Spinal Arteriovenous Malformations Associated with Klippel-Trenaunay-Weber Syndrome: A Literature Search and Report of Two Cases

**CASE REPORT**

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**SUMMARY:** Patients with Klippel-Trenaunay-Weber syndrome present with venous varices, cutaneous capillary malformations, and tissue hypertrophy, usually involving an extremity. A small but important subset also harbors arteriovenous malformations (AVMs) of the spine. We report 2 such cases, 1 with 3 concurrent spinal arteriovenous fistulas. These cases and our review of the literature emphasize the importance of screening the spine for AVMs. In addition, it is also important to investigate for the presence of multiple spinal AVMs.

Patients with Klippel-Trenaunay-Weber (KTW) syndrome present with venous varices, cutaneous capillary malformations, and tissue hypertrophy.1 Klippel and Trenaunay described the association of the 3 findings in 1900 and Parke Weber later added the important finding of arteriovenous fistulas (AVFs) to the syndrome complex.2 The exact cause of KTW syndrome is variable.4 There are many reports of other associated congenital anomalies with this syndrome. Anomalies of the fingers and toes and arteriovenous malformations (AVMs) are among these anomalies.1,3,5

In this report, we discuss 2 patients with KTW syndrome who presented with neurologic symptoms related to associated AVMs involving the spinal cord and spine. We also performed a review of the literature.

**Case 1**

A 37-year-old woman was referred for a second opinion for symptoms associated with a spinal arteriovenous shunt. She had been treated for limb hypertrophy as a child by closure of the physcal plates and had had surgical removal of venous malformations from the right lower extremity. At the current presentation, the patient showed subtle residual findings of KTW syndrome consisting of venous varices involving the right foot and a temperature difference in the feet (warmer on the right) but no evidence of cutaneous capillary malformation. She complained of increasing right lower extremity radicular pain and some perineal pain. The pain increased with activities increasing central venous pressure, such as performing sit-ups or crunches, or with prolonged standing. MR images of the lumbar and thoracic spine demonstrated multiple abnormal enlarged intradural flow-voids, especially at the level of the conus medullaris, with serpentine vascular structures extending cranially and caudally (Fig 1). There was no spinal cord signal intensity abnormality. Dynamic gadolinium-enhanced MR angiography (MRA) demonstrated an intradural vascular malformation, with the largest abnormal flow voids in the central spinal canal from T12 to L2 (Fig 1). A limited spinal angiogram performed at an outside institution demonstrated a type 4 (pial) fistula with moderate flow and variceal dilation of the recipient venous pouch at the level of the conus medullaris. A large radiculomedullary artery arising from the left lateral sacral artery provided good access to the recipient venous pouch. Additional supply was also seen from the anterior spinal artery (ASA). Because the frequency and intensity of the patient’s symptoms was increasing, endovascular treatment was offered to the patient.

After explaining the procedure and its potential risk of complications, informed consent was obtained for treatment under monitored anesthesia care. The right common femoral artery was accessed with a 6F arterial sheath, and a catheter was used for selective catheterizations and injections of the right T12 to L3 and left L1 to L3 arteries. Because type IV fistulas are generally single-hole fistulas, the spinal arteriogram was limited to the pedicles listed. The arteriogram revealed a type IVa arteriovenous fistula, fed by the ASA, and an enlarged radiculomedullary artery arising from the left lateral sacral artery. The venous varix draining the fistula was located primarily inferior to the conus medullaris and was drained by 3 veins, 2 draining inferiorly and the other draining superiorly. One of the 2 inferiorly draining veins was larger and extended to the sacral region and exited one of the sacral foramina. Endovascular treatment was begun by a guide sheath into the left internal iliac artery, through which a 5F catheter was placed into the lateral sacral artery. Using a triaxial system, a microcatheter was advanced through the radiculomedullary artery and into the venous varix draining the fistula. The varix was embolized using 8 detachable complex platinum coils (DCS; Cordis, Miami Lakes, Fla). Because of concern about creating significant mass effect on the conus by placement of additional coils, a standard mixture of n-butyl cyanoacrylate (n-BCA), ethiodized oil, and tantalum powder was injected to fill in the interstices of the coils and the venous varix. Control angiography done immediately after n-BCA embolization demonstrated one collateral artery arising from the lateral sacral artery, more proximal to the enlarged radiculomedullary artery with delayed filling of a very small part of the varix but without any flow beyond the varix. Control angiography of the left internal iliac artery, followed by a distal abdominal aortogram, demonstrated no filling of the varix or draining veins and no evidence of residual fistula at that time.

