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Adhesive Arachnoiditis

A CLINICAL UPDATE

A first-generation diagnostic and treatment guide for managing this inflammatory, painful condition of the lower spinal canal.

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Adhesive arachnoiditis (AA) is an inflammatory disease that occurs inside the lumbar and sacral regions of the spinal canal.[1-6] Simply put, arachnoiditis means inflammation of the arachnoid layer of the meninges. It may occur in other areas of the central nervous system (CNS) but, as used in this report, only refers to arachnoid inflammation in the lumbar-sacral area.

The disease inflames nerve roots of the cauda equina and the arachnoid-dural covering (meninges) of the spinal canal. This inflammation produces adhesions that merge or "glue" these two separate anatomic structures together into an inflammatory-adhesive mass inside the spinal canal. Multiple mass areas can form, and one or more of these areas can enlarge, entrap nerve roots, and block normal spinal fluid flow. Unless this inflammation is controlled and suppressed, it causes dysfunction and death to the entrapped nerve roots which results in intractable pain, multiple neurologic impairments, and autoimmune manifestations. Progressive enlargement of the mass or masses may occur in a manner analogous to the growth of a cancerous tumor. AA requires aggressive anti-inflammatory treatment and pain control.

Adhesive Arachnoiditis Is No Longer a Rare Disease

In the past, AA has been considered a rare disease, but this is no longer the case. An analysis of multiple, publicly available, scientific epidemiologic surveys of people with back pain suggests that 1.75 million to 7 million adult Americans presumably may have AA.[7-13] Regardless of the precise number, it is now clear that AA is found in every community and medical practice in the modern world. Consequently, it has become incumbent on every primary care and pain practitioner to be able to identify persons with AA and participate actively in the care of these individuals.

Since AA has become one, if not the most, common reason people develop severe intractable pain of the back and spine, the authors have established a research and education project to study AA and develop first-generation diagnostic and treatment guides for medical practitioners. Our latest observations

Table I: Clinical Profile of 80 MRI-Documented Cases of Adhesive Arachnoiditis.

Demographic Factor	Number (Percent)
Females	65 (81%)
Males	15 (19%)
Age range in years	18 to 80
Mean age ± S.D. in years	48.9 ± 13.7
Predisposing spinal conditions*	61 (76.3%)
Herniated discs	44 (55%)
Spondylolisthesis	17 (21.25%)
Osteoporosis	6 (7.5%)
Spine arthritis	23 (28.75%)
Scoliosis	9 (11.25%)
Tarlov cysts	9 (11.25%)
Prior surgeries or injections	
One or more spinal surgeries	43 (53.8%)
Total No. of spine surgeries in 43 cases	91
Range of surgeries in 43 cases	1 to 8
No. who had 2 or more spine surgeries	22 (27.5%)
No. who had 1 or more epidural injections	69 (86.3%)
Total No. epidural injections in 69 cases	236
Range of epidural injections in 69 cases	1 to 20
No. reported over 8 epidural injections	16 (20.0%)
Symptoms/complications reported by over 55% of cases	
Pain relief on standing	70 (87.5%)
Standing too long causes need to lie down	69 (86.3%)
Hurts to lie flat on back	67 (83.8%)
Pain always present	66 (82.5%)
Shooting pains, tremors, or jerking in legs	64 (80%)
Burning pains in feet	63 (78.8%)
Cold hands or feet	58 (72.5%)
Crawling of insects on skin	58 (72.5%)
Water dripping/running down legs	53 (66.3%)
Difficulties starting urination/defecation	51 (63.8%)
Leg raise hurts back	50 (62.5%)
Blurred vision	47 (58.8%)
Pain behind eyes	45 (56.3%)

***Some cases reported more than one condition. Based on authors' clinical experience.**

and recommendations are presented in this report. To date, we have analyzed medical information from more than 300 cases confirmed by magnetic resonance imaging (MRI), and observed treatment results in more than 200 cases. This report summarizes our observations and findings to date.

Today's Causes of AA

In the 19th century, adhesive arachnoiditis was known as a dread disease, causing unbearable suffering and early death. The initiating causes at that time were usually tuberculosis or syphilis, which had invaded the arachnoid-dura meninges covering. In the 20th century, the most common reported cause was the use of insoluble irritating oil-based dyes called myelograms that were directly injected into the spinal fluid to enhance x-ray visualization of the spine.

