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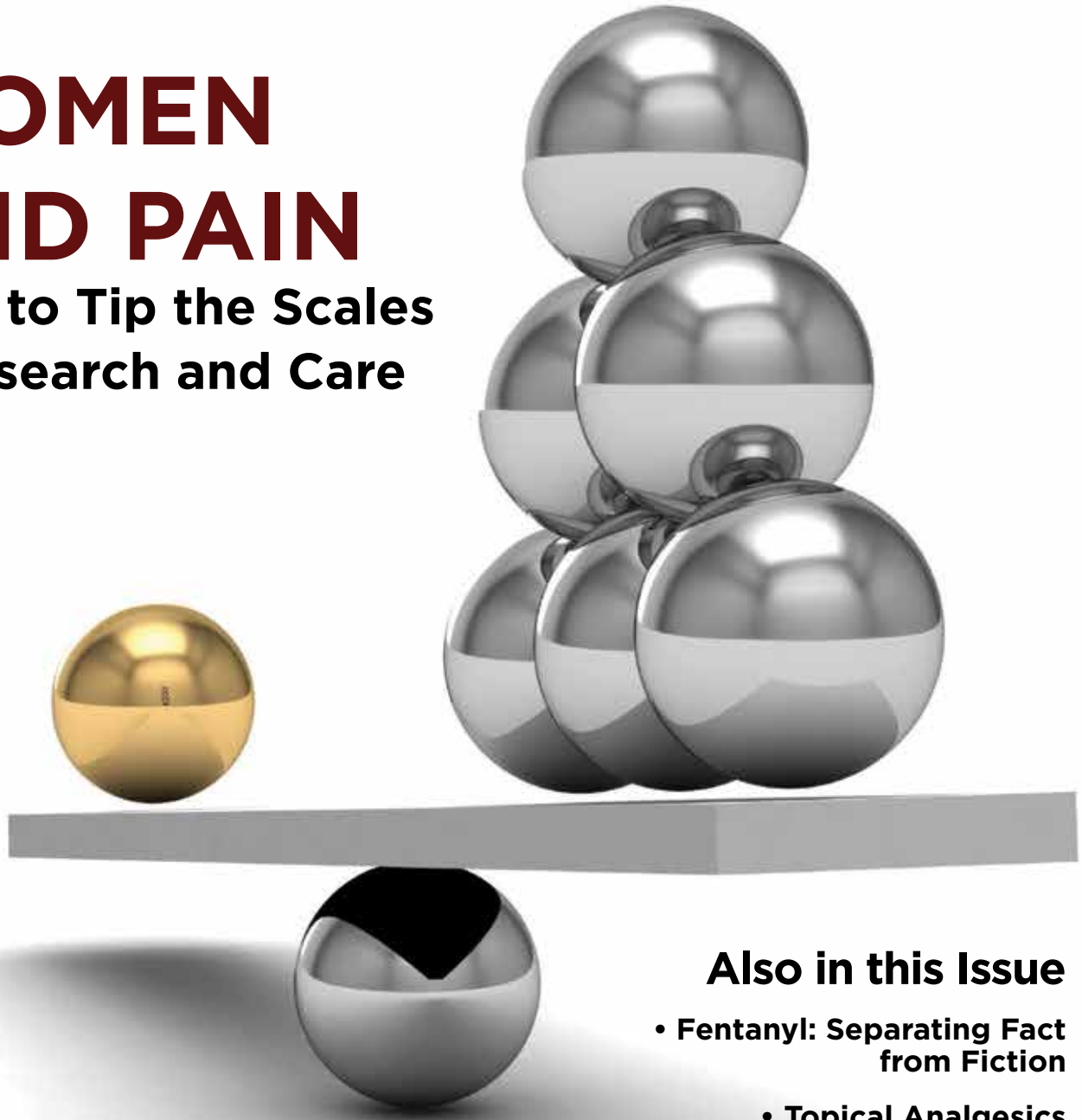
WOMEN AND PAIN

