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CASE OF AN EPIDURAL HEMATOMA FOLLOWING A LUMBAR EPIDURAL STEROID INJECTION IN A PATIENT TAKING ASPIRIN AND DULOXETINE

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Background: Epidural hematoma (EDH) formation is one of the most feared complications associated with epidural steroid injections (ESI) as persons may experience permanent neurological deficits including paraplegia. The risk of developing an EDH following an ESI is expectedly increased in the context of concomitant anticoagulant and/or antiplatelet agent usage. While there exists significant evidence for the risks associated with anti-coagulant and anti-platelet agents in epidural procedures, the anti-platelet effects of serotonin reuptake inhibitors medications (SRIs) in particular have received less attention.

Case Report: A 70-year-old female with numerous cardiovascular comorbidities (on aspirin 81 mg daily for primary prevention of coronary artery disease) and fibromyalgia (on duloxetine 60 mg daily) underwent a fluoroscopically guided L3-L4 level interlaminar ESI for lumbar radiculopathy. Starting 6 hours post-procedure, the patient started to manifest severe back pain, bowel and bladder incontinence, and paraplegia. Magnetic resonance imaging (MRI) of the thoracic and lumbar revealed a large epidural fluid collection compressing the spinal cord and cauda equina. Unfortunately, a delay in care prevented the patient from receiving neurosurgical decompression.

Conclusion: SRI associated coagulopathy may predispose to EDH formation by diminishing platelet aggregation. Therefore, weaning these medications, as dictated by the latest guidelines, should be highly considered, if possible and reasonable, to ensure favorable safety profiles for ESI procedures, especially in persons with multiple risk factors. Regardless of appropriate strategies to mitigate ESI associated bleeding risks, proceduralists should always maintain a healthy index of suspicion for EDH formation in the post-procedural phase as early diagnosis and intervention may prevent devastating neurological outcomes.

Key words: Epidural hematoma, paraplegia, aspirin, duloxetine

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BACKGROUND

Transforaminal and interlaminar epidural steroid injections (ESIs) are a commonly used interventional treatment for discrete source(s) of pain (inflamed nerve roots, spinal stenosis, discogenic pain) with proven efficacy (1,2). Currently, the only other treatments for these sources of pain are invasive surgical options. Other minimally invasive procedures for treating these sources of pain are being developed, such as disc decompression procedures and interspinous prosthesis placements (3-6). These procedures appear to have risk/benefit ratios more similar to the ESI, but currently are utilized when other minimally invasive procedures do not yield adequate relief of symptoms.

The risk/benefit ratio of both transforaminal and interlaminar ESI is excellent compared to surgery with the risks of severe complications both short and long term being logarithmically in the favor of minimally invasive treatment (1-8). Despite the potential benefits, the risk for both forms of ESIs is not absent and can be associated with life altering complications. Transforaminal ESI have been associated with paraplegia secondary to interruption of the blood supply to the thoracolumbar spinal cord (9-11). Interlaminar ESIs have been associated with paraplegia secondary to the development of epidural hematomas (EDH) (12-15).

At this time, there is only one reported case of a foraminal hematoma following a transforaminal ESI and there was no chronic motor sequela (16). There have been multiple cases of EDH formation following interlaminar ESIs, but no case of paraplegia secondary to interruption of the blood supply to the spinal cord as these procedures do not endanger the arteries supplying the spinal cord (9-17). Of note, these cases report EDH formation following cervical, thoracic, and lumbar ESIs (9-17).

EDH formation is one of the most feared complications associated with ESI procedures (2,8,12-19). With significant bleeding, EDH can produce a mass effect within the spinal canal and cause subsequent spinal cord edema and compression. Patients with suspicion of EDH formation warrant emergent neurosurgical intervention to prevent catastrophic and irreversible neurological outcomes. Despite the appropriate management, persons with EDH may still experience permanent neurological deficits (13,19).

The risk of developing an EDH following an ESI is expectedly increased in the context of concomitant anticoagulant and/or antiplatelet agent usage (19,20). In

an effort to address these concerns, the American Society of Regional Anesthesia and Pain Management (ASRA) has released evidence based guidelines for the appropriate discontinuation of these agents before undergoing neuraxial procedures. However, cases of EDH formation following ESIs have still been reported in recent years despite strict adherence to these recommendations (13-15,19).

While there exists significant evidence for the risks associated with anticoagulant and anti-platelet agents in epidural procedures, the anti-platelet effects of serotonin reuptake inhibitors medications (SRIs) has received less attention. A recent survey found that a significant number (36%) of pain practitioners were unaware that these medications were associated with anti-platelet effects (21). Below, we present an unfortunate case of a patient who developed an EDH following a lumbar interlaminar ESI while on a combination of low dose aspirin and duloxetine. Although others have reported cases of EDH formation in patients taking aspirin, we wish to use this case as an opportunity to convey and discuss the risks and complications associated with SRI agents in ESI procedures (12).