Today, the major cause lies with spine disorders that alter the natural anatomic structure and posture of the spinal column. Protrusion of lumbar and sacral intervertebral discs into the spinal canal are the most common culprits, as they cause narrowing (stenosis) of the canal along with compression and displacement of the free-floating nerve roots of the cauda equina. Stenosis of the spinal canal, combined with nerve root compression, eventually cause irritation, friction, and inflammation that leads to adhesion formation.

Other spine disorders prevalent among adults in modern society include scoliosis, spondylolisthesis, osteoporosis, and arthritis. Each of these disorders has the potential to cause the cauda equina nerve roots to undergo the compression and inflammatory process that leads to AA. These conditions appear to be related to sedentary lifestyle, inactivity, obesity, and longer lifespan.[14,15]

Next to spinal conditions, our experience has been that genetic connective tissue/collagen disorders of the Ehlers-Danlos syndrome (EDS) type are the most common conditions that can lead to AA. Trauma, autoimmune disorders, Lyme disease, and possibly viral, fungal, and bacterial infections make up an estimated 10% to 15% of cases.[16,17] Although surgery and epidural corticoid injections are often cited as the cause of AA, they are actually co-factors, as the person who receives surgery and/or epidural injections has some underlying spinal disorder that medically indicates the need for surgery or an epidural corticoid injection. Further, clinical data collected by the authors suggests that spine surgeries and epidural injections done on some individual patients may be excessive and even causative of adhesive arachnoiditis.[11,18]

The AA Clinical Profile

To the authors' knowledge, no clinical data on AA has been published in recent years.[18,19] As a component of our research and education project, we compiled a basic clinical profile from 80 cases of MRI-confirmed AA (see Table I). These patients sent us their MRIs with a clinical history to develop a profile, which is described and summarized in Table I. Fe-

Table II. Complications of Adhesive Arachnoiditis.

- Neurologic impairments (paralysis, urinary, bowel, sexual dysfunction)
- Spinal fluid flow obstruction (headache, blurred vision, tinnitus)
- Spinal fluid seepage (back pain, paraspinal tissue contractures, tissue atrophy)
- Autoimmunity (myalgias, arthralgias, mast cell activation)
- Anatomic derangements (leaning, splinting, aberrant posture, arthritic)
- Intractable pain syndrome (hormone deficiencies, hypertension, insomnia, fatigue)
- Shortened life span (cardiac arrest, adrenal failure, cachexia sepsis)

Based on authors' clinical experience.

males outnumbered males, and the age of these patients was generally in the older ranges. Sixty-one (76.3%) of the cases had one or more spinal conditions as a predisposing cause. Over half (53.8%) had one or more spinal surgeries, and 69 (86.3%) had undergone one or more epidural injections.

The majority (over 55%) reported symptoms of burning feet, tremors or jerks, the sensation of crawling insects and/or water dripping, difficulty starting urination or defecation and blurred vision. This symptom profile is important in identifying AA in patients who report back pain. Sixty-six (82.5%) among the 80 cases in the clinical profile reported here indicated their pain was always constant.

Complications of AA

Adhesive arachnoiditis can have serious complications that are briefly described below (see Table II).

Neurologic Impairments

The most common site for nerve root inflammation and destruction seems to be around the lumbar-sacral junction (eg, L5-S1). Nerve roots that transverse this area connect directly to the lower extremities, bladder, bowel, and sex organs. The lower extremities may suffer a variety of neurologic leg, ankle, or foot impairments including weakness and immobility ("foot-drop"). In severe cases outright paraparesis or paralysis may occur requiring the person with the disease to use a walker, cane, or wheelchair. Bladder impairment is almost uniform. Impairments include hesitancy, urgency, over-flow incontinence, leaking, and even the necessity of self-catheterization. Paresthesias of the lower trunk and extremities are common and include the feelings of insects crawling or water dripping on the skin.

Table I lists some of the most common symptoms derived from 80 patients with confirmed AA.

