Case Report

Watershed cerebral infarction - A case report

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Abstract

Watershed cerebral infarctions, also known as border zone infarcts, occur at the border between two main cerebral arterial territories where the tissues are very far from arterial supply and vulnerable to reductions in perfusion. The reduction of perfusion in the distal regions of the arterial territories makes them vulnerable to infarction. Two types of Watershed cerebral infarctions are known: external (cortical) and internal (subcortical). Internal Watershed cerebral infarctions are caused by hypoperfusion, whereas external Watershed cerebral infarctions are caused by embolism and sometimes along with hypoperfusion. Different types of Watershed cerebral infarctions require different modalities of treatment and depend on their causative factors. Advanced imaging technologies like Diffusion-weighted MR imaging and transcranial Doppler US can detect watershed infarctions. We herewith present a case report that had cerebrovascular accident (CVA) -Water Shed Infarction – Internal Water Shed infarction (IWS) on left side in Posterior border zone between the left posterior cerebral artery (PCA) and left middle cerebral artery (MCA) territories, resulting in right hemiparesis with hypertension.

Key words

Watershed Cerebral Infarction, Right Hemiparesis.

Introduction

Watershed cerebral infarctions, also known as border zone infarcts, occur at the border between two neighboring main cerebral arterial territories where the tissues are vulnerable to reductions in perfusion as these areas are very distant from main artery. Watershed cerebral infarction accounts for 5-10% of all cerebral infarctions [1]. They occur usually in the elder age group, who has a higher incidence of arterial stenosis and hypotensive episodes, and also microemboli [2].

Pathophysiology

Border zone infarcts involve the junction of the distal fields of two non-anastomosing cerebral arterial systems [3]. The commonly accepted hypothesis holds that decreased perfusion in the distal regions of the vascular territories leaves them vulnerable to infarction. Internal (subcortical) border zone infarcts are caused mainly by hemodynamic compromise. External (cortical) border zone infarcts are believed to be caused by embolism, sometimes with associated hypoperfusion. Watershed infarctions usually occur with episodes of systemic hypotension alone or along with severe stenosis or occlusion of the main feeding cerebral arteries, particularly the intracranial and extracranial carotid arteries. Microemboli are formed on the surface of inflamed atherosclerotic plaques. These microemboli cause an embolic shower in periphery of feeding main arteries. Clearance of these emboli is impaired in watershed zones due to poorer perfusion or hypotension. It has been proposed that both episodes of hypoperfusion and microemboli from inflamed atherosclerotic plaques play a role in pathophysiology of water shed infarctions, although the latter is less well established. A watershed zone infarct in an isolated area is more likely to be secondary to microembolism, particularly in the absence of systemic hypotension and/or arterial stenosis. In severe carotid stenosis, lesions are on same side as the stenosis. Prolonged hypotension, as in cardiac surgery or cardiac arrest, usually results in a bilateral pattern even in the absence of severe stenosis.

The conventional theory implicates the hemodynamic compromise caused by episodes of hypotension in presence of severe arterial stenosis or occlusion. In such setting the low perfusion pressure within the border zone areas, leads to an increased susceptibility to ischemia and infarction [4, 5]. The typical clinical manifestations of syncope, hypotension, and episodic fluctuating or progressive weakness of the limbs are also support the theory of hemodynamic compromise [6, 7].

Radiologic studies also support the hypothesis that border zone infarcts distal to internal carotid artery disease are more likely to occur in the presence of a non-competent circle of Willis. In sharp contrast with this interpretation, several pathologic investigators have emphasized an association between border zone infarction and microemboli, and embolic material has been found within areas of border zone infarction in autopsy series [8]. Border zone infarctions are better explained by the combination of two often interrelated processes: hypoperfusion and embolization [9].

