Chiropractic Management of Ehlers-Danlos Syndrome: A Case Report

By Joseph J. Morley, DC, PhD;* and Terence Parrault, DC, DACBR*

Address all correspondence to:
Terence Perrault, DC, DACBR
Associate Professor of Clinical Sciences
University of Bridgeport College of Chiropractic
75 Linden Avenue
Bridgeport, CT 06604
Tel: (203)-576-4281
E-mail: terence@bridgeport.edu

* Associate Professor of Clinical Sciences, University of Bridgeport College of Chiropractic

ABSTRACT

Objective: To structure chiropractic care for the symptomatic relief of musculoskeletal symptoms in a patient with Ehlers-Danlos Syndrome (EDS).

Clinical Features: A patient with EDS presented with chronic dorsal, neck, and low-back pain. She also had joint hypermobility, skin hyperelasticity and spontaneous glenohumeral dislocations.

Intervention: Treatment included soft-tissue work and chiropractic manipulation. Treatment lasted for 7 months.

Outcome: The patient reported a noticeable reduction in neck, dorsal, and low-back pain during treatment.

Conclusion: Chiropractic care helped relieve some of the more common musculoskeletal symptoms in this patient and may prove of value in other EDS patients. Doctors of chiropractic who are aware of EDS and its associated symptoms may be able to offer significant relief in selected EDS cases. A large-scale trial of chiropractic management of EDS needs to be done to demonstrate efficacy or lack thereof.

Key Indexing Terms: Ehlers-Danlos Syndrome; musculoskeletal pain; chiropractic

INTRODUCTION

Ehlers-Danlos Syndrome (EDS) is an inherited disorder of connective tissue characterized by heterogeneity and variance in clinical symptoms.1 Mao2 identifies 3 mechanisms by which the disease can occur:

- deficiencies of enzymes that produce collagen
- mutation of collagen alpha chains

Enzyme deficiencies or mutations affecting different collagens involved in EDS will become
manifest in tissues in which that particular type of collagen predominates functionally, i.e., skin, ligament, vascular tissue, bowel tissue, and oral structures.

- Haplo-insufficiency

This results from a lower level of a gene product and affects the cell’s ability to function normally.

Research has also concentrated on tenascin-X deficiency in connective tissues. This is an extracellular-matrix protein. However, tenascin-X deficiency is not found in a large percentage of EDS patients but seems to be associated more with the hypermobility type of EDS. Malfait suggests that other genetic factors and gender both contribute to EDS. Most of those suffering from the joint hypermobility type of EDS and associated pain were women.

Although joint hypermobility may be the most noticeable symptom, skin hyperelasticity, extensive bruising and scarring, and connective tissue fragility can be common features. Typical examples of skin hyperelasticity and joint hypermobility associated with EDS are seen in Figs. 1 and 2, respectively.

More serious symptoms associated with EDS can include joint dislocations, rupture of blood vessels and hollow viscera, and mitral valve prolapse. Other reported manifestations of EDS can include periodontal problems, psychological problems, epilepsy, cerebral cortical lesions, cephalalgia, and musculoskeletal pain.

Previously, Ehlers-Danlos was divided into 10 types. This was based on single-gene disorders. More recently, the Villefranche classification (Table 1) was developed. The Villefranche classification categorizes Ehlers-Danlos into 6 groups based on the severity of the clinical features, biochemical defects, genetic defects, and inheritance pattern.

The most common form of EDS is autosomal dominant in the older classification, hypermobility type in the newer Villefranche classification. The major diagnostic criteria are joint hypermobility and skin described as soft, smooth, and velvety. Joint hypermobility can lead to dislocation, which Beighton lists as one of the minor diagnostic criteria. Other minor criteria include chronic joint or limb pain and a positive family history. Beighton stated that one or more of the major criteria must be present for a definitive clinical diagnosis. Minor criteria aid in the diagnosis but are not sufficient in themselves.

