vessel type: Low-flow V-Ms (venous malformation (VM), lymphatic malformations (LM), capillary malformations (CM), and high-flow V-Ms (arteriovenous malformations (AVM)).

Low flow vascular malformations

Venous malformation (VM)

VMs are the most common type of V-M and present as soft, compressible lesions. VMs are commonly infiltrative in nature, and violate multiple tissue planes such as the subcutaneous fat and muscle. Focal, non-infiltrating presentations can be seen. The lesions vary in size from very small to extensive involving multiple compartments.

VMs are serpiginous T2 hyperintense lesions, which often show phleboliths. Hemorrhage, thrombosis or phleboliths may reveal variable degree of T1 hyperintensity within the VM. Some degree of fat tissue or muscle tissue may be observed interspersed between the venous channels.

Presence of phleboliths and internal enhancement in the venous phase of DCE-MRA are the best diagnostic clue in diagnosis of VM (Fig 3 on pg. 6). Variable degrees of internal contrast enhancement can be seen, depending on the presence of internal thrombosis, phleboliths and prior embolization (Fig 3 on pg. 6). VMs do not have arterial feeders, and may communicate with systemic veins, which is crucial to know before embolization. DCE-MRA demonstrates progressive contrast filling within the VM during the venous phase.

Lymphatic malformations (LM)

LMs are present as a soft non-pulsatile. They are the second most common type of vascular malformations after VMs [13]. Morphologically, they can present as macrocystic, microcystic or mixed macro- and micro-cystic LM. Variable size and trans-spatial infiltration can be observed.

LMs are commonly T2 hyperintense and high T1 signal can be seen in the presence of internal hemorrhage/high protein content.

Fluid-fluid level can be seen in LM likely reflecting debris from inflammation or hemorrhage, however it should be noted that fluid-fluid level is a sign of slow-flow malformations, and can be seen in VMs as well, therefore it shouldn’t be taken as a sole diagnostic criteria or pathognomonic for the diagnosis of LM.

LMs do not show internal enhancement after intravenous contrast administration, which is the most decisive finding on MR in the differentiation from other VAs [13]. However, septa/wall enhancement is commonly observed. In patients with diffuse microcystic LM, enhancing walls may challenge the interpretation as they may mimic areas of relatively solid enhancement.

Capillary Malformations (CM)

CMs are limited to superficial layers of the skin, however over time can become nodular and thicker especially with thickening of the underlying subcutaneous fat. Previously called, “port wine stains“, CM can be seen in Sturge-Weber syndrome, Klippel-Trenaunay, or Parkes-Weber syndrome. They are diagnosed on clinical basis. Given the superficial involvement MR imaging has a very limited value except for ruling out other underlying vascular malformations.

High flow vascular malformations

Arteriovenous Malformations (AVM)

AVMs are high flow lesions characterized by direct connections between arteries and veins without an intervening capillary bed. They are most common in the head and neck region, and nearly 70% involve the midface.
Vascular Anomalies continued from page 4

They are considered as the most aggressive type of vascular malformations.

AVMs are made of multiple feeding arteries with increased diastolic flow and increased venous return with systolic/diastolic flow. They present with ill-defined borders without associated soft tissue mass. Hyperplasia if the surrounding fat tissue can be observed. Unlike hemangiomas, there is always arterIALIZATION of all the draining veins (i.e. pulsatile flow) in AVMs.

Bone infiltration is most commonly seen in AVMs amongst all vascular malformations. Tangle of serpiginous signal voids are typically observed in both T1-W and T2-W Spin echo (SE) sequences, whereas increased signal is observed on gradient-echo and angiographic sequence indicating a high-flow lesion [14]. DCE-MRA typically shows early venous filling during the arterial phase. Systemic arteries feeding the AVM and draining veins can also be assessed in DCE-MRA [15] (Fig 5 on pg. 6).