Hypoperfusion, or decreased blood flow, is likely to impede the clearance of emboli. Because perfusion is most likely to be impaired in border zone regions, clearance of emboli will also be impaired in these regions. Severe occlusive disease of the internal carotid artery causes both embolization and decreased perfusion. Similarly, heart diseases are often associated with microembolization from the heart and aorta with periods of diminished systemic and brain perfusion [2]. In their study Ramez R. Moustafa, et al. [10], provides direct evidence that in symptomatic internal carotid artery disease, watershed infarcts may result from hemodynamic impairment through severe lumen stenosis, but also from microemboli alone through plaque inflammation (**Figure - 1**).

Types of watershed infarctions

Two types of border zone infarcts are recognized: external (cortical) and internal (subcortical). Various terms for these lesions have been used in the literature, with the most common summarized in the **Table - 1**. Infarcts of the lenticulostriate–middle cerebral artery border zone, are the most commonly seen [2].

The various watershed infarctions both internal and external and their probable locations of external (blue) and internal (red) border zone infarcts are well described in schematic, axial T2-weighted magnetic resonance (MR) images of normal cerebrum as shown in **Figure - 2**.

Figure – 1: Pathophysiological flow chart for the origin of water shed (WS) infarction in symptomatic 50% to 99% carotid stenosis based on the findings from the present investigation [10].

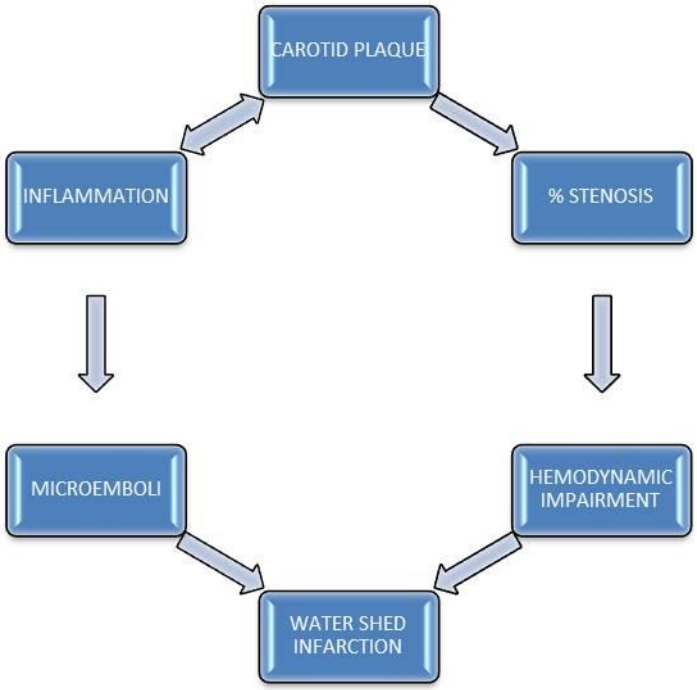


Table – 1: Classification of Border Zone Infarcts [2].

External (cortical) infarcts
Frontal cortex (between the anterior and middle cerebral arteries)
Occipital cortex (between the middle and posterior cerebral arteries)
Paramedian white matter (between the anterior and middle cerebral arteries)
Internal (subcortical) infarcts
Between the lenticulostriate and middle cerebral arteries*
Between the lenticulostriate and anterior cerebral arteries
Between the Heubner and anterior cerebral arteries
Between the anterior choroidal and middle cerebral arteries
Between the anterior choroidal and posterior cerebral arteries