A major symptom, joint hypermobility, is also shared with Marfan’s Syndrome, Benign Joint Familial Hypermobility Syndrome, and Osteogenesis Imperfecta. The heterogeneity of EDS and the fact that symptoms and severity can overlap with other conditions can lead to difficulty in diagnosis.
CASE REPORT
This case study dealt with the hypermobility type of EDS, which may be the type that is characterized by the most functional musculoskeletal problems.14

A 5’ 4” 120 lb., 20 year old female college student suffering from chronic spinal pain sought evaluation of her condition at a chiropractic clinic.

This patient had been diagnosed with EDS prior to seeking chiropractic care. Her family history included a brother also with EDS. She reported that he had a more severe form than she did, but did not elaborate any further. Past medical history included pyloric stenosis as an infant and an appendectomy 2 years previously.

Her lifestyle and dietary history revealed that she was a non-smoker, consumed very little alcohol, had a regular intake of fruits and vegetables, and ate chicken in preference to red meats. She did not drink coffee and drank at least a quart of water per day. She did not report taking any supplements.

Her major complaints were thoracic and cervical pain that worsened after a car accident 3 years ago. Prior to this accident, she had had periodic discomfort in these areas, but not to the extent now reported. She reported the pain as ranging from 3 to 8 on a 10-point scale. The spinal pain had become worse recently, tending toward 8.

Her secondary complaints included repeated bilateral shoulder dislocations and hip and finger dislocations. Other secondary complaints included:

- difficulty sleeping due to the thoracic and cervical pain
- occasional low-back pain that seemed to worsen with menstruation, but did not worsen after the accident

Previous treatments included:

- 2 months of physiotherapy for thoracic and cervical pain immediately following her car accident
- massage therapy for thoracic and cervical pain
- spontaneous reductions of dislocations or self-reductions of shoulder dislocations
- 2 hours of cardiovascular and weight exercises regularly
- dihydrocodeine for spinal pain
- carbamazepine for epilepsy
- sodium valproate for epilepsy
- phenytoin for epilepsy
- beclometasone for asthma
- salbutamol for asthma
- iron tablets for blood loss anemia

Informed consent was obtained from the patient and a physical examination was performed.

General Findings
Vital signs were within the normal range for a female of her age. The skin was elastic and smooth. A scar was noted at the mid-sternal area and the patient reported that a keloid had been removed years ago. There was hyperextension of both knees, both elbows, over-pronation of the feet, and loss of the normal medial longitudinal arches.

Cervical Exam
Hypolordosis
Head anterior to gravity line
Cervical distraction produced some pain radiating toward her right shoulder but not in her neck. Passive bilateral rotation, lateral flexion,
flexion, and extension were negative. An active trigger point was found in the right upper trapezius.

**Thoracic Exam**
Rotation and lateral flexion were restricted bilaterally from T5-T10. Active trigger points were found in the rhomboid majors, thoracic paravertebral musculature bilaterally, and middle trapezius.

**Lumbo-sacral Exam**
*Hypolordosis*
Right SI motion was restricted. Palpation of right SI joint elicited tenderness.

**Radiological Exam**
A radiological report for lumbar, thoracic and cervical x-rays taken elsewhere stated that there were no fractures or dislocations. A loss of normal cervical lordosis was also reported.

**Diagnoses, Rationale, and Treatment**
Exam and history findings supported a diagnosis of myofascial pain related to specific trigger points in the mid and upper trapezius, rhomboid majors, and thoracic paravertebral muscles. In addition, there was pain associated with fixation of the right SI joint and vertebrogenic pain associated with restriction of movement of T5-T10.

Given the above findings, the connective tissue characteristics associated with EDS, and the non-specific palliative care common for EDS, it was decided to treat this patient symptomatically, utilizing gentle soft-tissue work and gentle vertebral adjusting. She had reported getting relief from dihydrocodeine, a drug used for the treatment of musculoskeletal pain. This indicated that her symptoms could be relieved. If relief could be provided with chiropractic care, the side effects associated with an opioid drug might be avoided.

