WATERSHED STROKES

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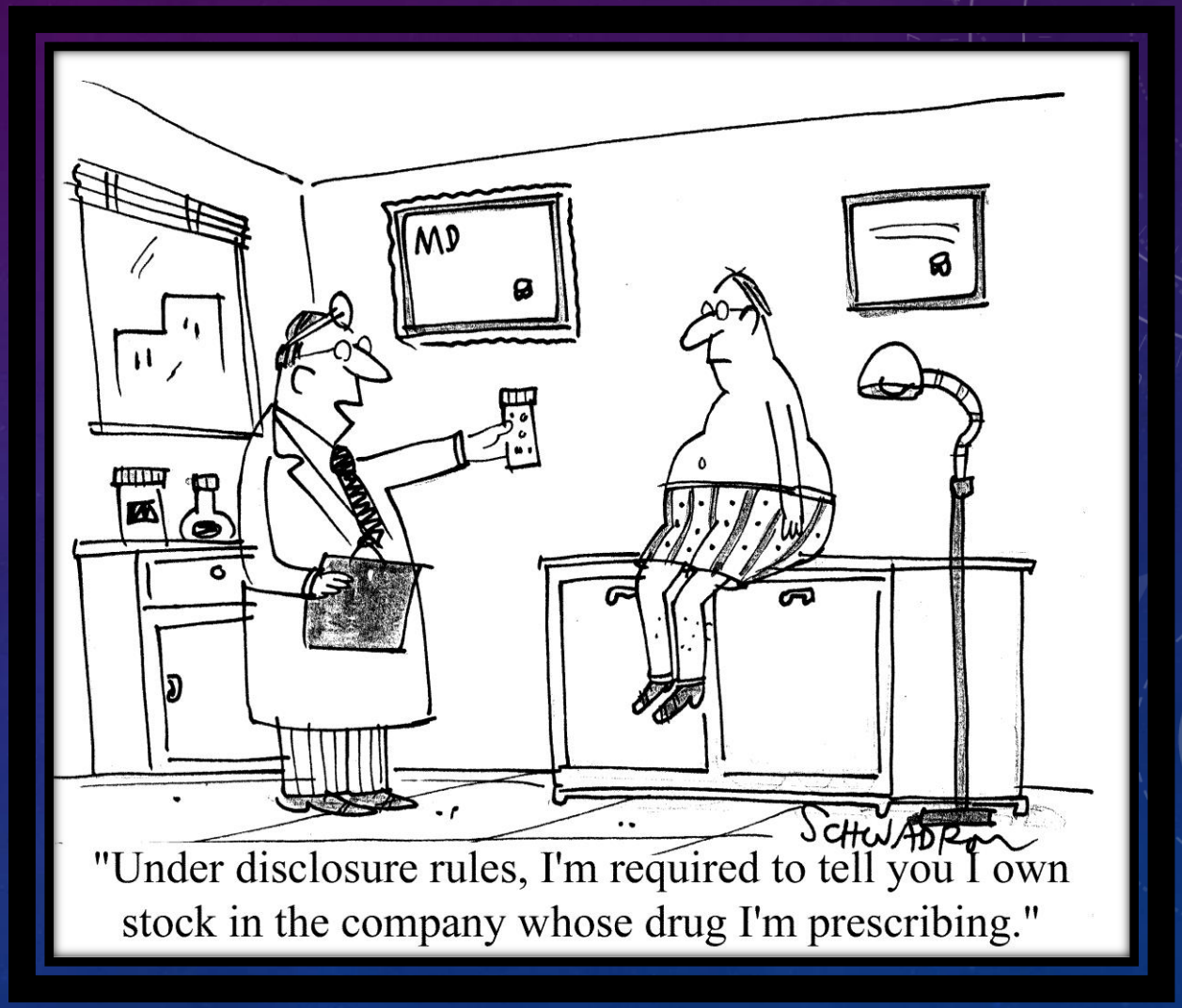
- I have no disclosures



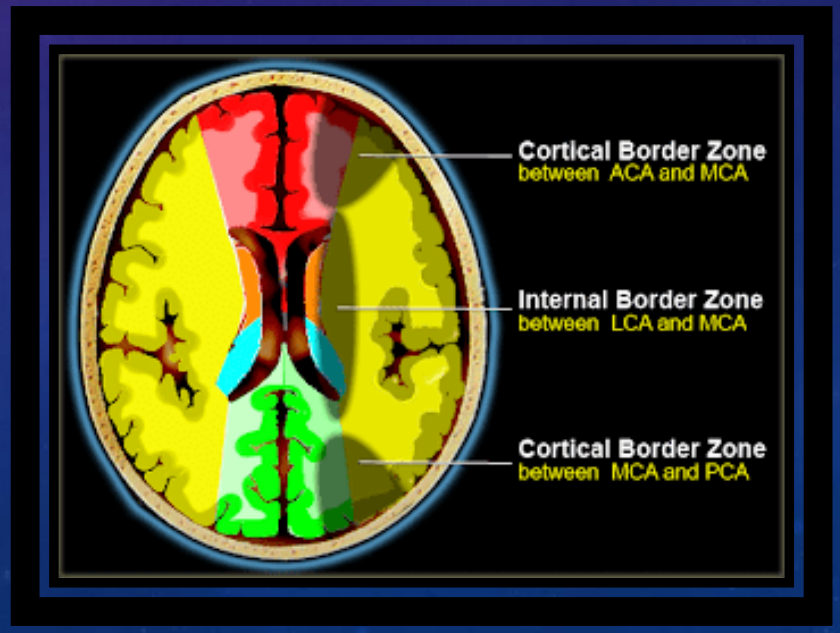
BORDER ZONE OR WATERSHED INFARCTS ARE ISCHEMIC LESIONS THAT OCCUR IN CHARACTERISTIC LOCATIONS AT THE JUNCTION BETWEEN TWO MAIN ARTERIAL TERRITORIES. THEY COMPRISE APPROXIMATELY 10% OF ALL ISCHEMIC STROKES

Internal Border Zone Infarcts

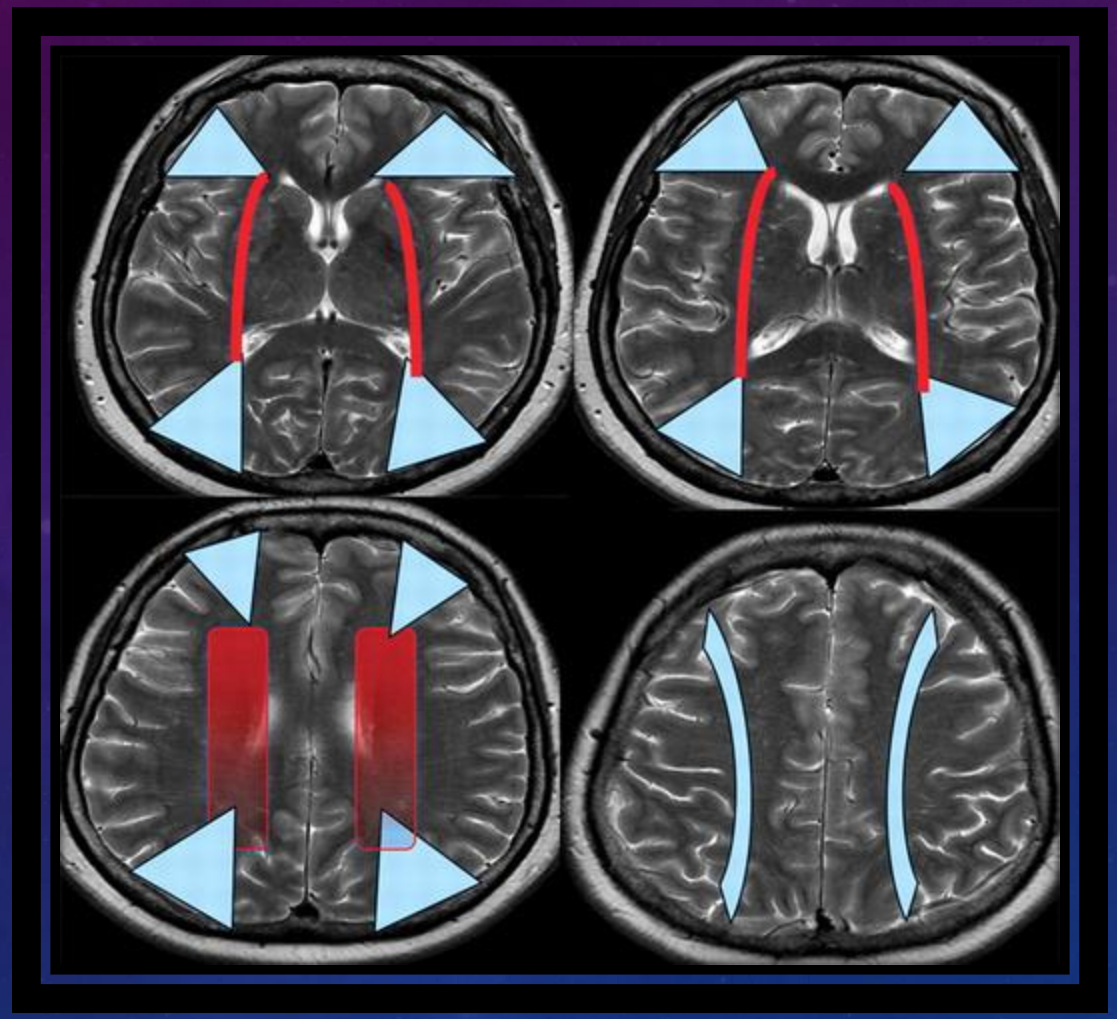
- The internal or subcortical border zones are located at the junctions of the anterior, middle and posterior cerebral artery territories with the Recurrent Artery of Heubner, lenticulostriate and anterior choroidal artery territories

