Coexistence of multiple cavernous angiomas in the spinal cord and skin: a unique case of Cobb syndrome

Case report

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Cobb syndrome is a rare, noninherited, neurocutaneous disease characterized by vascular abnormality of the spinal cord and is associated with vascular lesions in the skin at the same metamere. The majority of spinal vascular lesions are arteriovenous malformations, and skin lesions are mostly port-wine angiomas. The authors report the first case of multiple intramedullary cavernous angiomas (CAs) accompanied by skin CAs within the same metamere. A 42-year-old man presented with an acute onset of gait disturbance, low-back pain, and urinary incontinence. Magnetic resonance imaging of the thoracolumbar spine showed homogeneously enhanced lesions on a contrast-enhanced T1-weighted image and a hypointense area on a T2*-weighted image surrounding this enhanced lesion, between the T-12 and S-1 levels. Purple protruding skin lesions were detected on the left side of his gluteal region. The patient received a laminectomy followed by evacuation of the hematoma and partial removal of the tumor, which completely resolved his neurological symptoms. Pathological examinations showed that the spinal and skin lesions were CAs, suggesting that these vascular lesions developed congenitally. Cavernous angiomas associated with Cobb syndrome present with multiple lesions spanning more than 3 vertebral levels, making it difficult to completely resect these tumors. Although Cobb syndrome is an uncommon disease entity, it should be considered if a patient manifesting with neurological deficits has skin vascular lesions, including CAs.

Key Words • cavernous angioma • Cobb syndrome • cauda equina • oncology

Case Report

History and Examination. A 42-year-old man presented with acute onset of gait disturbance and visited the outpatient clinic of a nearby hospital. Four weeks later he began to experience low-back pain and urinary incontinence, and was referred to our hospital. Neurological examinations showed bilateral lower-limb hyperesthesia and weakness of bilateral toe flexors (Grade 4/5). His deep tendon examination showed normal reflexes and symmetry. He had multiple verrucous purple skin lesions on the left side of his gluteal region (Fig. 1A). Magnetic resonance imaging of the thoracic and lumbosacral spinal cord showed a well-demarcated mass at the conus medullaris accompanied by poorly defined multiple small lesions around the cauda equina between T-12 and S-1. On contrast-enhanced T1-weighted MR images, tumors showed

Abbreviations used in this paper: AVM = arteriovenous malformation; CA = cavernous angioma.
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weak homogeneous enhancement (Fig. 2A). A hypointense area on a T2*-weighted image indicated bleeding from the tumor (Fig. 2B). Spinal angiography revealed no pathological findings, such as an arteriovenous shunt. An FDG-PET study showed increased uptake in the lesion of the conus medullaris, with a standardized uptake value of 3.23 at the delayed phase, with no uptake for other lesions in the cauda equina and skin (Fig. 2C).

Operative Course. To improve his symptoms, at least partially, we recommended resection of the tumors. Laminectomy was performed at T12–L1, and the dura was opened. The conus medullaris was surrounded by port-wine colored tumors originating from the fine vasculature on the spinal cord. Importantly, the origin of the cauda equina was involved by the tumor, and several bundles of nerve fibers of the spinal cord were also attached by different pieces of the tumor (Fig. 2D). Because the tumors were so adhesive that it was difficult to remove them completely without damaging the spinal cord, we cut 1 fiber of the cauda equina along with a block of the tumor for histopathological examination, under electrophysiological monitoring. A hematoma observed in the conus medullaris was evacuated as much as possible (Fig. 2E).

Histopathological Findings. Histopathological analysis showed thin-walled vascular channels surrounded by fibrous tissues without any evidence of neuronal or glial tissue (Fig. 2F). The patient was diagnosed with CAs with hemorrhagic manifestation. He had two purple lesions of the skin tumor in the sacral area (S1–5) and biopsy of the tumor also showed typical features of CA (Fig. 1B).