Misnomers and Pitfalls

MR studies should be performed with the suggested VA protocol described earlier in this paper. Depending on the body part, modifications can be done with appropriate field of view, slice thickness, or use of respiratory/cardiac gating. MR imaging with standard MR protocols for required body parts should be avoided. To accomplish this important task, radiologists and the ordering clinical team should communicate closely, and radiologist should be aware of the suspected VA diagnosis.

Common misnomers should be avoided, such as: “strawberry or capillary hemangioma” should be replaced by “infantile hemangioma”; “cavernous hemangioma” should be replaced by “venous malformation”. “Port-wine stains” are now known to represent “capillary malformations”. Lymphatic malformations are not vascular tumors therefore the suffix “-oma” should be avoided: “lymphangioma” and “cystic hygroma” should be replaced by “lymphatic malformation”. Phleboliths are seen in VMs, not hemangiomas.

Lack of fat suppression can lead to misdiagnosis of persisting hemangiomas (Fig 2 on pg. 6). Relying on conventional MRI findings only may lead to misclassification of the VAs (Fig 6 on pg. 6).

Limitation of MR imaging should be recognized in diagnosis of superficial VAs especially CM. Major value of MR in such cases is to rule out presence of deep tissue involvement. In addition, although coronal plane generally serves well as the default plane for DCE-MRA, midline VAs may benefit from sagittal DCE-MRA.

Conclusion

Multidisciplinary approach integrating the clinical presentation and imaging findings is mandatory in the evaluation of VAs. Communication between referring clinical teams and the radiologist is critical. Dedicated VA MRI protocols should be implemented to make the most out of MR imaging. Standard use of classification system as accepted by ISSVA should set the basis of “common language” between different clinical teams involved in the care of VAs.

References:

Figures for: Radiological Diagnosis of Vascular Anomalies in the Head and Neck: Conventional Contrast Enhanced MRI and Dynamic MRA Imaging Features

**Figure 1.** Infantile hemangioma (IH) in the soft tissues of the right nose. A) Axial T2-W image with fat saturation demonstrates a well-defined hyperintense mass (arrow). B) Pre-contrast and C) Post-contrast T1-W image with fat saturation demonstrates avid, homogenous internal contrast enhancement of the solid mass (arrows). D) Time resolved dynamic contrast enhanced MRA (DCE-MRA) performed in the sagittal plane demonstrates enhancement of the IH starting in the arterial phase, and progressively increases in the venous phase (arrow). Sagittal plane is more suitable for DCE-MRA in the evaluation of midline VA (arrow).

**Figures 2.** 9 year old boy returns to clinic with the complaint of a non-resolving left parotid IH. A) Contrast enhanced T1-W image without fat saturation demonstrates a bright mass in the left parotid gland B) After fat suppression, it becomes clear that the T1 bright mass is in fact fat tissue. IH can resolve with fibro-fatty residuum. In the absence of fat saturation misdiagnosis of a persisting IH could have mislead the patient and the referring physician.

**Figure 3.** Venous malformation (VM) of the left cheek A) Coronal T2-W fat saturated image demonstrates lobular T2 hyperintense mass in the left masseter muscle. Multiple round T2 dark foci are noted within the VM representing phleboliths (arrow). B) Axial T2-W image focusing on the VM demonstrates fluid-fluid level (arrow), a feature of slow-flow vascular malformations. C) Pre-contrast, and D) Post-contrast T1-W images focusing on the VM demonstrate heterogenous contrast enhancement in the VM. E, F) Coronal DCE-MRA in the arterial phase doesn’t demonstrate any enhancement in the VM, because VMs don’t have any arterial feeders. Note the contrast enhancement in the venous phase (arrow), typical feature of VM (F).

**Figure 4.** Lymphatic malformation of the left cheek: A) Axial T2-W image with fat saturation demonstrates a multicycstic mass in the left masseter muscle. B) Axial T2-W image focusing on the VM demonstrates fluid-fluid level (arrow), a feature of slow-flow vascular malformations. C) Pre-contrast, and D) Post-contrast T1-W images focusing on the VM demonstrate heterogenous contrast enhancement in the VM. E, F) Coronal DCE-MRA in the arterial phase doesn’t demonstrate any enhancement in the VM, because VMs don’t have any arterial feeders. Note the contrast enhancement in the venous phase (arrow), typical feature of VM (F).