External Border Zone Infarcts

- The external or cortical border zones are located at the junctions of the anterior, middle and posterior cerebral artery territories

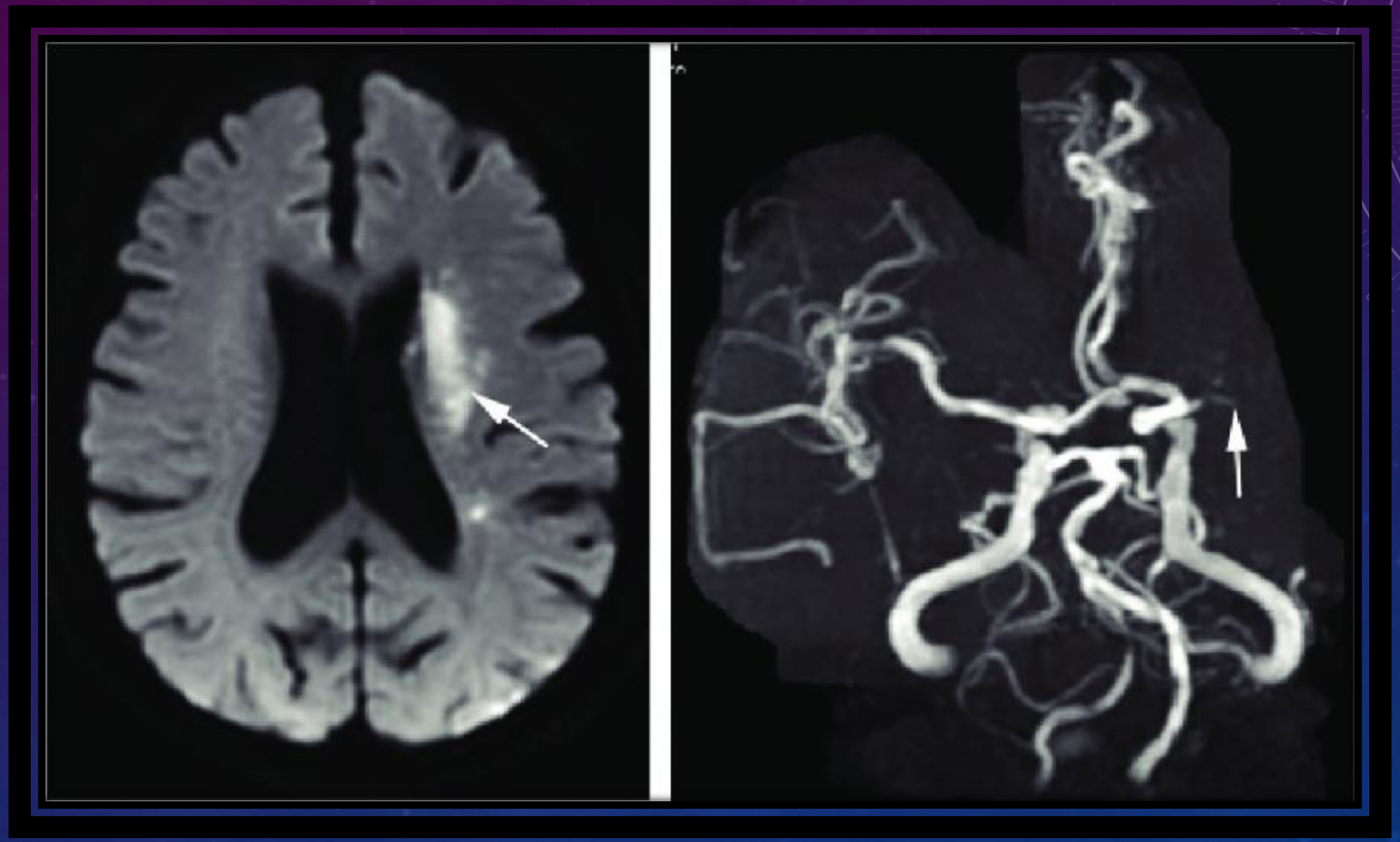


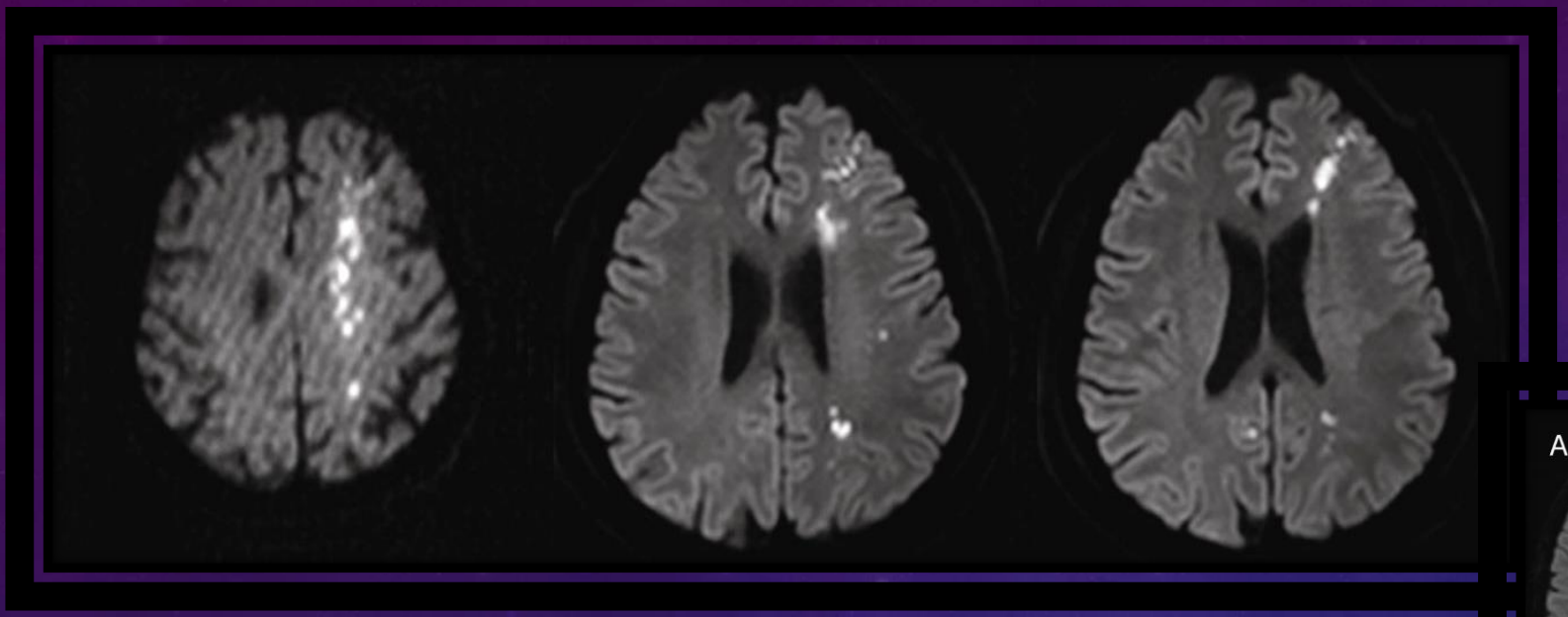
External border zones—light blue
Internal border zones—red

