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Chronic Superior Vena Cava Syndrome: Demonstration of Systemic Venous Circulation Inversion and Continuous Venous Blood Shunting Toward the Cerebrospinal Venous Circulation. Physiologic and Clinical implications for Neurodegenerative Disease

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Abstract

In superior vena cava syndrome (SVCS), one or more of the major veins are occlused or deeply stenosed. In these cases. Venous blood from the head, neck, chest and upper limbs regularly reaches brachiocephalic veins and the right atrium through collateral vessels. Several angiographic and echocardiographic studies have reported that in the left brachiocephalic venous stenosis venous blood, instead of flowing toward the superior vena cava and taking the compensation circles to reach the heart, reverses its flow direction through the jugular and then the cerebral veins.

In the venous system, flows direction is always centripetal one-way, and a completed flow inversion is possible only in presence of venous stenosis associated with a compensatory circle. Thus, we are here hypothesizing that in SVCS inversion of flows into a jugular vein, already clearly described in the literature, is due to the presence of a compensatory circle that finally connects the superior vena cava to the inferior vena cava.

Given that jugular and cerebrospinal veins join with full-channel connections to become a single conduit, we hpothesized that the "new" compensatory circle, deriving from the hemodynamic consequences of SVCS, may include the entire cerebrospinal venous system. This hypothesis is corroborated by the current knowledge on the cerebrospinal venous system: it is a unique, valveless, bidirectional flow circuit that freely communicates with superior and inferior vena cava.

In the SVCS, venous blood coming from the head, neck and upper extremities may not descend towards the brachiocephalic vein, as expected from literature, but reverses its flow direction towards the jugular vein and the cerebral spinal venous system, to reach the inferior vena cava.This means that constantly, in the SVCS, part of venous blood coming from the head, neck and upper limbs must cross the brain and the spinal cord to finally reach the right atrium, and that there is a direct contact between the venous blood of the superior vena cava and the cerebrospinal venous system. The continuous passage of venous blood from the superior cava system into the cerebrospinal circulation opens new perspectives in understanding the etiopathogenesis of many neurodegenerative diseases. In vena cava stenosis then, the cerebrospinal circle is subjected to an increase both in pressure and in volume overload, thus creating the possibility that infections, emboli or tumors migrate directly from the peripheral tissues to the brain through the venous route (as already demonstrated in literature).

From 2010 to now we have operated for plastic enlargement with patches of saphenous vein, 120 patients with congenital stenosis of the superior vena cava system. These compassionate interventions were undertaken as the "last therapeutic chance" of improving a series of severe and invalidating symptoms, completely non-responsive to each and all clinical practise therapy recommended by updated guidelines, and possibily depending on this blood flow inversion in SVCS.

Here we are reporting the angiographic findings of the first two patients with vena cava stenosis. In one we describe the inversion of flow from the site of the obstruction towards the cerebrospinal circle, and in the other we describe the passage of venous blood from peripheral tissues to the cerebrospinal circle.

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Introductio

It is thought that in the presence of a significant stenosis of the superior vena cava, the cerebrospinal venous circle normally flows into the jugular veins and brachiocephalic veins and, by means of the superior intercostal veins and the mammary veins, it reaches the azygos system and superior-inferior vena cava [1-5].

Recent studies have demonstrated that in the presence of a stenosis of the brachiocephalic or jugular veins, venous blood can invert the direction of its flow and move towards the cerebrospinal circle. As generally agreed, there is a venous reflux when the circle inversion exceeds 0.88 sec.

The cause of the reflux has been attributed to increased central venous pressure [6-10]. On this matter, the Scientific Community still assumes that in the venous system a countercurrent flow is not possible, the direction of the flows being always monodirectional and centripetal (such as a postulate). On the contrary, the cerebrospinal venous system, due to the absence of valves, is considered as single circuit with a bidirectional flow.