**Figure 5.** Arteriovenous malformation (AVM) of the left upper lip: A) Coronal T2-W image demonstrates a focal area of increased T2 signal with small serpiginous flow-voids. B, C) Sagittal DCE-MRA demonstrates early arterial filling of the AVM continuing into the venous phase, typical feature of AVM.

**Figure 6.** Venous malformation of the right frontal scalp. A) Coronal T2-W image with fat saturation, B, C) Pre-contrast and post contrast T1-W images with fat saturation demonstrate the features that have been described in Fig. 1, however this is not a VM. Note the signal void in A) which have been described in IH in the literature. D, E, F) Sagittal DCE-MRA demonstrates no enhancement in the arterial phase, and progressively increasing...
Introduction

Pediatric spine trauma is unique because of various reasons. First of all, the biomechanical properties of the initially predominantly cartilaginous pediatric spine are very different compared to the adult spine. In the early years of life, the stability of the pediatric spine relies predominantly on the cartilaginous spine and relatively lax ligaments. The pediatric spine is consequently relatively mobile and deformable. Traumatic forces will be absorbed differently; vertebral fractures are consequently rare in young children. Dislocations, ligamentous injuries, epiphyseal detachments and lesions of the ossification centers are more frequent. With progressing age and physical activity of the child the paraspinal musculature will develop and contribute to the dynamic stability of the spinal column. In addition the proportions of the pediatric body changes dramatically in the first years of life. Young children have a relatively large and heavy head compared with the torso. Later in life, the head-to-torso ratio progressively decreases. This is of particular importance for the crano-cervical junction. Next to the large head and the “weak” neck musculature, the “young” pediatric spine is also more mobile due to the shallow occipital condyles, the horizontal orientation of the facet joints and the immature uncovertebral joints. The transverse (extension/flexion) and rotational mobility of the cervical spine is increased compared to adults. This makes the crano-cervical junction and upper cervical spine very vulnerable for sudden acceleration and deceleration forces and trauma related injuries. The thoracic spine is less mobile due to the stabilizing impact of the adjacent rib cage, the lumbar spine is again more mobile.

Translational forces at the crano-cervical junction may result in devastating, frequently life-long lasting injuries to the lower brainstem and upper cervical spinal cord. Young children with traumatic brain injury should be evaluated for concomitant injuries to the crano-cervical junction. Next to the immediate injury to the spinal cord, injuries to the developing cartilaginous vertebral column and discoligamentary apparatus may also interfere with the ongoing development of the spinal column. Epiphyseal ring detachments, injuries to the ossification centers or dislocations possibly may result in spinal maldevelopment and long lasting spinal instability including scoliosis.

Finally, it is important to be aware that infants and children, depending on their age and physical activity are exposed to different kind of traumas. In neonates, the spine and spinal cord may be injured during a traumatic, forceful delivery; in young infants shaken baby injuries and non-accidental injury may result in trauma of the cranio-cervical junction; in older children direct blows to the spine may occur after falls or aggressive sport activities. Later in life, children predominantly suffer spinal injuries from high speed motor vehicle accidents. Airbag related injuries compromise a relatively new group of spinal injuries that depend on the size and position of the infant or child in relation to the rapidly expanding airbags in modern cars.

Knowledge about the kind of trauma, age dependent vulnerability of the spinal column and cord as well as risks of associated injuries outside of the central nervous system (CNS) are a sine qua non for correct diagnosis. Frequently, trauma to the spinal column and cord occurs as part of a more extensive accident including traumatic brain injury. In addition, simultaneous traumas to the chest and abdomen with possible cardio-pulmonary or parenchymatous complications may aggravate the injury of the spinal cord. Hypoxia-ischemia, spinal cord swelling, epidural hematomas, release of excitatory neurotransmitters, and various additional complex inflammatory processes to mention a few, may result in significant secondary injury.

