CASE 5.2
Crohn Disease | Level 2

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1. What subjective and objective evidence suggests active CD in this patient?

SUBJECTIVE FINDINGS: Abdominal pain, fatigue, bloody diarrhea

OBJECTIVE FINDINGS: Abdominal tenderness and pain (8/10), underweight, appears fatigued, and appears mildly malnourished on PE; important laboratory tests: + guaiac stool test, leukocytosis, elevated ESR, elevated fecal calprotectin, anemia, hypocalcemia, hypoalbuminemia, and a Pediatric Crohn Disease Activity Index (PCDAI) of 42

The PCDAI score can be used to determine the severity of CD based on symptoms and laboratory data. The score uses a 0 to 100 scale, and a score of >30 indicates active moderate-to-severe disease. It is important to understand that this patient has chronic CD with an active flare-up.

2. What risk factors does this patient have for the development of active CD?

The potential risk factors for active CD in this patient are her age, sex, ibuprofen use, and race. Although age does not necessarily cause CD, the majority of CD diagnoses occur between 15 and 40 years of age. Females have a higher incidence of CD compared to males, although this is reversed in ulcerative colitis (UC). The connection between ibuprofen use and development of CD is controversial, but ibuprofen has been reported to acutely worsen CD disease and cause active disease. Her symptoms seem to have occurred before she started using OTC ibuprofen, but it may be worsening her active disease. Compared to those of African-American and Hispanic descent, Caucasians have a higher incidence of inflammatory bowel disease (IBD).

Psychosocial factors, mainly stress, have also been known to induce active disease in some patients. There is not enough information in this case to determine if stress is a contributing factor. Contraceptive use has been implicated to increase the risk of IBD, but reports are conflicting, and it appears to be higher when combined with smoking and when used for postmenopausal hormone replacement. Other accepted risk factors not present in this case include family history, level of physical activity (more physical activity decreases risk), and a history of smoking. Associations with CD have also been noted with various diets, nursing as an infant (breastfed infants may have less risk), antibiotic use, infections, obesity, and isotretinoin use for acne

vulgaris, but these are not well-defined risk factors.

3. Assess the current pharmacologic management of this patient's CD.

The patient is currently exhibiting steroid dependent moderate-to-severe CD as indicated by the need for multiple steroid bursts this year and the resumption of symptoms while being tapered off the current steroid burst. Her disease has not been controlled with mesalamine. Various 5-ASA preparations have been used for treatment of mild-to-moderate CD. Although few studies have been completed in pediatrics, a meta-analysis of adult studies found that the role of 5-ASA remains unclear, and they are likely ineffective in severe disease.

Her steroid wean is not being tolerated, and she is having break-through symptoms. Budesonide is an alternative steroid with more localized action. Although fewer adverse reactions have been reported, studies have shown similar or less effectiveness compared to prednisone. Thus, switching to budesonide will likely not increase efficacy in this patient and is not a reasonable option. More aggressive CD treatment is warranted to induce and maintain remission. If an intervention is not made, multiple complications could occur. The patient may require long-term steroid treatment, which is not optimal treatment due to the numerous metabolic- and endocrine-related adverse reactions associated with long-term steroid use. Without adequate treatment, the extensive inflammatory disease could worsen and cause more severe complications such as fistulas and necrosis in her gastrointestinal tract. These complications may require extensive surgical management. She also will continue to have excessive bowel movements and will be malnourished, potentially requiring nutritional supplementation via parenteral nutrition.

The patient is *C. diff* toxin (-), and antibiotic therapy is not warranted for this patient's current presentation. Antibiotic therapy, usually ciprofloxacin or metronidazole, is often only used in patients with fistulas.

4. Develop a pharmacologic plan to induce remission for this patient's CD.

The goal of therapy in this patient is to induce a remission and then try to maintain it. Remission can be evidenced by a decreased number of bowel movements, absence of melena in her stools, decreased abdominal pain, decreased fatigue, improved oral intake, and appropriate weight gain. A decrease in the PCDAI score (overall disease severity) can also be used to determine a remission (scores of <10 have been used to define a remission). Initial treatment of CD is controversial and strategies have changed over the past decade. There has been a shift toward earlier immunomodulatory therapy after diagnosis. This patient may have been started on a 5-ASA agent at diagnosis because of a milder presentation. However, her current disease is more severe and thus requires more aggressive treatment to induce and maintain a remission.

An anti-tumor necrosis factor (anti-TNF) alpha agent would be an ideal treatment to induce remission in this patient. Recent studies (in both pediatric and adult populations) suggest earlier use of anti-TNF therapy after CD diagnosis leads to higher rates of remission, faster time to remission, and longer duration of remission compared to historical immunomodulatory treatments (e.g., methotrexate and azathioprine). Infliximab, although only FDA approved for induction and maintenance therapy of CD in children ≥6 years of age who failed conventional therapy, would be an appropriate treatment for this patient. An appropriate dose for this patient would be infliximab 200 mg (~5 mg/kg/dose) IV on weeks 0, 2, and 6 followed by 200 mg every 8 weeks. If treatment response is not achieved, the dose can be increased to 400 mg (10 mg/kg/dose) at the same frequency. Adalimumab has also been used to treat CD but is not approved by the FDA for use in pediatric patients, and data supporting its use in pediatrics are limited compared to infliximab. Although it may be beneficial in the ambulatory setting because it is administered subcutaneously and does not require hospital or infusion clinic admission for IV infusion, compliance can be a concern. This treatment should be reserved to failure with infliximab. Other biologics have