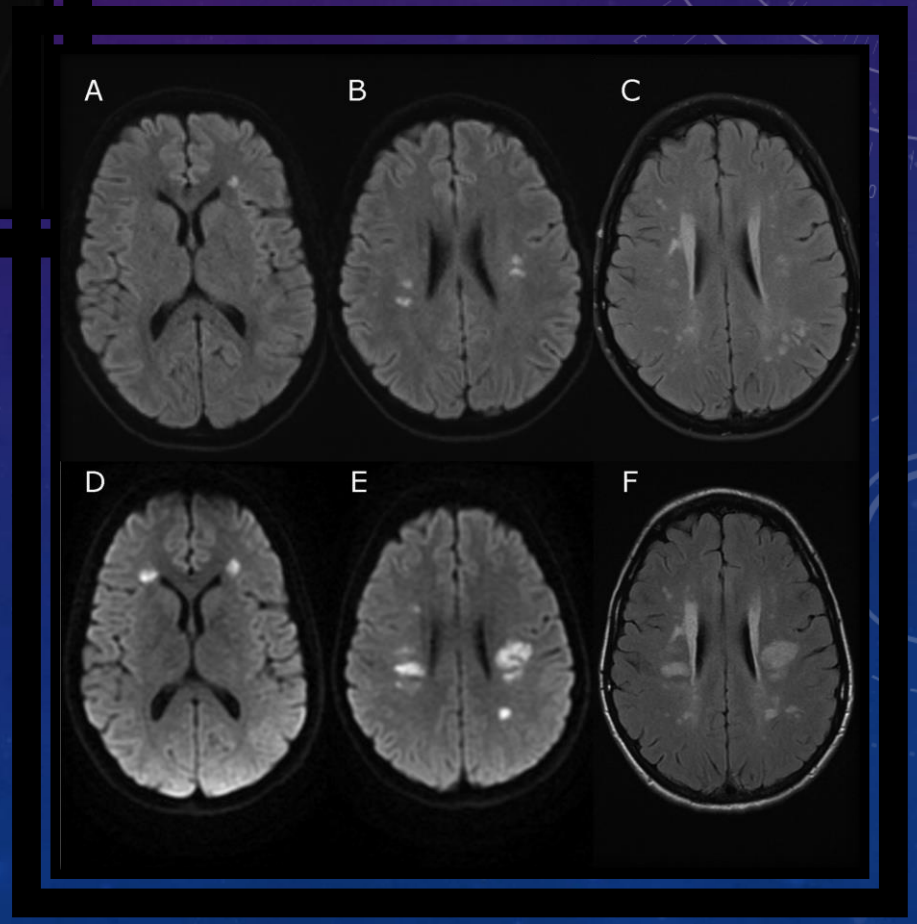


INTERNAL BORDER ZONE INFARCTS

- Often manifests as a series of 3 or more lesions, each with a diameter of 3 mm or more, arranged in a linear fashion parallel to the lateral ventricle in the centrum semiovale or corona radiata (rosary/bead)
- Can be confluent or partial; perhaps a briefer episode of hemodynamic compromise leads to a partial infarct, while a confluent infarct may be manifested by step-wise hemiplegia related to a longer period of hemodynamic compromise
- Caused mainly by arterial stenosis or occlusion, usually paired with hemodynamic compromise
- Thought to be much less likely than external border zone infarcts to be secondary to emboli
- Often associated with a more poor prognosis and clinical deterioration when compared with external border zone infarcts



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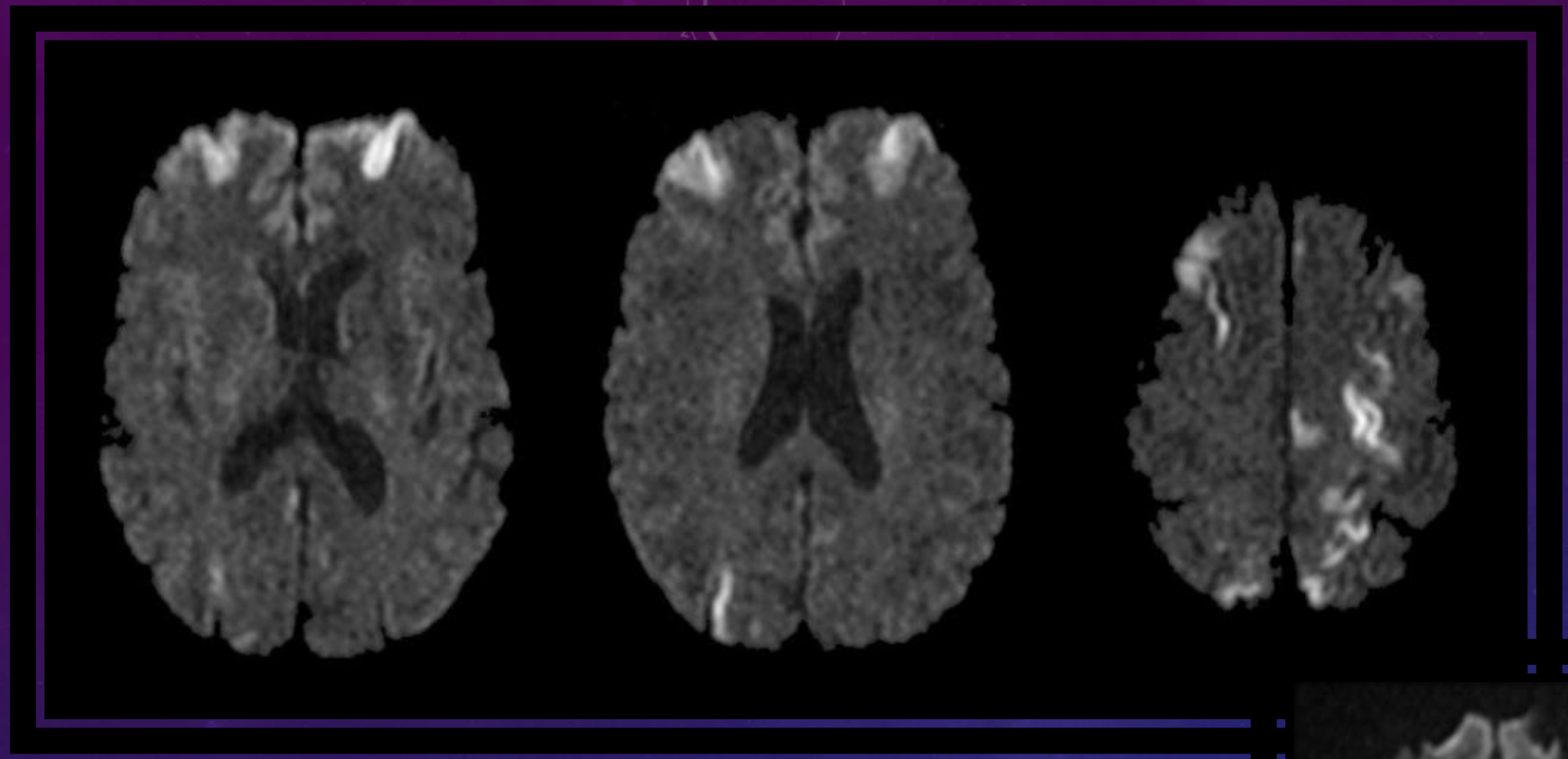
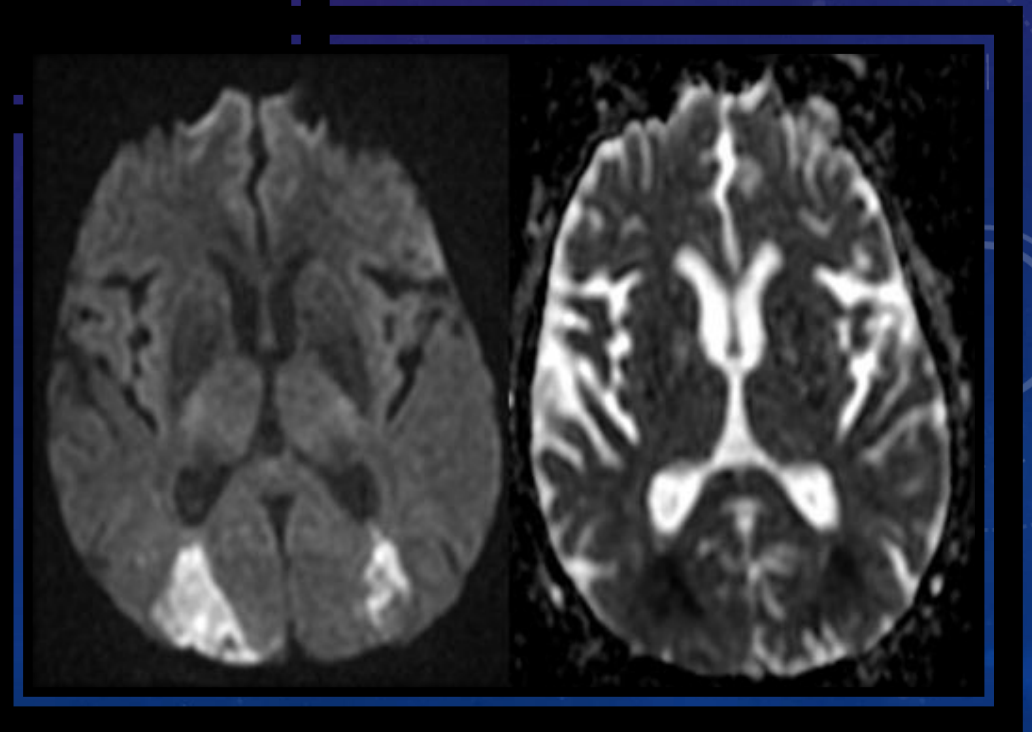
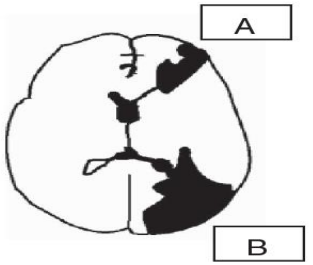
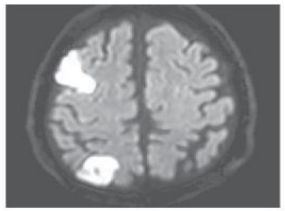
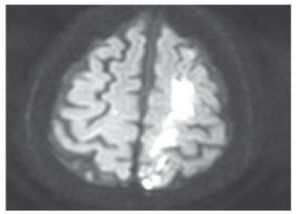
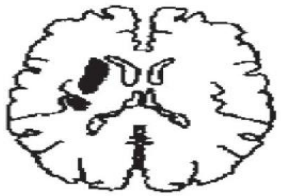
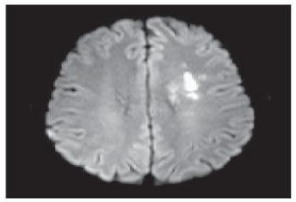
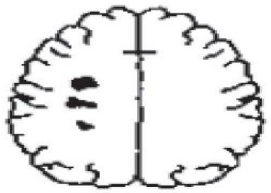
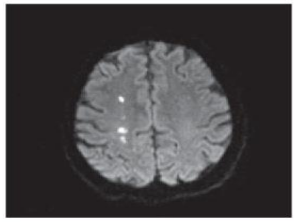
EXTERNAL BORDER ZONE INFARCT