She was advised to continue with her exercises. Her regular routine included weight lifting for the legs and arms (biceps and triceps curls, knee extensions, squats) and walking and jogging. These exercises are beneficial for maintaining muscle mass, minimizing osteoporosis, and maintaining the cardiovascular system in good health. Advice regarding the importance of Vitamin C for connective tissue was given.

Over a 10-month period, she was seen a total of 20 times. Within a week, after 3 visits, she reported an improvement of overall pain, down from an 8 to a 4. By the end of the second week of treatment (visit 5), she reported that her menstrual period was lighter and shorter than normal. At visit 6, she reported an exacerbation of thoracic pain, a 7 on the pain scale. At visit 7, she reported that she had responded to the last treatment but the thoracic pain had returned after a few days. There had been a spontaneous shoulder dislocation and subsequent neck pain on her right side. By visit 9, she had been under care for almost 2 months. She reported a significant reduction in her neck and back pain from the last visit until the current visit. Her pain was at a 2. She also reported that her menstrual periods were shorter and less painful than normal.

She was a student and did not return for 2 months during the summer break. Her symptoms were at about a 2 or 3 during this period. At the 12th visit, she reported that her cervical area had been quite sore after the last treatment. This is an indication of the necessity to ensure that soft-tissue work and manipulations are not done too vigorously.

By the 14th visit, her symptoms were once again reduced to a 3. Symptomatically, she remained at a 2 or 3 for the remainder of her visits. We lost contact with her after she finished her degree.

**Discussion**
In general, it is possible to determine the cause of a patient’s pain following an accident. However, the superimposition of a motor vehicle...
accident on defective connective tissue as seen in EDS complicated the diagnosis. How much of the spine-related pain was due to EDS and how much was due to the accident cannot be determined precisely. We can state that her spine-related pain worsened after the accident. We can also state that this patient improved symptomatically under chiropractic care. Although one case study does not prove that chiropractic care is an effective treatment for musculoskeletal symptoms common in EDS, it is a reasonable hypothesis that a trial period of chiropractic care could demonstrate significant relief of musculoskeletal pain in EDS as long as the complications associated with EDS are known. There are several factors that favor this approach:

- back and neck pain are common
- joint pain is common
- headache is common
- musculoskeletal symptoms start early and get progressively worse
- current medical treatment is non-specific and palliative
- in a survey of EDS patients, chiropractic care was one of the treatment methods used
- two case studies have been published previously that involved chiropractic treatment of EDS

**Radiographic Findings in EDS**

The radiographic picture of Ehlers-Danlos syndrome can be connected, at least in part, with the joint hypermobility and connective tissue/skin manifestations. Due to the increased joint motion, dislocations and subluxations are common. This would present with typical x-ray findings of dislocation/subluxation, such as loss of apposition of articular surfaces, or complete disassociation of opposing bones. The more frequent sites of dislocation include the glenohumeral, and acromioclavicular joints of the shoulder, as well as interphalangeal, patellofemoral, sternoclavicular, radiocapitellar, and temporomandibular joints. Pes planus of the feet, recurvatum of the knee and congenital hip dislocation are also findings commonly seen in these patients resulting from joint laxity. The increased motion found at articulations can often result in premature and severe degenerative changes. The metacarpophalangeal and interphalangeal joints of the hand may demonstrate severe degeneration resembling neuropathic joints. Acroosteolysis is also a potential radiographic finding.

Radiographic findings in the axial skeleton can include pectus excavatum or carinatum, hyperkyphosis/hypokyphosis, and scoliosis. Verterbral body scalloping is also visible. The scalloping is usually along the posterior vertebral body, and is the result of dural ectasia. However, at least one author suggests lateral scalloping is possibly due to dysplasia. Spondylolysis and spondylolisthesis are also possible findings in EDS.