Postoperative Course. After the operation, the patient demonstrated immediate improvement in motor weakness and sensory disturbance. Sensorimotor deficits were completely resolved within 1 week and urinary disturbance also disappeared within 6 months. Postoperative MRI showed a reduced size of the main tumor mass, which lost contrast enhancement, while other lesions remained unchanged (Fig. 3A and 3B). No differences were observed in MR images obtained 18 months after the operation (Fig. 3C and 3D). The patient experienced no neurological deterioration during an 18-month follow-up period.

Discussion

Spinal CAs account for approximately 5% of those occurring in the CNS. Gross et al. reviewed 27 publications and analyzed 352 cases of intramedullary spinal cord CAs. They reported that the mean age at presentation was 42 years, without sex predominance. Thirty-eight percent of the cases were cervical, 57% thoracic, 4% lumbar, and 1% in an unspecified location, indicating that lumbar spinal cord CA is extremely rare (14 cases). Approximately 90% of CAs, either intramedullary or extramedullary, have been reported to be completely removed by surgery. However, it appears to be more difficult to completely resect CAs in the cauda equina without damaging nerve roots. Of 15 cases of CAs occurring in the cauda equina, 7 required surgical dissection of the nerve roots because of strong adhesion of the tumors to the nerve roots. Of these 7 cases, 4 developed neurological deficits. In our case, the origin of the cauda equina, as well as the conus medullaris, was encapsulated by adherent tumors that were difficult to dissect, and several pieces of tumor were attached to different nerve roots. Repetitive hemorrhage in and around CAs might induce inflammation, which causes adhesion of the tumor to its surrounding tissue. We left most parts of the tumors untouched because resection of these tumors was likely to result in severe neurological deficits, according to electrophysiological monitoring. A similar decision was made by Miyake et al., who left 4 pieces of a CA that was adherent to distinct nerve roots. In addition, the difficulty in resecting angioma appears to be different between multiple angiomas and solitary angiomas. Multiple angiomas in the cauda equina failed to be completely resected in previous reports, although solitary angiomas were safely resected. Therefore, partial removal of CAs could be a treatment option if tumors apparently adhere to the nerve roots and electrophysiological examinations indicate a

![Figure 1](image1.png) Images showing characteristics of the skin lesions in the patient. (A): Purple verrucous skin lesion in the gluteal region. Inset shows a higher magnification (×4). (B): Photomicrograph showing typical features of CAs, including thin-walled vascular channels surrounded by fibrous tissues, without any evidence of neuronal or glial tissue. H & E, original magnification ×40.
high risk of neurological complications in dissecting the nerve root, although the first-line treatment for symptomatic spinal CAs is complete resection of the tumor. The annual risk of hemorrhage of intramedullary CAs has been reported to be 1.6%–4.5%. Although we detected no signs of rebleeding on MR images at the 18-month follow-up, because there is a higher risk of bleeding for symptomatic CAs compared with asymptomatic CAs, we need to maintain a rigorous follow-up of the patient (such as MRI examinations every 6 months).

Increased uptake of FDG is not common in CAs, and FDG-PET has been reported to be useful for differentiating a lesion from a malignant tumor. However, the FDG-PET study in our patient showed increased uptake of the tracer in the largest tumor at the conus medullaris, making it difficult to exclude malignancy. Miyauchi et al. reported a patient with a CA who showed increased uptake of FDG, and they speculated that inflammation induced by the hemorrhage might account for the increased uptake. In our case, the lesion with increased uptake of FDG showed CAs with intra- or peritumoral hemorrhage, which might reflect inflammation induced by the hemorrhage.

