

Critically Appraised Topic

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Cerebral Angiography and Diagnosis of CNS Vasculitis

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Conventional cerebral angiography was neither specific nor sensitive in the diagnosis of primary CNS vasculitis, but the evidence was very weak

Clinical Problem: A 55-year-old female presents with a 5-month history of mental status changes including increased forgetfulness, slurred speech and transient mild lower extremity weakness. Her MRI brain shows non-specific white matter changes. A diagnosis of CNS vasculitis is considered.

Clinical Question: What are the sensitivity, specificity and likelihood ratio of conventional cerebral angiography in the diagnosis of CNS vasculitis?

Search Strategy: SUMSearch: "Vasculitis" [MESH] (Focus: DIAGNOSIS, Ages: ALL, Subjects: HUMAN) resulted in 128 articles. Pubmed: "Vasculitis" [MESH] and "central nervous system" with clinical query "diagnosis" (Limits: human, English) resulted in 25 articles. No new articles were found in the PubMed search. The majority of the articles focused on temporal arteritis, MRI only, or comparison of MRI and conventional angiography. The chosen article¹ was the only study which compared brain biopsy, the most definitive investigation (ie. the current gold standard), to conventional cerebral angiography.

Clinical Bottom Lines:

1. Using brain biopsy as a gold standard, conventional cerebral angiography was neither sensitive nor specific in the diagnosis of primary CNS vasculitis, although the evidence was extremely weak. (sensitivity 0% (95%CI 0-58), specificity 61% (95%CI 45-77), LR positive test – not known, LR negative test 1.64 (95%CI 1.26-2.12)).
2. The sensitivity was difficult to interpret and unreliable, given a low number of positive biopsies.
3. In the two cases of positive brain biopsies, the cerebral angiography was not diagnostic of vasculitis.

The Evidence: Retrospective review of 38 patients at a single centre with suspected CNS vasculitis investigated with both a brain biopsy and conventional cerebral angiography. Patients were drawn from a neuropathology database. Seventy-three patients with a brain biopsy in which the term "vasculitis" appeared in the clinical summary, indications or description were identified. Thirty-eight of these patients underwent conventional cerebral angiography prior to the biopsy and were included in this study. An investigator that was blinded to the brain biopsy assessed the angiographic data. Angiography findings were classified as vasculitis (isolated multiple cerebral arterial segmental narrowings), normal or other pathology. The pathological diagnosis of vasculitis was fulfillment of the following criteria: 1) transmural inflammation of small- or medium-sized blood vessels of the meninges and/or cortex of the brain; 2) fibrinoid necrosis of the vessel wall; and 3) alternative diagnoses must be excluded.

Data:

		Brain Biopsy Diagnosis of Vasculitis		Total
		Present	Absent	
Conventional Cerebral Angiography Diagnosis of CNS Vasculitis	Positive	0	14	14
	Negative	2	22	24
Total		2	36	38

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Diagnostic Strength of Conventional Cerebral Angiography Compared with Brain Biopsy

		95% Confidence Intervals
Sensitivity	0%	0 to 58
Specificity	61%	45 to 77
LR +	Not able to calculate	-
LR -	1.64	1.26 to 2.21

Comments:

1. The evidence is extremely weak; mainly due to selection bias.
2. Of 73 patients screened, the gold standard (brain biopsy) and diagnostic test (conventional angiography) were applied to only 38 patients. Inclusion of these other patients may have greatly affected the results. It is not known how these 38 patients were chosen.
3. This is a retrospective study; therefore selection bias may exist thereby influencing the results.
4. In this study, the low number of positive biopsies for CNS vasculitis makes the sensitivity unreliable.
5. No clinical information was provided on the patients or the referral pattern, which makes it difficult to generalize results or apply to our practice.
6. The angiography results were reviewed in a blinded fashion.
7. Although brain biopsy is considered the gold standard for diagnosis of CNS vasculitis, given the patchy nature of the disease there are often false negative results. (see appendix)

REFERENCE ARTICLE APPRAISED:

1. Kadkhoyan Y, Alreshaid A, Moran CJ, Cross DT, Powers WJ, Derdeyn CP. Primary angiitis of the central nervous system at conventional angiography. *Radiology*. 2004; 233:878-882.

KEY WORDS

Primary CNS Angiitis, CNS vasculitis, Angiography, Biopsy

APPRAISER

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APPENDIX**Articles of Interest**

1. Calabrese LH. Diagnostic strategies in vasculitis affecting the central nervous system. *Cleve Clin J Med*. 2002;69(S2):105-108.
2. Alrawi A, Trobe JD, Blaivas M, Musch DC. Brain biopsy in primary angiitis of the central nervous system. *Neurology*. 1999;53:858.

EXPERT OPINION: Neuroradiology

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Primary CNS vasculitis remains a diagnostic challenge for neurologists and neuroradiologists. Often a diagnosis of exclusion, it is part of many differential diagnoses, sometimes it is even the prime suspect, but it is rare to actually find the "smoking gun" imaging evidence prior to open biopsy. As the accompanying article demonstrates, conventional digital subtraction cerebral angiography (DSA) is neither sensitive nor specific for the diagnosis. The classic "starry sky" appearance of multiple small vessel irregularities is rarely seen, and is actually more common in atherosclerotic disease. Although the risks of modern DSA are low, there is no convincing evidence that this invasive investigation is indicated to definitively diagnose CNS vasculitis.

How then should these patients be efficiently investigated? Magnetic resonance imaging (MRI) has shown some promise, with analysis of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) images proving useful^{1,2}. Some authors have found MR angiography (MRA) to show changes³ and others have shown the value of leptomeningeal enhancement⁴ and petechial cortical hemorrhages⁵ in making the diagnosis. Although most patients with CNS vasculitis will show abnormalities on MRI, many will not⁶. It may be that only the combination of MRI and DSA can guide the neurosurgeon to an appropriate location for biopsy. As yet, no one imaging modality can reliably make the diagnosis.

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5. Ay H, Sahin G, Saatci I, Soylemezoglu F, Saribas O. Primary angiitis of the central nervous system and silent cortical hemorrhages. *AJNR Am J Neuroradiol*. 2002;23:1561-3.
6. Wasserman BA, Stone JH, Hellman DB, Pomper MG. Reliability of normal findings on MR imaging for excluding the diagnosis of vasculitis of the central nervous system. *AJR Am J Roentgenol*. 2001;177:455-9.