Endometriosis of the conus medullaris causing cyclic radiculopathy

Case report

JEFFREY A. STEINBERG, M.D., DAVID D. GONDA, M.D., KARRA MULLER, M.D., PH.D., AND JOSEPH D. CIACCI, M.D.

Division of Neurosurgery, University of California, San Diego, California

Intramedullary spinal cord hematomas are a rare neurosurgical pathological entity typically arising from vascular and neoplastic lesions. Endometriosis is an extremely rare cause of intramedullary spinal cord hematoma, with only 5 previously reported cases in the literature. Endometriosis is characterized by ectopic endometrial tissue, typically located in the female pelvic cavity, that causes a cyclical pain syndrome, bleeding, and infertility. In the rare case of intramedullary endometriosis of the spinal cord, symptoms include cyclical lower-extremity radiculopathies and voiding difficulties, and can acutely cause cauda equina syndrome. The authors report a case of endometriosis of the conus medullaris, the first to include radiological, intraoperative, and histopathological imaging. A brief review of the literature is also presented, with discussion including etiological theories surrounding intramedullary endometriosis.

(http://thejns.org/doi/abs/10.3171/2014.7.SPINE14117)

Key Words • conus medullaris • lumbar spine • hemorrhage • radiculopathy • endometriosis • spinal cord • hematoma

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

Abbreviations used in this paper: ER = estrogen receptor; LE = lower extremity.

This is the first case to provide radiological, intraoperative, and histopathological images of the disease.

Case Report

History and Examination. A 29-year-old woman was referred to our neurosurgery clinic for progressive difficulty voiding and lower-extremity (LE) radiating radicular pain. Her LE radiculopathies fluctuated in severity with her menstrual cycle, and had been gradually worsening over the past year to the point that she was having difficulty walking. The temporal relationship between her menstrual cycles and radicular pains raised concerns of endometriosis along the sciatic nerve, because she had undergone a chemical induction of menopause with danazol. This had halted the worsening progression of the symptoms, but her radicular pains and voiding difficulty...
Persisted. On physical examination the patient’s right LE strength was mildly weak (4+/5), and she had decreased sensation to sharp and dull point discrimination. The patient’s surgical history included a posterior instrumented fusion of L5–S1 performed 5 years prior at another hospital for recurrent low-back pain with radicular symptoms. She later underwent a decompressive lumbar laminectomy at T-11 to L-1 after discovery of a subacute intradural hematoma by the same surgeon. There had been no attempt to evacuate the hematoma or explore for an underlying lesion at that time.

An admission MRI study of the patient’s lumbar spine demonstrated postsurgical changes related to her prior lumbar operations, in addition to a 2.5-×1-cm oblong lesion at the L-1 level centered in the conus. The lesion was hyperintense on T1-weighted and isointense on T2-weighted images, suggesting the presence of a subacute hematoma (Fig. 1). Given the rarity of spontaneous intramedullary hematomas, as discussed previously, our differential diagnosis included underlying neoplasm or vascular lesion; we thus scheduled her for evacuation and exploration of her conus lesion.

**Operation.** Intraoperative neuromonitoring with electromyography and somatosensory evoked potentials was performed to protect against neural injury. The dura mater was carefully dissected free from the overlying scar tissue of the previous laminectomy operation. The operating microscope was used for a midline dural opening. The conus medullaris was noted to be enlarged and hypervascular, and exiting nerve roots were identified bilaterally (Fig. 2 left). While dissecting the arachnoid adhesions to displace the overlying nerve roots there was spontaneous rupture of the intramedullary lesion, providing a corridor for access along the posterior lateral border of the conus (Fig. 2 right). Contents of the cystic lesion were a dark green sludge, which we collected for pathological analysis. Visualization of the cyst walls demonstrated a hemosiderin-stained gliotic appearance, with areas of darkening that were similar in color to the dark greenish-brown sludge. Initial frozen sections were reported as gliotic spinal cord with hemosiderin staining. The cyst walls were gently scraped with a ring curette. There was no discrete mass or source of the hematoma. Hemostasis was obtained with normal saline irrigation, and the dura and incision were closed in a watertight fashion.

**Postoperative Course.** Postoperatively the patient’s mild right LE weakness and radicular pains improved, with complete resolution of her voiding difficulties. At 6-month follow-up the patient remained symptom free, with 5/5 strength and intact sensation in bilateral LEs to sharp, dull, and vibratory stimulus. Importantly, the patient also remained free of voiding difficulties. She remained in a chemically induced menopausal state per her gynecologist, with ongoing management of her endometriosis.