CASE REPORT

History and Presentation

We present a case of a 70-year-old female who presented to an emergency room in a community hospital with intractable left hip pain. Her pain was described as constant, burning, shooting pain that radiated down her left lateral thigh, knee, calf, ankle, foot, to her toes. Her past medical history included hypertension, diabetes type 1, hyperlipidemia, hypothyroidism, morbid obesity, osteoporosis, fibromyalgia, failed back surgery syndrome following an L5-S1 spinal fusion 11 years prior, and multiple pelvic fractures. Her home medications taken included hydrochlorothiazide, losartan, carvedilol, aspirin, aspart and detemir insulin, rosuvastatin, levothyroxine, pregabalin, duloxetine, and hydrocodone as needed for breakthrough pain. Additionally, this patient received an unknown number of ESIs in the past for chronic lumbar radiculopathy. She had no history of coagulopathy or liver disease. Despite her morbid obesity and chronic pain conditions, she was ambulatory with the assistance of a walker.

On physical examination, she demonstrated limited active range of motion in the left lower extremity with relative left patellar hyporeflexia; no other focal neurological or musculoskeletal deficits were appreciated.

Plain films of the hip and lumbar spine did not reveal any gross abnormalities. However, a computed tomography scan of the lumbar spine revealed a fragment of disc material that was compressing the left L4 nerve root. The patient's pain continued to be poorly controlled over the next day despite adjunct usage of opioid medications. Therefore, the anesthesia pain management service was consulted to evaluate the patient for nonsurgical interventions of noted radiculopathy.

Procedural Parameters

All of the previously mentioned home medications were continued while inpatient; notably, the patient received her daily scheduled aspirin 81 mg and duloxetine 60 mg 15 hours prior to the procedure. She underwent a fluoroscopically guided L3-L4 level interlaminar ESI under midazolam sedation 2 days after admission. A 20-gauge Tuohy needle was used and a 2 mL mixture of triamcinolone 80 mg and lidocaine 1% was administered with loss of resistance technique. Only one puncture attempt was required. No immediate post procedural complications, including lower extremity weakness, tingling, or numbness, were noted.

Post Procedural Course

Approximately 6 hours post procedurally, the patient started to report severe, dull back pain, which was not alleviated with 2 administrations of 2 mg hydro-morphone intravenous push, delivered 2 hours apart. Subsequently, about 9 to 10 hours post procedurally, the patient reported the inability to move her legs and had an episode of urinary incontinence. Of note, the patient also received her daily scheduled aspirin 81 mg and duloxetine 60 mg 9 hours post procedurally. Within 24 hours post procedurally, the patient exhibited profound bilateral lower extremity weakness and incontinence to both stool and urine, which required diaper placement and foley catheterization. Due to unclear logistical difficulties, the patient was unable to obtain an MRI and required transfer to a tertiary care center for higher level of care.

Due to unclear barriers that precluded timely patient transfer, the patient was finally transitioned to the tertiary institution 4 days following the ESI. MRI of the thoracic and lumbar revealed evidence of a large, heterogeneous posterior epidural fluid collection extending anteriorly into the spinal canal from the T10 to L2/3 level, suggestive of an EDH that compressed the spinal cord and cauda equina anteriorly. Her physical examination

at this time revealed 0/5 strength in the bilateral lower extremities and absent knee- and ankle-deep tendon reflexes. No sensory deficits, however, were reported. Unfortunately, the neurosurgical service felt that given the now protracted length of paraplegia, there was a low probability that surgical intervention would lead to restoration of lower extremity function. A plan was then made to transition patient to an inpatient rehabilitation facility.

DISCUSSION

Although not precisely known, the prevalence of EDH associated with ESI procedures is estimated to be less than 1 case per 150,000 injections (22). This rate far outweighs the 1 case per 1,000,000 persons incidence of spontaneous EDH formation (23,24). Of these already rare instances, only 40% are estimated to be idiopathic in origin, thus conferring only a 1 case per 2,500,000 person incidence of this rare phenomenon. This stark disparity suggests that cases of EDH following ESI procedures are extremely unlikely to be resultant of idiopathic and spontaneous processes, but are rather influenced by a host of procedural and preprocedural risk factors.

Preprocedural risk factors for EDH formation in this case include female gender, elder age, and prior spinal surgeries, all of which are nonmodifiable (19, 25). Admission laboratory studies did not reveal any thrombocytopenia, liver dysfunction, or coagulopathy. Procedural risk factors, including difficult or repeated spinal punctures, were not reported in this case. Consequently, the usage of anti-platelet and SRI medications as in this case, represents the risk factor that conferred the greatest preventable risk.