- Typically wedge shaped or ovoid shaped, size is variable because of anatomic variation and minimal/maximal distribution of each of the large vessel territories (MCA, ACA, PCA) from person to person
- Also may vary secondary to the development of leptomeningeal collateral vessels
- Often caused by hemodynamic compromise and may pair with moderate or severe narrowing of the carotid or proximal cerebral arteries
- As opposed to internal border zone infarcts, microemboli from the heart or atheroembolic events can propagate to the cortical border zones; these areas have a lower perfusion than more proximal regions, so less ability to “wash out” the microemboli
    - Recent intraplaque hemorrhage/plaque rupture may play a role
- Patients often have a more benign clinical course and better prognosis than those with internal border zone infarcts, especially if unilateral or only in one border zone

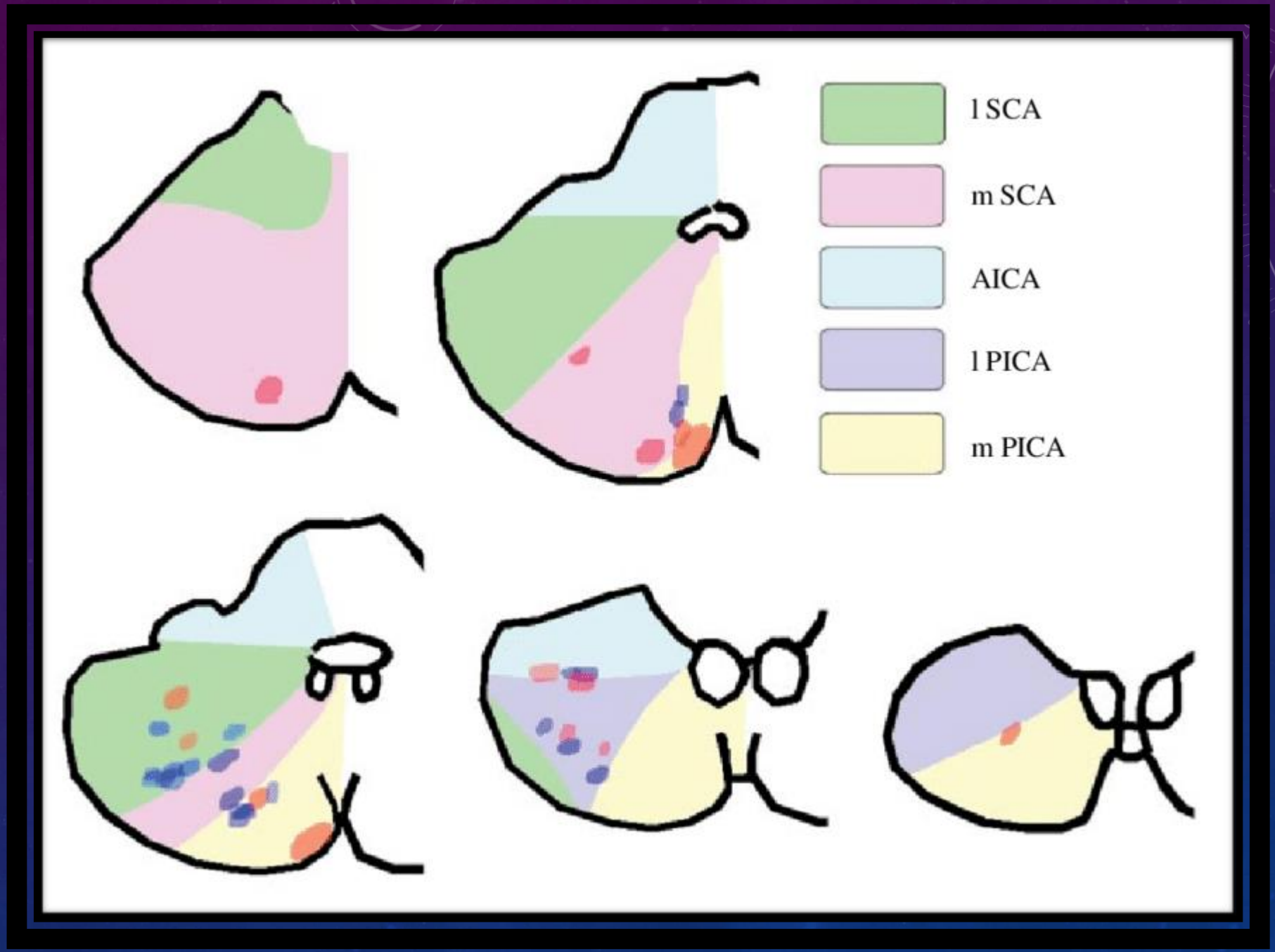




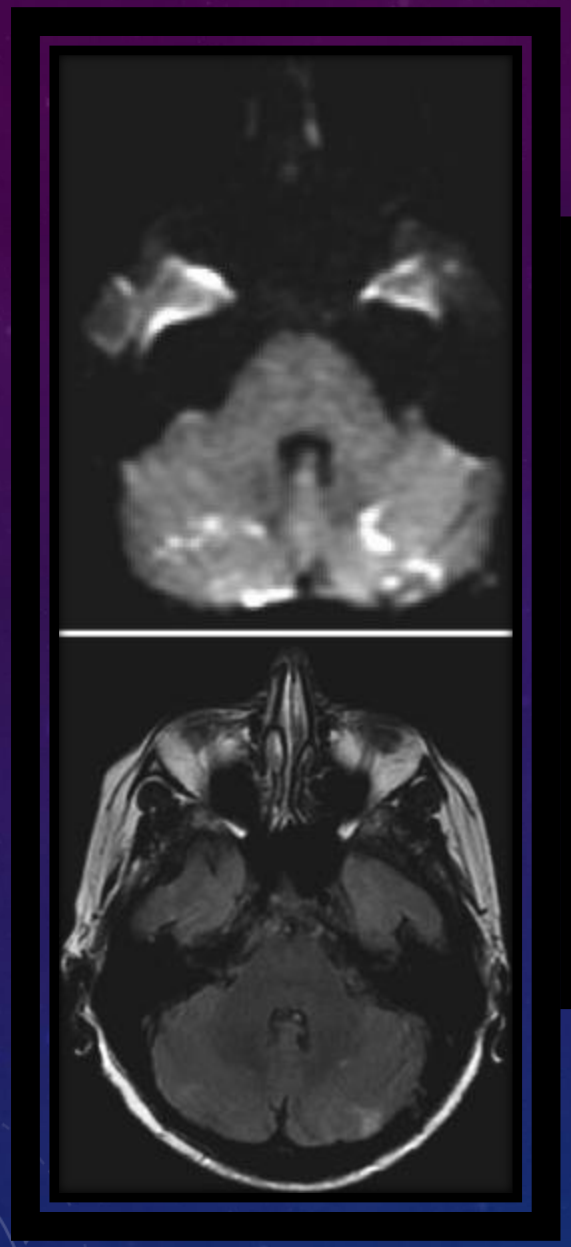
Pattern	Type of Lesion	Borderzone Location	Example	Example on MRI