Soft-tissue findings may include persistent joint effusions or hemarthrosis, as well as both olecranon and prepatellar bursitis. One of the most common radiographic findings within the soft tissues, occurring in approximately one third of the patients, is small foci of subcutaneous calcification. These small densities usually demonstrate lucent centers and resemble phleboliths. The calcifications are the result of either hemorrhage or fat necrosis, and are often seen along the forearms, shins, and extensor surfaces of the extremities. Other calcifications of the soft tissues may be seen as a result of myositis ossifications or scarring. Heterotropic ossification is also seen in EDS and occurs primarily in the region of the pelvis and hips.

One unusual manifestation of soft-tissue calcification is detected specifically in the Type IX Ehlers-Danlos syndrome (using the older classification system mentioned in the Introduction). The radiographic appearance of “occupi-
tal horns,” or horn-shaped excrescences on the occipital bone, is rare to all other categories of EDS.\(^{21,22}\) The cause of this osseous manifestation is unknown.

**Goal Setting**
Goal setting for conditions such as EDS must take into consideration the heritable nature of the disease. Therapy should be designed to provide temporary relief of symptoms and make the activities of daily living easier to perform. An added benefit is that success in reducing pain, albeit only temporary, can reduce the quantity of pain killers that the EDS patient may be taking. This point is discussed well by Colloca\(^{20}\) in the previous report of chiropractic management of EDS. All of this must be explained to the patient so that realistic expectations can be made and false hopes not promoted or assumed.

**Exercise/Home Care**
It was fortunate in this case that the patient was already committed to daily exercise that included both aerobic and weights. One of the psychological ramifications of chronic pain is a loss of interest in doing exercises and onset of depression. Since exercises can help to reduce the impact of pain, motivating the EDS patient to get on a regular program needs to be incorporated into the treatment regimen. There is a sound mechanical reason for doing exercises with weights. Tendons, ligaments, and muscles all hypertrophy in response to exercises with weights. How this can be beneficial is illustrated by the dimensionless formula for stress:

\[
\sigma = \frac{F}{A}
\]

where \(\sigma\) = stress, \(F\) = force, \(A\) = area

Hypertrophy of muscle, tendon, or ligament increases its size or area, the denominator \(A\). This thus can reduce the force \(F\) per unit area and can help to minimize mechanical damage to the affected structure.

**Neurology and Nutrition**
The various types of EDS mainly involve collagen types I, II, III, V and XI.\(^9\) Interestingly, muscle spindles are reported to be rich in type-IV collagen, which is not implicated in EDS.\(^{27}\) This would suggest that afferent information from the spindles is normal. However, spindles are activated by passive stretch. Faulty mechanics, such as carrying the head anterior to the gravity line could also lead to passive stretch of posterior cervical muscles, contributing to aberrant afferent input into the spinal cord. Passive stretch of genetically weak connective tissue could lead to an increase in neck pain in this situation. This would justify attempting to minimize mechanical faults in the EDS patient. Colloca\(^{20}\) points out that the inherent weakness of the connective tissue in EDS could result in spinal instability, ligamentous laxity, and vertebral deformity. Mechanical faults, especially in the lower lumbar spine, can lead to an increase in shear forces on discs. Given an already weakened connective-tissue condition, increasing shear force can further exacerbate low-back problems in the EDS patient. Joint capsules and ligaments are well supplied with mechanoreceptors and proprioceptors.\(^{28-30}\) Inherent weakness in connective tissue, as in EDS, means that afferent input from joint capsules and ligaments in these patients could result in muscle spasm and pain. The chiropractor needs to try to minimize faulty biomechanics through exercise and manipulation tailored to the EDS patient to normalize afferent input.

