Ankylosing Spondylitis Versus Internal Disc Disruption: A Case Report Treated Successfully with Intradiscal Platelet-Rich Plasma Injection

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Abstract

We report the case of a 21-year-old female who presented with severe disabling low back pain radiating to both buttocks for 1 year. She was initially diagnosed with ankylosing spondylitis (AS) based on her complaints of persistent low back pain with bilateral sacroiliitis found on magnetic resonance imaging (MRI) of the sacroiliac joints. Despite testing negative for HLA-B27 and lack of other positive imaging to support the diagnosis, she was still treated presumptively as a patient with this disease. These symptoms were debilitating to the point where she withdrew from college, discontinued horseback riding, developed depression, and required antidepressant treatment. She did not improve with oral non-steroid anti-inflammatory drugs, neuropathic and opiate pain medications, or a trial of Etanercept (Enbrel). She then presented to our outpatient physiatry office for a second opinion. Her axial low back pain was exacerbated with positions of increased disc load (sitting/lifting/forward bending), and the physical exam was positive for pain-limited spine range of motion in flexion greater than extension and dural tension signs. Therefore, a clinical impression was formed that her pain may be more related to an internally disrupted disc (IDD) than AS. This diagnosis was further supported when she failed to obtain any relief with fluoroscopically guided bilateral sacroiliac joint injections. MRI of the lumbar spine was ordered, which revealed a small posterior annular fissure at L5-S1 that was later confirmed as the pain generator with provocative discography. The patient's pain and function improved transiently with a caudal epidural steroid injection and were significantly alleviated with two serial intradiscal platelet-rich plasma (PRP) injections. The patient returned to college, discontinued anti-depressant and pain medications, and resumed all activities 1 year from the second PRP injection. Additionally, she has had no further treatment of her presumed AS.

Keywords: Ankylosing spondylitis; Annular fissure; Discogenic low back pain; Internal disc disruption; Intradiscal therapies; Platelet-rich plasma; Regenerative medicine; Sacroiliac joint pain; Sacroiliitis

Introduction

The differential diagnosis of patients who present with primarily low back and bilateral buttock pain without any clear inciting event is wide. In general, common musculoskeletal etiologies that may explain such pain patterns include lumbar discogenic pain from internal disc disruption (IDD), facet arthropathy, myofascial pain, or referred hip pain from greater trochanteric pain syndrome. The sacroiliac (SI) joint is another commonly cited pain generator that may present with similar symptomatology. The prevalence of SI joint pain is reported to be 13% to 15% and as high as 30% in patients who present with both low back and buttock pain [1,2]. Bilateral sacroiliitis is even more uncommon and often represents an early, hallmark sign of ankylosing spondylitis (AS), a seronegative spondyloarthropathy. The estimated prevalence of this rheumatologic condition ranges from 0.1 to 1.4% [3]. Differentiating among these numerous conditions may be challenging, but may be further elucidated with an understanding of the known epidemiology and risk factors of these disorders, the gathering of an effective history, the results of a neuromusculoskeletal physical exam, and the judicious use of relevant studies and/or select image-guided injections.

Case Presentation

A 21-year-old female with history of Graves' disease status following iodine and radiation treatment in 2012 presented with a 1-year history of low back pain radiating to the bilateral buttocks and intermittently to the posterior thighs. Her symptoms started insidiously and were refractory to physical therapy, non-steroidal anti-inflammatory drugs (NSAIDs), Gabapentin, Duloxetine, Enbrel (etanercept), and opiates. The pain was described as constant and severe, and ranged from a scale of 4 to 10 out of 10. It was exacerbated with prolonged standing, walking, or sitting, and was particularly bothersome

in the morning. She could not identify any alleviating factors. She denied any lower extremity weakness, bowel/bladder changes, or constitutional symptoms, but endorsed feelings of depression and poor quality of life due to her pain. There was no family history of rheumatologic conditions. In retrospect, she did report being involved in a minor motor vehicle accident 3 months prior to the onset of symptoms.

