Test Summary

Inflammatory Bowel Disease Differentiation Panel

Test Code: 16503(X)

Specimen Requirements: 2 mL room-temperature serum (red-top tube); 1.4 mL minimum.

CPT Codes*: 86021 (x3); 86671 (x2)

Clinical Use

- Differentiate ulcerative colitis (UC) from Crohn disease (CD) in patients with inflammatory bowel disease (IBD)

Clinical Background

UC and CD, the most common forms of IBD, are both characterized by inflammation of the digestive tract lining. The inflammation associated with UC is relatively superficial and affects continuous regions of the colon, usually beginning with the rectum and extending proximally. UC is generally confined to the colon, although in rare cases involvement may extend to the terminal portion of the ileum. In CD, inflammation extends deeper into the tissue and can affect any portion of the digestive tract, often "skipping" regions. Both may present with severe bloody diarrhea, abdominal pain, fever, and malnutrition. Accurate diagnosis is critical, as the treatment and prognosis of UC and CD differ.

Although UC and CD can usually be differentiated on the basis of clinical, radiographic, endoscopic, and histologic findings, these conditions can be difficult to distinguish in about 10% to 15% of IBD patients.[1] Numerous studies have investigated the utility of 2 serologic markers in differentiating between UC and CD: atypical perinuclear anti-neutrophil cytoplasmic antibody (pANCA) and anti-*Saccharomyces cerevisiae* antibody (ASCA). Unlike the pANCA or cytoplasmic ANCA found in vasculitis, the IBD-associated pANCA has an "atypical" perinuclear staining pattern. This atypical pANCA is detected in about 40% to 80% of UC patients but only 5% to 25% of CD patients.[2,3] ASCA, on the other hand, is detected in 40% to 68% of CD patients[2,3] but only about 6% to 12% of UC patients.[1,4] Table 1, based on a meta-analysis of 60 studies comprising 7,860 IBD patients, summarizes the sensitivity and specificity of pANCA/ASCA combinations for UC and CD.[2]

Practice guidelines note that the combination of these markers may be useful in patients with IBD that cannot be differentiated as UC or CD on the basis of traditional criteria (ie, indeterminate colitis; IC).[5] However, few studies have directly examined the utility of atypical pANCA and ASCA in such patients; most have involved patients in whom UC or CD had been differentiated using conventional approaches. In a prospective study of 97 individuals with an initial diagnosis of IC, serologic testing provided limited information for differentiation, as most patients (n = 66; 68%) retained the IC diagnosis throughout a mean follow-up period of nearly 10 years.[12] The pANCA+/ASCA– pattern was 50% sensitive and 35% specific for UC, and the pANCA–/ASCA+ pattern was 47% sensitive and 31% specific for CD.[6]

Some reports have also noted the potential utility of serologic testing, combined with other clinical and laboratory information, to identify children with suspected IBD who may not require invasive testing.[7,8] These serologic assays may also be helpful in stratifying CD: pANCA-positive CD has been associated with colonic involvement and a clinical phenotype similar to that of UC (UC-like CD), whereas positivity for ASCA may be associated with non-UC–like CD.[4,9,10]

Proteinase-3 (PR-3) antibody and myeloperoxidase (MPO) antibody assays have been recommended by an international consensus group to provide supportive information for ANCA indirect immunofluorescence (IIF) assays.[11] PR-3 and MPO

Table 1. Sensitivity and Specificity of pANCA/ASCA Combinations for UC and CD in Patients with IBD[a]

Marker	UC		CD	
	Sensitivity	Specificity	Sensitivity	Specificity
pANCA+/ASCA–	51%	94%	—	—
pANCA–/ASCA+ (IgA or IgG)	—	—	55%	93%

[a] Studies were largely retrospective, comprising patients in whom inflammatory bowel disease (IBD) had been classified as ulcerative colitis (UC) or Crohn disease (CD) on the basis of clinical, radiographic, endoscopic, and histologic findings.[2]

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Test Summary

are rarely the targets of the atypical pANCA associated with UC, and ELISAs for these antibodies typically show absence of strong binding in IBD patients.[1]

Individuals Suitable for Testing

- Individuals with IBD

Method

- ANCA screen: cell-based indirect immunofluorescence; positive results reflexed at an additional charge to:
  - –pANCA titer,
  - –cANCA titer, and
  - –atypical pANCA titer
- ASCA IgG and IgA: enzyme-linked immunosorbent assay (ELISA)
- Myeloperoxidase antibody: ELISA
- Proteinase-3 antibody: ELISA

Reference Ranges

Table 2. Reference Ranges for Components of IBD Differentiation Panel

Assay	Range		
	Negative	Equivocal	Positive
ANCA Screen	Not detected	—	Detected
ASCA IgA	≤20 U	20.1-24.9 U	≥25 U
ASCA IgG	≤20 U	20.1-29.9 U	≥30 U
MPO Antibody	<1 AI	—	≥1 AI
PR-3 Antibody	<1 AI	—	≥1 AI

Interpretive Information

In patients with IBD, positivity for atypical pANCA is associated with UC, whereas positivity for ASCA is associated with CD. ASCA negativity increases specificity for UC, and pANCA negativity increases specificity for CD. Because of the relatively low sensitivity of these assays, negative results do not rule out the presence of UC or CD. Among patients with an initial diagnosis of IC, those seropositive for either atypical pANCA or ASCA may be more likely than seronegative individuals to have a final diagnosis of UC or CD.[6]

In patients with CD, pANCA positivity has been associated with disease limited to the colon, a more UC-like phenotype, and a lesser association with small bowel disease.[9] Detection of ASCA in patients with CD has been associated with small bowel disease and a more severe phenotype.[9,10,12]

MPO is associated with pANCA, and PR-3 is associated with cANCA. However, patients with IBD are typically negative for MPO and PR-3 antibodies.[1] Detection of either does not rule out UC or CD. PR-3 positivity is associated with granulomatosis with polyangiitis (Wegener's), and MPO positivity is associated with autoimmune vasculitides including microscopic polyangiitis and crescentic glomerulonephritis.

References

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4. Abreu MT, Vasiliauskas EA, Kam LY, et al. Use of serologic tests in Crohn's disease. *Clinical Perspectives in Gastroenterology*. 2001;4:155-164.
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