Cobb syndrome is a rare clinical entity, which includes the combination of a vascular skin nevus and a spinal angioma present at identical dermatomal levels. Arteriovenous malformations are a main spinal vascular pathology of Cobb syndrome, but Johnson and Petrie suggested that Cobb syndrome is accompanied by a wide variety of vascular pathologies, including telangiectatic angioma, venous angioma, hemangioblastoma, and CA. A total of 47 AVMs and 6 CAs, including our case, have been reported to date. Six cases of CAs associated with Cobb syndrome are summarized in Table 1. The reason why CAs are less frequently observed in Cobb syndrome than AVMs or port-wine angiomas is unclear. We speculate that spinal CAs are less likely to...
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<th>Authors &amp; Year</th>
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<th>Spinal CAs</th>
<th>Neurological Findings</th>
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<tr>
<td>Gourie-Devi &amp; Prakash, 1978</td>
<td>25, M</td>
<td>deep purple nevus involving the whole of the rt UE &amp; neck at C4–T2*</td>
<td>C7–T2 epidural laminctomy, subtotal re-oval of tumor</td>
<td>LE weakness completely free</td>
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<td>Kaito et al., 1989</td>
<td>63, F</td>
<td>port-wine stain at chest, back, lt arm &amp; shoulder</td>
<td>C2–7 epidural laminctomy, partial re-oval of tumor</td>
<td>UE &amp; LE weakness, positive neurological reflex in both LEs good recovery</td>
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<td>Basappa, 1996</td>
<td>26, F</td>
<td>port-wine stain on rt side of back at T2–6 &amp; infraaxillary region</td>
<td>not examined C5–T5 not described laminctomy</td>
<td>LE weakness flaccid paraplegia</td>
</tr>
<tr>
<td>Wakabayashi et al., 2000</td>
<td>8, M</td>
<td>multiple angiokeratomas in the rt C4–T1, S3–4 &amp; the lt L3–4, S1–4 areas</td>
<td>angiokeratoma C5–7, T1–3, T12–L1 intramedullary gradually improved w/o surgical intervention</td>
<td>urinary disturbance, upper back pain slight sensory disturbance in left foot &amp; pathological reflex in both LEs</td>
</tr>
<tr>
<td>Gatzonis et al., 2010</td>
<td>32, F</td>
<td>large skin nev at the lt back, rt arm &amp; lt lateral abdominal wall at T2–3, T5–6, T9–11</td>
<td>not examined T-1, T-4, T-5, T-7, T-8 intramedullary posterior longitudinal myelotomy, partial re-oval of tumor</td>
<td>LE weakness numbness &amp; hypesthesia, flaccid paraparesis, prominent spasticity</td>
</tr>
<tr>
<td>present case</td>
<td>42, M</td>
<td>multiple protruded purple skin lesions in the gluteal area</td>
<td>cavernous angioma T12–S1 intramedullary laminctomy, partial re-oval of tumor</td>
<td>LE weakness &amp; hypesthesia, urinary disturbance, low-back pain completely free</td>
</tr>
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* The lesions may be associated with Klippel-Trenaunay-Weber syndrome. LE = lower extremity; UE = upper extremity.
cause symptoms compared with spinal AVMs, and might be underdiagnosed. Spinal CAs in previous reports were observed in the cervicothoracic spine in 5 cases,2,5,6,13,24 whereas the CAs in our case were observed mainly in the lumbar spinal region. Patients in the previous reports were treated by laminectomy with or without partial removal of the tumor in all cases except for 1, and complete or partial recovery of clinical symptoms was obtained in 3 patients. Given that permanent morbidity is 6%–12% in patients with spinal CAs,7,17 the long-term outcome of patients with this syndrome may not be as good compared with patients with spinal CAs alone. Notably, CAs associated with Cobb syndrome present with multiple lesions, which spanned more than 3 vertebral levels in all 5 published cases, and in our case, whereas most spinal CAs present with solitary lesions.7,17 Multiple lesions in Cobb syndrome could be associated with incomplete resection and worse neurological outcome in patients. None of the previous reports described pathological findings of both spinal and skin lesions. However, in the present case, pathological findings of the spinal and cutaneous tumors were the same, showing typical features of CA. This is the first report of pathologically confirmed multiple intramedullary lumbar spinal CAs associated with skin CAs within the same metameric region. Coexistence of identical pathology in spinal and skin lesions at the same metamere suggests that CAs in our patient developed congenitally. Abnormality may occur in the mesoderm and the adjacent neural crest, which share the same metameric origin, before migration of these cells.16 Broad distribution and multiple lesions observed in Cobb syndrome could be associated with the timing of the development of CAs.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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