**Histopathological Findings.** Cyst fluid aspirate sent to the cytopathology department was prepared as a cell block and stained with H & E. This cell block showed the most valuable diagnostic material, with fragments of intact epithelial cell–lined tissue and underlying stroma. The epithelium was cuboidal to columnar and in a single-cell layer with distinct cytoplasmic borders and ovoid bland nuclei (Fig. 3A). Multiple foci of epithelial cells contained cilia (Fig. 3A inset). The stroma was composed of bland ovoid cells admixed with some lymphocytes and many hemosiderin-laden macrophages. Taking into account the patient’s clinical history, this tissue appeared reminiscent of endometrial epithelium, some with tubal (ciliated cell) metaplasia, and endometrial stroma. On immunohistochemical staining, both epithelial and stromal cells showed scattered positivity for estrogen receptor (ER) (Fig. 3B). In addition, the epithelium was positive for pancytokeratin, whereas the stroma was positive with antibodies against CD10.

This immunohistochemical pattern confirmed the presence of endometrial tissue, and, combined with the location and presence of hemosiderin-laden macrophages, a diagnosis of endometriosis was given. In addition, tissue fragments received by the neuropathology department revealed hemorrhagic whitish-tan soft tissue grossly. As mentioned above, an intraoperative consultation showed only spinal cord with reactive gliosis and some hemosiderin-laden macrophages by frozen section. Formalin-fixed and paraffin-embedded permanent H & E–stained sections confirmed that the majority of the specimen was made up of spinal cord parenchyma, with reactive astrocytes, eosinophilic granular bodies, and eosinophilic hyaline corkscrew-shaped Rosenthal fibers, all consistent with reactive gliosis. Fresh hemorrhage and embedded hemosiderin-laden macrophages were also seen. Slender ribbons of epithelium lined a few fragments of tissue, reminiscent of the endometrial epithelium seen on the cytology preparation (Fig. 3C and D). The epithelium was likewise positive for ER (Fig. 3D inset) and pancytokeratin by immunohistochemistry. The final tissue diagnosis was endometriosis and spinal cord with reactive gliosis.

**Discussion**

Endometriosis, a common gynecological disorder affecting 6%–15% of the female population, is defined by the presence of ectopic endometrial tissue located outside...
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Although it most commonly occurs within the pelvic regions near the uterus, such as the ovaries, fallopian tubes, and uterosacral ligaments, more distant cases of endometriosis in the gastrointestinal tract, lungs, and other visceral organs have been described. Endometriosis occurring within the CNS, however, is extremely rare, with only a handful of cases reported within the spinal cord.

The clinical presentation of intramedullary endometriosis of the spinal cord involves a young woman of fertile age who presents with back pain and radicular symptoms that occur in synchrony with her menses, termed cyclic lumbago and/or sciatica. Endometriosis occurring solely along pelvic nerves, such as the sciatic and obturator, causes a similar constellation of cyclic symptoms but without the back pain, and is much more common than intramedullary endometriosis. Imaging of the spine shows an intradural mass lesion suggestive of a well-circumscribed tumor or hemorrhagic cyst, but is nondiagnostic.

The management of intramedullary spinal endometriosis, as in our patient, involves both medical and surgical therapies. Surgical biopsy of the lesion is necessary for diagnostic purposes. Once diagnosis is established,

Fig. 2. Intraoperative photographs demonstrating a hypervascular and expansile region of the conus medullaris. Left: Nerve roots can be seen traveling alongside the conus in addition to the filum terminale. Right: Dissection at the right lateral aspect of the conus medullaris demonstrates a cystic dark green area consistent with endometriosis.

Fig. 3. A and B: Photomicrographs of specimen prepared as a cell block in the cytology department. A: Endometrial epithelium and stroma surrounded by fresh hemorrhage. Ciliated epithelium consistent with tubal (ciliated cell) metaplasia, indicated by the asterisk, is visualized (inset). H & E, original magnification ×200 (inset ×400). B: Endometrial epithelium and stromal cells positive for ER immunohistochemistry. Original magnification ×400. C and D: Photomicrographs of specimen prepared as formalin-fixed, paraffin-embedded permanent sections in the neuropathology department. C: Spinal cord parenchyma with many hemosiderin-laden macrophages and a thin strip of endometrial epithelium. H & E, original magnification ×400. D: Endometrial epithelium overlying spinal cord, with inset showing ER positivity of the epithelium. H & E (main panel), ER immunohistochemistry (inset), original magnification ×400 (inset and main panel).
evacuation of cystic contents through the surgical fenestration of the mass lesion can relieve compression of neural elements, including the conus and adjacent nerve roots, providing symptomatic improvement. Oral contraceptives and gonadotropin-releasing hormone agonists are used to decrease the cyclical proliferation and degradation of hormonally sensitive ectopic endometrial tissues to prevent reaccumulation of mass effect and recurrent symptoms. As Table 1 shows, of the previous 5 reported cases, medically induced menopause was used for treatment in 4, in addition to surgical evacuation of the hematoma, with oophorectomies also performed in 2 cases.