Due to the direct communication with the jugular vein at one end and the azygos vein at the opposite extreme, we hypothesized that the cerebrospinal venous system behaves like a compensatory circuit that connects the superior cava with the inferior cava and that the flow direction is regulated by pressure gradients at its ends. In case of stenoses of the left brachiocephalic vein or jugular veins, blood flows from the point of stenosis to the cerebrospinal circle and to the azygos vein. In the presence of a stenosis of the azygos vein, the blood flow cannot arrive, as usual, into the superior vena cava but must reverse the flow direction and must pass through the spinal and cerebral circulation to reach the superior vena cava.

This means that in left brachiocephalic or in giugular veins stenosis, venous blood coming from the head, neck must cross the veins of the cerebrospinal system and the azygos vein to reach the heart, and that the cerebrospinal venous system represents the first and most important compensatory collateral pathway.

To confirm this hypothesis, we are here describing the angiographic pattern of two patients with significant stenosis of the superior vena cava system. After the patients were repeatedly administered contrast agents at various sites, we were able to trace the passage of peripheral venous blood, from the point where the stenosis was, toward the cerebrospinal circle.

Clinical Cases

First Case

A sixty-seven-year-old female weighing 63 kg recently underwent reconstructive surgery because of an ascending aorta aneurism. During the time that the left brachiocephalic trunk was isolated from the aortic arch, a tear took place at the junction point of the vena cava that was repaired with direct suture. During the post-operative period, a stenosis of the brachiocephalic vein was suspected because of edema of the left superior extremity, together with swelling of the neck.

Angiographic examination was carried out through the right femoral vein. An injection of 15 ml of iodinated contrast agents (lomeprol 300 mg/ml) made it possible to visualize the superior vena cava and the brachiocephalic trunk, as well as the right jugular vein, which appeared free from obstruction and with a normal centripetal flow. A second injection into the left brachiocephalic vein uncovered a dense stenosis corresponding to its junction in the superior vena cava. The contrast medium, which was injected immediately after the stenosis, did not drain into the intercostal veins, but inverted its direction and moved prevalently into the left internal jugular vein and into the cerebral circle. It was also noted that even the non-contrasted blood coming from the left subclavian vein also showed a preferential flow towards the jugular vein and the cerebral circle diluting the contrast medium. A third injection in the third proximal part of the jugular vein found a scarce outflow in the centripetal direction; instead,

the reflux towards the cerebral venous system was evident and prevalent. In this projection, moreover, the non-contrasted blood coming from the subclavian vein is clearly seen flowing into the jugular vein and into the cerebral circle.

Second case

The patient was a fifty-two-year-old male with a "collar of stokes" edema, turgor of the jugular veins, congestion of the face and the conjunctiva, and marked venous circle of the thorax. An echocolorDoppler examination revealed vena cava thrombosis due to precedent positioning of a central venous catheter and reflux in the right jugular vein. An injection of contrast medium in the right basilic vein confirmed that there was a stenosis of the superior cava vein, above the junction of the azygos vein. Once the contrast liquid reached the subclavian vein, it flew prevalently into the right jugular vein and cerebral veins, instead of into the superior intercostal vein and azygos vein, as has been described in the literature.

In both cases, the angiographic examination carried out after surgical elimination of the stenoses showed normalization of the blood flow direction from cerebral venous circle to superior vena cava.

Discussion

The SVC syndrome results from obstruction of the SVC or its major tributaries by intraluminal occlusion or by extrinsic compression or invasion from malignant and benign diseases. The severity of the symptoms depends on the degree of narrowing of the superior vena cava, the speed of the onset of the narrowing and the development on the collateral vascular system. The interruption of the normal venous blood flow from the vena cava to the heart causes an increased venous pressure (20 to 40 mmHg). (1.2) In the SVCS, venous blood coming from the head, neck, shoulders and arms cannot directly reach the right atrium, and blood flow is redirected through the collateral circulation, in order to bypass the obstruction and restore the venous return. There are four possible collateral systems which were first described in 1949 by McIntire and Sykes: the azygos veins, the internal thoracic veins, the vertebral venous system and the external thoracic vein [2, 3].