The patient had significant relief of her symptoms, with disappearance of the radicular symptoms, and a mild residual amount of perineal pain. Follow-up contrast-enhanced and time-resolved MRA...
of the spine performed on the day after embolization revealed a persistent arteriovenous shunt, despite clinical improvement. This MRA showed a persistent draining vein extending inferiorly from the AVM. Some venous structures also extended cranially from the AVM. The venous varix seen the day before was now less well-defined as a result of embolization. Given the MRA evidence for persistent arteriovenous shunt surgery, and despite continued symptomatic improvement, the decision was made to perform a follow-up spinal arteriogram 3 month later. On re-examination at that time, angiography revealed 2 additional separate smaller pial AVFs (type IVa). These 2 AVFs were located at the level of the inferior endplate of T11, on the dorsal surface of the cord, supplied by the posterior spinal arteries. Each of these 2 fistulas drained into short separate venous channels, which converged, in a Y-shape, into a dorsal longitudinal vein, extending inferiorly, to drain into the venous variceal pouch, previously partially embolized. An attempt was made to access 1 of the 2 smaller fistulas using the smallest braided and flow-guided microcatheters available. Because of the small size of the segmental arteries supplying the ASA and the fistula, access to the ASA was not possible.

During the subsequent 3 months, she again began to experience increasing pain, primarily in the perineal region. The previous radicular right lower extremity pain had not recurred.

The case was discussed at the multidisciplinary neurovascular conference. Given the relative youth of the patient, and the progressive nature of the symptoms, treatment was recommended. Given the multiplicity of pial fistulas (3 total), the categorization of the 2 additional fistulas as type IVa, and the location of the 2 remaining fistulas on the dorsal surface of the cord, surgical treatment was recommended. The patient underwent open surgical treatment 8 months after her first admission to our center. The fistula was approached through a T11–L1 laminectomy. Intradural exposure of the fistula revealed the coil mass packed into the inferior aspect of the varix with persistent arterialized flow as expected from the presurgical angiogram. Inspection of the varix revealed 3 arterialized draining veins with connections to the superior aspect of the fistula as well as several enlarged arteries coursing inferiorly toward the conus. Numerous nerve roots and the varix mass made identification of the arterial venous varix connections difficult. Temporary vascular clips were placed across the arteries and the varix was checked with a flow Doppler for persistent flow. The presence of flow despite the arterial occlusions suggested that the fistula had numerous smaller connections and would require skeletonization and removal of the varix to eliminate the shunt surgery. A number of small AVF connections were encountered that were coagulated and divided as the entire varix was mobilized out of the conus. With the removal of the varix and elimination of the arterialized flow, the normal conus veins darkened, serving as a direct indicator that the fistula had been successfully eliminated. Further inspection in the region of the conus revealed what was
felt to be a true small AVM that was resected as well. Postprocedure angiography confirmed that the fistula was completely obliterated. The patient had some postoperative bowel and bladder dysfunction that improved significantly on subsequent follow-up.

**Case 2**

The patient was a 29-year-old woman with known KTW syndrome, with a history of multiple documented venous malformations involving the extremities, chest wall, spleen, and pulmonary parenchyma with pulmonary vein varicosities. The venous malformation in the left posterior chest wall had presented with left chest wall pain and discomfort and had been successfully treated by embolization 4 years before. Approximately 2 months before her office visit, she had experienced a sudden onset of neck pain that occurred after her right upper extremity was pulled hard while she was walking her dog. Approximately 2 weeks later, she began to experience significant right upper extremity weakness and numbness, primarily involving the hand and forearm, with relatively sparing of the shoulder girdle.

MR imaging of the cervical and thoracic spine with and without contrast performed at an outside institution demonstrated a prominent epidural lesion that extended from the level of C5 down to T2. The signal intensity characteristics were compatible with an epidural hematoma centered in the right posterolateral aspect of the spinal canal, causing mass effect on the thecal sac and cord and the right C8 and T1 nerve roots (Fig 2). The patient was placed on oral corticosteroids because of the obvious mass effect on the cord, and surgical decompression was advised. An early appointment was made for her to see a vascular neurosurgeon (C.C.G.).