Time to Tip the Scales in Research and Care



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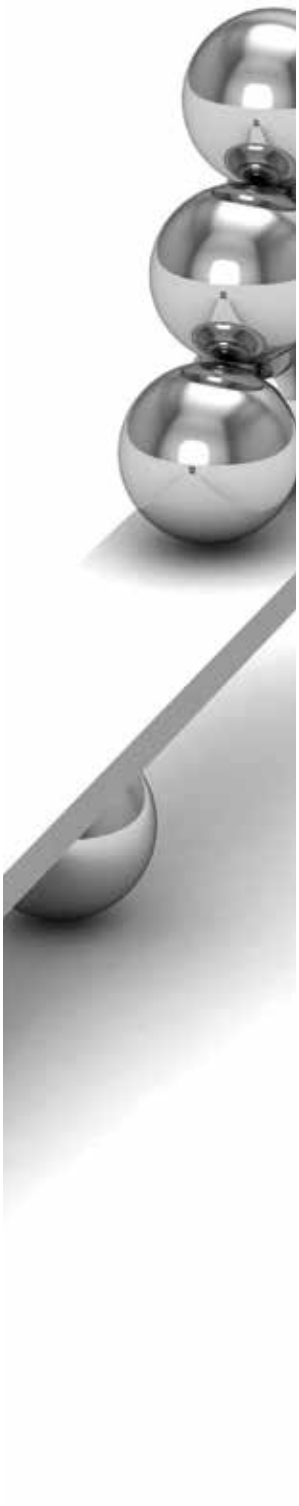
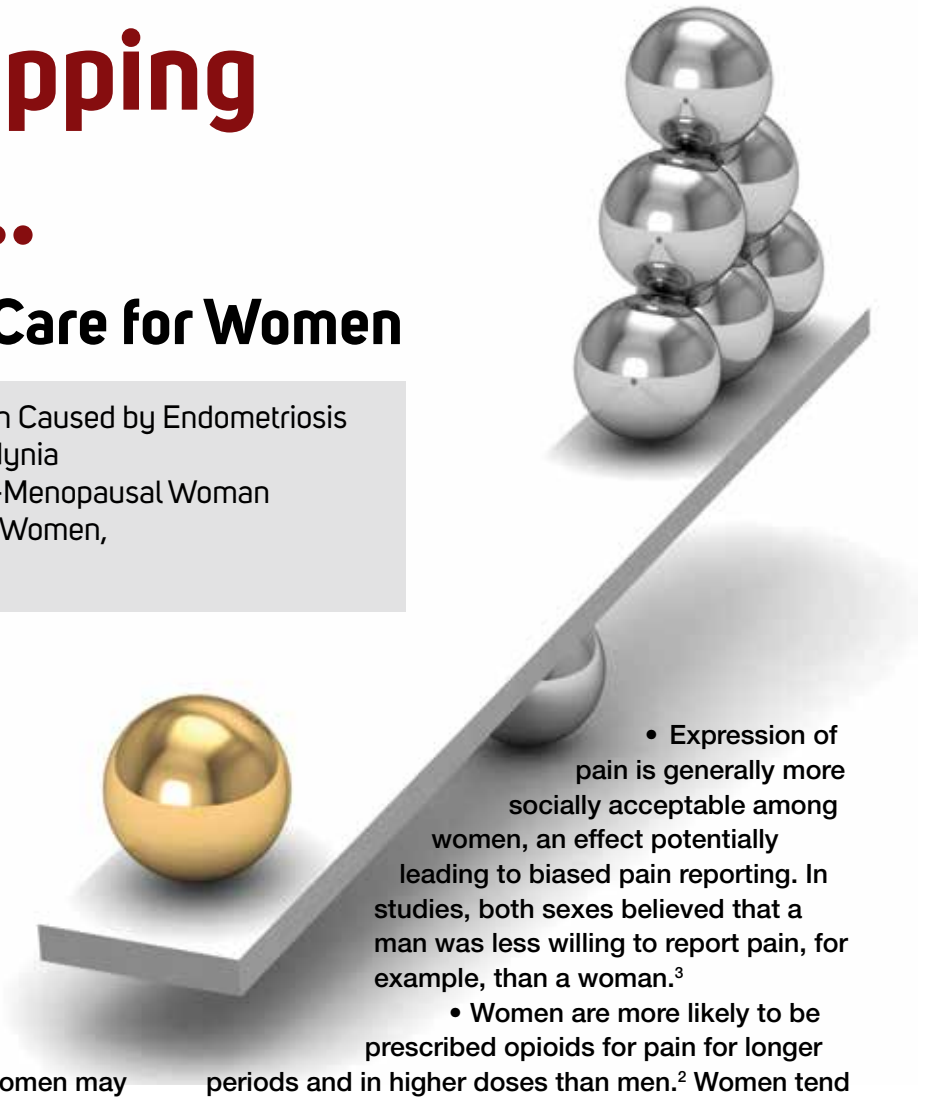


Women and Pain, featuring:

Special Focus on Topicals, including:

Here's to Tipping the Scales...

in Pain Research & Care for Women



The Stats

- Women report more intense pain than men in virtually every disease category, and women are at increased risk for opioid misuse.[1,2]
- The literature reveals that men and women differ in their responses to pain and in responses to pain interventions, with increased sensitivity and risk for clinical pain commonly observed among women.[3]
- A high proportion of reproductive-age women may be experiencing pelvic pain that goes untreated. Roughly one-third of women reported that they have experienced chronic pelvic pain that has gone untreated for six months or longer.[4]
- It has been acknowledged in recent decades that clinical trials have not always adequately enrolled women or analyzed sex-specific differences in the data.[5] Approximately 80% of pain studies are conducted on male mice or human men, despite the fact that 70% of chronic pain conditions primarily affect women.[6]
- Endometriosis affects 1 in 10 women worldwide, and as many as 16% of women in the US suffer from vulvodynia at some point in their lives.[7,8]
- The sex of both the patient and the healthcare provider may influence pain care, with one study showing that female practitioners are more likely to recommend psychosocial treatments for female than for male pain patients.[9]
- Expression of pain is generally more socially acceptable among women, an effect potentially leading to biased pain reporting. In studies, both sexes believed that a man was less willing to report pain, for example, than a woman.[3]
- Women are more likely to be prescribed opioids for pain for longer periods and in higher doses than men.[2] Women tend to become dependent on prescription pain relievers more quickly than men and may experience more cravings;[10] despite this, co-prescribing opioids with medications that may increase overdose risk, such as benzodiazepines, is more common in women.[11]
- Among those in need of medication-assisted treatment, or MAT, men are much more likely to obtain treatment than women.[10]
- Women are more likely to have co-occurring mental health and substance use disorders than men.[12]