Spinal Fluid Flow Obstruction

Unfortunately, the inflammatory-adhesion process causes the nerve roots to clump and a tumor or mass to form when the clump attaches to the arachnoid-dura covering. This inflammatory-adhesive mass acts like a cancerous tumor. It may grow, expand, and capture more and more nerve roots. The net result is more pain and neurologic dysfunction. Inflammatory-adhesive masses most often occur near the lumbar-sacral spine junction (L5-S1), which is the joint that must endure the most pressure when we sit. Therefore, persons with AA often cannot sit very long without causing themselves great pain as they are compressing the inflammatory-adhesive mass that is inside the spinal canal.

There may be multiple small masses inside the spinal canal caused by the inflammatory-adhesive process of AA. They act like boulders or a dam in a stream or river. Spinal fluid constantly flows inside the spinal canal to bring nutrients, lubricate the spinal cord and nerve roots, and carry away any toxins, including inflammation waste products and dead cellular material.[20,21] These intraspinal masses may interfere with spinal fluid flow, causing such symptoms as headache, blurred vision, dysphoria (opposite of euphoria), and ringing in the ears or tinnitus.

Spinal Fluid "Seepage"

As noted, the term arachnoiditis simply means inflammation of the arachnoid layer of the meninges or spinal canal covering. When inflamed, nerve roots become attached to the arachnoid-dural covering of the lower spinal canal; inflammation involves not only the inner arachnoid layer but also the outer dural layer. Just like leakage from a rusty pipe, spinal fluid may chronically seep out of the dural layer into the soft tissues that surround the spinal column. When this occurs, lower back pain develops. Paraspinal tissues may become inflamed and contract since spinal fluid is a toxic irritant to tissues outside the spinal canal. Considerable anatomic and tissue alterations may occur (see Figures 1-3).

Autoimmune Sequelae

Moderate through severe stages of AA may cause autoimmune sequelae.[22-24] There may include arthralgia, myalgia, carpal tunnel syndrome, and thyroiditis among autoimmune manifestations that have been observed with other diseases. The aegis of autoimmunity in AA is likely related to inflammatory waste and/or spinal fluid that reaches either the general vascular circulation or tissues outside the spinal canal. Inflammatory waste can reach the general circulation by being transported from the lower spinal canal up into the brain and neck where the glymphatic and lymphatic systems empty waste into the general circulation.

AA may cause erosion of the spinal canal covering (arachnoid and dural layers) and allow chronic seepage of spinal fluid into the paraspinal soft tissue producing an inflammatory response. This can ignite an autoimmune reaction.

Anatomic Derangement

AA plus any underlying spine abnormality causes profound anatomic derangement of paraspinal muscles and soft tissue. The derangement is due to anatomic spine abnormalities plus chronic bending and leaning to minimize pain. The result is abnormal posture with excess stress and pressure on joints including facet and sacroiliac joints. If spinal fluid seepage has chronically occurred, paraspinal tissue may construct toward further anatomic derangement (see Figures 1-3) These complications may require soft tissue and intra-articular measures such as corticoid injections, topical lidocaine, homeopathy, electric current (TENS) or electromagnetic therapy. Physical stretching of the upper back, shoulder girdle, and hips is essential to counter the anatomic derangement found in AA patients.

Intractable Pain Syndrome (IPS)

IPS is defined here as a disorder that produces constant (24/7) pain, insomnia, and anorexia and has measurable, adverse impacts on the endocrine and cardiovascular systems. IPS raises blood pressure and pulse rate, alters glucose metabolism, and overstresses the pituitary-adrenal-gonadal axis to produce multiple hormonal deficiencies. In the authors' experience, IPS can result from the activation of glial cells and the formation of neuroinflammation within the CNS (ie, centralization or sensitization).

Diagnosing Adhesive Arachnoiditis

A preliminary diagnosis of AA may be made in a patient who has an inciting event or disorder such as herniated discs, trauma, or EDS, and who has the typical symptom profile. The authors recommend that all patients presenting with typical AA symptoms be screened for EDS (see Table I). Although non-specific, persons with AA tend to have some physical, neurologic abnormalities of the lower extremities; examination of the back will almost always show asymmetry, leaning, possible contractures, or skin indentation (see Figures 1-4).