Although all of her malformations to date had been venous, a decision was made to better identify the type of vascular malformation before treatment. At first, a time-resolved MRA was performed (Fig 2) that demonstrated definite arteriovenous shunt surgery in the cervical epidural space, thus excluding a pure venous malformation and suggesting an AVM. A conventional arteriogram was performed. An aortic arch injection demonstrated an AVM within the spinal canal extending from the top of C6 to the bottom of T1, with the nidus located in the right dorsolateral aspect of the spinal canal. The AVM drained via the paraspinal veins superiorly and inferiorly. Arterial supply to the AVM arose from segmental branches of the right vertebral artery, as well as the right and left costocervical trunks. The venous drainage included a varix in the right posterolateral epidural space, with subsequent extraspinal drainage extending superiorly, as well as a smaller separate vein draining into the ventral epidural venous plexus and then the right external jugular vein. There was a focal stenosis at the connection of the epidural varix with the extraspinal veins. The venous varix caused erosion and widening of the right C6/C7 and C7/T1 intervertebral foramina. After careful consideration, endovascular embolization of the lesion followed by surgical resection was recommended to the patient.

Embolization of the AVM was performed in 2 sessions. In the first
session, the right-sided supply from the costocervical trunk was embo-
libized using a combination of polyvinyl alcohol (PVA) particles and 
$\alpha$-BCA. In the second session, the left costocervical trunk supply was 
embolized using a combination of PVA particles and $\alpha$-BCA. After the 
final session, the lesion was nearly completely devascularized. No 
complications were encountered.

The patient underwent surgical removal of the AVM with lami-
nectomies at C5–T2 the day after the last embolization. The objective 
of surgery was to decompress the spinal cord at the level of the mal-
formation with resection of as much of the vascular tissue as feasible. 
A bilateral cervical laminectomy was performed from C5–T2. A sig-
nificant amount of bleeding was encountered during the exposure of 
the lamina from numerous emissary veins coursing through the T1 
lamina. Inspection of the epidural space upon completion of the lam-
nectomies revealed a thick plaque of arterialized dilated vascular 
channels extending from C6 to T2 where the tissue tapered out. The 
tissue was divided carefully in the midline using bipolar electrocau-
tery with controllable bleeding. The tissue peeled easily laterally to the 
edges of the laminectomies, where it was amputated and sent en bloc 
for pathologic examination. The surface of the dura also contained 
engorged venous channels that were coagulated. There was no evi-
dence of the malformation extending into the intradural compart-
ment. One small connection from the dural venous channels to the 
epidural vascular malformation was coagulated and divided. Hemo-
stasis was achieved, and the incision was closed. A postoperative ar-
teriography was performed revealing complete elimination of the 
AVM.

Discussion

KTW syndrome consists of a classic triad of venous varices, 
cutaneous vascular nevi, and limb hypertrophy and may in-
clude AVMs. The KTW syndrome is generally thought to oc-
cur sporadically, following a somatic mutation model. How-
ever, in some cases, clinical manifestations of the syndrome 
have been found in family members, suggesting an autosomal 
dominant inheritance. Ceballos-Quintal et al reported KTW 
syndrome in a family where the family tree supported an au-
tosomal dominant inheritance. There are also some reports of 
chromosomal abnormalities in some cases of KTW syn-
drome. These observations all suggest a genetic contribu-
tion to the occurrence of KTW syndrome with multiple pos-
sible genes involved. Timur et al cloned a susceptibility 
gene (named AGGF1) for KTW syndrome. AGGF1 encodes a 
potent angiogenic factor. KTW syndrome-associated muta-
tions enhance the activity of this gene, suggesting increased 
angiogenesis as one molecular mechanism for the pathogene-
sis of this syndrome. Some authors have grouped this syn-
drome with neurocutaneous hereditary diseases such as Von 
Hippel-Lindau, neurofibromatosis, Sturge-Weber syndrome, 
and tuberous sclerosis. Furthermore, several case reports 
showed no clear distinction between the KTW syndrome and 
related entities such as Sturge-Weber syndrome or Proteus 
syndrome. Vascular malformations are a common feature in all 
these syndromes, malformations that might be due to gene 
mutations that cause dysregulation in the signaling involved in 
vascular morphogenesis, growth, and development.