Sources: 1-Stanford University School of Medicine Release, Jan. 23, 2012. 2-CDC, "Prescription Painkiller Overdoses: Overview," Updated March 23, 2017. 3-Bartley EJ, Fillingim RB, Sex differences in pain, *Br J Anaesth.* 2013;111(1):52–58. 4-Schliep KC, et al., Pain typology and endometriosis, *Hum Reprod.* 2015;30(10):2427-2438. 5-Liu KA, Dipietro Mager NA, *Pharm Pract,* 2016;14(1):708. 6-Kiesel L, "Women and pain," *Harvard Hlth Blog*, Oct. 9, 2017. 7-Endometriosis Foundation of America. 8-National Vulvodynia Assoc. 9-Hirsh AT, et al., The influence of patient sex, provider sex, and sexist attitudes on pain treatment decisions, *J Pain.* 2014;15(5):551-559. 10-HHS Office on Women's Health, "White Paper: Opioid Use, Misuse, and Overdose in Women," 2016. 11-Hwang CS, et al. Trends in the concomitant prescribing of opioids and benzodiazepines, *Am J Prev Med.* 2016;51(2):151-160. 12-NIDA, "Substance Use in Women," Rev. June 2018.

Cross-Linked Hyaluronic Acid for the Management of Neuropathic Pelvic Pain

A case presentation and injection technique for targeting chronic neuropathic pelvic pain caused by endometriosis.

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Endometriosis, the presence of endometrial tissue outside of the uterus, is a frequent, estrogen-related condition, affecting approximately 176 million women in the world, or 1 in 10 women between the ages of 15 and 49.[1] The condition may lead to infertility in 30 to 50% of those diagnosed,[2] as well as multiple types of related pain including: dysmenorrhea, dyspareunia, intestinal and bowel pain, dysuria, and chronic low back and pelvic pain.

The management of endometriosis-related pelvic pain requires medical and, at times, surgical therapy.[3] Medical modalities are directed at relieving pain through various mechanisms, including the suppression of: inflammation, cyclical ovarian hormone release, estradiol, and menses. Surgical treatment may be used as a first-line approach or after medical failure. Surgery may consist of a variety of techniques including: fulguration, excision, or ablation of endometrioma implants, as well as resection of rectovaginal nodules, lysis of adhesions and nerve pathways interruption.[4] It should be noted that clinical staging of the disease often assists in the selection of treatment in a given case,[5] and may include: Stage 1-Minimal, Stage 2-Mild, Stage 3-Moderate, and Stage 4-Severe. The stages are dependent upon the presence, location, extent and severity of endometrial implants, endometriomas, and adhesions.

The following case presents a woman with severe, chronic lumbosacral and pelvic neuropathic pain due to Stage 4 endometriosis-related endometrioma implants, after undergoing multiple surgical interventions that failed to improve her pain control, wherein she is then successfully treated with cross-linked hyaluronic acid (CL-HA). The diagnosis is supported by electromyography (EMG) findings of multilevel lumbosacral radiculopathy[6-8] and a negative imaging workup for other causes. The use of CL-HA to treat neuropathic pain was initially presented at the 2015 annual meeting of the American Academy of Pain Medicine.[9] This form of treatment is designated as Cross-Linked Neural Matrix Antinociception, or simply XL-NMA.[10] CL-HA is made of chemically cross-linked hyaluronic acid – a linear, anionic proteoglycan polysaccharide composed of glucuronic acid and N-acetylglucosamine repeating units.

The Case

A 41-year-old woman, G, P, M, A: 4, 2, 2, 0, presented with persistent, worsening pelvic and low back pain that she described having for 15 years. The pain would intermittently radiate down both lower extremities, right greater than left, and up her lower back. Overall, her pain was worsening; it had persisted daily for the past six years, with localized pain over the anterior and posterior right greater trochanter.

Pain initially began in the right lower quadrant and was attributed to endometriosis in 2000. She had undergone six endometriosis surgeries (most recent was 6 months prior, excisional type, no change). She was status post-appendectomy, complete hysterectomy, with left ovary remaining, lumpectomy for right breast carcinoma (7 years prior) and self-referred to our center for evaluation. Pain interfered with sleep; weight was stable, as was bowel and bladder function. There was dyspareunia due to pain upon penetration. There was no loss of sensation or weakness, but her legs weakened when the pain became severe. She underwent trigger point injections and radiofrequency denervation, three years prior, with no relief.

Her current analgesic regime included:

- Hydromorphone IR (4 mg; 1 to 1 1/2 tabs, q. 4 to 6 hrs, prn severe pain, as an Oxycodone sparing drug)
- Oxycodone IR (10 mg; 1 to 1 1/2 tabs, q. 4 to 6 hrs, prn severe pain)
- Methocarbamol (750 mg; 1 tab, qid, prn muscle spasm).

Self-reported symptoms as shown on Figure 1 revealed pain over the anterior and posterior pelvis, radiating down both lower extremities, anterior and posterior aspects, to just above

the knees. The patient noted the pain indicated on the left was referred or radiating from its mirror origin on the right (as shown in Figure 2). She described the pain as: aching, sharp, tight, pulling, and constant. The pain score intensity range was (lowest-average-highest): 3, to 5, to 10/10, aggravated by prolonged sitting, standing, lying, touching, stress, driving and/or riding in a vehicle, vacuuming, and pulling. The patient found some relief from "self-determination," pain medication, rest, heat, cold, and lying down in a fetal position.