The introduction in the vascular diagnostics of angiography, TAC, echocardiography and MRI has brought new knowledge on the flow's direction that contrast much with the literature extablishments. In a patient whith marked obstruction to the flow at the region of the left brachiocephalic vein, injected a rapid intravenous bolus (1 ml) of 99mTcsodium pertechnetate into the left antecubital vein. What he observed and described is that the tracer, instead of flowing towards compensatory circles to reach the azygos vein or inferior vena cava, rose into the internal jugular vein and then the cerebral veins. Subsequently, numerous angiographic studies have reported that in the left brachiocephalic venous stenosis, there is a reversed flow in the left internal jugular and in cerebral vein [5-8].

Even with the use of ecocolor Doppler, in SVC syndrome studies of the flow in the jugular and cerebral veins have shown that there is an inversion of flow direction towards the jugular veins (JVR). Found a cutoff value for the duration of the detected retrograde flow during VM, to differentiate between a physiologic jugular venous reflux and a true IJVVI. This value is equal to or greater than 0.88s. Continuous JVR has been reported in patients with central venous obstruction as in the mediastinal masses, aortic aneurysm and central venous thrombosis (superior vena cava syndrome). identified a new nosological vascular model defined as chronic cerebrospinal venous insufficiency (CCSVI), characterized by more strictures/obstructions affecting the internal jugular veins (IJV) and the azygous vein [9-11]. Zamboni hypothesized that once the cerebral venous flow reaches the point of stenosis, due to the high resistance encountered, it reverses direction, reaches the cerebral venous circulation and returns to the heart mainly through the collateral cervical circles. Assuming that in the venous circulation, the direction of the flows is always centripetal and monodirectional and that a countercurrent flow is possible only in collateral venous circles, we hypothesized that the inversion of the flow in the jugular vein should be associated with the presence of a collateral circle able to connect the superior vena cava with the inferior vena cava. We believe that this collateral circulation can be represented by the same cerebrospinal venous system. This hypothesis is validated by current knowledge of the anatomy and physiology of the cerebrospinal venous system that is considered a unique, valveless, bidirectional flow circuit that freely communicates with both superior and inferior vena cava.

Before the 18th century, the vertebral venous plexus (VVP) was not investigated and was largely ignored by anatomists and physicians. Demonstrated the continuity of the CSVS from the pelvis to the cranium and established that retrograde flow from the VVS into the brain was possible because

of the lack of venous valves. In living humans, Anderson and Diodrast similarly demonstrated that contrast material injected into the VVS reached the intracranial venous sinuses and the internal cerebral veins in a retrograde fashion [12, 13].

Used Doppler to measure cerebral blood flow and ultrasound to measure the cross-sectional area of the internal jugular vein in healthy human in the supine and standing positions, before and during a Valsalva maneuver. Unlike the other venous systems, the direction of the cerebral venous flow is not centripetal but dynamic and varies with posture and respiratory acts. When standing, the jugular veins are collapsed and venous efflux from the brain occurs through the VVS, in the supine position the internal jugular veins are the main route of venous exit from the whole head. This has to be considered in the understanding of how works the intracranial pressure and flux regulation of venous blood from the brain to the vena cava [14].

Due to its unique anatomical features: single duct, bi-directional flow, absence of valves, connected to the extremities with both the superior and the inferior vena cava, it can be hypothesized that, in the SVC syndrome, the cerebrospinal venous system behaves like the first and most important compensatory circle. In the superior vena cava syndrome, because of the direct communication between the two caval systems, the presence of a stenosis induces a gradient pressure between the superior vena cava and the inferior vena cava, this causing an inversion of the flows with a continuous passage of venous blood coming from the head, neck, shoulders and upper limbs into the cerebrospinal venous system. And then from it throgh the azygos vein into the inferior vena cava. In the SVC syndrome, therefore, the venous blood must cross the cerebrospinal venous circles to reach the heart. Based on this updated and revised knowledge, in the SVCS the behaviour of the venous flows is completely different from that described in the literature.