The cause of intramedullary endometriosis of the spinal cord is unknown, although several hypotheses exist. John Sampson was one of the first to conceptualize a theory of endometriosis, hypothesizing that retrograde menstruation allowed endometrial cells within menstrual fluid to travel in a retrograde manner up the fallopian tubes, enter the pelvic cavity, and deposit on nearby structures.[13,27,36] Evidence for this theory includes the fact that viable endometrial cells have been observed in menstrual flow, retrograde menstruation is a common occurrence in females, endometrial cells can be artificially implanted onto discrete tissue in the laboratory, and a correlation between obstructed menstrual flow and endometriosis has been demonstrated.[36] However, Sampson’s theory does not address how endometriosis can occur at distant noncontiguous sites of the body such as the spinal cord.

The hematogenous/lymphatics dissemination theory of endometriosis overcomes some of these hurdles by providing a clear route for endometrial cell dissemination throughout the body via the lymphatic-vascular system. It has been demonstrated in animal models that intravascular injection of endometrial cells can cause pulmonary endometriosis, evidence that once these cells enter the hematogenous system they are capable of implanting at distant sites, resulting in ectopic endometriosis.[21] Interestingly, as with our patient, every reported case of intramedullary endometriosis of the spinal cord to date has occurred at the conus medullaris.[2,5,17,24,30] None of the aforementioned hypotheses by themselves offer a rationale for this focal anatomical predilection. An alternative theory for spread to the spinal cord may involve a migratory route of endometrial tissue along roots of the lumbar plexus to the conus. Evagination of pelvic peritoneum into the retroperitoneal space is thought to allow for retrogradely menstruated endometrial cells to come into proximity to pelvic nerves.[14,25] Endometrial cells then invade the epineurium and perineurium of the lumbosacral nerves.[1,2,25,40] Furthermore, studies examining endometriotic nociception have shown that endometrial cells possess considerable neurotropic properties, secreting factors such as nerve growth factor, which stimulates neurite growth. Mechanisms allowing endometrial cells to migrate, adhere, and infiltrate nervous tissue are under investigation, but involve the complex interactions of integrins, cadherins, and matrix metalloproteinases.[1,9,23,32,33,36]

Conclusions

Although most neurosurgeons will never be actively

| TABLE 1: Literature review of intramedullary endometriosis of the spinal cord* |
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| Patient | Presenting Sxs | Lesion Location | Diagnostic Studies |
| Agrawal et al., 2006 | progressive bilateral radiculopathies & urinary incontinence | conus | MRI/histopathology |
| Barsi et al., 2006 | bilateral lower extremity weakness & numbness, sensory loss below L1 | conus | MR/CT/USM |
| Erbayraktar et al., 2002 | recurrent bilateral radiculopathies of 3 yrs duration associated with menopause | conus | MRI/CT/USM |
| Lombardo et al., 1998 | chronic bilateral radiculopathies of 1 year, headache (SAH) | | MRI/CT/USM |
| Sahu et al., 2013 | chronic LBP, difficulty voiding | conus | MRI/CT/USM |
| | | | |
| Authors & Year | Age (yrs) | Presenting Sxs | Location |
| Agrawal et al., 2006 | 40 | progressive bilateral radiculopathies & urinary incontinence | conus |
| Barsi et al., 2006 | 42 | bilateral lower extremity weakness & numbness, sensory loss below L1 | conus |
| Erbayraktar et al., 2002 | 28 | recurrent bilateral radiculopathies of 3 yrs duration associated with menopause | conus |
| Lombardo et al., 1998 | 26 | chronic bilateral radiculopathies of 1 year, headache (SAH) | conus |
| Sahu et al., 2013 | 25 | chronic LBP, difficulty voiding | conus |

* LBP = low-back pain; LP = lumbar puncture; SAH = subarachnoid hemorrhage; Sxs = symptoms.
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involved in the management of endometriosis, this case illustrates 2 key points for neurosurgical practice and pathophysiological understanding. First, a differential diagnosis should remain broad when evaluating patients with lesions of the spinal cord, with a comprehensive history being an integral aspect of each patient’s workup. Subtleties from the history that may seem irrelevant or coincidental should be contextualized. Second, in considering the proposed causes of CNS endometriosis, an indirect review of basic theories surrounding metastatic disease is considered. Questions focusing on cellular invasion, migration, and replication, evasion of the immune system, genetic and epigenetic influences, and angiogenesis are as relevant to endometriosis as they are to oncological metastasis. Future treatments and understanding of this enigmatic disease may bring greater understanding of other disease processes that spread to the CNS.

Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Steinberg, Gonda, Muller. Acquisition of data: Steinberg, Muller. Analysis and interpretation of data: Muller. Drafting the article: Steinberg, Gonda. Critically revising the article: Steinberg, Gonda, Ciacci. Reviewed submitted version of manuscript: all authors.

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