Patient's Neuropathic Painful Dysesthesias

Right hip and anterior pelvic region:

- The painful dysesthesias from this region proceeded downward and laterally, anteriorly, and medially.

Right sacral region:

- The S1, S2 and S4 dysesthesias proceeded horizontally across the buttock, to the anterior pelvis.
- The S3 dysesthesias, which were the strongest, proceeded in the same direction as the others, but felt deeper, like a level below S1, S2 and S4, and were more intense.

Initial Assessment

Examination: In examining the abdomen/pelvis, there was diffuse tenderness to the lower hemi-abdomen and pelvis, right greater than left, with mild palpation. The vaginal vault was moist, mildly reactively constricted, but admitted two digits. Upon digital pressure superiorly and to the right, right-sided abdomino-pelvic pain was evoked. In assessing the spine, percussion tenderness was noted from L2-3 to S3-4, greatest at L5-S1. The anterior and posterior loading maneuver (ALM/PLM) were both positive at L5-S1. However, the PLM was more severe, with pain noted to the right coxofemoral and greater trochanter region. Palpation over right sacral foramina and greater trochanter revealed additional hyperalgesia and hyperpathia, supporting the presence of neuropathogenicity.

Records review: X-ray of both hips from 3 years prior were noncontributory. A CT Scan of the abdomen/pelvis from two years prior noted previous swelling of the mesentery in the right lower quadrant was not seen, although there was persistent induration in the mesentery (considered: intermittent mesenteric volvulus or internal hernia).

Etiology: Given the patient history, physical assessment, and records, the following differential diagnoses were considered:

1. Endometriosis related-lumbosacral plexopathy, secondary to radicular implants, with secondary neuropathic pain syndrome
2. High-lumbar lesion with referred pain to hips/pelvis, with secondary radiculopathy
3. Intermittent mesenteric volvulus and/or internal hernia, with secondary visceral pain syndrome
4. Metastatic process due to history right breast cancer (7 years prior), lumpectomy.

New Tests Orders and Results

To refine the above differential diagnoses, several tests were ordered. See Table I for diagnostics and results. Based on the

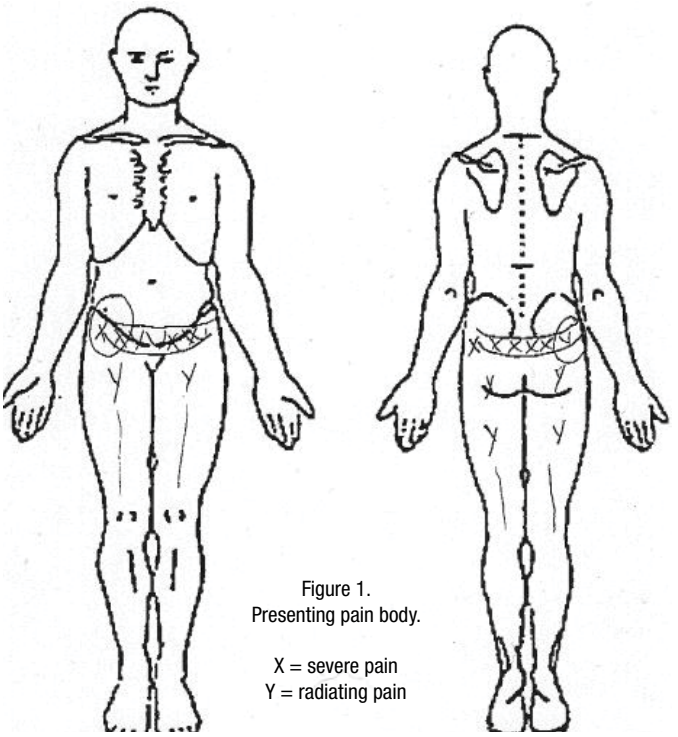

Figure 1.
Presenting pain body.

X = severe pain
Y = radiating pain

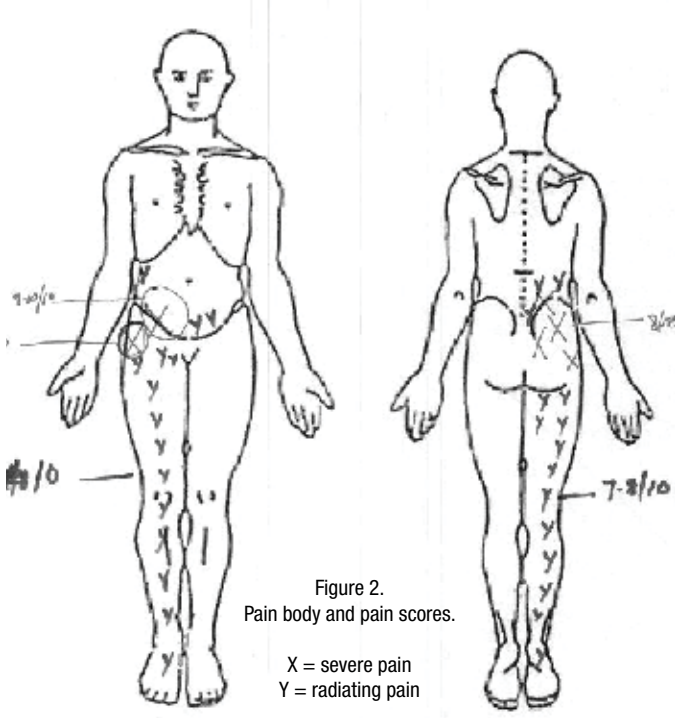

Figure 2.
Pain body and pain scores.