The patient was previously managed with AS by her rheumatologist and was treated for 2 months with Enbrel with no improvement in her symptoms. Her original plain films of the lumbar spine, pelvis, and sacrum did not show any pathognomonic signs of AS, such as vertebral body squaring, syndesmophyte formation and lumbar fusion, or symmetrical sacroiliitis. However, a magnetic resonance imaging (MRI) of the sacrum demonstrated mild bilateral sacroiliitis (left greater than right) with no evidence of ankylosis **(Figure 1a and 1b)**. She did not have any MRI of her lumbar spine before presenting to our clinic. Her blood work was negative for HLA-B27, rheumatoid factor, and antinuclear antibody, with normal complement and inflammatory marker levels (C-reactive protein: 34; erythrocyte sedimentation rate: 0.5). She also tested negative for Lyme's disease, Sjogren's antibodies, and hepatitis.

On physical exam, the patient had restricted lumbar spine range of motion in all planes, especially with flexion. Hip range of motion was full and pain free. No scoliotic deformities were noted. She had diffuse tenderness to palpation to the lumbar paraspinals at L4-5, L5-S1, and at the posterior superior iliac spines (PSIS) bilaterally. There was no tenderness over the greater trochanteric bursas. No weakness was appreciated on strength testing, with her lower extremity reflexes symmetric without ankle clonus bilaterally. Sensation was intact to light touch in both limbs. Gait was slow, but non-antalgic. Her exam was significant for interspinous tenderness at the lower lumbar levels and mild dural tension in the form of positive bilateral straight leg raise and seated Slump's testing. These tests reproduced her usual low back and radiating symptoms in an S1 distribution. While provocative tests such as FABER and FADIR testing did not reproduce her pain symptoms. Schober's testing could not be adequately performed secondary to pain.
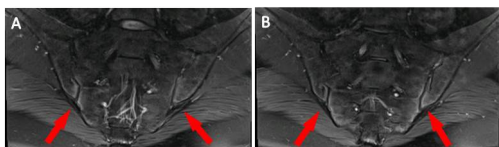
Figure 1 (a and b) Coronal T2-weighted fat-suppressed magnetic resonance imaging (MRI) of sacroiliac joints demonstrating mild marrow edema and erosive changes in both sacroiliac joints (left greater than the right).

An MRI of the lumbosacral spine was performed 2 months after the MRI of the sacrum. It was significant for an annular fissure at L5-S1 **(Figure 2a and 2b)**. It remained unclear whether the pain generator was the presumed sacroiliitis

versus an IDD at the L5-S1 segment. Diagnostic fluoroscopically guided bilateral SI injections provided no relief. A fluoroscopic epidural anesthetic and steroid injection was then performed to assess for discogenic low back pain as a result of IDD. We used a caudal approach, because in our experience, this provides the most reliable means of achieving central ventral epidural flow to cover the posterior annulus at the L5-S1 segment. Immediately following the procedure, the patient had anesthetic relief of her low back and radiating buttock pain. One week after the procedure, she reported significant relief for the first time in 1 year. However, this relief was transient and dissipated over the ensuing 3 weeks.
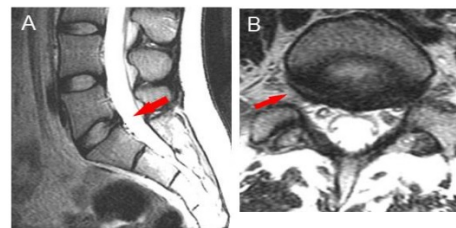

Figure 2 (a and b) T2-weighted sagittal and axial MRI of the lumbar spine study performed 2 months after an outside MRI sacroiliac study. The sagittal and axial images show a high intensity zone along the posterior periphery of the L5-S1 disc.

Because the caudal epidural steroid injection was well-received, a lumbar discogram was performed to confirm if the symptoms were consistent with IDD at L5-S1. The discogram produced no pain at L4-L5, but did confirm the presence of a symptomatic annular fissure at the L5-S1 level. At the same time as the discogram, we injected 2 cc of platelet-rich plasma (PRP), which was prepared using the Harvest centrifuge system (Harvest Technologies Corporation, Plymouth, MA), at the L5-S1 level. At 1 month post-PRP injection, the patient reported about 20% improvement in pain symptoms. She also reported a slightly decreased need for Percocet 10/325 mg, which was lowered from 1 tablet 5 times a day to 4 times a day, as well as an increased tolerance for positions that normally would aggravate her symptoms. She was able to tolerate a light physical therapy program for the first time. One month later, she reported decreased depression and pain levels that were 30% of pre-intradiscal PRP pain levels; however, she continued taking pain medications. In collaboration with her rheumatologist, Enbrel was stopped with no change in symptoms.

