The Association between the Myelodysplastic Syndromes and Crohn Disease
Charis Eng, MD, PhD; Francis A. Farraye, MD; Lawrence N. Shulman, MD; Mark A. Peppercorn, MD; Celeste M. Krauss, MD; Jean M. Connors, MD; and Richard M. Stone, MD


The myelodysplastic syndromes are a heterogeneous group of bone marrow stem-cell disorders characterized by peripheral cytopenias and hypercellular dysplastic bone marrows (1, 2). The myelodysplastic syndromes, as defined in the French-American-British classification (2), include refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia. Crohn disease, an inflammatory bowel disease, is characterized by specific pathologic and endoscopic gastrointestinal mucosal findings; these include chronic inflammation, noncaseating granulomas, skip lesions, and aphthous ulcerations (3). Unlike the frequent occurrence of clonal chromosomal abnormalities in the bone marrow cells of patients with a myelodysplastic syndrome, karyotypic abnormalities in intestinal cells have not been seen in patients with inflammatory bowel disease (3, 4). We describe four patients who had both a myelodysplastic syndrome and Crohn disease; three of these patients had bone marrow karyotypes that showed abnormalities in chromosome 20.

**Patient 1**
An 83-year-old woman presented in 1985 with refractory anemia with ringed sideroblasts (Table 1). The bone marrow karyotype was 46,XX,t(4;20)(p16;q11.2). In 1989, she developed nonbloody diarrhea and experienced weight loss. Stool cultures and small-bowel follow-through radiograms were negative. Colonoscopy showed focal ulcerations, and histologic evaluation was diagnostic of chronic active colitis, which is consistent with the diagnosis of Crohn disease. Sulfasalazine therapy alleviated the gastrointestinal symptoms, but the anemia persisted.

**Patient 2**
A 78-year-old woman was diagnosed with refractory anemia with ringed sideroblasts (see Table 1) in 1988. The bone marrow karyotype was 46,XX,del(20)(q11). In the next 2 months, she experienced diarrhea, weight loss, worsening anemia, and leukocytosis. Stool cultures were negative. An upper gastrointestinal series showed mucosal irregularity and ulcerations of the terminal ileum. Scattered aphthous ulcerations with intervening normal mucosa and multiple stellate ulcerations were seen colonoscopically. A biopsy specimen showed chronic inflammation consistent with the diagnosis of Crohn disease. Sulfasalazine treatment was associated with a decrease in diarrhea, but the hematocrit remained at approximately 0.30.

**Patient 3**
A 56-year-old man developed oral aphthous ulcers in May 1991. A bone marrow examination done to evaluate thrombocytopenia showed refractory anemia (see Table 1). The bone marrow karyotype was 46,XY,del(5)(q); +8; t(4;13). Three months later, he developed abdominal pain and watery diarrhea and had temperatures to 39.4 °C. Stool cultures were negative. Colonoscopy showed scattered aphthous ulcerations throughout the colon, a finding consistent with the diagnosis of Crohn disease. Histologic findings indicated mild chronic colitis. Although the patient's gastrointestinal symptoms responded to steroid therapy, he developed acute myeloid leukemia in September 1991.

**Patient 4**
A 68-year-old woman developed bloody diarrhea in 1982. Stool cultures were negative. Colonoscopy

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**Table 1. Hematologic Profile of Patients at Presentation**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count, × 10⁹/L</td>
<td>7.4</td>
<td>7.1</td>
<td>7.0</td>
<td>5.9</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>102</td>
<td>107</td>
<td>...</td>
<td>96</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.29</td>
<td>0.30</td>
<td>0.33</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean corpuscular volume, fL</td>
<td>105</td>
<td>98</td>
<td>88</td>
<td>94</td>
</tr>
<tr>
<td>Platelet count, × 10⁹/L</td>
<td>276</td>
<td>400</td>
<td>90</td>
<td>239</td>
</tr>
<tr>
<td>Bone marrow Cellularity, %</td>
<td>60</td>
<td>60</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Trilineage dysplasia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ringed sideroblasts, %*</td>
<td>&gt; 90</td>
<td>5</td>
<td>&lt; 5</td>
<td>80</td>
</tr>
<tr>
<td>Myeloblasts, %</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

* Percent of nucleated red cells.
showed Crohn colitis. Severe perianal disease and symptoms that were unresponsive to steroid therapy prompted total abdominal colectomy and ileostomy in 1983. Pathologic examination revealed chronic transmural colitis with numerous granulomas and “skip” areas. In 1984, a bone marrow examination was done because of the patient’s persistent anemia and showed refractory anemia with ringed sideroblasts (see Table 1). Karyotype analysis revealed one of 20 mitoses with 46,XX,der(20),t(20;?)p13;?).

Discussion

Although an association between inflammatory bowel disease and lymphoreticular neoplasms or leukemia has been described anecdotally (5, 6), our four cases represent the first series of patients with coexistent myelodysplastic syndrome and Crohn disease. All patients had either refractory anemia or refractory anemia with ringed sideroblasts (2). None showed the stigmata of the Turner or Hermansky-Pudlak syndromes, which are associated with an increased risk for both inflammatory bowel disease and hematologic disorders.

Although the association between myelodysplastic syndromes and Crohn disease may be coincidental, the apparent pathophysiological links suggest otherwise. Immune dysfunction, including impairment of T-cell and natural-killer-cell function, has been described in patients with inflammatory bowel disease (3) and in those with myelodysplasia (1, 7). Whether underlying immunologic irregularities account for the development of both myelodysplastic syndromes and inflammatory bowel disease or whether the additional immunosuppression caused by one disease predisposes to the development of the other is unknown. Except in the case of Patient 4, the immunosuppressive agents prednisone or sulfasalazine were not administered before the development of the myelodysplastic syndrome (3) and those with myelodysplasia (1, 7). Whether underlying immunologic irregularities account for the development of both myelodysplastic syndromes and inflammatory bowel disease or whether the additional immunosuppression caused by one disease predisposes to the development of the other is unknown. Moreover, whether a disruption of a gene or proto-oncogene, hematopoietic cell kinase, s-adenosyl homocysteine hydrolase, and adenine deaminase, are located on 20q11-13 (10), the precise role of these genes in the myelodysplastic syndromes is unknown. Moreover, whether a disruption of a gene or proto-oncogene, hematopoietic cell kinase, s-adenosyl homocysteine hydrolase, and adenine deaminase, are located on 20q11-13 (10), the precise role of these genes in the myelodysplastic syndromes is unknown.

Although our findings show the potential significance of anemia in Crohn disease and of diarrhea in myelodysplastic syndromes, the exact relation between Crohn disease and the myelodysplastic syndromes is unclear. The validity of this potential association should be tested in a case-control fashion.

Requests for Reprints: Richard M. Stone, MD, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115.

Current Author Addresses: Drs. Eng and Stone: Division of Medical Oncology, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115.
Dr. Farurray: Division of Gastroenterology, Harvard Community Health Plan, 2 Fenway Plaza, Boston, MA 02115.
Drs. Shulman and Connors: Division of Hematology and Oncology, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115.
Dr. Peppercorn: Division of Gastroenterology and Department of Medicine, Center for Inflammatory Bowel Diseases, Beth Israel Hospital, 330 Brookline Avenue, Boston, MA 02115.
Dr. Krauss: Division of Medical Genetics, Harvard Community Health Plan, 185 Dartmouth Street, Boston, MA 02116.

References