X = severe pain
Y = radiating pain

new test results, the following determinations were made:

1. Probable: endometriosis-related lumbosacral radiculoplexopathy, as suggested by EMG plus secondary neuropathic pain syndrome, with referred pain to hips/pelvis
2. Not found or resolved: intermittent mesenteric volvulus and/or internal hernia
3. Not found: metastatic process.

Treatment

To localize potential sites for neuromodulation, the patient was scheduled for differential neural blockade with local anesthetic (lidocaine 2%, plain) at: right dorsal cutaneous nerve branches (see Figure 3) of T11, T12, L1, L2, L3, L4, L5, S1, S2, S3, S4. See sidebar "Step-by-Step Injection Technique" for further detail. *Note*: The left-sided pain areas were not treated as the patient felt that the primary pain generators were on the right, and that those sites were referring pain to the left side.

With the exception of the anterior pelvic region (see patient commentary), the patient reported good relief and began periodic injections at the same sites, with pain control maintained using an injectate of: 4 cc, 2% plain lidocaine; 7.95 cc, 0.25% plain bupivacaine; and 0.25 mg/0.05 cc, morphine sulfate-MSO4 (5 mg/cc), administering 0.5 to 1.5 cc per site. The patient related that these injections, which provided relief for about 7 days, in combination with her opioids improved substantially her ability to perform daily activities, as well as tend to her children and family, including serving as the primary caregiver of her mother who was undergoing treatment for breast cancer. The patient's reduction in pain was significant (see Figure 4).

XL-NMA – Neural Matrix Aninociception

Approximately 20 months after the patient first presented to the clinic, she underwent an initial trial of XL-neural matrix antinociception at the same sites, using the same technique, except the volumes of the injectate were reduced to one-tenth of the lidocaine/bupivacaine/MSO4 injectate used (this varied from 0.15 cc to 0.25 cc of cross-linked hyaluronic acid, with a concentration varying from 20 mg/ml (Restylane) to 24 mg/ml (Juvederm) per site.[11,12] The patient responded well, with no adverse reactions noted, and achieved a duration of relief of 3 to 4 months for the sacral sites, 4 months for the lumbar sites, and 6.5 months for the greater trochanter region. The patient rated overall improvement after the CL-HA injections at 90%. Change in pain scores was remarkable (see Figure 5).

Since that time, the frequency of injection sessions dropped from three to four times per month on the previous injectate of lidocaine/bupivacaine/morphine, to once every five to six months. There have been no adverse reactions and the patient continues on this regimen to date.

Table I: Initial Testing and Results of the Case Patient.

Test	Results
X-Ray: Lumbo-sacral spine, with Flex, Ext & Oblq views	Left convex scoliosis; left L5-S1 facet arthropathy
MRI: Lumbo-sacral spine, +c/-c	Negative
MRI, Abdomen/Pelvis, +c/-c	Abdomen, mildly enlarged and fatty liver; pelvis, s/p hysterectomy; normal left ovary
Bone Scan: TC-99 nuclear, whole body	Negative
Pudendal EMG / attention: S2-S4	Negative
EMG/NCVs: Both Lower Extremities / attention: L1, L2, L3, L4, L5, S1	Chronic L1, L4, L5 radiculopathy, greatest at L5.

Figure 3.
Sensory Dorsal Cutaneous nerve branches subserving painful region.

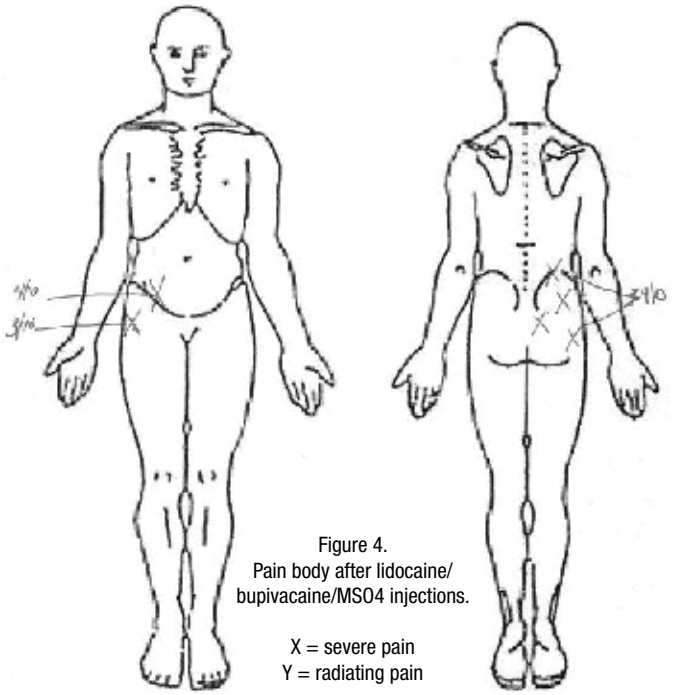

Figure 4.
Pain body after lidocaine/bupivacaine/MSO4 injections.