4	***Cortical borderzone infarcts	Junctions between the cortical frontal, *ACA and MCA (A) or cortical occipital, MCA and **PCA		
		(B) Paramedian borderzone infarct located between the MCA and the *ACA		
5	****Internal borderzone infarct	Infarct at the junction between the deep and the superficial arterial system of the MCA, a confluent pattern		
		Infarct at the junction between the arterial system of the *ACA and MCA, a typical rosary-like pattern		

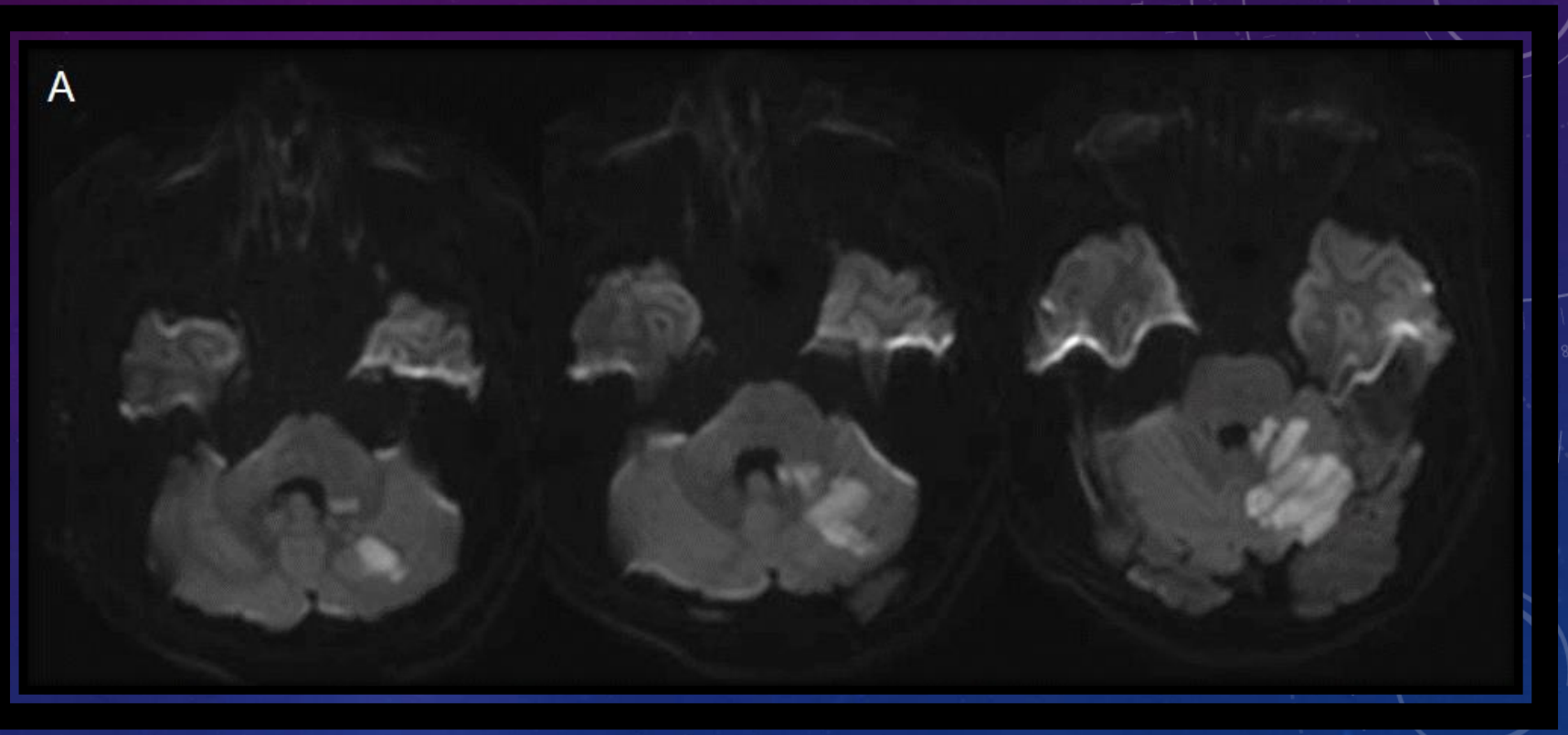
BORDER ZONE INFARCTS IN THE CEREBELLUM

- These are usually < 2 cm in size and are seen at the borders of the AICA, SCA and PICA (and their branches)
- Due to stenosis or embolism. Embolic events can come from the heart or atherosclerotic disease
- May be see with vertebral dissections
- Typically not disabling in an of themselves, but often coexist with large territorial lesions
- They can be silent if small, or similar in presentation to larger cerebellar infarcts, with vertigo and ataxia


l SCA
m SCA
AICA
l PICA
m PICA

Red is AICA
Dark Green is lateral SCA
Light Green is medial SCA
Dark Blue is lateral PICA
Light Blue is medial PICA

