Correspondence

Diagnosis of vasculitis

To the Editor

We read with interest the review article by Abdul-Aziz and Faizal.[1] We would like to emphasize that the diagnosis of vasculitis is a histopathological one and not serological. If the clinical scenario is suggestive, a tissue biopsy should be obtained whenever possible. In severely ill patients, therapy can be initiated but as soon as the patient is stable, a biopsy must be organized. Treatment of systemic vasculitis with corticosteroids and cytotoxic therapy may be associated with serious complications such as systemic infections, hemorrhagic cystitis, bladder cancer and even death. Establishing a definite diagnosis becomes even more important before subjecting the patient to intensive and potentially dangerous therapy. An alternative to biopsy for diagnosis is conventional angiography and it has been the gold standard for medium- and large-vessel vasculitis for decades especially in cases of Takayasu's arteritis and classic polyarteritis nodosa (PAN). In PAN, the arteriography is often diagnostic, showing multiple aneurysms and irregular constrictions in the larger vessels with occlusion of smaller penetrating arteries. Less invasive techniques such as computerized tomography, MRI scan whole body positron emission tomography isotope study can also be used.[2]

There are limitations to the value of an anti-neutrophilic cytoplasmic antibodies (ANCA) test. For example, 10% of patients with severe Wegener's granulomatosis (WG), 40% of patients with limited WG, 30% of all patients with microscopic polyangiitis and almost half of those with Churg Strauss syndrome are ANCA-negative.[3] In a significant number of patients with idiopathic small vessel vasculitis, the ANCA test results (either in immunofluorescence or ELISA) are negative.[4] Anti-neutrophilic cytoplasmic antibodies may also be detected in a variety of gastrointestinal and other rheumatic disorders, particularly by immunofluorescence. The clinical significance of a positive ANCA in these disorders is unclear.[3] Even in cases of vasculitis such as giant cell arteritis that are not associated with a positive serological test, obtaining a histopathological diagnosis is also important. Temporal artery biopsy should also be attempted in all cases of suspected giant cell arteritis. Hamidou et al reported 7 cases of temporal arteritis in patients with systemic vasculitis without classic giant cell arteritis. Non-giant cell arteritis, such as necrotizing vasculitis, polyarteritis and "hypersensitivity" angiitis, have also been reported earlier to involve the temporal arteries by other aurhors,[6-10] The prognosis of those patients with non-giant cell arteritis may be less favorable, probably due to the less beneficial effect of single-corticosteroid therapy on the course of polyarteritis.[10] Clinicians and histopathologists should be aware of the possibility of non-classic giant cell arteritis in elderly patients presenting with temporal arteritis. A temporal artery biopsy should be performed in patients with temporal arteritis, as patients with systemic necrotizing vasculitis may require cytotoxic drugs in addition to corticosteroids.[11] The overall prognosis of these patients may be effectively less favorable if other sites are involved, and clinicians must be aware of renal, cardiac, digestive, or central nervous system involvement, defining requirements of the "5 factors score".[12]

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Reply from the Author

We would like to thank Drs Jawad and Saeed for showing interest in our published review on immunological diagnosis of vasculitis.[1] Prompt diagnosis and treatment of vasculitis is of paramount importance in order to prevent the high morbidity, and mortality, that is associated with untreated patients. However, diagnosis of vasculitis can prove very difficult and, therefore, extensive laboratory and radiological investigations may be required. In our review, we concentrated on the contribution of the clinical immunology laboratory in the investigation of vasculitis. Many of the immunological investigations can produce results that are almost diagnostic (such as granular C-ANCA/PR3 for Wegner granulomatosis) and, in life threatening conditions, treatment can be initiated on the bases of immunological findings. However, as we stated in our review, conformation of the diagnosis required a biopsy. Due to the limited histopathological lesions, histopathological findings may not always prove diagnostic of a specific vasculitic condition (such as cryoglobulinemia, Henoch Schönlein purpura). In such situations, definitive diagnosis may only be obtained from a combination of histopathological (leukocytoclastic lesions) and immunological (such ascomplements, cryoglobulins, immunoglobulins,

immune deposition on biopsies) findings. With regards to medium and large vessel vasculitides (such as Giant cell (temporal) arteritis, Takayasu's arteritis, polyarteritis nodosa, Kawasaki disease), currently there are no specific immunological tests for these conditions. The clinical immunology laboratory is increasingly involved in the diagnosis, and monitoring, of variety of other autoimmune diseases beside vasculitis.[1,13-17] The results produced can be highly sensitive and specific for a given disease and, in some instances, prove far more sensitive and specific than histopathological investigations.[5] With time, and with more research, it is anticipated that immunological investigations in many conditions may well replace other more invasive diagnostic procedures.