Imaging

Goal of any diagnostic imaging should be to collect as much relevant and specific information about the location, degree and quality of primary injury to start immediate treatment and to limit or prevent secondary injury. Imaging should be fast, readily available, not interfere with the immediate treatment and should of course be highly sensitive and specific.

The tool box of available imaging modalities is diverse and includes static and dynamic conventional radiography (CXR), computer tomography (CT) and magnetic resonance imaging (MRI). Depending on the patients acute physical status and the available equipment different diagnostic approaches may be chosen. CXR of the spine is still being used as a first line of imaging. However in many institutions, children who suffered from serious traumas typically first receive a CT study of the region of trauma. In particular, children who suffered from an unwitnessed traumatic brain and/or spine injury, unconscious children, rapidly deteriorating children and children with focal neurological deficit receive primarily a head and spine CT. Multiplanar reconstructions of the spine show fractures and dislocations with high sensitivity and specificity. Next to bone algorithm reconstructions, soft tissue images are necessary to depict focal spinal cord injuries, epidural hematomas and adjacent soft tissue injuries. In addition, occasionally vascular injuries may be noted. Finally, if additional injuries to the chest and abdomen are present or suspected, whole body CT imaging may be performed. MRI is typically performed after a CT study if a spinal cord lesion is suspected (focal neurological deficits), or if the CXR or CT imaging findings do not explain the clinical/neurological symptoms. In addition, MRI is frequently used as follow-up imaging tool in order to reduce the radiation dose. Even in children who have stabilizing hardware in place, MRI may be considered. The hardware that is nowadays being used is usually non-ferromagnetic and will typically only induce a focal signal loss in the immediate region of the hardware. The segments above and below the surgical site are usually free of significant artifacts. MRI typically includes multiplanar T1 and T2-weighted imaging as well as either short TI inversion recovery (STIR) or fat saturated T2-weighted sequences. Intravenous contrast injection is rarely necessary. High resolution PST continued on page 8
heavily T2-weighted sequences like the three dimensional constructive interference in steady state CISS sequence can be helpful to study the exact anatomy of the spinal cord and nerve roots as well as the spinous ligaments. Ultrasound has only a very limited role in the diagnostic work-up of traumatic spine injuries. In the neonates, the spinal canal can be evaluated in between of the ossification centers, however spinal US is predominantly used for the evaluation of spinal malformations rather than for posttraumatic lesions. Bone scintigraphy may be considered if a complicating osteomyelitis is suspected and hardware prevents a diagnostic MRI study of the region of interest. Conventional radiography remains important in children suspected of non-accidental injury (skeletal survey). Depending on the age of the child, various “typical” posttraumatic lesions are seen. Child abuse should be suspected if the imaging findings cannot adequately be explained by the reported trauma history and if “peculiar” fractures are noted like e.g. isolated spinous process fractures.

Mimickers of pediatric spinal injuries

IHs make up to at least 90 % of all vascular tumors. The developing pediatric spinal skeleton may be challenging. The cartilaginous nature of the young skeleton, the presence of multiple ossification centers and complex synchondroses as well as a high variability in the normal development may result in misdiagnosis. Synchondroses, not yet ossified parts of skeleton or residual cartilaginous components may be misinterpreted as fractures. The different shape of the pediatric vertebral bodies with physiological anterior wedging may be interpreted as a compression fracture. In addition, the hypermobility of the spine with physiological subluxation of especially C2 relative to C3 may mimic traumatic injury/dislocation (Fig 1 on pg. 10). Finally, various metabolic disorders and skeletal dysplasias may result in a deformity of the osseous elements (mucopolysaccharidoses) suggesting traumatic injuries. Also various connective tissue disorders as well as chromosomal anomalies (e.g. trisomy 21) may result in an increased mobility of the spinal column. Frequently, widening of the prevertebral space, especially along the cervical spine is used as an indirect sign for an adjacent spinal injury. However, depending on the degree of inspiration the prevertebral space may show a significant physiological variability in width. Moreover, the adenoids and cervical lymphatics are more pronounce in children than in adults. Finally, it should not be forgotten that on the contrary traumatic injuries and fractures may be missed on CXR and CT because the injured components may not yet be ossified.