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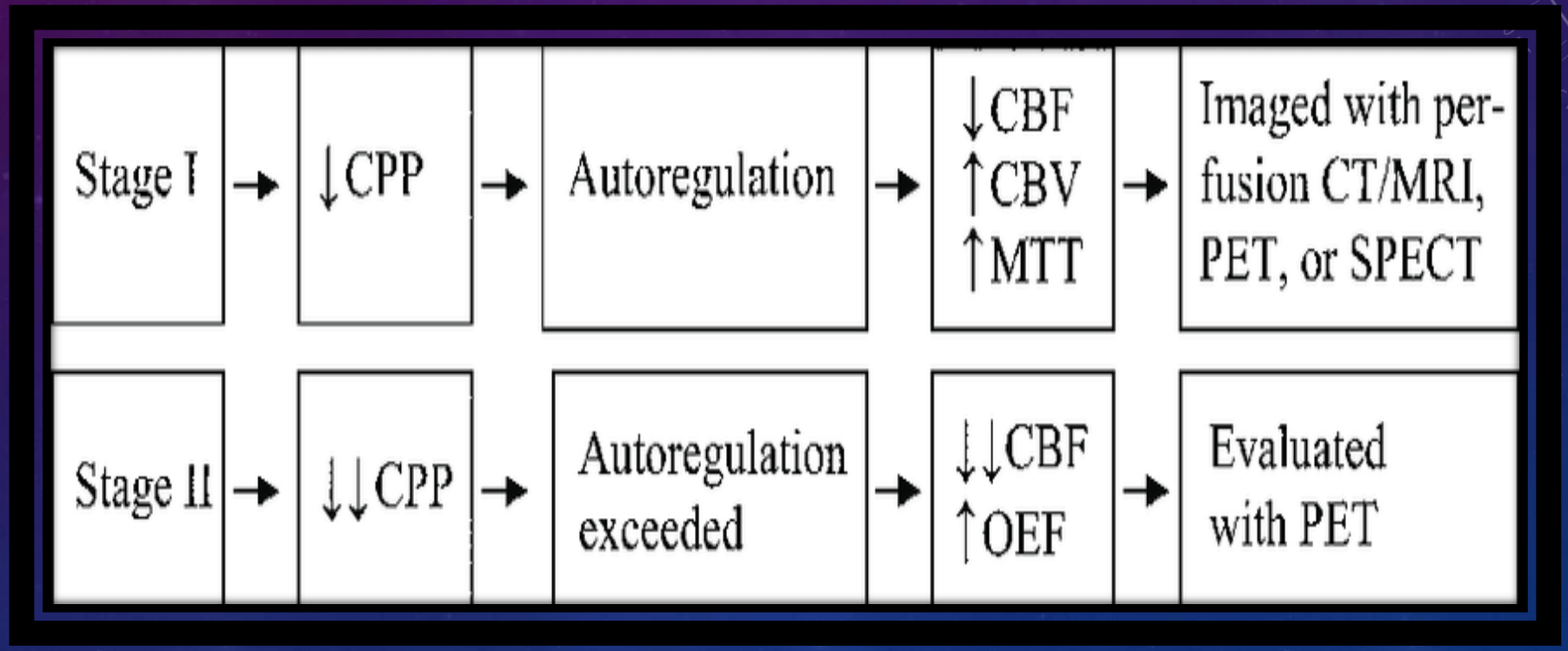
STAGES OF HEMODYNAMIC IMPAIRMENT

- In stage I impairment, a decline in cerebral perfusion pressure leads to autoregulatory vasodilatation of resistive vessels of the brain
- This can be measured with various methods, including xenon-enhanced CT, CT perfusion, MR perfusion, SPECT and PET
- Mainly, the modalities measure cerebral blood flow, cerebral blood volume and mean transit time
- To measure cerebrovascular reactivity, cerebral blood flow measurements can be repeated after a vasodilatory challenge
- Normally, an increase in CBF is expected; however, with hemodynamic compromise, the CBF is often not increased because autoregularotion has already caused maximum vasodilatation in response to decreased CPP

STAGES OF HEMODYNAMIC IMPAIRMENT

- In stage II, further reduction in CPP causes inadequate autoregulatory vasodilation, and CBF decreases
- As blood flow decrease, the oxygen extraction fraction in the brain may increase, and can be measure with PET
- The increased oxygen extraction fraction in the ischemic region has been described as misery perfusion, where the metabolic demand of tissue is greater than its blood supply
- Patients with misery perfusion, which is a significant disturbance of cerebral autoregulation, have a significantly higher stroke recurrence ratio than patients without misery perfusion

STAGES OF HEMODYNAMIC IMPAIRMENT



Border Zone Infarcts: Pathophysiologic and Imaging Characteristics[1]

Rajiv Mangla, MD • Balasubramanya Kolar, MD • Jeevak Almast, MD
Sven E. Ekholm, MD, PhD

CME FEATURE

See www.rsna.org/education/rg_cme.html

LEARNING OBJECTIVES FOR TEST 1

After completing this journal-based CME activity, participants will be able to:

- Define the types of border zone infarcts.
- Describe the pathophysiologic and radiologic imaging features of each type of border zone infarct.
- Discuss the role of imaging in management of patients with border zone infarcts.

TEACHING POINTS

See last page

Border zone or watershed infarcts are ischemic lesions that occur in characteristic locations at the junction between two main arterial territories. These lesions constitute approximately 10% of all brain infarcts and are well described in the literature. Their pathophysiology has not yet been fully elucidated, but a commonly accepted hypothesis holds that decreased perfusion in the distal regions of the vascular territories leaves them vulnerable to infarction. Two types of border zone infarcts are recognized: external (cortical) and internal (subcortical). To select the most appropriate methods for managing these infarcts, it is important to understand the underlying causal mechanisms. Internal border zone infarcts are caused mainly by hemodynamic compromise, whereas external border zone infarcts are believed to result from embolism but not always with associated hypoperfusion. 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 (eg, multiple small internal infarcts) have proved to be independent predictors of subsequent ischemic stroke. A combination of several advanced techniques (eg, 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.

Abbreviation: MIP = maximum intensity projection

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[1]From the Department of Imaging Sciences, University of Rochester, School of Medicine and Dentistry, 601 Elmwood Ave, PO Box 648, Rochester, NY 14642-8648. Presented as an education exhibit at the 2008 RSNA Annual Meeting. Received January 28, 2010; revision requested March 12; final revision received April 17, 2011; accepted May 2. For this journal-based CME activity, the authors, editor, and reviewers have no relevant relationships to disclose. **Address correspondence to** R.M. (e-mail: *manglarajiv@yahoo.com*).

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RESEARCH Open Access

Microemboli versus hypoperfusion as an etiology of acute ischemic stroke in Egyptian patients with watershed zone infarction

Ahmed ElSadek*, Ahmed Gaber, Hossam Afifi, Sherin Farag and Nouran Salaheldien

Abstract

Background: Brain perfusion is most likely to be impaired in border zone regions, and clearance of emboli will be most impaired in these regions of least blood flow. Severe occlusive disease of the internal carotid artery causes both embolization and decreased perfusion as well as some cardiac diseases that cause microembolization.

Objectives: To differentiate between hypoperfusion and microemboli as etiology of acute ischemic stroke in watershed zone.

Subject and methods: Fifty patients of acute ischemic stroke in watershed zones were recruited within 7 days from stroke onset. Methods used were transcranial Doppler (TCD) monitoring for the intracranial vessels to detect microembolic signals and magnetic resonance imaging (MRI) perfusion image to detect hypoperfusion signs.

Results: We detect embolic causes of watershed infarction (WSI) by using TCD with 61.1% sensitivity and 84.4% specificity and hypoperfusion causes of WSI by using MRI perfusion studies with 94.9% sensitivity and 54.5% specificity.

Conclusion: We detected the etiology of WSI, either embolic by using TCD or hypoperfusion by using MRI perfusion. The embolic causes of WSI usually cause external or mixed WSI, and hypoperfusion causes of WSI cause internal WSI.

Keywords: Microemboli, Hypoperfusion, Watershed zone infarction

Introduction

Watershed strokes are named because they affect the distal watershed areas of the brain. The term "watershed" refers to those areas of the brain that receive dual blood supply from the branching ends of two large arteries [1]. These events are localized to two primary regions of the brain: Cortical watershed strokes (CWS), or outer brain infarcts, are located between the cortical territories of the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA). Internal watershed strokes (IWS), or sub cortical brain infarcts, are located in the white matter along and slightly above the lateral ventricle, between the superficial systems of the MCA and ACA, or between the deep and the superficial arterial systems of the MCA [10]. The conventional theory implicates hemodynamic compromise produced by repeated episodes of hypotension in the presence of a severe arterial stenosis or occlusion. The lower perfusion pressure found within the border zone areas in this setting confers an increased susceptibility to ischemia, which can lead to infarction [5]. 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 [9]. Hypoperfusion, or decreased blood flow, is likely to impede the clearance (washout) of emboli. Because perfusion is most likely to be impaired in border zone regions, clearance of emboli will be most impaired in these regions of least blood flow. Severe occlusive disease of the internal carotid artery causes

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Editorial

The Pathogenesis of Watershed Infarcts in the Brain

ANSGAR TORVIK, M.D.