In conclusion, we would like to re-emphasize the fact that a large repertoire of tests exists in the immunology laboratory for the investigation of vasculitis. These tests, which are simple and have quick turn around times, should be used in the early stages of the investigation of vasculitis. The results produced can provide an early picture of the type of vasculitis involved and thus allows early institution of treatment. Reliance on more sophisticated radiological investigation as the first line of investigation can lead to delay in the diagnosis of vasculitis as well as prove costly.

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References

1. Abdul-Aziz K, Faizal A-A. Immunological diagnosis of vasculitis. ***Saudi Med J*** 2006; 27: 1105-1115.
2. Schmidt, WA. Use of imaging studies in the diagnosis of vasculitis. ***Curr Rheumatol Rep*** 2004; 6: 203.
3. Stone JH, Rose BD. Clinical spectrum of antineutrophil cytoplasmic antibodies. Available from URL: http://patients.uptodate.com/topic.asp?file=glom_dis/16776&title=HIV+infection
4. Hagen EC, Daha MR, Hermans J, Andrassy K, Csernok E, Gaskin G, et al. For the EC/BCR project for ANCA assay standardization. Diagnostic value of standardized assays for anti-neutrophil cytoplasmic antibodies in idiopathic systemic vasculitis. ***Kidney Int*** 1998; 53: 743.
5. Hamidou MA, Moreau A, Toquet C, EI Khouri D, de Faucal P, Grolleau JY. Temporal arteritis associated with systemic necrotizing vasculitis. ***J Rheumatol*** 2003; 30: 2165-2169.
6. Wagener HP, Hollenhorst RW. The ocular lesions of temporal arteritis. ***Am J Ophthalmol*** l958; 45: 617-630.
7. Fronhert PP, Sheps SG. Long-term follow-up of periarteritis nodosa. ***M J Med*** 1967; 43: 8-14.
8. Torvik A, Bemtzen AE. Necrotizing vasculitis without visceral involvement. ***Acta Med Scand*** 1968; 184: 69-77.
9. Trepo C, Thivolet J, Lambert R. Four cases of periarteritis nodosa associated with persistent Australia antigen. ***Digestion*** 1972; 5: 100-1007.
10. Morgan GJ Jr, Harris ED. Non-giant cell temporal arteritis. Three cases and a review of the literature. ***Arthritis Rheum*** 1978; 21; 362-366.
11. Jawad ASM. Temporal arteritis associated with systemic necrotizing vasculitis. ***J Rheumatol*** 2005; 32: 1173.
12. Guillevin L, Lhote F, Gayraud M, et al. Prognostic factors in polyarteritis nodosa and Churg-Strauss syndrome. A prospective study in 342 patients. ***Medicine (Baltimore)*** 1996; 75: 17-28.
13. Abdul-Aziz K, Faizal AA. Utilization of complement testing in clinical medicine. ***Saudi Med J*** 2006; 27:
14. Abdul-Aziz K. Significance of anti-glomerular basement membrane antibodies in type 2 diabetic patients. ***Saudi Med J*** 2006; 27: 915.
15. Aziz KA, Faizal AA. The role of the clinical immunology laboratory in the diagnosis and monitoring of connective tissue diseases. ***Saudi Med J*** 2004; 25: 1796.
16. Aziz KA, Polson RJ. Serological diagnosis of celiac disease. ***Saudi Med J*** 2005; 26: 1340.
17. Abdul-Aziz K, Faizal AA. Serological diagnosis of autoimmune hepatobiliary diseases. ***Saudi Med J*** 2005; 26: 1875.