

Internal jugular vein and multiple sclerosis story

Abstract

The cause of Multiple sclerosis (MS) is unknown. Multiple theories for pathogenesis of MS postulated. The most accepted is autoimmune inflammatory process. In recent years the role of internal jugular vein abnormality in MS pathogenesis has been considered as “Big Idea” that raised hopes for MS treatment. But although the earlier studies were promising, their results were not reproducible and recent finding disputed the theory.

Keywords: CCSVI, Multiple sclerosis, Internal jugular vein, Liberation treatment

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Amir Azarhomayoun,¹ Iman Azarhomayoun²

¹Department of Neurosurgery, Tehran University of medical sciences, Iran

²Tehran University of medical sciences, Iran

Correspondence: Amir Azarhomayoun MD, Department of Neurosurgery, Tehran University of Medical sciences (TUMS), Sina trauma and surgery research center, Gundishapur academy of neurosciences (GAN), Chamran Hospital, Hasan abad square, Tehran, Iran, Tel +98-912-1959851, Fax +98-21-88071231, Email dr.azarhomayun@gmail.com

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Abbreviations: MS, Multiple Sclerosis; IJV, Internal Jugular Vein, CCSVI, Chronic Cerebrospinal Venous Insufficiency ; DU, Duplex Ultrasound; VHISS, Venous Hemodynamic Insufficiency Severity Score

Introduction

Multiple sclerosis (MS) considered as autoimmune inflammatory disease. In the recent years correlation of the internal jugular vein (IJV) abnormality and MS was investigated in several studies and still controversies about this issue remained to be clarified. In this review we discuss about the story of the IJV abnormality and MS.

Discussion

The term of CCSVI was first used by Zamboni et al. for jugular vein abnormalities associated with MS.¹ He described criteria for diagnosis of CCSVI based on duplex ultrasound (DU) standards for detecting reflux or stenosis in the extra cranial venous system. Even the location of venous obstruction was contributed to clinical course of the disease.¹ This hypothesis states that MS is caused by the obstruction at different vein levels, namely the internal jugular veins (IJVs), azygos vein (AV), and vertebral veins. It is postulated that CCSVI may lead to blood-brain-barrier disruption and iron-dependent inflammation.² The reports after that had variable results. Various pathologic findings have been reported with different definition without any agreement in etiologic relationship with MS.

Meanwhile, the hypothesis lead to venous stenting in MS patients published in open case series.³ The Liberation treatment was coined by Zamboni et al. for endovascular procedure. Venous Hemodynamic Insufficiency Severity Score (VHISS) developed to use as indicator of treatment effect. Social media and other public media raised hopes. Many MS interest groups began feverishly advocating the procedure and in response Europe, the US, and Canada committed millions of dollars for research to validate the concept of CCSVI and the seemingly effective procedure.⁴ Several subsequent prospective open-label, nonrandomized studies investigated safety and efficacy of venous angioplasty in MS. Findings from some of these studies showed positive effect of the treatment while other studies not only showed no potential treatment benefit even increase in disease activity reported. In an RCT by Siddiqui et al.⁵ patients with MS and extra cranial venous abnormality proved by Doppler Sonography criteria underwent venoplasty. it is showed that clinical and imaging

outcomes are no better or worse in patients with MS identified with venous outflow restriction who receive venous angioplasty compared to sham controls who do not receive angioplasty.⁵

In the Systematic review in 2014, Tsvigoulis et al.⁶ concluded that there is no evidence for performing liberation treatment In MS patients and in fact its main source is “sensational” but inaccurate information.⁶ Although ,It looks as the end of great Idea but still researcher continue to investigate jugular vein pathologies in MS. today no study were reproduce findings such a Zamboni and external validity of Zamboni criteria has been be questioned. Zamboni partly blamed this discrepancy on the fact that others did not use the high quality equipment manufactured by SoNos, a high resolution ultrasound machine made by the very company he has financial stakes in, raising serious ethical concerns.⁴

Comi et al.⁷ published the results of their “Italian multicenter observational study of the prevalence of CCSVI in multiple sclerosis” (CoSMo study) which attempted to validate the presence of CCSVI in MS using Zamboni’s DU criteria. He CoSMo group found that in MS patients, the presence of CCSVI was 3.26%. In patients with other neurodegenerative disorders, the presence of CCSVI was 3.1% and in healthy controls 2.1%. Given the low frequency combined with the presence of CCSVI in all cohorts analyzed, the authors concluded that CCSVI was not associated with MS. There are several important variables, including physiologic, technical, and criterion definitions, in the application of sonographic assessment of chronic cerebrovascular venous insufficiency that may affect diagnostic accuracy.⁸ Recent studies using MRI and high technical imaging also disputed the theory. Some authors have tried to study the ultra structure of extra cranial veins in patients with MS. The vein tissue in patients with CCSVI studied by several methods .although they showed some histological alteration these could be due to endothelial chronic stress secondary to altered hemodynamic.

Conclusion

There is now numerous evidence to consider CCSVI as a failed concept. There is Evidence Level I that extra cranial venous angioplasty should be abolished as a treatment in patients with MS.

Acknowledgments

None.

Conflicts of interest

None.

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