WATERSHED INFARCTS are ischemic lesions which are situated along the border zones between the territories of two major arteries, for example the anterior and middle or the middle and posterior cerebral arteries (fig. 1). They may also be located between the territories of the major cerebellar arteries and they have even been described between the territories of the small arteries in the basal ganglia.[17] However, the exact nature of the latter lesions is more uncertain. The infarcts may be pale or hemorrhagic or mixed but generally the hemorrhagic component is not prominent.

Altogether, approximately 10% of all brain infarcts are watershed lesions.[6] Similar infarcts are also found in other organs, such as the heart and the kidneys, but they are more easily recognized in the brain because of the well defined course and extent of the cerebral arteries.

The mechanisms whereby watershed infarcts develop have been debated for many years and they have been variously ascribed to cerebral thromboangiitis obliterans,[7, 12] episodes of systemic hypotension,[1, 9, 11, 17] carotid occlusions[4, 5, 15] and to microembolism.[6, 13, 16] It has now been convincingly shown that both hypotension and microembolism may cause such lesions. However, in some cases, particularly in those with a progressive or stepwise clinical course, the mechanism still remains uncertain.

Watershed Infarcts Caused by Hypotension

A sharp drop in the systemic blood pressure is the most frequent cause of watershed infarcts.[1, 3, 11, 17] Apparently, the reduction in the blood flow becomes most severe in the terminal areas of the vascular fields. However, this is not the whole explanation because unpredictable combinations of partial uni-and bilateral infarcts may occur. The most striking and most frequent location is the territory between the fields of the anterior and middle cerebral arteries. Sometimes there may be a diffuse nerve cell loss in the cortex in addition to the localized infarcts but the hippocampus appears to be remarkably resistent.[1]

The watershed infarcts caused by hypotension are rarely grossly hemorrhagic. This is somewhat unexpected, since the circulation obviously becomes reestablished after the initial ischemic damage to the vascular endothelium. It is also remarkable, and of relevance to certain findings discussed below, that the small leptomeningeal vessels overlying the infarcts rarely become occluded by secondary thrombosis.[1, 16]

Watershed Infarcts Caused by Microemboli

It has often been speculated that the platelet aggregates which so frequently block the small leptomeningeal arteries over watershed infarcts are microemboli and thus the cause of the infarcts rather than secondary events. However, secondary thrombi formed *in situ* may have a similar appearance and it has therefore been difficult to distinguish between emboli and thrombi in this location.

It has now been shown in a considerable number of cases that showers of cholesterol crystals or of tumor emboli can block the vessels in these areas and cause watershed infarcts.[2, 8, 10, 16] Although admittedly rare causes, these examples of unusual embolic material prove beyond doubt that particles of a certain size may lodge preferentially in the watershed areas and cause infarcts in the underlying brain. Generally, emboli tend to pass as far distally as their size permits along the superficial vascular tree, and they rarely follow the sharp angles of the branches passing to the deeper sites of the brain. Presumably, the microemboli to the watershed areas are extreme examples of this general rule.

Watershed Infarcts Caused by Carotid Occlusions

It has been known for many years that thrombi at the bifurcation of the carotid artery in the neck may cause watershed infarcts between the territories of the anterior and the middle cerebral arteries, and more rarely, between the middle and posterior cerebral arteries. Frequently, these cases present clinically with either transitory ischemic attacks or a stepwise type of development, or with evenly increasing clinical symptoms.[11, 15] Several authors have also commented upon the frequent occurrence of platelet aggregates in the overlying leptomeningeal vessels.[5, 11, 15]

The watershed infarcts in carotid occlusions have mostly been considered to be due to a reduced blood flow analogous to the situation following systemic hypotension and the occluded leptomeningeal vessels a

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WATERSHED STROKES AFTER CARDIAC SURGERY

- Watershed distribution strokes are seen more frequently in patients with postcardiac surgery stroke than in the general population (> 40% vs 2-5%)
- These patients are more likely to require long-term care than other postcardiac surgery stroke patients
- Probably involves a combination of hypoperfusion and embolization
- In cardiac surgery, global systemic hypoperfusion caused by severe intraoperative hypotension is known to be associated with poor outcomes
- One randomized trial showed improved neurological and cardiac outcome in patients with MAP maintained at 80 to 100 mm Hg vs 50 to 60 mm Hg

WATERSHED STROKES AFTER CARDIAC SURGERY

- One study done at John Hopkins followed patients who underwent cardiac surgery between 1998 and 2003 and developed a focal neurologic deficit post operatively. Data was reviewed for patients with watershed infarctions
- Intraoperative blood pressure was defined as blood pressure while on CPB, so patients who underwent off-pump CABG were excluded from the part of the study involving BP measurements
- Only those patients who had MRI/DWI imaging were included, although patients also underwent CT
- Standard MAP goal during CPB at John Hopkins is (was) 60 to 80 mm Hg
- 91 patients were included, with 5 patients excluded that underwent off-pump CABG and 2 that developed symptoms over 10 days post-operatively

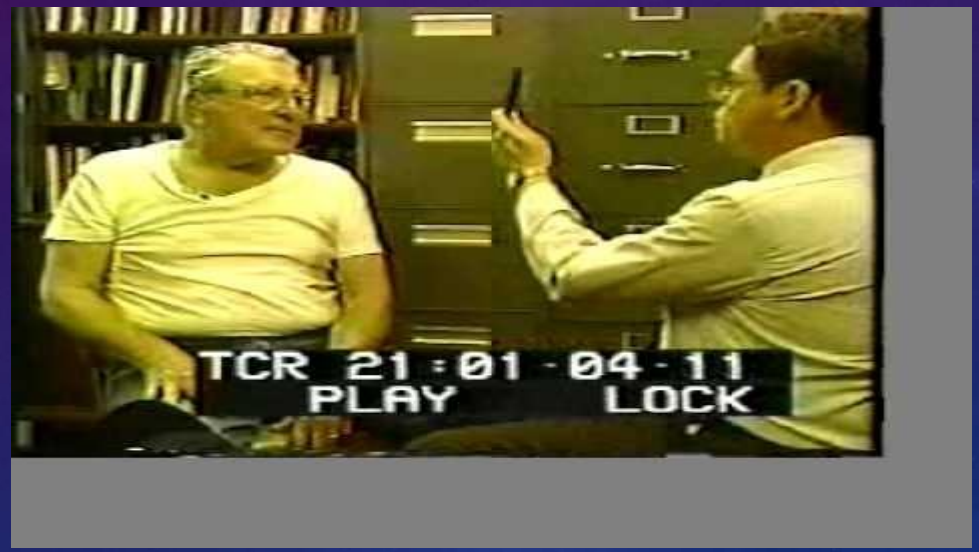
WATERSHED STROKES AFTER CARDIAC SURGERY

- Patients with bilateral watershed infarctions were more likely to have undergone an aortic procedure and less likely to have undergone a simple or redo CABG
- Patients with bilateral watershed infarcts were 6.23 times as likely to be discharged to an ARF, 12. 46 times more likely to be discharged to subacute rehab or to SNF, and 17.28 times more likely to die in the hospital than be discharged home
- Patients with a length of stay > 14 days were more likely to have bilateral watershed infarcts than other stroke patterns
- Patients with a drop in MAP or at least 10 mm Hg were 4.06 times (adjusted OR: 95% CI: 1.05, 15.98) as likely to develop bilateral watershed strokes as those patienrs who had a smaller drop or no drop in bp
- Data showed that bilateral watershed strokes were more readily detected by DWI MRI (than CT) and were associated with poor short-term outcomes, and MAY have been related to a decrease in intraoperative blood pressure from a preoperative baseline

DEFICITS/FINDINGS RELATED TO LOCATION(S)