Each radiologist and physician who is interpreting pediatric spine studies should consequently be familiar with the normal, developing pediatric skeleton to prevent misdiagnosis.

PEdiatric Spinal Injuries

Cranio-cervical junction and cervical spine

A spectrum of posttraumatic lesions may be encountered at the cranio-cervical junction. Depending on the trauma mechanism translational, flexion/extension, distraction and compression injuries or fractures may be noted. Most of the lesions are noted at the immediate cranio-cervical junction. In its mildest forms the ligaments are stretched or torn with or without dislocation. In more severe cases epiphyseal detachment or fractures may be seen. Most importantly, compression, contusion or transection of the adjacent brainstem and spinal cord may occur. Neurological deficit is typically acute and has a poor prognosis.

• In mild forms, the alignment is preserved but the ligaments are stretched or torn. CXR and CT may be unremarkable with exception of a straightening of the physiological cervical lordosis (guarding) and a mild paravertebral edema or an epidural retroclival or intraspinal hematoma. T2-weighted MRI may show an increased T2-signal of the injured ligaments, occasionally with T2-hyperintense edema of the injured ligaments. The high resolution T2-weighted CISS sequence may directly show the interruption of the ligaments. This sequence is especially helpful for the alar and apical ligaments as well as the tectorial membrane. Retroclival hematomas may displace the tectorial membrane and extend into the epidural space of the upper spinal canal (Fig 2 on pg. 10). T2-hyperintense edema may be seen along the epiphyseal plates as well as along the insertion of the ligaments within the subchondral bone. Adjacent soft tissue edema or hematomas may be seen. Vascular injuries like dissections should be ruled out.

• Due to the high mobility and flexibility of the pediatric spine, an intermittent subluxation/luxation may have occurred during the time of trauma which has spontaneously recovered on follow up. The CXR and CT findings are consequently underestimating the degree of injury, MRI is however able to show the resulting injuries that affect the ligaments and possibly also spinal cord and brainstem. This category of injury is also overlapping with an entity known as SCIWORA (spinal cord injury without radiographic abnormality). Pang and Wilberger defined this entity as marked by objective signs of spinal cord injury resulting from trauma, with no evidence of ligamentous injury or fractures on plain films or tomographic studies. This entity has typically been described to affect children and is believed to affect the cervical spine most frequently. Flexion and extension but also lateral bending, distraction, rotation, axial loading or combinations of these forces are the most common mechanism of injury. Again, MRI usually shows the trauma related injuries that remained undetected on CXR or CT.

• In the more severe forms an axial dislocation of C1 in relation to the occiput (atlanto-occipital dislocation) may be encountered or between C1 and C2 (atlanto-axial dislocation). The spinal canal is typically narrowed with compression and injury to the spinal cord. Anterior dislocations are the most common mechanism of injury. Again, MRI usually shows the trauma related injuries that remained undetected on CXR or CT.

• In the most severe forms a significant axial/vertical atlanto-occipital dislocation, better known as dissociation may be encountered (Fig 3 on pg. 10). These injuries typically occur in high speed motor vehicle accidents and are characterized by a complete rupture of the ligaments between the occiput and
C1/C2 with subsequent “separation” of the spinal column from the skull. The spinal cord is usually severely injured with poor prognosis. These injuries may also be seen in young children who were struck by a rapidly deploying airbag while seated in a forward facing car seat. Large pre- and paravertebral hemorrhages occur.