X = severe pain
Y = radiating pain

Step-by-Step Injection Technique Targeting Endometriosis-Related Neuropathic Pelvic Pain

Figure A. CL-HA procedure tray.

Supplies and Materials

The injectates used in the presented case came prepackaged in a 1 mL syringe (Restylane[11] and Juvéderm[12]). The hyaluronic acid (HA) content was 20 mg/mL and 24 mg/mL, respectively. The procedure tray is shown in Figure A. The volumes used ranged from 0.15 to 0.25 mL per site. However, the amount used was a function of the virtual injection compartment's volume surrounding the neural target. For the S3 and S4 site, 0.25 ml was necessary. However, as the dose increases per site (0.5 to 1mL), extra-arterial tamponade must be considered and immediately treated if it supervenes (ie, hyaluronidase [Hylenex] or recombinant hyaluronidase administered to quickly dissolve the injectate, along with any other measures to maintain and support arterial blood flow). In this case, no significant arterial blood flow was at risk.

The following steps were applied in the case presented and may be considered in similar cases.

XL-NMA Technique

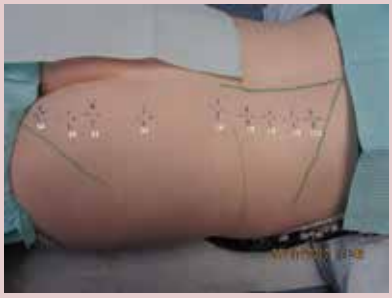

Figure B. Sensory nerve sites subserving painful region.

Figure C. Patient Lt. lateral decubitus - localization of sensory neural points and nerves subserving painful region of greater trochanter (sclerotomal sciatic nerve and L5 nerve root).[22]

Step 1. Subserving Sensory Nerve Identification:[20-21] Clinically determine the principal sensory nerve or neural complex subserving the affected painful area (ie, rt. dorsal cutaneous nerve branches of T11-L5, S1-S4, sciatic nerve, and L5 nerve root (see Figures B-D).

Note that sensory afferent pathways may be variable (eg, the respective innervated dermatome, sclerotome, myotome, or all three). This variation is typical in a chronic pain state.

Figure D. Localization of sensory neural points and nerves subserving painful region, T11-L5.

Step 1a. When several nerves are involved, perform differential nerve blocks separately (test injections of possible nerves with local anesthetic, 1 to 2 mL, 2% plain lidocaine). After 10 min, assess the relief after each neural point injected. The neural point that provided the most relief will be the first target for the cross-linked neural matrix antinociception (XL-NMA). Keep anesthetic volumes low to avoid local anesthetic spread across various nerves. After the most responsive nerves have been identified, wait 3 to 7 days for complete anesthetic washout and then schedule XL-NMA.

Figure E. CL-HA injection, tissue resistance plane, L4.

Step 1b. Identify and mark the target sensory nerve points for the rt. dorsal cutaneous nerve branches of T11-L5, S1-S4, sciatic nerve, and L5 nerve root as shown in Figures B-D. The various target points for the dorsal cutaneous nerve branches of T11-L5, are for the most part, just lateral to the transverse process at the level of the myofascial plane (see Figure E). For the S1-S4 targets, these are located at the level of the posterior sacral foramina's myofascial plane S1-S4 and the affected anatomical region of the sciatic nerve and L5 nerve root sclerotomal innervation are also found at the level of the myofascial plane, lateral aspect of the greater trochanter, where usually three distinct sites can be identified.

For all nerves, with the exception of S3 and S4 (S4 sacral nerve is variable, and not present in all patients, hence, for completeness, it is treated routinely), aim perpendicularly and inject just above the myofascial plane. For the S3 and S4 nerves, enter and aim the needle at a 30° angle laterally from the perpendicular. The S5 sacral nerve was not treated in this case. However, it may be a valid target in other cases as it is a component of the coccygeal plexus, which also includes a branch from S4, and the coccygeal nerve, forming the anococcygeal nerve and thereby providing sensory innervation to the skin in the coccygeal region.

Figure F. Skin wheal preparation.

Step 2. Skin Wheal Preparation
Cleanse the target treatment area with alcohol, and raise a skin wheal with a mixture of 0.5 mL 2% plain lidocaine and 1 mL plain bupivacaine using a 30-gauge, ½-inch needle (see Figure F).

Injection of Cross-Linked Hyaluronic Acid

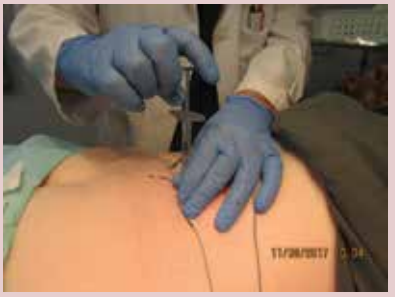

Figure G. CL-HA injection, 0.15 cc, L5.

Step 3a. For the dorsal cutaneous nerve branches of T11-L5, slowly insert a 1½-inch, 25G hypodermic needle perpendicularly through the skin wheal until it encounters tissue resistance. At that point, with the opposite hand, fix the hub of the needle to lock its position in place (see Figure G), and then slowly introduce 0.15 cc of the injectate at each site.

Step 3b: For the S1-S2, slowly insert a 1½-inch, 25G hypodermic needle perpendicularly through the skin wheal until its first encounters tissue resistance (take caution not to perforate the sacral foramen and enter the sacral hiatus portion of the spinal canal). As above, fix the hub of the needle with the opposite hand to lock its position in place (see Figure G), and then slowly introduce 0.15 cc of the injectate at each site.

