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CASE REPORT

Horner Syndrome After Lumbar Epidural Analgesia in a Patient with Ehlers-danlos Syndrome

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Abstract: Horner syndrome is a facial triad of miosis, ptosis, and anhidrosis. It is produced by a lesion of the sympathetic pathway supplying the head, eye, and neck. Causes range from benign to serious. Epidural anesthesia is widely used during obstetrics and general surgery. Although generally a safe procedure, it can cause neurologic and ophthalmologic complications. We report a case of unilateral Horner syndrome in a 43-year-old woman with Ehlers-Danlos syndrome (EDS). The patient underwent bowel and urogenital surgery under general anesthesia supplemented with L4-L5 epidural anesthesia. Horner syndrome may have been promoted by increased local anesthetic spread permitted by the connective tissue dysfunction of EDS. Furthermore, the patient suffered chronic constipation as a complication of EDS, and straining may have promoted upward spread of the local anesthetic. In addition, weakness of the dura and/or ligamentum flavum might predispose to subdural migration of epidural catheters in patients with EDS. Accordingly, EDS may increase the likelihood of a Horner syndrome following epidural anesthesia.

Keywords: Horner Syndrome, Epidural analgesia, Ehlers-danlos syndrome, Sympathetic pathway.

1. INTRODUCTION

Horner syndrome refers to the constellation of signs resulting from the interruption of sympathetic innervation to the eye and ocular adnexa. There is blepharoptosis, pupillary miosis, and facial anhidrosis. Etiologies of sympathectomy range from simple migraine to life-threatening conditions, such as carotid dissection and malignancy. Horner syndrome can be seen following several regional anaesthetic techniques, including brachial plexus block and epidural anaesthesia. Lumbar or low-thoracic epidural anesthesia is widely used during obstetrics and general surgery. Although generally regarded as a safe procedure, epidural anesthesia can cause neurologic and ophthalmologic complications. As a recognized complication of epidural anesthesia, Horner syndrome has mainly been described in obstetrical patients. It is rare and unpredictable, and its course is usually benign and transient. Although typically a benign side effect that resolves spontaneously, Horner syndrome is likely to cause anxiety in patients, surgeons, and anesthesiologists, and it may prompt emergent and costly investigations.

We report a case of Horner syndrome in a woman with Ehlers-Danlos syndrome (EDS) undergoing bowel and urogenital surgery under general anesthesia supplemented with lumbar epidural anesthesia.

2. CASE PRESENTATION

A 43-year-old woman presented for laparoscopic sigmoid colectomy, repair of cystocele, and repair of rectocele because of pain and constipation. Associated diagnoses included gastroesophageal reflux, asthma, hypothyroidism, and

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bipolar mood disorder. She also had a history of EDS. This was Type III with symptoms of joint and spine hypermobility, joint dislocations, chronic joint pain, soft and smooth skin, megacolon, and delayed gastric emptying. Previously, she underwent a partial colectomy, a repair of pelvic floor laxity, and another subtotal colectomy with ileorectal anastomosis. During previous anesthetic techniques, epidural anaesthesia was not administered. General anesthesia was supplemented by regional *via* a pre-operatively placed lumbar epidural catheter (L4-L5). The catheter was placed *via* a 17G Touhy needle in a midline approach, guided by loss of resistance to saline while the patient was in the sitting position. The placement was uneventful, and there was no leak of cerebrospinal fluid (CSF). The epidural catheter was fixed at around 5 minutes. There was an unremarkable test dose of 3 mL of 2% lidocaine with epinephrine. This was followed by an infusion of a mixture of 0.1% bupivacaine and 10 mcg/mL hydromorphone at 8 mL/h. There were occasional boluses of 2 mL of the bupivacaine/hydromorphone mixture at intervals of at least 20 min. A total of 32 mL local anesthetic solution was given over about 2 hours. Surgery was performed in the lithotomy position. A laparoscopic colectomy with ileorectal anastomosis was affected uneventfully. Postoperatively, the patient was extubated and transferred to the postoperative anesthesia care unit (PACU), where she was afebrile and hemodynamically stable. Because of gastrointestinal effects of the EDS, she had feelings of constipation and responded with frequent straining in the manner of Valsalva maneuvers. Anisocoria was noted in the PACU. Upon evaluation, the patient had miosis and ptosis of the right eye with no other neurological signs or symptoms. The Horner syndrome resolved within 24 h with no sequelae. The patient did not manifest any other symptoms or signs.