There is no specific blood test. Inflammatory markers of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and various cytokines may be elevated.[25] Hormonal deficiencies of cortisol, pregnenolone, dehydroepiandrosterone (DHEA), and testosterone may be present.[26]

A contrast MRI of the lumbar-sacral spinal canal is required for a confirmatory diagnosis providing the history, symptoms, and physical examination are also compatible (see Table I). Contrast techniques (injected dye or high-resolution MRI) differentiate cauda equina nerve roots and spinal fluid so the typical appearance of AA can be visualized.[18,27,28]

Table III. Suggested Categories of AA Severity.

Mild
- Full range of motion
- No back indentation or contracture
- Normal inflammatory markers
- No bladder impairment
- No MRI evidence of spinal fluid leakage or obstruction
- No hormone abnormalities
- Can sit and stand in one position for 10 minutes

Moderate
- Full range of motion and walking without assistance
- Mild to zero lower extremity weakness
- Normal inflammatory markers
- Some bladder hesitancy, urgency, dripping
- No MRI or physical evidence of spinal fluid leakage
- Mild constant pain but no need for sleep medication
- Can sit and stand in one position for 10 minutes

Severe
- Some range of motion impairment and needs assistance (cane or other) to ambulate
- Weakness in lower extremities with neurologic symptoms (eg, burning feet, bugs crawling, jerking or other)
- Elevated inflammatory markers and/or hormone abnormalities
- Bladder impairment symptoms (eg, hesitancy, urgency, or incontinence)
- MRI and/or physical evidence of chronic spinal fluid leakage and/or flow obstruction
- Constant pain that impairs sleep
- Cannot sit and stand in one position for 10 minutes

Catastrophic
- Requires assistance with activities of daily living (eg, dressing, toileting, eating)
- Significant lower extremity impairment (needs walker, wheelchair, braces)
- Bladder impairment of hesitancy, urgency, incontinence
- Mental deficiencies such as memory loss, reading ability
- MRI and physical evidence of chronic spinal fluid obstruction and leakage
- Elevated inflammatory markers and hormone abnormalities
- Constant pain that impairs sleep
- Unable sit or stand in one position for 10 minutes

Based on authors' clinical experience.

Categorization of Severity

Like all diseases, AA has degrees of severity. The authors recommend a four-level categorization that is based on clini-

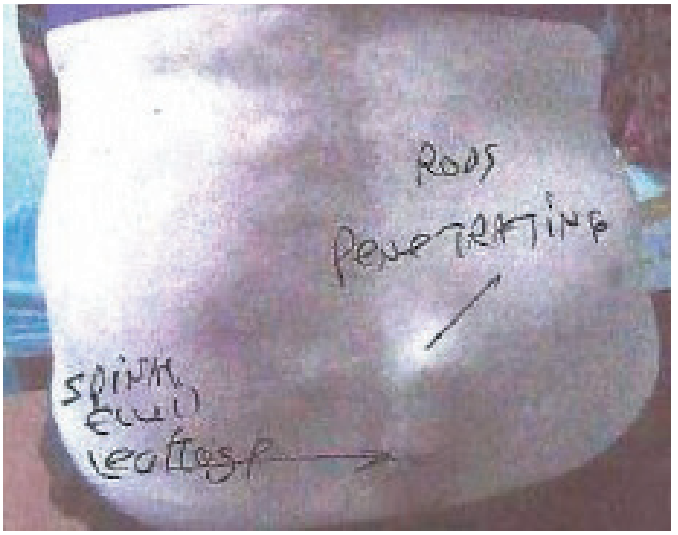

Figure 1. Spinal fluid leakage and rods penetrating in AA patient

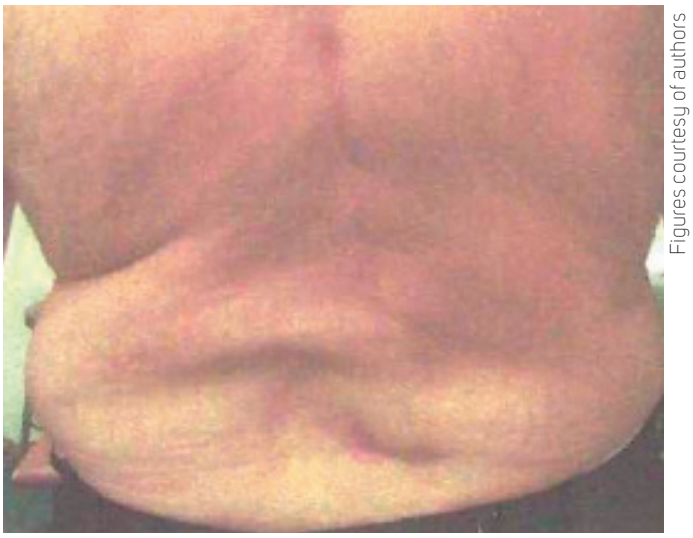

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Figure 2. Multiple spine surgeries in AA patient. Note the areas of tissue atrophy and crease of left side.

