Upper Cervical Vertebral Subluxation in Multiple Sclerosis Subjects with Chronic Cerebrospinal Venous Insufficiency: A Pilot Study

Sandro Mandolesi, MD,1 Giuseppe Marceca, MD,2 Stephen Conicello, DC,3 Eriece Harris, DC4

ABSTRACT

Objective: The purpose of this study is to evaluate the relationship between Atlas vertebra misalignments identified via radiographs and patients with multiple sclerosis (MS) and chronic cerebrospinal venous insufficiency (CCSVI).

Clinical Features: Four patients with MS and CCVSI, three women and one man were evaluated according to revised McDonald criteria. These four patients were compared to a control group of four patients of similar age but with no neuro-degenerative diseases.

Intervention and Outcomes: This is the first report on Atlas (C1) misalignment in MS patients with CCVSI. Four patients were evaluated using the Zamboni’s criteria using the following: Echo Color Doppler (ECD) MyLab Vinco System Esaote, Upper cervical x-ray examination, Myofunctional Map, and Tytron thermal scanning instrumentation. In this study we found different alterations of C1 alignment in the MS patients versus the control group. Analysis of the x-ray examination permits us to identify a severe rotation and anterior intrusion of C1 in the MS patients with CCVSI.

Conclusion: We found not only endovenous congenital malformations, but also external venous compression that blocks drainage flow. This confirms the validity of our Mechanical Posture Vascular Compressive Block. We hypothesize that extracranial venous compression is linked to severe misalignment of C1. We can also catalogue misalignments into two types of degrees: moderate and severe. This staging permits us to begin to distinguish paraphysiologic misalignments from true pathological misalignments.

Keywords: Multiple sclerosis, chronic cerebrospinal venous insufficiency, upper cervical, subluxation

Introduction

Multiple sclerosis (MS) is considered a chronic disease of the nervous system, characterized by inflammation, demyelination, and neurodegeneration. MS affects over 400,000 individuals in the United States, with new cases annually. It is estimated that MS currently affects 400,000 individuals in the United States, with 12,000 being new cases annually, with more people being diagnosed now than in the past. MS affects twice as many women as it does men, mimicking the unexplained bias found in other neurological disorders.

Multiple Sclerosis


1. Professor – Cardiovascular and Respiratory Science Department, Sapienza University of Rome, Rome, Italy
2. Professor – School of Medicine, Sapienza University of Rome, Rome, Italy
3. Private Practice of Chiropractic, Rome, Italy
4. Private Practice of Chiropractic, Naples, FL
autoimmune disorders. This autoimmune disorder usually begins in subjects around the ages of 20-40. The majority of MS patients (80%) present with the relapsing/remitting form of the disease. This form is characterized by relapsing of symptoms followed by full recovery, relapse with persistent deficit, and finally secondary progression. In about a quarter of the patients, MS never affects activities of daily living; conversely 15% become severely disabled in a short period of time. Recognized and described over 150 years ago by a French neurologist Charcot, the exact cause of the disease remains unknown.

In general, we consider MS to be caused by an autoimmune mechanism with multiple etiological factors such as genetic, infectious, and environmental. Recently, chronic cerebrospinal venous insufficiency (CCSVI) has been described as a condition that may possibly contribute to the symptoms often experienced by patients with MS. CCSVI has been described as a vascular condition characterized by anomalies of the main extra-cranial cerebrospinal venous routes that interfere with normal venous flow. These anomalies have been reported to affect the internal, vertebral and azygous veins.

The origin of CCSVI related venous anomalies has not been determined. It has been suggested that the origin of these abnormalities could be physiological, age-dependent, congenital, and a possible consequence of an inflammatory process or environmental factors. It has been hypothesized that cerebrospinal venous anomalies may cause alterations to blood flow that result in iron deposition, decreased brain parenchyma metabolism, degeneration of neurons and characteristic brain injury patterns found in MS. This hypothesis is referred to as “The Big Idea”.

The Big Idea hypothesis was created by Paolo Zamboni. In 2006 Zamboni researched and published a paper in the Journal of the Royal Society of Medicine entitled “The Big Idea: Iron-dependent inflammation in venous disease and proposed parallels in multiple sclerosis”. His paper outlines the mechanism of pathology in CCSVI and MS. This paper also suggests that there is a connection due to similarities in tissue response. To summarize the findings of the paper, the correlation begins with increased iron stores in areas of the body - mainly the legs, due to extravasation of red blood cells (RBC) in conditions of significant venous stasis in CCSVI.