In normal circulation, the blood flows in the brachiocephalic vein at the confluence of the subclavian vein and the internal jugular vein, and into other collateral branches represented by the external thoracic veins and the superior intercostal veins. In the presence of a SVCS, while the subclavian vein has a constantly centripetal blood flow, the jugular vein, the internal mammary vein and the superior intercostal vein reverse their flow direction.The jugular veins carries venous blood, coming from the head and neck and part of the blood coming from the shoulders and upper limbs to the cerebrospinal venous circulation, while the internal mammary veins and the superior intercostal veins carry the blood from the brachiocephalic veins to the inferior vena cava.

This hypothesis was confirmed by angiographic examinations of 120 patients with congenital stenosis of internal jugular veins or brachiocephalic veins and undergoing plastic surgery to widen the point of stenosis, with a patch in saphenous vein or in bovin pericardium. In these patients, the preoperative angiographic study documented a constant reverse flow, from the point of vein stenosis to the cerebrospinal circulation [15, 16].

We are reporting the angiographic description of the first two operated patient. In the first case, the stenosis was located in the cava above the azygos vein. An injection of contrast liquid in the right basilic vein, once the contrast reached the vena cava, showed that it did not flow into the brachiocephalic vein and then into the superior intercostal vein, as expected from the literature, but preferentially into the right jugular vein.

In the second patient with stenosis of the left brachiocephalic vein, repeated injections of contrast medium in different sites demonstrated a constant flow of venous blood in the left jugular vein and in the cerebral circle, but not in the intercostal veins. It was also shown that the non-contrasted blood coming from the left subclavian vein did not flow into the brachiocephalic vein but inverted its flow and drained into the jugular vein. A second injection in the upper third part of the left jugular vein showed scarce flow in the centripetal direction and prevalent amount toward the venous cerebral system. In this projection, non-contrasted blood coming from the subclavian flew into the left jugular vein, and not into the brachiocephalic veins.

In both cases, the angiographic examination carried out after removing the stenosis showed a complete normalization of the blood flow, again from the cerebral circle to the superior cava. These two cases, together with agreat amount of evidence already published in recent years, confirm that stenosis of the cava system determines a pressure gradient between the two ends of the cerebrospinal venous circulation with a reversal of the cerebrospinal venous circulationIn superior vena cava syndromes, then, the continuous outflow of blood coming from the peripheral tissues into the venous cerebrospinal circle causes a volume overload which, in association with an overload of pressure, may be responsible of pathological anatomic lesions as well as of yet unknown

diseases [5-7].

Several neurologic disorders have already been associated with internal jugular vein reflux, includ¬ing: transient global ischemia, transient blindness, cough headache and primary exertional headache. It has also been shown that, in caval syndromes, venous blood from peripheral tissues may represent a direct vascular pathway for the spread of infections, emboli, and tumors in the brain Additional investigations are expected to increase and better define the knowledge of the damage caused by continuous passage of venous blood coming from superior vena cava tissues in the cerebrospinal venous circulation. In patients with superior vena cava stenosis, reaching a better understanding of each particular clinical pattern associated with each hemodynamic change in venous circulation might contribute deeply in defining the pathogenesis of different neurodegenerative syndromes [17-21].