3. DISCUSSION

Horner syndrome is a rare sequel of epidural anesthesia [1, 2]. It is intriguing to consider whether EDS might have facilitated the phenomenon in our patient. The various types of EDS involve defects in the integrity of connective tissue and could plausibly permit increased spread of local anesthetic fluid. The increased spread might be akin to that deliberately produced by addition of the connective tissue-degrading enzyme hyaluronidase to local anesthetic solutions [3]. Increased local spreading with hyaluronidase has been shown in many sites, including the epidural space [4 - 8]. Of note, hyaluronidase has been particularly popular in ophthalmic blocks [9]. Most cases of Horner syndrome following epidural anesthesia have been reported in obstetric cases [10]. Perhaps epidural connective tissue changes in EDS may mimic those of pregnancy. The possibility that EDS might predispose to post-epidural Horner syndrome is important because Horner syndrome could herald dangerous vascular complications of EDS, such as arterial aneurysm [11 - 14]. Another EDS-related factor that may have contributed to this patient's Horner syndrome is the postoperative straining.

Horner syndrome was first described by Johann Friedrich Horner in 1869 [15]. Manifestations include facial anhidrosis, pupillary miosis, and ipsilateral blepharoptosis. A Horner syndrome could result from a pathological change anywhere along the sympathetic pathway which originates from hypothalamus and supplies the neck, eye and head (Table 1). Causes of Horner syndrome can range from serious to benign and require a methodical approach to diagnostic evaluations. They are based on the location of the pathological changes, and could divide Horner syndrome into 3 subtypes: first-order syndrome (central Horner syndrome), second-order syndrome (preganglionic Horner syndrome) and third-order syndrome (postganglionic Horner syndrome) (Table 2) [16].

Epidural anesthesia can lead to a Horner syndrome due to pharmacologic disruption of the preganglionic neuron as it exits the spinal cord [17, 18]. Post-epidural Horner syndrome is most often reported in obstetrical procedures. A variety of mechanisms have been put forward to explain the occurrence and development of Horner syndrome in epidural anesthesia. Sympathetic pre-ganglionic nerves originate from anterior horn cells from C8 to T1 [19]. The small fibers are particularly sensitive to anesthetics, thus being easy to be blocked by a large volume of local anesthetics during epidural anesthesia. In obstetrics, Horner syndrome may involve increased epidural pressure and higher cephalad spreading of local anesthetics caused by straining and by uterine contractions [19]. High progesterone levels of pregnancy can increase the sensitivity of nerve fibers. Our patient experienced feelings of constipation in the postoperative anesthesia care unit and was performing frequent Valsalva-like straining maneuvers. Another cause of high sympathetic block is an accidental subdural placement of an epidural catheter. Total spinal block may be caused by exaggerated cephalad spreading within the CSF.