The RBC’s are degraded by interstitial macrophages and the released iron is converted into ferritin. Eventually the ferritin is transformed into haemosiderin and then deposited into venous tissue. This increase of iron storage in the body as well as interstitial proteins attracts potent chemicals that represent the initial chronic inflammatory signal response for white blood cell recruitment and migration in the matrix. The predominate cells migrating into the extra cellular matrix are macrophages and T-lymphocytes.

Similarly, the inflammation in MS is characterized by expression of adhesion molecules followed by the migration of macrophages and T-lymphocytes across the blood brain barrier. In both scenarios there is an over expression of matrix metallo-proteases (MMPs) that are not substantially balanced by their physiological tissue inhibitors (TIMPs). If MMP is unrestricted it leads to matrix break down and ulcer onset. Ajay has proposed the use of susceptibility weighted neuroimaging techniques to confirm the hypothesis of iron playing a role in the formation of MS. This imaging is able to detect the iron deposits in the brain tissue.

The proposed correlation in the two diseases comes from the similar altered venous haemodynamics. The altered venous haemodynamics are considered the trigger mechanism that caused the inflammatory process in CVD. This has to be studied further in relation to MS.

Methods

Eight patients were selected to participate. Four of the patients were diagnosed with MS according to the revised McDonald criteria and CCSVI. The median age for the patients is 33 with a maximum age of 36 and minimum of 30. The gender of the patients consisted of three women and one man. Disease duration for the patient group did not exceed 15 years. The other four patients were the control sample group composed of subjects of the same age, without any neurodegenerative diseases.

Each patient was examined using the following: ECD, Doppler Ultrasonography dynamic test, total body myofunctional map, upper cervical radiography, and Tytron C-5000 thermal scanning.

Results

Echo Color Doppler

According to Menegatti ECD demonstrated to be an ideal non invasive tool for screening patients. There was a question of the reproducibility of the instrumentation based on the training of the individual performing the exam. The conclusion of the 36 subject study showed ECD is a powerful non-invasive and reproducible tool for screening CCSVI and MS but the individual needs special training. ECD was used to measure outflow in veins and inflow in arteries. In the MS sample the venous outflow assessment showed: jugular vein stenosis in 50%, not visible vertebral veins in 25%, reflux in 50%, blockage in 50%, and compression block in 25% of the sample. The control sample assessment revealed ectasia of the jugular vein only in 50% of the sample. The ECD arterial inflow assessment of MS sample showed thoracic outlet syndrome on the left side in 100%, kinking in vertebral arteries in 75% of the sample. The control sample showed kinking of the carotid arteries only in 25% of sample.

Myo-functional Map

Myo-functional assessment is an objective hand examination of the skeletal muscle system that allows us to find, in an objective way, the muscular contractures perceived (spontaneous painful) from those not perceived (spontaneously not painful). We then draw specific symbols on an accurate Myo-functional Map. In the MS sample we found muscular contractures of the total body examination: Median 47±21, Points min: 22 and Points max: 28. In the control sample we found muscular contracture of the total body examination: Median 15, Points min: 2, Points max: 28.
Cervical Radiographic Examination

Each patient received a series of cervical radiographs. The following projections were taken and measured for each sample group: APOM (anterior posterior open mouth), lateral cervical and base posterior.

APOM

This projection is used to measure left or right laterality of C1. To measure this a horizontal line was drawn through the upper ½ to 1/3 portion of the foramen magnum. The foramen magnum is then bisected with a vertical line. A line is then drawn from the vertical line to the edge of the lateral mass on the right and left side. Measure both sides and the longer side is the side of laterality of C1.

Base Posterior

This projection is used to measure anterior intrusion of C1. This is measured by drawing a line from the posterior foramen magnum to the posterior neural canal of axis. This will be labeled as line A. Another line is then drawn from the posterior portion of the neural canal of the posterior arch of atlas to the posterior of foramen magnum. This line will be labeled line B. Another line is then drawn from the posterior of the neural canal of the posterior arch of the atlas to the posterior neural canal of axis. This line will be labeled line C. Measure the distance from the point where B and C meet at posterior neural canal at the posterior arch of atlas to line A at a perpendicular angle.

The normal values for these radiographs are as follows: tilt of 18-22 degrees, no laterality, no rotation, and no intrusion into the spinal laminar line (neural canal). The moderate category values are as follows: inferior tilt of 16-18 degrees, superior tilt of 22-24 degrees, laterality of < 1.5mm, rotation of < 1 degree, and anterior intrusion of < 1.8mm. The severe category values are as follows: inferior tilt of <16 degrees, superior tilt of > 24, laterality > 1.5mm, rotation of > 1 degree, and anterior intrusion of > 1.8 mm.