The presentations of this syndrome are variable. The cuta-
neous vascular nevi can be in the form of port-wine stains, 
hemangiomas, or lymphangiomas. In some subsets of pa-
tients, on the other hand, only 2 of the 3 classic findings are 
present.

Our first patient had partial hypertrophy of a lower limb 
with associated varices; however, cutaneous capillary malfor-
mations were conspicuously absent. Our second patient had 
significant hypertrophy of the right lower extremity with as-
associated bony abnormalities. The venous abnormalities were 
not limited to a single extremity; rather, they involved the 
trunk and all 4 extremities.

The association of KTW syndrome and spinal cord vascular 
lesions has been reported in the medical literature. Djid-
jian et al described 5 cases of KTW syndrome associated with 
intramedullary spinal cord AVMs discovered at a variable time 
after the diagnosis of KTW syndrome. Benhaiem-Sigua et 
al reported a case of this syndrome associated with a ret-
romedullary spinal AVM. Alexander et al reported a case of 
extradural thoracic AVM in a known case of KTW syndrome.

To the best of our knowledge, 22 reported cases of the KTW 
syndrome are associated with spinal vascular malformations 
(Table). The selection of treatment modalities depends primarily 
on the type of spinal vascular malformation encountered, and a 
discussion of treatment for the various types of malforma-
tions is beyond the scope of this study. Treatment modalities 
include microsurgery, endovascular embolization, and, more 
recently, stereotactic radiosurgery. Concerning the treatment 
of perimedullary fistulas (ventral epidural or type IV), endo-
vascular treatment has the primary role for treatments of sub-
types B and C, as a result of the enlargement of the ASA, which 
allows for microcatheter access. Patients presenting with sub-
type A are usually considered better microsurgical candidates 
due to the small size of the ASA, which often precludes micro-
catheter navigation. Recently however, Oran et al reported 
successful endovascular treatment of 4 patients with Anson-
Spetzler type IV, subtype A perimedullary fistulas. With regard 
to the treatment of epidural AVMs, microsurgical removal is 
necessary in a case such as ours in which the patient presented 
with hemorrhage and mass effect on the spinal cord and exiting 
nerve roots. Preoperative embolization was thought to be 
necessary to make the operation safer and faster.

The recognition and proper categorization of spinal AVMs 
are crucial for planning the right treatment options. Because 
of the small numbers of published series, there is no consensus 
about the classification and optimal treatment options for spi-
nal AVMs in KTW syndrome. Spetzler et al introduced a 
modified classification for spinal AVMs in 2002. This more 
recent classification divides spinal AVMs into extradural-in-
tradural and intradural types. The former type—previously 
known as “juvenile” or Anson-Spetzler type III—is uncom-
mon, usually does not respect any tissue boundary, and usu-
ally needs a multidisciplinary approach consisting of emboli-
zation and surgical resection. The intradural AVMs are further 
classified into intramedullary, intramedullary-extramedul-
lary, and conus medullaris subtypes. The intramedullary sub-
type (previously known as glomus AVMs or Anson-Spetzler 
type II) can be supplied by multiple branches of the anterior 
and posterior spinal arteries and are characterized by high 
pressure, low resistance, and high blood flow. The conus med-
ullaris AVMs are always located in the conus medullaris and 
cauda equina and, unlike other spinal arteriovenous lesions,
frequently produce radiculopathy and myelopathy at the same time. Spetzler et al.32 also modified the classification for the predominant vascular abnormalities in these patients concerned with spinal vascular malformations. First, although Spetzler and Kazner18 emphasized 2 important points regarding patients with KTW syndrome. These cases and our review of the medical literature established that there is a high incidence of arteriovenous shunts, and appropriate investigation with MRA, CTA, or conventional angiography is indicated. Second, it is extremely important to evaluate these patients for the presence of more than one spinal vascular malformation.

