ANCA Screen with MPO and PR3, with Reflex to ANCA Titer

Test Code: 70159(X)

Specimen Requirements: 2 mL room temperature serum; 0.8 mL minimum

CPT Codes*: 86021 (x3)

CLINICAL USE

- Differential diagnosis of systemic vasculitis
- Monitoring patients with systemic vasculitis

CLINICAL BACKGROUND

Systemic vasculitis is characterized by inflammation of and damage to blood vessels. Subsequent disruption of the blood supply leads to tissue and organ damage. Vasculitis may be a primary or secondary manifestation of disease and can be caused by certain infections, malignancy, rheumatic disease, medications, and a wide variety of autoimmune disorders. Differential diagnosis is required to determine the appropriate therapy.

Differential diagnosis can be aided by testing for specific antineutrophil cytoplasmic antibodies (ANCA), which have been associated with several of the autoimmune systemic vasculitis disorders. These include granulomatosis with polyangiitis (GPA, formerly Wegener's), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss).[1] Each disorder is associated with predominance of a specific ANCA type.[2] The ANCA types are revealed by fluorescent patterns obtained in the indirect immunofluorescence ANCA screen. For example, the cytoplasmic pattern (C-ANCA) is very common in GPA, but not MPA or EGPA. The perinuclear pattern (P-ANCA), on the other hand, is rare in GPA, common in MPA, and moderately common in EGPA cases. The atypical P-ANCA pattern is rare in all 3 of these; it is usually associated with nonvasculitic conditions such as inflammatory bowel disease.[3] The sensitivity and specificity of these markers for the various disorders are summarized in the **Table**.[4-6]

The diagnostic accuracy of the ANCA screen can be improved by combining it with immunoassays specific for myeloperoxidase (MPO) and proteinase-3 (PR3) antibodies. An international consensus group recommends this approach.[2] Though the C-ANCA pattern typically reflects specificity to PR3, there is not 100% concordance between C-ANCA and PR3 antibody as C-ANCA has multiple targets. Similarly, the P-ANCA pattern predominantly reflects MPO specificity.

ANCA can also be used to help guide patient management. A persistently positive ANCA is associated with relapse if treatment is stopped;[7] thus continued treatment should be considered as long as the ANCA is positive. ANCA titers may start high, decline during treatment, and increase again in relapse. ANCA titers do not closely reflect disease activity, though.[7] Thus when titers increase, the patient should be monitored more closely but not necessarily receive increased treatment.[7] Additional measures of disease activity should be used before modifying treatment.[7,8]

Table. Diagnostic Sensitivity (Specificity) (%) of ANCA, PR3 Antibody, and MPO Antibody for Various Diseases

Marker	Vasculitides					Other Autoimmune Disease		
	GPA[a,6]	MPA[a,6]	EGPA[4]	PAN[a,6]	GCA[a,6]	UC[5]	SLE[a,6]	RA[a,6]
ANCA	85 (93)	68 (87)	31	15	3	55	11	9
C-ANCA	81 (100)	3 (93)	5	0	1	ND	0	0
C-ANCA+/PR3+	69 (100)	0	1	0	2	ND	0	0
P-ANCA	4 (94)	65 (94)	21	15	2	55	11	9
P-ANCA+/MPO+	2 (99)	48 (100)	20	0	1	15	2	0

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis; PAN, polyarteritis nodosa; GCA, giant cell arteritis; UC, ulcerative colitis; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; and ND, not determined.
[a] Sensitivity and specificity based on patients tested for ANCA in a rheumatology clinic.

INDIVIDUALS SUITABLE FOR TESTING

- Individuals with symptoms of systemic vasculitis (eg, unexplained systemic illness with multiple organ involvement, unexplained ischemia)

METHOD

ANCA Screen

- Cell-based, indirect immunofluorescence using fixed human neutrophils
- Results reported: negative or positive
- Positive results reflexed to titer of the relevant pattern(s) (eg, C-ANCA, P-ANCA, atypical P-ANCA) at additional charge (CPT code 86021)

Myeloperoxidase and Proteinase-3 Antibodies

- Semiquantitative multiplex immunoassay
- Analytical sensitivity: 0.2 AI for each antibody
- Analytical specificity: no known cross reactivity with antibodies associated with infection and immune disorders

Panel components can be ordered separately: ANCA screen (70171), MPO antibody (8796), PR3 antibody (34151).

REFERENCE RANGES

ANCA Screen	Negative (titer <1:20)
Myeloperoxidase Antibody	<1.0 AI (no antibody detected)
Proteinase-3 Antibody	<1.0 AI (no antibody detected)

INTERPRETIVE INFORMATION

A positive ANCA screen supports a diagnosis of autoimmune-related systemic vasculitis in a symptomatic patient (**Table**). Positive results are also seen in inflammatory bowel disease (ulcerative colitis) and occasionally in other autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis, autoimmune hepatitis). Exposure to certain drugs (eg, propylthiouracil, hydralazine, methimazole) and infectious agents (eg, hepatitis C virus) can result in secondary vasculitis and an ANCA-positive screen result.[8,9]

A negative ANCA, MPO antibody, and/or PR3 antibody result does not rule out systemic vasculitis.

An increase in serum ANCA levels suggests the need for closer clinical monitoring.[7] Patients who are persistently ANCA negative after treatment may be at less risk for a relapse.[10]

Owing to limitations in sensitivity and specificity, ANCA, MPO antibody, and PR3 antibody test results should be interpreted carefully in light of clinical and other laboratory data.

References

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