- The spectrum of cervical fractures in children is similar to the “adult” fractures, however the incidence, distribution and location differs. Atlas fractures like the Jefferson fracture is typically seen as a result of an axial compression after a fall onto the head (diving accidents) while anterior and posterior arch fractures of the atlas typically result from a focal C1/2 hyperextension. Fractures of the axis include the Anderson fracture which typically occurs as complication of a traumatic hyperflexion and the Hangman fracture which in turn is seen after a traumatic hyperextension. Compression fractures (C3-C7) typically result from traumatic hyperflexion and present with an increased anterior wedging of the cervical vertebral bodies. CXR and especially multiplanar coronal and sagittal CT reconstructions usually easily identify the kind and degree of injury/ fracture. MRI may help to characterize and date the fracture. Occasionally it is difficult to differentiate between a physiological wedging of the vertebral bodies as a normal variant or as part of a systemic disorder versus a posttraumatic anterior reduction in height. T2-hyperintense bone marrow edemas as well as paravertebral soft tissue edema suggest acute injury.

With progressing age, the middle and lower cervical spine will be more frequently affected. The region of maximal mobility migrates from the C2/C3 region towards the adult region at the level of C5/C7/T1. Consequently, more frequently posttraumatic lesions resulting from hyperextension/hyperflexion will be seen in the middle and lower cervical spine.

Thoracic and lumbar spine

With progressing static and dynamic stability, the predominant location of spinal injuries migrates towards the thoracic and lumbar spine (children >10 years). Fractures are typically seen at the thoraco-lumbar junction and in the region of the lumbar spine. Fractures occur less frequently in the thoracic spine because of the stabilizing effects of the rib cage. Thoracic and lumbar fractures include compression fractures (typically from falls), burst fractures, Chance fracture (flexion-distraction injury) and focal, direct impact fractures. Compression fractures are characterized by a wedge shaped deformity of the involved vertebral body with interruption/fracture of the anterior vertebral contour. Compression fractures are typically stable. Burst fractures occur as complication of an axial force resulting in a fracture of both the anterior and posterior contour of the involved vertebral body. Bony fragments may be dislocated into the spinal canal, compressing the adjacent neuronal structures (Fig 4 on pg. 10). Additional dislocations may be seen in more severe injuries. These fractures result from various combinations of flexion and axial compression. Lateral forces may also result in compression or burst fractures, however in these trauma lateral dislocations can be noted (Fig 5a,b on pg. 10).

The Chance fractures, named after the British radiologist G.C. Chance who described this group of fractures first in 1948 for the lumbar region, is characterized by a transverse or oblique fracture that involves all three longitudinal vertebral columns. This fracture results from a combined flexion-distraction mechanism around a fulcrum, most commonly a seat belt (seat belt or lap belt fracture). The anterior vertebral body is typically compressed while the posterior vertebral body height is increased by the distraction component of the injury. The posterior extension of the distracting forces distracts the posterior elements with increased interspinous distance and widened facet joints. Concomitant ligamentous injury, e.g., rupture of the posterior longitudinal ligament and interosseous ligament occurs in variable degrees and determines stability. Anterolysisis at the fracture level may result in significant compression of the spinal cord or cauda equine. Most injuries of the lower back are at the thoracolumbar junction because of its relative high mobility. Children with seat belt injuries frequently have additional internal injuries because of less stable rib cage and pelvis compared to adults. Imaging should consequently also include evaluation of the thoracic and abdominal organs and vasculature.

Non-accidental injury

The spinal column may also be involved in non-accidental injury or child abuse. Depending on the used force and mechanism of trauma nearly any kind of spinal injury may result. There are no pathognomonic injury patterns to confirm the non-accidental nature of the trauma. Some lesions may suggest non-accidental injury like isolated fractures of the spinous processes (resulting from direct blows to the back of the child), especially when no adequate trauma history is given by the caregivers. A complete diagnostic work up with skeletal survey, physical examination and a psycho-social evaluation should be performed.

Birth-related injury

Traumatic vaginal delivery may result in injuries of the cranio-cervical junction and cervico-thoracic junction. Next to ligamentous and cartilage-osseous lesions, the spinal cord may be injured ranging from smaller focal hemorrhages up to complete transections. In addition, nerve root avulsions and brachial plexus injuries may be seen.