### Summary of reported cases of Klippel-Trenaunay-Weber Syndrome associated with spinal arteriovenous malformations

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Reported AVM(s)</th>
<th>Age and Sex of Patient</th>
<th>AVM Location</th>
<th>Type</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Den Hartog Jager et al16</td>
<td>1949</td>
<td>1</td>
<td>27 years, male</td>
<td>Spine (T9–T10)</td>
<td>Intramedullary*</td>
<td>* Subtype not specified.</td>
</tr>
<tr>
<td>Schulz et al20</td>
<td>1966</td>
<td>1</td>
<td>24 years, male</td>
<td>Spine (T5–T7)</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td>Kravenbühl et al33</td>
<td>1970</td>
<td>1</td>
<td>20 years, male</td>
<td>Spine (T5–T8)</td>
<td>Extradural</td>
<td>Presented as leg spasticity</td>
</tr>
<tr>
<td>Förster and Kazner18</td>
<td>1971</td>
<td>1</td>
<td>11 years, female</td>
<td>Spine (T9–L2)</td>
<td>Intramedullary</td>
<td></td>
</tr>
<tr>
<td>Saito et al26</td>
<td>1975</td>
<td>1</td>
<td>49 years, female</td>
<td>Spine (T4–L4)</td>
<td>Spinal cord</td>
<td></td>
</tr>
<tr>
<td>Pitagoras de Mattos et al29</td>
<td>1975</td>
<td>1</td>
<td>33 years, male</td>
<td>Spine (T9–T10)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td>Eber et al37</td>
<td>1976</td>
<td>1</td>
<td>32 years, male</td>
<td>Spine (L1)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td>Djindjian et al36</td>
<td>1977</td>
<td>5</td>
<td>13 years, male</td>
<td>Spine (T9–T12)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>22 years, female</td>
<td>22 years, female</td>
<td>Spine (T5–T6)</td>
<td>Intramedullary*</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>28 years, female</td>
<td>28 years, female</td>
<td>Spine (T9–L2)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>13 years, female</td>
<td>13 years, female</td>
<td>Spine (L1–L2)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 years, male</td>
<td>15 years, male</td>
<td>Spine (L1–L2)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td>Vajda et al29</td>
<td>1983</td>
<td>1</td>
<td>10 years, male</td>
<td>Spine (T12–L2)</td>
<td>Intramedullary*</td>
<td></td>
</tr>
<tr>
<td>Benhaim-Sigaux et al15</td>
<td>1985</td>
<td>1</td>
<td>9 years, female</td>
<td>Spine (T11–T12)</td>
<td>Extramedullary</td>
<td>Presented with headache, lower limb pain, weakness, and swallowing difficulties</td>
</tr>
<tr>
<td>Komatsu et al22</td>
<td>1985</td>
<td>1</td>
<td>13 years, male</td>
<td>Spine (L4–L5)</td>
<td>Not specified</td>
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<tr>
<td>Jyoichi et al26</td>
<td>1989</td>
<td>1</td>
<td>67 years, male</td>
<td>Spine</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td>Kojima et al31</td>
<td>1989</td>
<td>1</td>
<td>28 years, female</td>
<td>Spine (T11–L2)</td>
<td>Spinal cord</td>
<td>4-month history of steadily progressive weakness and dysesthesia</td>
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<tr>
<td>Tan et al28</td>
<td>1990</td>
<td>2</td>
<td>19 years, male</td>
<td>Spine (T2–T6 and T10–T12)</td>
<td>Juvenile/glomus</td>
<td>Sudden onset of thoracic pain and paraplegia, severe impairment of all sensory modalities below T4 level and bilateral clonus</td>
</tr>
<tr>
<td>Nakstad et al24</td>
<td>1993</td>
<td>4</td>
<td>13 years, female</td>
<td>Spine (T11–T12)</td>
<td>Extramedullary</td>
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<tr>
<td>Szajner et al27</td>
<td>1999</td>
<td>1</td>
<td>48 years, female</td>
<td>Spine (C6–C7)</td>
<td>Epidual</td>
<td>10-month history of progressive myelopathy, bilateral lower-extremity weakness, and numbness</td>
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<tr>
<td>Alexander et al3</td>
<td>2002</td>
<td>1</td>
<td>30 years, male</td>
<td>Spine (T3–T4)</td>
<td>Extradural</td>
<td></td>
</tr>
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</table>

*Subtype not specified.

### References