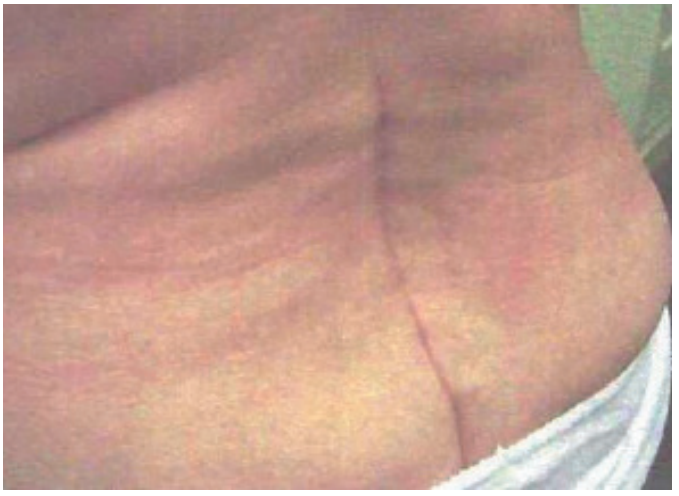

Figure 3. Mid-line indentation and skin contractures in an AA patient.

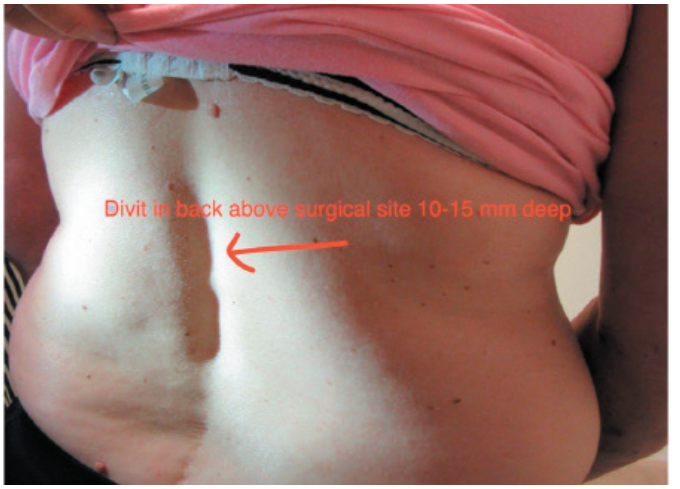

Figure 4. Mid-line indentation in an AA patient.

cal assessment as MRI findings are not specific enough to determine clinical severity. Our recommended classification is mild, moderate, severe, and catastrophic (see Table III). Those persons in the severe and catastrophic levels appear to have sustained permanent and irreversible neurologic damage. Consequently, they will likely not respond to anti-neuroinflammatory or neuroregenerative therapies. These individuals will usually require palliative pain care.

Those persons with AA who are in the mild or moderate categories have appeared to have good response to anti-neuroinflammatory and neuroregenerative treatment in our clinical experience. This reasonable assumption is based on the fact that these individuals do not have total irreversible neurologic damage, as do those persons in the severe and catastrophic categories. As with other diseases, the earlier the case is diagnosed and treated, the better the outcome (see Table III).

Treatment Approaches

Treatment for adhesive arachnoiditis should consist of both physical and pharmacologic measures. Highly recommended physical measures include daily walks and stretching to full extension the upper and lower extremities and paraspinal muscles. The primary purpose of these measures is to prevent paralysis and contractions of paraspinal musculature.

Other recommended physical measures based on anecdotal evidence include water soaking, deep breathing, rocking in a rocking chair, or mini-trampoline walking. Although no scientific evidence is available to support these measures, they may enhance spinal fluid flow leading to improved CNS nutrition and cleansing of inflammatory waste.