The likelihood of a subdural misplacement of an epidural catheter may be increased in EDS. EDS refers to a group of uncommon genetic disorders of connective tissue which are characterized by one or several features, including tissue fragility, joint hypermobility, and skin hyper-extensibility [20]. In most types of EDS, the underlying pathophysiology involves inherited alterations in genes affecting the synthesis and processing of different forms of collagen, which are important in the structure of many tissues and organs, including the skin, tendons, ligaments, vasculature, skeleton, and

eyes [20]. The spinal ligaments provide a natural brace to help protect the spine from injury. The ligamentum flavum, as the strongest, runs from the base of the skull to the pelvis, in front of and between the lamina, and protects the spinal cord and nerves. It is composed of elastin and collagen fibers in a 2:1 ratio [21]. The elastin fibers provide elasticity to the ligament, while the collagen fibers provide stiffness and stability. In EDS, the structure and proportion of collagen are significantly changed, resulting in fragility and weakness of the spinal ligaments. This may increase mobility of an epidural catheter. Of note, the sense of constipation that troubled our patient in the PACU was probably a sequel of the chronic EDS. Gastrointestinal involvement is a well-known complication of EDS. Problems include structural anomalies (such as intestinal intussusception, internal pelvic/organ prolapse, and diaphragmatic/abdominal hernia) and functional features (such as constipation/diarrhea, recurrent abdominal pain, dyspepsia, gastro-esophageal reflux, and dysphagia) [22]. Curiously, patients with EDS may have reduced response to local anesthetic agents. The reason is unknown but does not appear to be caused by abnormally rapid dispersal through the lax connective tissues [23].

Table 1. Neuroanatomical features of Horner syndrome-related three-neuron sympathetic pathway.

Neuroanatomy	Anatomical features of the three-neuron sympathetic pathway
First-order neuron	Descends caudally from the hypothalamus to the first synapse, which is located in the cervical spinal cord (levels C8-T2) and is also called ciliospinal center of Budge.
Second-order neuron	Travels from the sympathetic trunk, through the brachial plexus, and over the lung apex. It then ascends to the superior cervical ganglion, which is located near the angle of the mandible and the bifurcation of the common carotid artery.
Third-order neuron	Ascends within the adventitia of the internal carotid artery, through the cavernous sinus, where it is in close relation to the sixth cranial nerve. The oculo-sympathetic pathway then joins the ophthalmic (V1) division of the fifth cranial nerve (trigeminal nerve).

Table 2. Etiologies and features of different types of Horner syndrome.

Subtypes	Etiologies and features of the three types of Horner syndrome
First-order syndrome	Lesions of the sympathetic tracts in the brainstem or cervicothoracic spinal cord can produce a first-order Horner syndrome. The most common cause is a lateral medullary infarction, which produces a Horner syndrome as part of the Wallenberg syndrome. Typically the patient presents with vertigo and ataxia, which overshadow the Horner syndrome. Strokes, tumors, and demyelinating lesions affecting the sympathetic tracts in the hypothalamus, midbrain, pons, medulla, or cervicothoracic spinal cord are other potential causes of a central Horner syndrome.
Second-order syndrome	Trauma or surgery involving the spinal cord, thoracic outlet, or lung apex can cause a second-order Horner syndrome. Other cases are related to malignancy, which can be occult at the time of presentation with the Horner syndrome. Ipsilateral axillary or arm pain often accompanies the Horner syndrome in these cases. Lumbar epidural anesthesia can also produce a Horner syndrome due to pharmacologic disruption of the preganglionic neuron as it exits the spinal cord (as in the present case).
Third-order syndrome	Third-order Horner syndromes often indicate lesions of the internal carotid artery such as an arterial dissection, thrombosis, or cavernous sinus aneurysm. Carotid endarterectomy and carotid artery stenting can also produce a Horner syndrome. Other causes of postganglionic Horner syndrome include neck masses, otitis media, and pathology involving the cavernous sinus.

CONCLUSION

Valsalva-like straining maneuvers may have contributed to Horner syndrome in our patient. These were prompted as a complication of the EDS. Weakness of the dura and/or ligamentum flavum might predispose to subdural migration of epidural catheters in patients with EDS. With this case, we emphasize that EDS may increase the likelihood of a Horner syndrome following epidural anesthesia.

PATIENT'S CONSENT

Written, informed consent was obtained from the patient for publication of this case.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Declared none.

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