The radiographic results of the study are displayed in Figure 1.
The MS sample group results show that 25% of participants presented with severe inferior tilt, severe left laterality, moderate right laterality, severe right laterality, moderate anterior right rotation, severe anterior right rotation, severe posterior right rotation, and severe posterior left rotation. Normal superior tilt was found in 75% of the MS sample group and no left rotation was found in any participants. The major finding is that 100% of sample group presented with severe anterior intrusion into the neural canal with the maximum being 4.07mm.

The control sample group results show 25% of the participants presented with normal tilt values and no anterior intrusion. Fifty percent of the sample group presented with moderate left laterality, moderate right laterality, moderate impairment on left and right in anterior rotation. The control group also presented with moderate superior tilt and moderate impairment in anterior intrusion in 75% of participants. The major finding in this group is 100% of sample group presented with anterior rotation.

**Tytron Thermal Scanning**

Thermocouple devices have been used in chiropractic as early as 1924 to measure side-to-side skin temperature differentials. According to Owens the Tytron shows very high intraexaminer and interexaminer reliability with intraclass correlation coefficient values between .91 and .98. When scanned using the tytron the MS sample group had greater temperature alterations than the control group.

**Discussion**

CCVSI as a potential etiopathic entity in MS has recently been suggested and gained significant attention. It is widely accepted that MS is an autoimmune disease but now we are faced with a new model of it being possibly vascular or degenerative. There is also a possibility of there being a mechanical component involving the C1 vertebra. To begin to address these concerns we must first look at the current literature.

Williams created a study to evaluate the hypothesis of Zamboni in the Big Idea. In order to evaluate this hypothesis she developed an animal model. The conclusion of her study showed that MS caused the vascular abnormalities, not the other way around.

There is also controversy about the frequency and the role of CCVSI in patients with MS. Laupacis performed a systematic review and meta-analysis of all the peer review studies that compared the frequency of CCVSI among patients with MS. The meta-analysis published in 2011 included 8 studies and the article concluded that there was a strong and statistically significant association between CCVSI and MS. The article did have a limitation of a small sample size but found a strong association between CCVSI and MS. The study concluded that more high quality studies using identical ultrasound protocols are needed.

Awad published a critical review on the subject. He states the controversy of the subject is due to the inability of any other researchers to reproduce the results published by Zamboni. Awad goes on to list six different recent studies that have been done to recreate Zamboni’s results but have been unsuccessful. Awad goes on to discuss the plausibility of CCVSI being biologically linked to MS and states the gold standard to confirm would be a tissue diagnosis.

One common theme that seems to reoccur is the use of ECD in evaluating CCVSI. The instrumentation has been deemed reliable but only if the ultrasonographer is trained properly. More and better quality reasearch needs to be done on the subject in order to determine causality.

The presence of substitute circles in Zamboni type hemodynamic classification, when joined to external compression of the jugular veins, suggests to us that a venous vertebral and/or jugular postural venous compression block may be caused by misalignment of C1.

This intermittent compression block of vertebral and jugular veins may be one of the multi-factorial causes of the worst clinical conditions in MS patients with CCSVI, the Mechanical Postural Vascular Block (MPVB) (Mandolese-Marceca, 2010 hypothesis). These patients frequently had head and neck trauma.

There is a proposed relationship between MS and upper cervical subluxation. Elster conducted a study on upper cervical subluxation and it’s connection to MS and Parkinsons disease.

The retrospective study consisted of 81 patients. Of the 81 patients 44 had MS and all were diagnosed with upper cervical subluxations. These patients were diagnosed using paraspinal digital infrared imaging and laser-aligned radiography.

After the instrumentation and radiograph analysis were done, the patients were adjusted using Knee Chest technique. The result of this study showed 91% of the participants responded to care with improved or reversed symptoms, and no further progression of symptoms. The results suggested a link between trauma, upper cervical injury, and disease onset for both MS and Parkinsons. In addition to this study Stude presented a case study showing conservative spinal manipulations had positive effects in an MS patient. The patient presented in the case did not have any upper cervical subluxations but did have significant reduction in symptoms posttreament.

There seems to be some similarities in this study and the study done by Elster. Two of the same examinations were used, Tytron and upper cervical radiographs. They both also show a relationship between C1 subluxation and the presence of MS. The differences are Elster’s paper was focused on trauma as a possible cause of MS while this paper is focused the relationship between misalignment and CCVSI in patients with MS.

**Conclusion**

As far as we know, this is the first report on C1 misalignment in MS patients with CCSVI. In this study we found a significant parameter of C1 misalignment (anterior intrusion) in patients with MS with CCVSI versus control subjects.
We postulate that the severe rotation and anterior intrusion should be an important radiological marker for MS patients with CCSVI. Further study with a larger sample size of these CCSVI patients is recommended.

References

Figure 1. Results from Radiographic Study