Given her continued, gradual, but positive response to the first intradiscal PRP injection, a repeat intradiscal L5-S1 PRP injection was deemed to be of further therapeutic value **(Figure 3a and 3b)**. The second PRP injection was performed 3 months after the first. She then experienced further improvements in pain and function. Throughout the management course, all interventions were tolerated well without any adverse complications. Two months after the second intradiscal PRP injection, the patient reported intermittent mild pain in the lower back that occasionally radiated to the buttocks. However, these symptoms did not

interfere with her daily activities, and she was able to tolerate sitting and standing. She soon progressed to a full physical therapy program, tapered off all pain and anti-depressant medications, and returned to college to pursue her teaching major.
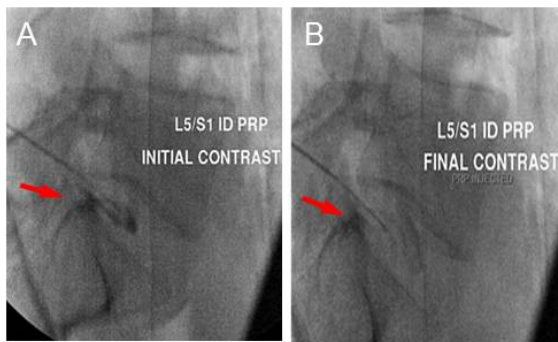
Figure 3 (a and b) Sagittal view of lumbar spine on fluoroscopic imaging demonstrating the repeat intradiscal PRP injection.

On the 1-year follow-up exam, she had minimal to no tenderness at the L5-S1 interspinous region, no tenderness over the PSIS joints, full, pain-free lumbar spine range of motion, and no neurological deficits. She had returned to full activities and discontinued all opiates.

Discussion

This case highlights the continued importance of a careful, comprehensive medical history, physical exam, and imaging in the diagnostic work-up of patients who present with chronic low back and buttock pain refractory to conservative treatment. As this case illustrates, positive imaging has the potential to mislead physicians to believe the abnormal structure is the primary pain generator. Even though bilateral sacroiliitis is present as a clinical feature in nearly 100% of AS cases, it must be weighed with more commonly encountered musculoskeletal and spine disorders [1]. Although a positive MRI increases the post-test probability of AS to 80% to 95%, this only occurs if patients present with signs and symptoms consistent with inflammatory back pain and positive HLA-B27 serology [4]. The patient presented in the current report did not fulfill all clinical criteria for inflammatory back pain, such as morning stiffness lasting greater than 30 minutes, improvement of back pain with exercise but not rest, or alternating buttock pain [5]. She also had negative serology for HLA-B27. In addition, her radicular pain was not consistent with AS patients. However, if one was to follow the modified New York 1984 criteria for AS, the minimal criteria would have been fulfilled as she did possess restriction of thoracolumbar motion and positive sacroiliitis confirmed on MRI [6,7].

Restriction of motion may be easily explained by her unrelieved pain from IDD. If sacroiliitis was suspected as being responsible for causing the patient's symptoms, the most facile way to rule in or exclude simple SI joint dysfunction would be a fluoroscopically or computed tomography-guided SI joint injection, which is the gold standard for the diagnosis of SI joint pain [1]. Our patient did not gain any relief from these injections, which suggested that her symptoms were more discogenic in nature.

The incidence of chronic low back pain that is attributable to discogenic causes is reported to be approximately 40% to 45% [8]. Degenerative disc disease begins as early as the second decade of life, and the risk factors include obesity, smoking, and activities involving repetitive lumbar spine flexion and rotation, and or history of trauma [8,9]. Genetic inheritance has also been cited in the development of low back pain [10]. Although the pathophysiology of discogenic pain is not fully understood, a multifactorial model proposes that the combination of decreased disc height, desiccation, reduced proteoglycan content in the nucleus pulposus, and increased mechanical disc pressure loads leads to the disruption of the normal disc architecture, often in the outer third of annulus fibrosis [8,11]. The presence of these defects leads to an inflammatory cascade, followed by a possible compensatory mechanism. The resulting highly innervated disc structure in the setting of a degenerated nucleus pulposus is believed to create this difficult-to-treat pain generator [8]. Vertebral endplate changes are also associated with this cycle (Modic changes on MRI) and appear to be associated with low back pain developing at the level of a disc herniation [12].