While several agents have some scientific research to suggest they suppress neuroinflammation, the authors currently

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recommend the following three agents as starting treatment for all patients diagnosed with adhesive arachnoiditis (all are potent neuroinflammation suppressors and provide direct analgesic action):

- naltrexone
- ketorolac[29-33]
- corticosteroid (methylprednisolone or dexamethasone).[34-38]

Pharmacologic treatment is primarily directed at control of the neuroinflammation actions of AA. In patients who are not on opioids, naltrexone is our primary drug preference as it has analgesic, as well as anti-inflammatory and autoimmune suppression properties. The starting dosage is 0.5 mg to 1.0 mg given twice a day. This dosage can be raised over 4 to 6 weeks to as high as 7.0 mg given twice a day.

At this point in our research, we regret we must highly recommend ketorolac and one of these corticosteroids – methylprednisolone or dexamethasone – as adjuncts to naltrexone or daily opioids if they are the patient's primary pain treatment. Although a number of agents, including diclofenac, metformin, indomethacin, acetazolamide, and prednisone, have some anti-neuroinflammatory properties, we have not found them to be consistently effective simply because they are not as potent as either ketorolac or methylprednisolone/dexamethasone.[29]

Also for agents to be effective in AA treatment, they must cross the blood-brain barrier, enter spinal fluid, and act on receptors in lower spinal canal tissue.[30-38]

The authors recognize the complications that ketorolac and the two potent corticosteroids can cause, so we recommend these agents be used intermittently at a low dose. Examples of recommended use are: 1 to 2 times a month, OR, 1 to 3 times a week avoiding two days in a row. Ketorolac must be used with great caution if used in persons over age 70, orally, or in persons with renal compromise. Preferred route of administration is intramuscular (IM) injection. Regular monitoring for GI bleeding or renal toxicity is recommended. Potential complications of AA, including a shortened lifespan, outweigh the risk of low dose, intermittent use of ketorolac, methylprednisolone, or dexamethasone.

In addition to the above-noted physical and pharmacologic therapies, the authors recommend a high protein, low carbohydrate, high content fruit/vegetable diet. Useful dietary supplements in our experience have been curcumin, pregnenolone, and B12. Pain control may have to be very aggressive and potent, especially in people with AA who fall into the severe and catastrophic categories. These individuals have usually had little anti-neuroinflammatory treatment and suffer severe intractable pain with many of the complications noted above. High-dose, opioid therapy, implanted electrical stimulators, and intrathecal opioid administration may be necessary (Table IV). It is also important to point out that AA patients in the severe and catastrophic categories may be too impaired to participate in physical measures or take pharmacologic agents recommended here.

New Therapeutic Approaches

Since adhesive arachnoiditis is now being recognized in every community, new therapeutic measures are being attempted. Our clinical experience as well as reports received by us indicate potential with two new approaches. The first is an anabolic or neuroregenerative effort with the neurosteroids human chorionic gonadotropin (HCG) and nandrolone. Second, intravenous infusions of ketamine, lidocaine, vitamin C, and nicotinamide adenine dinucleotide (NAD) have all been reported to us to give some patients relief for up to 3 months after a single infusion.

Various stem cell measures are now being examined as well. At the time of this writing, however, we have no specific recommendation on their use. Our major caution with the new approaches is that they are sometimes promoted as a substitute for daily physical measures, anti-neuroinflammatory treatment, and effective pain control. Also, some persons with long-standing AA who never had the benefit of specific treatment may not benefit from treatment other than palliative care.

Potential Complications

Pain in the Paraspinal Tissues

The soft tissues that surround the spinal column including muscle, fat, connective tissue, and large nerves that exit the spinal column may become inflamed and painful in patients

Table IV. Starting Treatment Regimen*

Pharmacological
- Low dose naltrexone 0.5 mg to 7.0 mg twice a day*
- Ketorolac (injection or troche) 15 mg to 60 mg on 1 to 3 days a week or bi-monthly
- Corticosteroid: methylprednisolone 2.0 mg to 4.0 mg or dexamethasone .5 mg to .75 mg 1 to 3 days a week or bi-monthly