Clinical Course

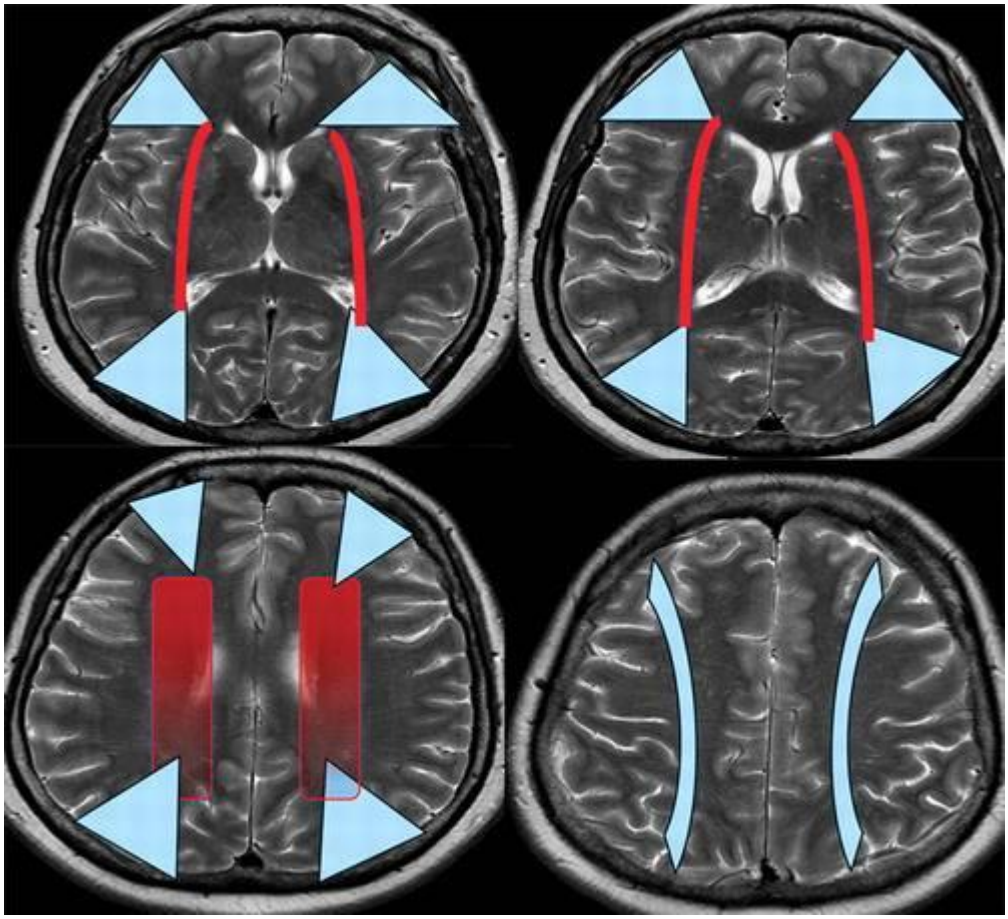
External border zone infarcts usually follow a benign clinical course, whereas internal border zone infarcts are associated with higher morbidity and a higher risk for future stroke in its clinical course [11, 12].

Imaging studies

Various imaging modalities have been used to determine the presence and extent of hemodynamic compromise or misery perfusion in association with border zone infarcts, and some findings (e.g., multiple small internal infarcts) have proved to be independent

predictors of subsequent ischemic stroke. A combination of several advanced techniques (e.g., diffusion and perfusion magnetic resonance imaging and computed tomography, positron emission tomography, transcranial Doppler ultrasonography) can be useful for identifying the pathophysiologic process, making an early clinical diagnosis, guiding management, and predicting the outcome [2].

Figure – 2: Color overlays on axial T2-weighted magnetic resonance (MR) images of normal cerebrum show probable locations of external (blue) and internal (red) border zone infarcts [2].



The exact pattern depends on the bordering territories, which are usually variable in different individuals. Imaging of watershed infarction should also aim to determine the presence and severity of arterial stenosis and occlusion. The external, cortical border zones are located between the anterior, middle, and posterior cerebral arteries and are usually wedge-shaped or ovoid. Internal border zone infarcts appear in multiples, in a rosary like pattern. Diffusion-weighted MR imaging has the advantage of enabling differentiation of acute stroke from chronic stroke in patients with border zone infarcts. It is more sensitive than standard MR imaging techniques and can better depict the location of border zone infarcts in relation to the vessel [2].

Therapeutic approach

Different therapeutic approaches may be required to prevent early clinical deterioration in patients with different types of border zone infarcts like I V fluids, vasopressors for hypotension, and hypoperfusion, low dose aspirin and statins for thromboembolic phenomenon and atherosclerotic plaque with embolic shower [2].