Clinically, patients with primarily axial low back pain report symptoms more frequently in the morning hours. The pain is often exacerbated with activities, such as lumbar flexion, prolonged sitting or standing, and Valsalva maneuvers. Lying supine relieves these symptoms [8,13]. The neurologic exam may be unremarkable but may be significant for restricted spine range of motion and dural tension signs. With respect to imaging, the best modality for visualizing disc pathology is MRI. Painful IDD is represented on MRI as a "high intensity zone," which is an increased T2 signal of the posterior portion of the annulus [14]. However, the "gold standard" diagnostic test for discogenic pain is provocative lumbar discography [8,14]. Although its use has been the subject of debate, it remains to be the only available method of correlating abnormalities seen on MRI with clinically reported pain [8,15]. Initial conservative treatment of chronic discogenic pain consists of a multidisciplinary approach of structured physical therapy, oral pain medications, and patient education. Other complementary treatments, such as chiropractic care, massage, and acupuncture, may be used as adjunct treatment options. Higher-tier treatments include fluoroscopically guided spinal epidural injections, if patients do not improve with the above. Surgical interventions, such as lumbar disc replacement and/or interbody lumbar fusion, are indicated when patients have exhausted all available conservative therapies [16,17].

For patients who suffer from chronic, lumbar discogenic back pain and are not amenable to standard conservative or surgical treatment regimes, intradiscal therapies are a potentially promising option. However, there is an ongoing debate regarding the long-term safety of the procedure, and there is no consensus on what injectate best alleviates discogenic pain without compromising the overall health of

the disc [15,18]. The intradiscal injection of stem cells as a possible regenerative therapy has been extensively studied in various animal models of intervertebral disc (IVD) degeneration and is currently being investigated in clinical trials. Despite promising preliminary results, rigorous studies on IVD cells suggest that transplanted cells are unable to survive and adapt in the avascular and hypoxic IVD environment [19]. Thus, the clinical utility of this intradiscal injectate will remain unclear until further research is concluded.

PRP is a biologically active solution that has gained popularity in the treatment of various musculoskeletal injuries and disorders [20,21]. It has been used to successfully heal injured tendons, which are predominantly avascular and are comprised of type I and II collagen. There is evidence to support its efficacy as a treatment in chronic tendinopathies, such as lateral epicondylalgia [22,23] and knee osteoarthritis [24,25]. More recently, PRP has been shown to be effective in the IVD [26,27]. Data in the IVD are promising, but are limited to preliminary studies. Its mechanism of action has not been fully explained, but the various growth factors present in PRP have been suggested to aid in bolstering the healing response to these injuries [17]. In the spine, PRP has historically been used to help augment bony spine fusion [17].

As the largest avascular structure in the human body, IVDs rely primarily on passive diffusion from adjacent endplate vessels for nutrition [28]. Therefore, the IVD has poor inherent healing potential. An analysis of PRP-infused human IVD specimens demonstrated up-regulated cellular proliferation/ differentiation, chondrogenesis, and proteoglycan synthesis [29]. Additionally, intradiscal PRP is associated with greater restoration of disc height, decreased inflammatory cells, and normal cellular architecture in experimentally-injured IVDs *in vivo* [30]. The injection of fibrin itself may catalyze the sealing of annular fissures [31]. Similarly, in an *in vitro* study of 5 bovine lumbar IVDs with annular defects, PRP preparations into these areas showed an increase histologically in annular fibrosis matrix and cell production in a course of 4 days [32]. By extension, the intention of injecting PRP in chronic, discogenic disease is to alter the inflammatory environment surrounding the disc and possibly prevent further deterioration and advancement of the degenerative disc cascade [33]. The risks associated with corticosteroid use on the nucleus pulposus and collagenous ring structures are minimized with PRP. Although the risk for further disc degeneration and infection is entirely possible in view of discography, such complications may be avoided when performed in a safe and sterile manner by an experienced physician. In addition, no significant adverse events using this route of delivery have been reported. Another possible beneficial effect of PRP is its impact on circulating systemic growth factors. Although it may be delivered locally to one region of the body, recent studies show that there is an increase in systemic growth factors (albeit temporarily), which theoretically may have an additional anti-inflammatory role [34].

Conclusion

This is the first, known described case of a patient with underlying lumbar discogenic pain with an additional diagnosis of AS, whose pain, quality of life, and function were significantly improved with a novel, regenerative intradiscal therapy consisting of autologous PRP. Clinicians should be both aware of how IDD may masquerade as AS, and how intradiscal PRP may become a promising treatment for patients with IDD. Further long-term randomized controlled studies are needed.

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