Additional risk factors

Preexisting spinal pathologies including spinal anomalies with defective or incomplete development of the neural elements, segmentation or formation anomalies of the osseous spine, spondylolysis as well as various systemic diseases like metabolic disorders, bony dysplasia, or infectious diseases including spondylitis and retropharyngeal abscesses may facilitate spinal injury. Finally, various chromosomal abnormalities like Down syndrome increase the risk for injuries due to the increased ligamentous laxity.

Conclusion

The pediatric spine is very different compared to the adult spine; incidence, epidemiology, distribution and character of spinal injury are unique for the age of the patient. Imaging should evaluate the ligamentous and osteo-cartilaginous elements of the spine as well as the spinal cord including nerve roots and paraspinal plexuses. CXR and CT predominantly study the osseous complications, MRI the soft tissue injuries of spinal trauma.
Figures for: Pediatric Spine Trauma: Relevant and Non-relevant Imaging Findings Including its Mimickers

**Figure 1.** Sagittal CT reconstruction of the cervical spine of a 4 year old child. Normal alignment is noted with physiological pseudoluxation of C2 relative to C3.

**Figure 2.** Sagittal T1-weighted brain and T2-weighted cervical spine MRI of a young child who sustained a combined head and spine trauma. A moderate sized retroclival hematoma is noted which elevates the tectorial membrane. Mild amount of blood is seen in the adjacent prevertebral space. In addition, the T2-weighted image shows some blood between the apex of the dens and the inferior tip of the clivus indicating ligamentous injury. The brainstem and spinal cord is mildly compressed, no focal lesion noted.

**Figure 3.** Lateral CT localizer, soft tissue and bone algorithm sagittal and coronal CT images of the cervical spine of an adolescent boy who sustained severe cranio-cervical junction dissociation after a high speed motor vehicle accident. He was ejected from the car and resuscitated at the scene. A significant vertical and anterior dissociation of the cranio-cervical junction is noted. High grade narrowing of the spinal canal as well as a large prevertebral and moderate sized anterior epidural hematoma is seen. Subarachnoid blood is seen outlining the brainstem. The child subsequently died.

**Figure 4.** Sagittal and coronal CT and sagittal T2-weighted MRI of the lumbar spine of a 14 year old female who fell of the swing show a burst fracture of L1 with retropulsion of bony fragments and minimal lateral subluxation. MRI shows compression of the cauda equine with mild T2-hyperintense cord edema. An additional superior endplate fracture is seen at the level of L4.

**Figure 5a.** Sagittal T2- and T1-weighted as well as sagittal curved reformatted T2-weighted MRI of a 17 year old male who fell 12 feet of a roof. Multilevel compression fractures are noted with significant T2-hyperintense bone marrow edema. The spinal canal is mildly narrowed; the spinal cord appears intact without significant edema.

**Figure 5b.** matching coronal 2D and 3D reconstruction of the same patient as shown in figure 5a. In addition to the multilevel compression fractures a significant lateral dislocation is noted with partial overriding of the vertebral bodies. Despite the significant dislocation no serious neurological deficits persisted. The dislocation is best seen on the coronal images.

Further Reading


Corresponding author

Thierry A.G.M. Huisman, MD
Professor of Radiology, Pediatrics and Neurology
Director Division of Pediatric Radiology
Director Pediatric Neuroradiology
Johns Hopkins Hospital
600 North Wolfe Street
Nelson B-173
Baltimore, MD 21287-0842
thuisma1@jhmi.edu
MESSAGE FROM THE PRESIDENT

Richard L. Robertson, MD

It’s July and now that a hectic spring meeting schedule is over, it is perhaps a good time to take a step back and reflect on goals for the coming year, and how we, as members of the ASPNR, relate to our specialty and the environment in which we practice.