Case report

84 years old male patient, admitted for right sided limbs weakness of 2 days duration. Patient

was apparently asymptomatic a day earlier, then he developed weakness of right sided limbs which was gradual in onset, No history of head injury, no history of syncope or loss of consciousness, no history of loss of sensations, No history of seizure like activity, No history suggestive of any cranial nerve palsy. Past history - Patient had ischemic stroke 4 years ago with left hemiparesis from which he recovered completely. He was a known hypertensive on irregular medications. He discontinued the treatment like anti-platelets and anti-hypertensives since 3 months. No history of NIDDM, TB, Epilepsy, Thyroid disorders. He was a smoker and alcoholic since 20 years.

General Examination

Patient was conscious, coherent, answering questions well, moderately built, moderately nourished, no icterus, cyanosis, clubbing, koilonychia, lymphadenopathy, pedal edema, no neurocutaneous markers, no peripheral nerve thickening, no trophic ulcers, head and spine was normal, no tenderness, thyroid was normal.

Vitals

Temp – Normal, PR =78/min, regular, BP = 200/120 mm of Hg, RR=18/min.

CNS examination

Intellectual functions were normal, All cranial nerves were normal, Motor system examination left sided limbs were normal. Right sided limbs-revealed, Bulk- normal, Power – 2/5, Tone – hypotonia, superficial reflexes were normal, corneal and conjunctival were normal, abdominalis was present, left plantar showed flexor response, the right plantar showed extensor response, deep tendon reflexes were exaggerated on right side and were normal on left side. Sensory system: pain, temperature - normal in all limbs, pressure, vibration, joint sensations normal in all the limbs. There were no cerebellar signs on left side, on right side could not be tested as power was 2/5, there were no signs of meningeal irritation, skull and spine was normal. Gait could not be seen as patient is not able to stand because of right hemiparesis (power – 2/5). Examination of Cardio Vascular System and Respiratory Systems were normal.

Investigations - CBP – Hb-12 gm%, TLC-9000, Plt-2,50,000, N- 73, L- 25, B-0, E-2, M-0, ESR: 06 mm, Bleeding Time- 4 mts,Clotting Time- 6 mts, Prothrombin Time- 12 seconds, CUE – Urine Albumin - Nil, Sugar – Nil, HIV – Non reactive, HbsAg – Negative, HBC – Negative, Lipid Profile – NAD, Bl Sugar – 114 mg/dl, Bl Urea – 24 mg/dl, S. Creatinine – 0.6 mg/dl, S. Electrolytes – Serum sodium-128 mmol/L, serum potassium 6.9 mmol/L, LFT- Normal, X Ray Chest PA View – NAD, ECG – LVH, 2D ECHO – Normal Study, USG abdomen – NAD, CT Scan shows chronic infarcts in right capsuloganglionic region and corona radiata, and chronic lacunar infarcts in right thalamus. Small vessel ischemic changes and age related cerebral atrophic changes were seen (**Figure - 3**), MRI axial T1, T2, DW, Flair and GRE Coronal - T2, Sagittal - T2, TOF Angio (**Figure - 4, 5, 6, 7, 8, 9**) - Shows acute infarcts in the left periventricular white matter, occipital lobe, corona radiata and centrum semi ovale. Chronic infarcts with cystic encephalomalacia and peripheral gliosis in right corona radiata with ex vacuo dilatation of the right ventricle. Discrete to early confluent small vessel ischemic lesions in bilateral periventricular white matter, corona radiata and centrum semiovale. MR Angiogram of intracranial arteries show severe narrowing of the P1 segment of left PCA with occlusion of the petrous segment, irregular moderate narrowing of M2 segment of the left middle cerebral artery with paucity of cortical branches of bilateral middle cerebral arteries. Carotid duplex ultrasound examination was normal on both sides.

Figure - 4, 5, 6, 7, 8, 9 shows acute infarcts in the left periventricular white matter, occipital lobe, corona radiata (CR) and centrum semi ovale (CSO), Chronic infarcts with cystic encephalomalacia and peripheral gliosis in right corona radiata with ex vacuo dilatation of the right ventricle, Discrete to early confluent small vessel ischemic lesions in bilateral

periventricular white matter, corona radiata and centrum semiovale. MR Angiogram of intracranial arteries show severe narrowing of the P1 segment of left PCA with occlusion of the petrous segment, irregular moderate narrowing of M2 segment of the left middle cerebral artery with paucity of cortical branches of bilateral middle cerebral arteries.