There is another type of proprioceptor contained within the muscle, the Golgi tendon organ (GTO). It is located at the junction of the muscle and tendon, and lies in series with the muscle. When stimulated, it can have an inhibitory effect on its own muscle and synergists, and an excitatory effect on the antagonists. It is stimulated slightly by passive stretching. It is also stimulated by the contraction of the muscle.
The fact that the GTO can have an inhibitory affect on its own muscle may seem contradictory at first. However, it acts in coordination with other sensory information, such as that from muscle spindles and mechanoreceptors, to allow for an appropriate response. The self-inhibition is a protective mechanism that occurs if the load on a muscle is so great that a continued contraction would result in tearing or rupture of muscle and/or tendon.

What load on a muscle/tendon arrangement is too great? The same load placed on a normal muscle/tendon complex and on a muscle/tendon complex in an EDS patient could have different consequences due to the inherent weakness of connective tissue in EDS. Weakened connective tissues are susceptible to damage due to tensile or shearing forces placed on them or if they are required to transfer loads.

Mantle et.al.\(^{31}\) have suggested that the inherent weakness in EDS connective tissue may be helped somewhat by selected nutritional support. Vitamin C and glucosamine sulphate are 2 of the nutrients that they discuss. EDS connective tissue bears comparison to connective tissue seen in the classical nutritional disease, scurvy. A lack of Vitamin C prevents the formation of normal connective tissue and leads to the weakening of tendon, ligament and vascular structures. Vitamin C is essential for hydroxylation of the amino acids proline and lysine, which are necessary steps in the formation of normal collagen. Shashikiran\(^{32}\) reported that Vitamin C supplementation resulted in an improvement in collagen synthesis in EDS patients suffering from recurrent respiratory infections. The Villefranche\(^{17}\) classification of EDS shows that the kyphoscoliosis type of EDS (formerly type VI) is characterized by a deficiency of lysyl hydroxylase. This enzyme is needed for the hydroxylation of lysine and hence normal collagen formation. Vitamin C is a requirement for this step. Supplementation of EDS patients with Vitamin C would seem to be a rational therapeutic choice.

Redaelli\(^{33}\) did a study in which he demonstrated that the transfer of force in a tendon is not all due to long tendon fibrils running the entire length of the tendon. There is some evidence that an extra-cellular matrix consisting of glycosaminoglycans (GAG) aids in force transfer. Glucosamine sulfate and chondroitin sulfate are both constituents of GAG. GAG helps to provide adherence between parallel shorter fibers. This is sufficient to allow for transfer of force between adjacent fibers and hence through the entire tendon. Mao’s\(^{2}\) investigation into collagen structure showed that collagen V is a factor in limiting the diameter of collagen fibrils. Typical in EDS hypermobility type is an increase in fibril diameter and the production of rare collagen cauliflowers. The mechanism by which the defect in collagen V contributes to biomechanical instability involves fibril disarray rather than hyper-extensibility of the collagen fibrils. Whether this cross force transfer could be helped in EDS patients by nutrition emphasizing glucosamine sulfate and chondroitin sulfate is not known at this time. Given the promising research of GAG in joint pain and mobility, this may prove to be beneficial in managing EDS patients.\(^{34}\)

It is interesting to note the patient reported an improvement in menstrual cramping during her care. Previous research has indicated that lumbar spinal manipulation might reduce the cramping and prostaglandin F2a metabolites associated with menstrual pain.\(^{35}\) This prostaglandin factor contributes to smooth muscle contraction and platelet aggregation, factors responsible for the cramping and excessive bleeding often noted during menstruation. Prostaglandins are hormone-like substances that are elaborated near or at the site of their activity. They can be either pro or anti-inflammatory. There are 3 series of prostaglandins that can be produced in the body;
series 1, 2, or 3. The series depends on the substrate of dietary fatty acid intake. Linoleic acid will produce type 1 prostaglandins, arachidonic acid will produce series 2, and linolenic acid will produce type 3. Series 3 prostaglandins are the least inflammatory, while series 2 are the most inflammatory. Diet may have a significant role and it may be helpful for the EDS patient to include oily fish or fish oil supplements in the diet. This type of fat will help the production of the series 3 prostaglandins and theoretically could minimize inflammation.