References

1. Macchiarini P (2008) Superior vena cava obstruction. In: Patterson GA, Cooper JD, Deslauriers J, Lerut AEM, Luketic JD, Rive TW, editors. Pearson's thoracic & esophageal surgery. 3rd edition, Philadelphia, PA: Churchill Livingstone, Elsevier pp1684-96.
2. Francesco Puma, Jacopo Vannucci (2012) Superior Vena Cava Syndrome, "Topics in Thoracic Surgery", book edited by Paulo F. Guerreiro Cardoso, ISBN 978-953-51-0010-2.
3. McIntire FT, Sykes EM (1949) Obstruction of the superior vena cava: A review of the literature and report of two personal cases. Ann Intern Med 30: 92.
4. Pucheu A, Evans J, Thomas D et al. (1994) Doppler ultrasonography of normal neck veins. J Clin Ultrasound 22: 367-373
5. Jehuda J Steinbach, Add G Maftar, Dorsey T (1976) Mahin Alteration of the cerebral bloodflow study due to reflux in internal jugular veins. J Nucl Med 17: 61-410.
6. Lumsden AB, MacDonald MJ, Isiklar H, Martin LG, Kikeri D et al. (1997) Central venous stenosis in the hemodialysis patient: incidence and efficacy of endovascular treatment. Cardiovasc Surg 5: 504-509.
7. Matsuyama T, Okuchi K, Seki T, Higuchi T, Murao Y (2006) Perimesencephalic nonaneurysmal subarachnoid hemorrhage caused by physical exertion. Neurol Med Chir (Tokyo) 46: 277-282.
8. Nishijima H, Tomiyama M, Haga R, Ueno T, Miki Y et al. (2011) Venous cerebral infarction in a patient with peripheral hemodialysis shunt and occlusion of the left brachiocephalic vein. J Stroke Cerebrovasc Dis 20: 381-383.
9. Nedelmann M, Eicke BM, Dieterich M (2005) Functional and morphological criteria of internal jugular valve insufficiency as assessed by ultrasound. J Neuroimaging 15: 70-75.
10. Chung CP, Hsu HY, Chao AC et al. (2007) Detection of intracranial venous reflux in patients of transient global amnesia. cerebral venous outflow impairment—insight from the abnormal flow patterns of the internal jugular vein. Ultrasound Med Biol 33: 1727.
11. Zamboni P, Galeotti R, Menegatti E, Malagoni AM, Tacconi G et al (2009) Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 80: 392-399.
12. Batson OV (1940) The function of the vertebral veins and their role in the spread of metastases. Ann Surg 112: 138-149.
13. Anderson R. Diodrast studies of the vertebral and cranial venous systems to show their probable role in cerebral metastases. J Neurosurg. 1951; 8:411-422
14. Gisolf J, van Lieshout JJ, van Heusden K, Pott F, Stok WJ et al (2004) Human cerebral venous outflow pathway depends on posture and central venous pressure. Journal of physiology 560: 317-327.
15. S Spagnolo (2018) The role of chronic superior vena cava syndrome and stenosis of jugular veins in neurodegenerative diseases. Surgical treatment and preliminary result J Clin Exp Cardiolog 9: 12.
16. S Spagnolo Chronic superior vena cava syndrome: Cause of continuous passage of blood from the territory of venous system to the cerebrospinal venous circulation and possible cohorts for several neurodegenerative diseases. J Clin Exp Cardiolog 9: 36.
17. Hsu HY, Chao AC, Chen YY, et al. (2008) Reflux of jugular and retrobulbar venous flow in transient monocular blindness. Ann Neurol 63: 247-253.
18. Batson OV (1967) The vertebral system of veins as a means for cancer dissemination. Prog Clin Cancer 3: 1-18.
19. Epstein HM, Linde HW, Crampton AR, et al. (1970) The vertebral venous plexus as a major cerebral venous outflow tract. Anesthesiology 32: 332-337.
20. Chung CP, Hsu HY, Chao AC, et al. (2007) Flow volume in the jugular vein and related hemodynamics in the branches of the jugular vein. Ultrasound Med Biol 33: 500-505.
21. Harbour RC, Trobe JD, Ballinger WE (1984) Septic cav-

ernous sinus thrombosis associated with gingivitis and parapharyngeal abscess. Arch Ophthalmol 102: 94-97.