Figure – 3: CT Scan shows chronic infarcts in right capsulo ganglionic region and carona radiata, and chronic lacunar infarcts in right thalamus. Small vessel ischemic changes and age related cerebral atrophic changes are seen.

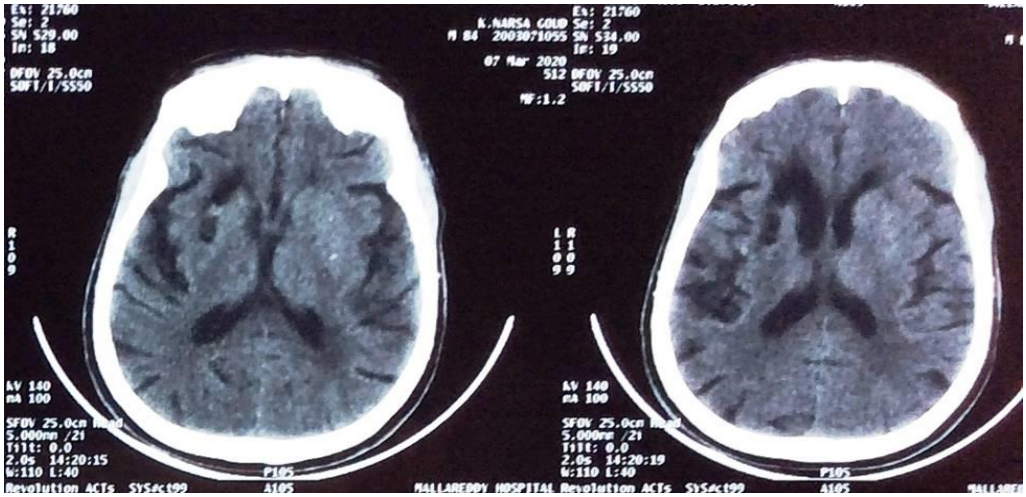


Figure – 4: MRI Axial T1.

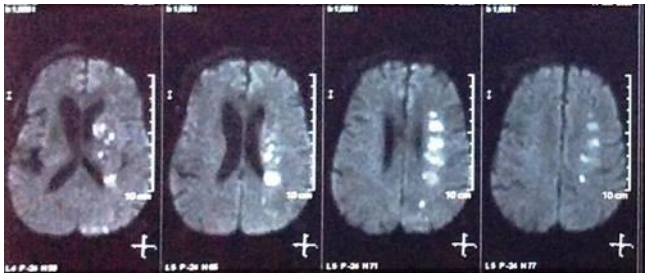


Figure – 5: MRI Axial T2.

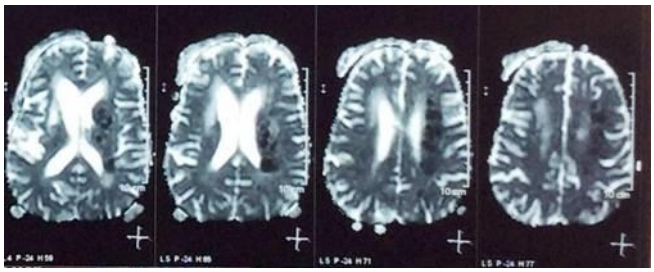


Figure – 6: MRI Axial DW.

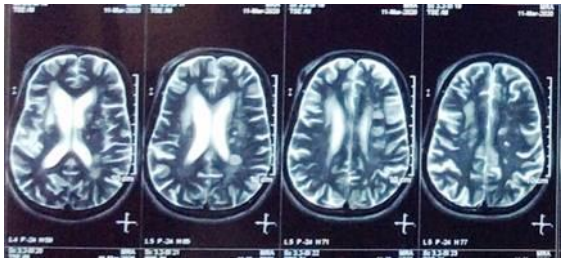


Figure – 7: MRI Axial Flair.