Figure H. CL-HA injection, 30-degree approach angle, S4

Step 3c: For the S3-S4, due to the normal convexity of the lower sacrum, slowly insert a 2-inch, 21G hypodermic needle at a 30° angle laterally from the perpendicular, through the skin wheal until it first encounters tissue resistance (take caution not to perforate the sacral foramen and enter the sacral portion of the spinal canal) (see Figure H). Fix the hub of the needle with the opposite hand to lock its position in place, and then slowly introduce 0.2 cc of the injectate at each site.

Figure I. Cl-HA injection, 0.15 cc, greater trochanter (sciatic nerve and L5 sclerotome).

Step 3d: For the regional and sclerotomal innervation of the greater trochanter (sciatic nerve and L5 nerve root), slowly insert a 1½ inch, 25G hypodermic needle perpendicularly through the skin wheal until its first encounters tissue resistance. Fix the hub of the needle with the opposite hand to lock its position, and then slowly introduce 0.15 cc of the injectate at each site (see Figure I).

Compression and Extension of CL-HA

Figure J. Compression and extension of the viscous CL-HA infero-laterally.

Step 4. The CL-HA is notably viscous. To increase its extension and coverage along the long axis of the target nerve, firmly compress the injectate infero-laterally using an applicator and/or the operator's digit (see Figure J). Dress the wounds with sterile adhesive bandages (see Figure K).

Figure K. Sterile dressings.

Post-Procedure Assessment & Follow-Up

Step 5. Assess the degree of pain relief/score at 20 min. There may be no change to a drop of 2 to 3 points. At 72 hours, maximal relief usually develops. Note that some patients may struggle in using the concept of pain scores; in this case, the patient was asked for a simple overall percent improvement in relief of pain.

Step 6. The need for additional treatment may be determined by contacting the patient at 72 hours and 1 week. A visual analog scale pain score of 0 to 4 out of 10 is to be expected, with a duration from 8 weeks to 6 months. These results may continue to improve after repeated CL-HA injections. In some cases, depending on the underlying pathology, there may be permanent relief of neuropathic pain.

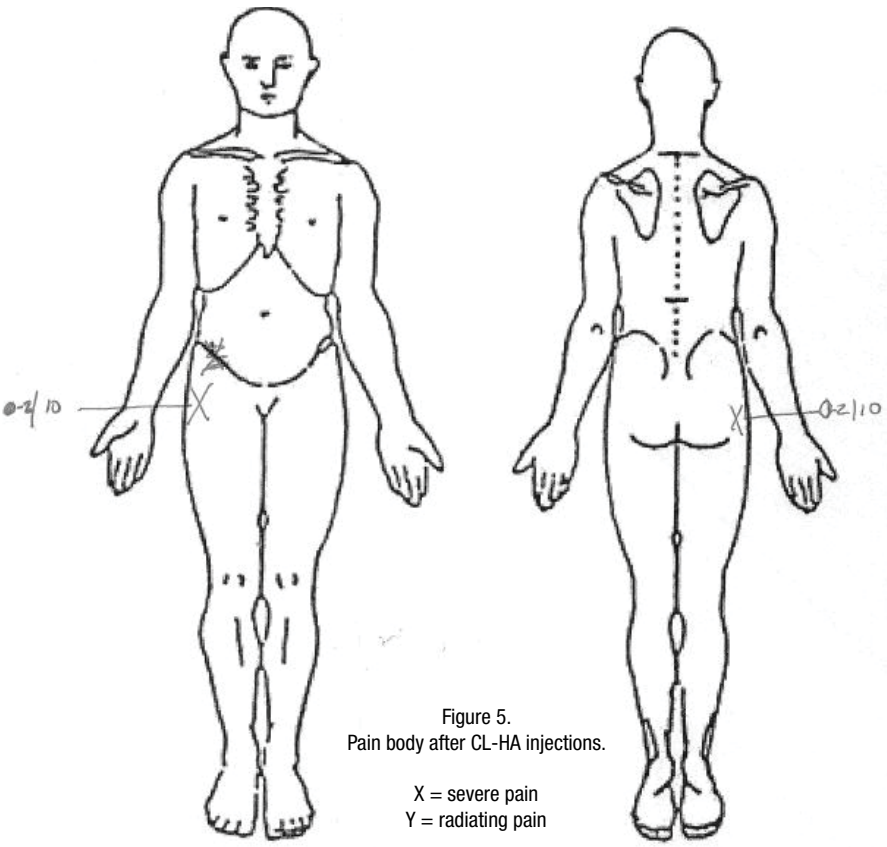

Figure 5.
Pain body after CL-HA injections.

X = severe pain
Y = radiating pain

Discussion & Recommendations

While the patient's outcome using cross-linked hyaluronic acid injections was successful, additional research is necessary to elucidate the mechanism of action of this complex substance, as well as to develop additional techniques for its use in neuropathic pain. In this case, the right anterior pelvic pain was essentially unaffected. Methods such as an intercostal T10-12, transforaminal L1, L2, lumbar sympathetic or celiac XL-NMA may be found to remedy this shortcoming.