The second edition of the ASRA guidelines for interventional spine procedures for persons on anti-platelet or anti-coagulant medications released in April 2018, recommends gradual tapering of SRI medications across 1 to 2 weeks in those persons with increased bleeding risk, who were defined as those with old age, advanced liver disease, or taking nonsteroidal anti-inflammatory drugs, anti-platelet, or anti-coagulant medications, as long as their severe depression and suicidality risks are accounted (19,26). Additionally, they recommend consideration of aspirin discontinuation in intermediate-risk procedures, like interlaminar ESIs, in persons where anatomical configurations increase procedural bleeding risk. This stems from the finding that as roughly 10% of circulating platelets are replaced on a daily basis, by the fifth day of aspirin discontinuation, approximately

50% of all platelets would have normal function (19,27). The extensive list of anatomical configurations includes prior surgical interventions, as studies have suggested that localized anatomical disruptions and scar formation preclude appropriate resorption of post procedural blood products (19,28,29). The latest American Society of Interventional Pain Physicians guidelines state good evidence for discontinuation of low dose aspirin for 3 days prior to procedures with a moderate to high risk of bleeding, however does not contain specific guidelines as it pertains to management of SRI's (30).

The case reported in this manuscript was in 2012, which predated even the first edition of the aforementioned ASRA guidelines. As such, the clinical practice patterns at the time do not reflect the current standard of practice. In one survey, it was found that only 32% of practitioners in 2012 discontinued aspirin prior to performing ESIs (19). Likewise, there also exists a knowledge gap in pain practitioners treating persons taking SRI medications. A significant number of practitioners (36%) were unaware that SRIs even conferred a bleeding risk. This knowledge gap is especially alarming given the high incidence of mood disorders and SRI usage in persons with chronic pain considered for ESI (19,31,32).

Although the precise pathophysiology of SRI-mediated coagulopathy has yet to be clearly elucidated, there exists increasing evidence that SRI medications diminish platelet aggregation (33,34). Appropriate intracellular serotonin concentrations are necessary to achieve effective primary hemostasis. Serotonin is packaged within dense granules of platelets, which are released upon cellular activation, and acts to recruit additional platelets to aid in aggregation. Both in-vitro and in-vivo studies have demonstrated that intra-platelet serotonin concentrations are markedly decreased after as little as 3 weeks of SRI usage and that this depletion confers a coagulopathic state (33-35).

SRI associated coagulopathy has also been established clinically for other presentations of bleeding, namely gastrointestinal and intracranial hemorrhage (36,37). The relationship between the anti-platelet effects of SRIs and bleeding has been instrumental in delineating the known risks of these medications in the latest ASRA guidelines for neuraxial procedures. Of note, these risks are not simply associations, but rather have been substantiated by high level of evidence concluding these risks to be attributable to SRI use (36-38).

An additional point of consideration was the pos-

sibility of using a caudal approach for ESI. While the interlaminar and transforaminal approaches for ESI can be targeted to a specific point in pathology, it has been shown that caudal ESI procedures, with needle entry through the sacral hiatus under fluoroscopic guidance, provides additional safety benefits, such as minimizing the risk of inadvertent dural puncture (39). Despite caudal ESI requiring larger volumes, it is considered to be the safest approach, and is the preferred method for those with spinal hardware (40,41). Despite the patient having fusion surgery at a level inferior to the level of interlaminar injection, the surrounding scar tissue stands as a complicating factor, which could have potentially been avoided with the use of caudal approach.

The most cited prevalence of EDH formation following ESIs suggests an incidence of 1:150,000, which itself is extrapolated from epidural anesthesia literature (22). Given that standard ESI procedures do not require catheter placement, EDH incidence is expected to be slightly lower in this population. Regardless, it is widely agreed that any ESI has a baseline risk for EDH formation secondary to needle puncture itself. However, differentiating the rate of this known and nonpreventable adverse event from those caused by modifiable risk factors, is challenging. The lack of epidemiological data of this phenomenon, compounded by the scarcity of high-level data delineating the precise risk of each contributing etiology, makes it difficult to directly establish EDH formation as sequela of SRI usage. However, given that SRI associated coagulopathy has been extensively shown to cause other hemorrhagic presentations, SRI discontinuation should be strongly considered, especially in patients with high bleeding risk, if reasonable and clinically appropriate.

CONCLUSION

As the prevalence of cardiovascular diseases is ever increasing along with the arsenal of anti-coagulant and anti-platelet medications, judicious preprocedural risk stratification is necessary to minimize adverse events related to bleeding. Although associations between many of the risk factors and their individual contributions to these bleeding events remain controversial and have yet to be clearly delineated, there exists growing data suggesting that SRI medications may predispose patients to EDH formation. Consequently, weaning these medications as dictated by the latest guidelines should be highly considered, if possible and reasonable, to ensure favorable safety profiles for ESI procedures,

especially in those persons with multiple risk factors for EDH formation. However, regardless of appropriate strategies to mitigate ESI associated bleeding risks, proceduralists should always maintain a healthy index

of suspicion for EDH formation in the post procedural phase, as early diagnosis and intervention within 8 hours may prevent devastating neurological outcomes (14).

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