CONCLUSION
Chiropractic management has the potential to help alleviate the pain and mobility restrictions that are associated with the hypermobility type of EDS. Vigorous manipulation must be avoided given the nature of the connective-tissue weakness and the potential for vascular damage. Soft-tissue work must also be gentle due to the hyperelasticity of the skin. Nutritional therapy has yet to be demonstrated to be effective on a large scale but preliminary results indicate that it is an avenue that needs further trials. Unfortunately, we did not follow up on whether this patient started taking Vitamin C. Exercise is important and it is here that motivating patients and frequently encouraging them becomes essential.

As Colloca stated, no definitive conclusions can be drawn from a case report. However, given the non-specificity of current medical care and the emphasis on symptomatic relief, chiropractic care could prove to be beneficial for the EDS patient. It is hoped that a proper large-scale study involving chiropractic and EDS will be undertaken soon in order to assess this issue.

Table 1. Villefranche Classification of types of Ehlers-Danlos Syndromes (reprinted with permission of the author and the publisher)

<table>
<thead>
<tr>
<th>Type</th>
<th>Inheritance</th>
<th>Previous Nomenclature</th>
<th>Major Diagnostic Criteria</th>
<th>Minor Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic</td>
<td>Autosomal dominant</td>
<td>Types I and II</td>
<td>Skin hyperextensibility, wide atrophic scars, joint hypermobility</td>
<td>Smooth, velvety skin; easy bruising; molluscoid pseudotumors; subcutaneous spheroids; joint hypermobility; muscle hypotonia; postoperative complication (e.g., hernia); positive family history; manifestations of tissue fragility (e.g., hernia, prolapse)</td>
</tr>
<tr>
<td>Hypermobility</td>
<td>Autosomal dominant</td>
<td>Type III</td>
<td>Skin involvement (soft, smooth and velvety), joint hypermobility</td>
<td>Recurrent joint dislocation; chronic joint pain, limb pain, or both; positive family history</td>
</tr>
<tr>
<td>Vascular</td>
<td>Autosomal dominant</td>
<td>Type IV</td>
<td>Thin, translucent skin; arterial/intestinal fragility or rupture; extensive bruising; characteristic facial appearance</td>
<td>Acrogeria, hypermobile small joints; tendon/muscle rupture; clubfoot; early onset varicose veins; arteriovenous, carotid-cavernous sinus fistula; pneumothorax; gingival recession; positive family history; sudden death in close relative</td>
</tr>
</tbody>
</table>
## Kyphoscoliosis
- **Autosomal recessive**
- **Type VI – lysyl hydroxylase deficiency**
- Joint laxity, severe hypotonia at birth, scoliosis, progressive scleral fragility or rupture of globe
- Tissue fragility, easy bruising, arterial rupture, marfanoid, microcornea, osteopenia, positive family history (affected sibling)

## Arthrochalasia
- **Autosomal dominant**
- **Type VII A, B**
- Congenital bilateral dislocated hips, severe joint hypermobility, recurrent subluxations
- Skin hyperextensibility, tissue fragility with atrophic scars, muscle hypotonia, easy bruising, kyphoscoliosis, mild osteopenia

## Dermatosparaxis
- **Autosomal recessive**
- **Type VII C**
- Severe skin fragility; saggy, redundant skin
- Soft, doughy skin; easy bruising; premature rupture of membranes; hernias (umbilical and inguinal)

### References
6. Fig. 1 courtesy of www.patient.co.uk/showdoc/40001375.
7. Fig. 2 courtesy of http://home-and-gaden.webshots.com/photo/147193643069923602AolCTL.