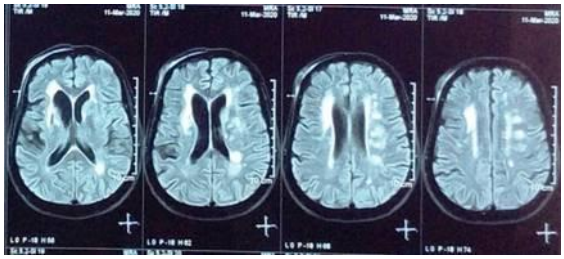
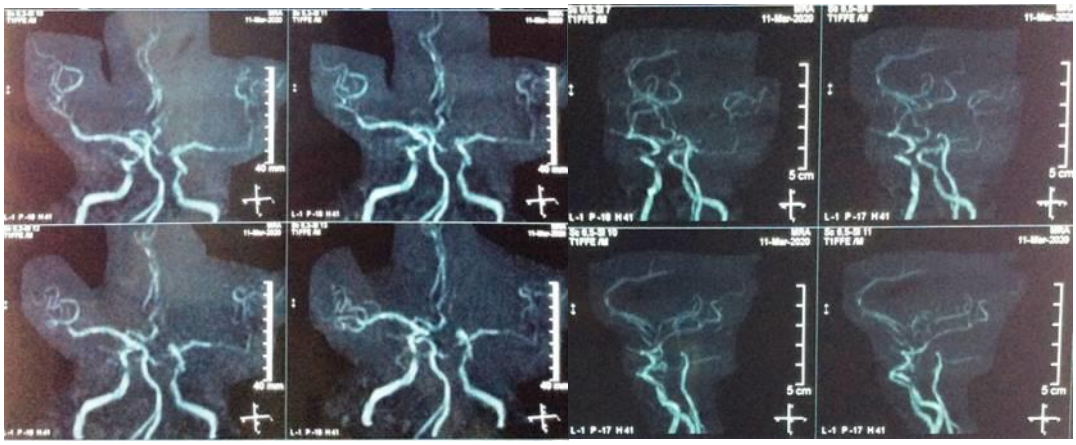


Figure – 8, 9: MRI Coronal - T2, Sagittal - T2, TOF Angio.



Diagnosis

CVA -Water Shed Infarction – Internal Water Shed infarction (IWS) on left side in Posterior watershed zone between the left PCA and left MCA territories, resulting in right hemiparesis + Hypertension

Treatment given

Tab. Ecosprin 75 mg OD
Tab. Nicardia Retard 10 mg 1 TID
Inj. Optineuron 1amp IV daily
Physiotheraphy
Patient improved completely within a month.

Discussion

Shinichi Nakano, et al. [13] studied the frequency of the different location patterns of large subcortical infarcts. In their study, the combination of striatocapsular and corona radiata infarcts was the most frequent pattern (14 of 38 (36.8%)), which usually was associated with middle cerebral artery (MCA) occlusive diseases occluding the orifices of all lenticulostriate arteries. Ten of 16 (62.5%), patients with MCA occlusive disease produced this combination pattern of infarct. On the contrary, it was not common for internal carotid artery (ICA) occlusive diseases to produce this combination pattern of infarct (4 of 22(18.2%)) [13].

It has been shown that periventricular white matter of the corona radiata is the watershed zone between the deep and superficial territories of the MCA and that supraventricular white matter of the centrum semiovale is the watershed zone between the superficial territories of the anterior cerebral artery (ACA) and MCA. White matter infarcts in these two regions were usually induced in patients with ICA or MCA occlusive disease and together called “terminal supply area infarcts” or “subcortical watershed infarcts [13].

Post-cardiac surgery watershed infarctions

Watershed-distribution strokes were seen more frequently in patients with post-cardiac surgery stroke than in the general stroke population. Patients with watershed infarcts by CT required long-term care than other post-cardiac surgery stroke patients. The mechanism underlying post-cardiac surgery watershed stroke probably involves a combination of hypoperfusion and

embolization, but the role of hypoperfusion is not well elucidated. Watershed strokes in the general population are usually secondary to global hypoperfusion, such as during cardiac arrest, or are attributable to stenosis of the carotid artery or other major vessels, leading to local hypoperfusion. Most of the patients with watershed strokes had favorable outcomes [14].