- Deficits are relative to stroke burden and locations
- Internal border zone infarcts, especially if more “cigar” shaped or multiple “beads on a string”, tend to do worse then isolated cortical border zone infarcts
- Bilateral infarcts also tend to do worse
- “Man in a Barrel” syndrome can occur if bilateral MCA/ACA cortical infarcts are extensive: proximal > distal UE weakness, inability to abduct arms; bilateral brachial weakness, can spare face, legs
- Balint’s syndrome can be caused by bilateral posterior MCA/PCA border zone infarcts
  - 3 classic findings are simultanagnosia, optic ataxia and oculomotor apraxia—severe visual-spatial abnormalities


Neurology
Clinical Practice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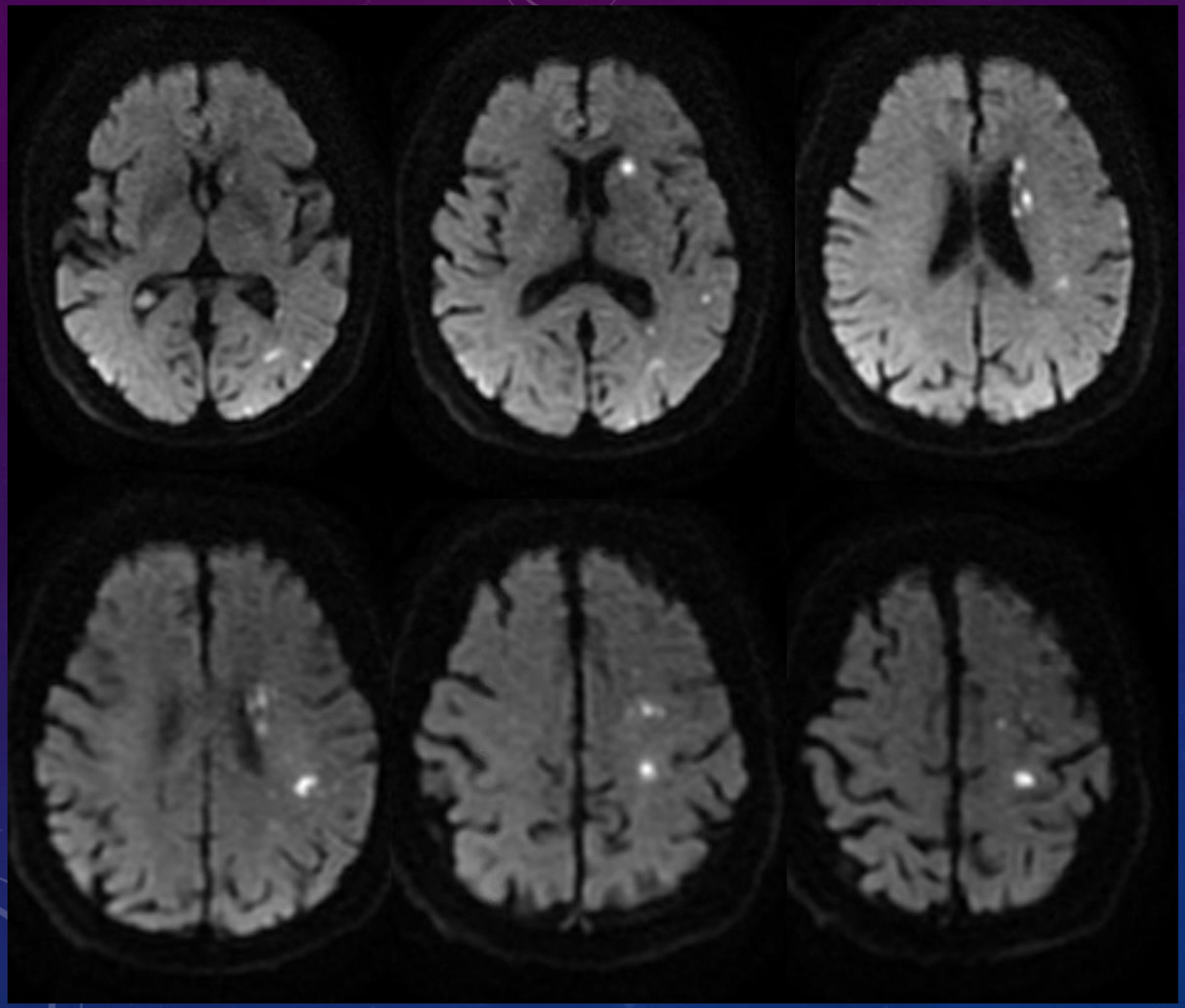
PLAY
LOCK

CASE STUDY

- 69 yo male presenting with chest pain radiating to left jaw, down left arm and increasing SOA x 1 week
  - Chest pain not relieved with nitro; also, nitro caused N/V
  - Further history revealed he had been sleeping in a recliner for 2 weeks
  - Wife reported confusion, which was very unusual, as well as increasing fatigue and easy bruising
- PMH significant for ischemic cardiomyopathy, CAD, s/p STEMI, PAD, PVD, OSA/CSA, CKD, DM, hxtn, bilateral carotid artery disease, s/p stents bilaterally at OSH
- Initial labs revealed glucose 124, remainder of CMP normal, troponin 0.03, Hgb 6.9, hct 21, WBC 1.7, Plt 37—significant thrombocytopenia

CASE STUDY

- Troponins elevated to 2, No ST elevation/depression
- Hgb worsened, pt transfused, nephrology, GI medicine, cardiology and Heme/onc all consulted
- Day 5, pt noted to be more somnolent, slurred speech, neurology consulted
- On exam, he was somnolent, clearly encephalopathic, no definite vision change, but right facial droop and subtle right sided weakness (superimposed on notable generalized weakness)
- Review of BPs over the previous 24 hours with SBP as low as 71, transiently, but often in the 90s
- MRI obtained. Pt continued to be markedly pancytopenic. Also ordered carotid Doppler/US



MRI slices showing watershed infarcts

Carotid Doppler/US indicated 70% to near total occlusion of LICA.

CASE STUDY

- The patient was recommended to transfuse to Hgb 9 or greater—both for neurologic and cardiologic reasons
- Recommend keep SBP > 110
- He underwent bone marrow biopsy prior to neuro consult—preliminary findings of myelodysplastic syndrome, 6-7% blasts
- He was improved significantly in regards to his encephalopathy and his right sided weakness within 2 days, but does continue to wax and wane in regards to his mental status. BP has mostly been > 110, and HGB > 8 with repeated transfusions

CONCLUSIONS

- Watershed or border zone infarcts are much more common than initially thought
- In addition to hemodynamic compromise, micro emboli likely play a role, especially in external or cortical border zone infarcts
- Internal border zone infarcts may be difficult to distinguish from other entities; chronically, WM lesions from demyelination, and when minimal, often thought to be “lacunar” infarcts
- Cerebellar border zone infarcts are also possible, and probably more common than initially recognized
- Hence, large vessel imaging is extremely important in ALL ischemic stroke work ups
- Longer times of hemodynamic compromise often leads to more severe stroke deficits
- Neurologic exams and, if focal deficits are found, MRI imaging are important post cardiac surgery, or any prolonged surgery with drop in MAP from baseline
- Quick hemodynamic support is imperative for good outcomes in cases where this is a problem

REFERENCES

- Google images
- Momijan-Mayor MD, Isabelle and Baron MD, FRCP, Jean-Claude, “The Pathophysiology of Watershed Infarction in Internal Carotid Artery Disease”, *STROKE,* 2005/https://doi.or/10.1161/01.STR.0000155727.82242.e1/Stroke. 2005; 36: 567-577.
- Mangla, MD, Rajiv, Kolar, MD, Balasubramanya, Almast, MD, Jeevak, Ekholm, MD, PhD, Sven E. “Border Zone Infarcts: Pathyophysiologic and Imaging Characteristics.” *Radiographics.rsna.org.* September-Octtober, 2011. 1201-1215.
- Gottesman, MD, Rebecca F., et al. “Watershed Strokes After Cardiac Surgery: Diagnosis, Etiology and Outcomes.” *STROKE.* DOI: 10.1161/01.STR.000023604 24.68020.3a. 2306-2311.

Thank You!