While we challenge ourselves and our trainees to master an ever-expanding body of knowledge and to continue to be passionate about the role of neuroimaging in the diagnosis and management of neurologic conditions in children, I believe we must look beyond the reading room to fulfill our professional obligations. As a membership united in advancing the care of children through the use of neuroimaging this is an exciting time of challenges and opportunities for our specialty and the ASPNR. As concerns about rising health care costs continue to mount, there is increasing pressure from payers, the government, businesses and consumers to control medical expenditures. Despite the enormous contribution of medical imaging to patient care over the last two decades, the expense of imaging has made it a target in cost reduction efforts. Whether through an emphasis on decreasing imaging utilization or redirection of patients to the lowest cost provider, attempts to reduce costs are often poorly informed and undervalue the contributions of the pediatric neuroimaging subspecialist. The membership of the ASPNR is uniquely qualified to help inform this dialog and it is incumbent upon each of us to promote an understanding of the unique requirements of pediatric neuroimaging and its importance to the diagnosis and management of pediatric neurologic conditions. While some of the decisions on care direction will come from the national or state agencies, our ability to effectively communicate our value to our patients, their families and referring clinicians remains a powerful factor in where and by whom care is delivered. Although each of us can subjectively speak to why effective pediatric neuroimaging requires expertise and dedication, our specialty is lacking in outcome studies that would enable us to more quantitatively and objectively articulate our contributions to patient care. As we think about academic projects for the upcoming year, I would encourage the membership of the ASPNR to be aware of the need that we all share for quantitative information to support our specialty and to consider submission of outcomes research on pediatric neuroimaging to our meeting next year in Montreal.

While health care reforms place challenges in front of the ASPNR membership, interest in pediatric neuroimaging continues to grow and we have opportunities to advance our specialty through collaboration with other professional groups equally committed to neuroimaging in children. One particularly exciting opportunity for international collaboration for the ASPNR is with our colleagues in the European Society of Neuroradiology. While there have long been affiliations between individual members of the ASPNR and ESNR, I am delighted to be able to announce that the ASPNR and ESNR will be jointly developing and sponsoring the pediatric neuroimaging programming for the 2014 ASNR meeting in Montreal. This is a wonderful opportunity for enhancing the relationship between two societies that have a mutual and deep interest in neuroimaging in children. It is hoped that this will be the start of an even closer affiliation between the ASPNR and ESNR.

Pediatric neuroimaging continues to be an exciting field of study and learning. As the demands of and on the specialty evolve over time, the commitment of the membership of the ASPNR to advancing health care in children is a reason for optimism for those of us fortunate enough to be pediatric neuroimagers. As President, I encourage your continued support of the Society as a professional resource and hope you can attend the ASPNR program at the 2014 ASNR meeting in Montreal.

ANSWER TO RETZIUS NEUROANATOMY QUIZ #9

Answer: for·nix, gen. for·ni·cis, pl. for·ni·ces (f r’niks, -ni-sis, -ni-s z), [L. arch, vault]

Discussion:
1. In general, an arch-shaped structure; often the arch-shaped roof (or roof portion) of an anatomic space.
2. The compact, white fiber bundle by which the hippocampus of each cerebral hemisphere projects to the contralateral hippocampus and to the septum, anterior nucleus of the thalamus, and mammillary body. Airing from pyramidal cells of the Ammon horn, the fibers of the fornix form the alveus hippocampi and the fimbria hippocampi, and in their further course compose, sequentially, the commissure of the fornix [TA], also called the hippocampal commissure [TA] (commissura hippocampi [TA]), the crus of fornix [TA] (crus fornici [TA]), the body of fornix [TA] (corpus fornici [TA]), and the column of fornix [TA] (columna fornici [TA]), which divides into a smaller portion of precommissural fibers [TA] that pass anterior to the anterior commissure to the septal area and a larger portion of postcommissural fibers [TA] that pass posterior to the anterior commissure to end mainly in the mammillary nuclei and to a lesser extent in the anterior thalamic nucleus.

Farlex Partner Medical Dictionary © Farlex 2012
For the etymologists among us, the word fornication derives from the activity commonly practiced under the “arches” during Roman times. Over 1 million served.