Dietary measures/supplements
- Curcumin 900 mg to 1800 mg a day
- Pregnenolone 200 mg to250 mg a day
- Diet: high protein, low carbohydrate, high vegetable-fruit

Physical measures to be done daily
- Walk with arm swings
- Full length stretching of arms, legs and feet
- Water soaking: tub, shower, jacuzzi, pool
- Side-to-side leaning and stretching

Pain control
- Standard treatment with analgesic, neuropathic, and adrenergic/stimulant agents

*Naltrexone should not be prescribed to pattients who take opioids. Substitutes include diclofenac, indomethacin, acetazolamide, or metformin.

with AA. Potential reasons are:
- anatomic and postural abnormalities caused by an underlying spinal disorder
- neurologic impairments
- chronic seepage of spinal fluid.

Any number of therapies that reduce inflammation and pain in soft tissues may provide some relief and recovery. Daily extension stretching of lower back muscles and arms and legs may be essential to prevent contractures. Topical agents, including lidocaine and diclofenac, may be helpful as well.

Local corticosteroid (non-epidural) injections may be necessary for localized, painful areas. A favored treatment of ours is pulsed electromagnetic energy administration (radio wave, laser, infra-red) to not only help heal inflamed soft tissues, but, hopefully, the electromagnetic energy waves will penetrate deep enough to help heal the spinal canal covering (arachnoid-dura) and stop spinal fluid seepage. Individual AA patients have reported that massage, TENS, homeopathy, and other soft tissue therapies are helpful.

Post-Injection Emergency Treatment

An unfortunate, small number of people develop AA following a spinal tap or epidural injection, based on our collected data. It is therefore critical that simple, emergency treatment be done if symptoms of AA develop within 60 days after the injection. These symptoms may include increased back pain, dizziness or vertigo, leg weakness, burning skin, and urinary hesitancy, frequency, or incontinence. It is essential to administer emergency treatment based strictly on symptoms, because signs of AA may not show on an MRI for up to 6 months after the injection.

The emergency treatment we recommend is simple and has not proved to cause any lasting complications:
- 6-day methylprednisolone dose pack
- ketorolac, 30 mg to 60 mg for 3 consecutive days
- medroxyprogesterone 10 mg twice a day for 5 days

Little is known about the optimal, post-injection treatment for symptoms of AA. We have used the above off-label protocol on 11 cases.

In the authors' experience, the emergency treatment recommended here has always stopped further progression into full-blown AA but some symptoms have remained in all 11 cases, and they have included mild to moderate, intermittent back pain and paresthesia in the legs. Intravenous use of methylprednisolone or dexamethasone can be a useful adjunct to this protocol. Following emergency treatment, naltrexone and the other measures described will need to be started and continued for at least a few weeks.

Summary

Adhesive arachnoiditis can no longer be considered a rare disease as it is emerging in every community. Major causes of AA cases today include degenerative spine disorders that anatomically compress cauda equina nerve roots and initiate a process of friction, inflammation, and adhesion formation. Genetic connective tissue/collagen disorders of the Ehlers-Danlos class appear to be the second most common cause based on the authors' collected case data.

AA should be suspected in a patient with back pain who complains of leg weakness, urinary symptoms, blurred vision, sensations of water or insects on their skin, and relief of pain on change of position such as standing or reclining from a sitting position. Elevated inflammatory markers may be present in serum; MRIs should be used to confirm diagnosis.

Because AA is a progressive, inflammatory disease of the spinal canal with the potential for severe neurologic impairments leading to an inability to care for oneself, immense pain, and early death, treatment must be aggressive and primarily directed at controlling intraspinal inflammation. The first drug preference is naltrexone in patients who do not take daily opioids, as naltrexone has analgesic, anti-inflammatory, and autoimmune suppression properties. The authors do recommend that naltrexone be accompanied by low intermittent dosages of ketorolac and one of these two corticosteroids: methylprednisolone or dexamethasone. This

aggressive approach to the intraspinal, inflammation-adhesion process is the basis of AA treatment.

Patients with AA may have intense, intractable pain that requires the most aggressive and potent pain control measures, which may include opioid medication for those who have already failed other treatments. In addition to control of intraspinal inflammation and pain control, several approaches are being attempted to regenerate tissue and provide some permanent relief and recovery. •

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