Mechanism of Action Summary

Purported mechanisms of action are complex and no doubt, multifactorial.[13] Nonetheless, it is possible that the antinociceptive effect may occur in a step-wise fashion over time (ie, immediately or in first 10 minutes after injection) and that the CL-HA acts as a physical shield, thereby forming a protectcive compartment and blunting spontaneous activity of C fiber and Remak bundle afferency, including aberrant nociceptive ephapse.[14] In addition, contemporaneous depolarization of the action potential due to its polyanionic nature and size of its negative charge

Patient Commentary

"I was officially diagnosed with severe endometriosis when I was 26 years old. Although, I am very certain it started years before when I was in my teens. My periods where always very heavy flow and extremely painful—painful enough that I would always need a day or two off from school or work. I started taking birth control pills when I was 18 and that seemed to suppress the progression of the disease or at least the symptoms. After I had my first child, when my cycle resumed, the pain returned. My doctor did ultrasounds, MRIs, and x-rays trying to find the cause. She decided to do an exploratory laparoscopy and that's when they discovered I had severe endometriosis.

Over the next 15 years, I had five more abdominal surgeries. My right ovary was removed, my uterus, my appendix, along with both of my tubes and my cervix because they were covered with the disease. The endometriosis continued to spread and do damage to many nerves in my pelvic area. The nerve damage caused severe pain in my right hip, low back, and my pelvic area.

The pain gradually got worse, increasing from a few days a month to everyday. I was put on countless medications. From pain meds to hormones, birth control pills, IUD and the worst was a medication that shut down my ovaries and put me into medical menopause. I used OTC pain relievers until my stomach couldn't handle them anymore, as well as ice, heat, and local lidocaine to no avail. Another pain management doctor gave me more medications to try as well as nerve ablation—none of which helped.

The pain was so intense that, most days, I was forced to stay home. I was unable to take care of my home or my children. I was also unable to have sex because it was too painful. When more surgery was no longer an option I began seeking someone to help me deal with the pain. At this point in my life my life quality was terrible. A friend recommended Dr. Campa [the author]. I saw him and he started a treatment plan with the injections. He gave me injections in my right hip, low back and my pelvic area.

Very early in the treatments I began to feel improvement. The injections would bring my pain scores from a 9 or 10 down to a 2 or 3. The only drawback was that it was short relief. While they were working I was able to start participating in my family life again. I would get the injections once a week. The first three and four days were great but over the next day or two the pain would return. Although while they were working, I could be active and have intercourse that wasn't painful. The only drawback was that the relief was so temporary.

When Dr. Campa started giving me the cross-linked injections the onset of pain relief was within 24 hours or so. The great thing about them was that they lasted for months not days! Comparing the two different injections, the cross-linked injections brought my pain scores of 9 or 10 to a 1 or 2. Only getting injections

(a function of its massive molecular size, 500 million daltons to 100 GDa), blocking any transduction of signal, may occur. Its long-term effect may be due to low/high molecular weight mismatch correction resulting in TNFα-stimulated gene 6 protein modulation of the subclinical, regional inflammatory response. Dysregulation at the level of the extracellular neural matrix is stabilized, promoting a restoration of the normal immunoneural cross-talk, thereby negating what is believed to be the root cause for the development of chronic pain.[15-18]

Furthermore, any injury or insult to the nervous system may cause deafferentation pain (defined as "severe spontaneous pain in body parts distal to the injury despite reduced or no sensitivity to external noxious stimuli to that body part (hypoalgesia or analgesia)"[19] as it represents a loss of information from the periphery to the brain. In the case presented, the nerve roots and spinal cord segments of the painful regions in question likely suffered deafferentation and neuropathic pain as a result of injury caused by the endometrial implants. It is this initial injury that likely initiated the cytokine cascade's proinflammatory, pronociceptive state. For a complete discussion of these mechanisms of action in this regard, see the author's previous report.[13]

Overall, this case provides a detailed look at the use and technique of targeted neural matrix antinociception injection of cross-linked hyaluronic acid in the successful treatment of chronic endometriosis pain of the thoraco-lumbar, sacral, and right greater trochanteric region that occurred in a 41-year woman who had previously undergone multiple endometriosis pain related surgeries with no change. The technique presented has resulted in the patient's enduring pain relief, and proved to be a safe and effective method in this patient. Its routine use should be considered early to manage pain in similar cases.

every 6 months or so compared to weekly has been so much easier and the time I saved I am able to devote to my family. The long-term pain relief has been an absolute blessing.

Before the cross-link injections, oxycodone and hydromorphone would help minimally with all the nerve pain and abdominal pain from the scar tissue and adhesions. The oral pain medication barely took the edge off of all the pain and I spent most of my time in bed or on the couch unable to move. The cross-link injections brought down my pain levels in my right hip, low back and pelvic area nerves enough that the oral pain medication made the scar tissue and adhesion pain more manageable. I continue to take oxycodone and hydromorphone to help with the severe pain that isn't nerve related. The scar tissue and adhesion pain is a pulling pain across my whole pelvic region, but the most intense pain originates from the lower right pelvic region. This pain is controlled with opioids, which lowers the pain score from a 9 or 10/ out of 10 to about a 6 out of 10.

In the areas treated with the cross link injections the pain is a least 90% better. The other areas seemed to improve some but it's hard for me to tell if they actually improved or if they are easier to manage since the other pain is so much better."

–Commentary provided by author with patient permission.

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