In autopsy studies, CWS and IWS infarcts also termed external and internal border-zone infarcts, respectively—together represent 10% of all brain infarcts [1]. Imaging studies in severe internal carotid artery (ICA) disease report an incidence ranging from 19% to 64%. This is probably an underestimate, as WS infarction is seldom fatal, [6, 15, 16]. Although the pathological [17, 18] and imaging characteristics [6, 19, 20] of WS infarcts are well-described, their pathogenesis is much debated. It is well-established fact that severe systemic hypotension can cause bilateral WS infarction, [5, 18], and hemodynamic failure is said to cause WS infarcts in ICA disease [15, 19, 20]. Susceptibility of the WS areas, result from their situation in "distal field" where perfusion pressure is the lowest, [21] and repeated episodes of hypotension in the presence of severe ICA disease, facilitates WS infarcts. The occasional occurrence of syncope at onset of WS stroke, [4, 22] and the typical clinical presentation of episodic, fluctuating, or progressive weakness of the hand, occasionally associated with upper limb shaking, are consistent with hemodynamic failure [6, 7, 23].

This interpretation is supported by radiological studies showing that WS infarcts distal to ICA disease are more likely with a non-competent circle of Willis. In contrast, embolism from ICA disease preferentially affects the stem and large branches of the MCA, producing cortical "wedge-shaped" and/or deep striato-capsular infarcts [24, 25, 26]. Several pathological studies suggest, the association of WS infarction with microemboli arising from unstable carotid plaques or from the stump of an occluded ICA [1]. Most of the occlusions seen in the leptomeningeal arteries over WS infarcts distal to ICA occlusion are due to microemboli occluding the terminal vascular field, and not due to slowing of the cerebral blood flow (CBF). Most importantly, there is experimental evidence that small thrombi travel preferentially to WS areas because of their distinctly small size [27]. Interestingly, cerebral amyloid angiopathy has recently been proposed as a risk factor for microinfarcts in the CWS areas [28].

Anatomy, Structural Imaging, and Angiography

The CWS regions are boundary zones where functional anastomoses between the two arterial systems exist, i.e., on the pial surface between the major cerebral arteries [29]. CWS infarcts represent the most familiar WS strokes. Anterior WS infarcts develop between the ACA and MCA territories, either or both as a thin fronto-parasagittal wedge extending from the anterior horn of the lateral ventricle to the frontal cortex, or superiorly as a linear strip on the superior convexity close to the interhemispheric fissure, whereas posterior WS infarcts develop between the ACA, MCA, and PCA territories and affect a parieto-temporooccipital wedge extending from the occipital horn of the lateral ventricle to the parieto-occipital cortex [30].

IWS infarcts can affect the corona radiata (CR), between the territories of supply of the deep and superficial (or medullary) perforators of the MCA, or the centrum semiovale (CSO), between the superficial perforators of the ACA and MCA. On the basis of their radiological appearance, IWS infarcts have been divided into confluent and partial infarcts [7].

Confluent infarcts correspond to large cigar-shaped infarcts alongside the lateral ventricle, whereas partial IWS infarcts may appear either as a single lesion or in a chain-like (or "rosary-like") pattern in the CSO. The absence of collateral blood flow via the anterior communicating (ACoA) and the posterior communicating artery has been associated with WS infarcts (both CWS and IWS) [26, 31]. Based on the anatomic study of Moody, et al.,

[32] Krapf [12] proposed that in patients with impaired hemodynamics, the rosary-like pattern may result from brief declines in blood pressure, whereas the confluent pattern may be caused by longer-lasting impairments of the cerebral perfusion. According to this hypothesis, rosary-like infarcts may be considered precursors to a more profound event. The current view is that hypoperfusion and artery-to-artery embolism coexists to explain WS stroke in patients with ICA disease [3, 9, 33].

Diagnosis may be difficult, and is done after excluding a possible embolic source. One should suspect the diagnosis on the basis of one or more of the following: documented episode of hypotension, a history of syncope or near syncope preceding the event, characteristic patterns of infarction on computed tomography (CT) or magnetic resonance imaging, or the presence of carotid occlusive disease [4, 6, 7, 15, 34, 35, 36, 37]. Shuaib and Hachinski [38] found watershed infarction to be more common in the elderly, largely due to hemodynamic disturbances e.g. postural hypotension, cardiac arrhythmias, and overzealous use of antihypertensive drugs. Orthostatic hypotension occurs in 14% to 33% of persons older than 60 years, with the degree of postural fall varying with activity, hydration, and timing of meals and medication." It has been identified as a significant risk factor for stroke in a number of prospective population based studies [39, 40, 41].

Watershed infarction is not adequately explained by embolic phenomena. Ringelstein, et al. [15] used TCD and angiography to examine 44 patients with carotid occlusion and watershed infarction and failed to reveal any evidence of secondary emboli to explain the CT findings; furthermore, no cases of watershed infarction were found among 60 consecutive cases of proven cardioembolic stroke [42]. Hemodynamic dysfunction was therefore proposed as the principal cause of this form of stroke. This is further supported by recent serial magnetic resonance imaging studies that show the development of "low-flow" strokes in fully anticoagulated patients undergoing therapeutic occlusion of the ICA [43]. Other studies have shown that patients with carotid occlusion and watershed infarction frequently have syncope or near syncope at stroke onset [6, 15, 19]. Watershed infarction occurred most frequently in the corona radiata (or centrum semiovale) [44] and has been described in up to 40% of patients with symptomatic carotid artery disease [15, 35, 37, 45].

Positron emission tomography and single-photon emission computed tomography studies have demonstrated that these white matter infarcts have reduced regional cerebral blood flow, reduced perfusion reserve (regional cerebral blood flow/regional cerebral blood volume), and an elevated regional oxygen extraction fraction, indicative of a hemodynamic origin [46, 47]. These blood flow imaging techniques may help in the differentiation between watershed infarction and deep lacunes (in the basal ganglia/ internal capsule) or striatocapsular infarcts [48], which have a different pathogenesis and outcome and preserved cerebral perfusion reserve [37, 49]. Infarction of cerebral watershed areas, the junction between territories of supply of major cerebral arteries, is generally attributed to hemodynamic mechanisms [6, 15, 19].

Prolonged severe hypotension after cardiac arrest sometimes causes bilateral watershed infarction, but unilateral lesions are more common and often occur in association with severe carotid disease. The extent of infarction depends on the severity and duration of hypoperfusion, the location and severity of occlusive vascular disease, and the adequacy of collateral blood supply. Involvement of cortical border-zone regions is the most familiar form of watershed infarction. However, watershed infarction may also occur in internal border zone regions between medullary arteries arising from the superficial pial plexus and deep penetrating arteries arising from the basal cerebral arteries [50]. These lesions lie in the corona radiata and centrum semiovale adjacent to the lateral ventricles [7].

Conclusion

In the beginning the diagnosis was difficult as the CT scan was inconclusive, but patient had dense hemiparesis. We went for further investigations like MRI and carotid duplex ultrasound and we made a diagnosis of CVA - Water Shed Infarction – Internal Water Shed infarction (IWS) on left side in Posterior watershed zone between the left PCA and left MCA territories, resulting in right hemiparesis + Hypertension. Interestingly it was posterior border zone - water shed infarction which is very unusual.

In this case there was no ICA pathology, hence, there was no occlusive ICA thrombosis and there was no thromboembolic episode. He did not have any cardiac disease to think of any valvular or coronary heart disease and also he did not undergo any surgery including cardiac surgery, to think of any microemboli. Patient was hypertensive; hence, the question of hypoperfusion does not arise. But, Noncompliance and irregular in taking treatment of HTN, and frequent change of anti-hypertensive drugs, might have caused hypoperfusion at some point of time.

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