

Case Study: Aphthous Ulcers in a 14-Year-Old Girl

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Briana is a 14-year-old, previously healthy, Jewish female, presenting to her primary care clinic accompanied by her mother. She has been complaining of mouth sores for the past 3 weeks. Her mother expresses concern because the sores are not going away and the mouth pain has caused both a decrease in appetite, and lately, absence from school.

Recurrent aphthous ulcers (RAUs), also known as canker sores, aphthous stomatitis, or aphthae, are a very common and often painful condition presenting in primary care. The majority of aphthous ulcers are benign, time-limited (7 to 14 days), and in some cases, require pain management until healed. However, RAUs can be a manifestation of a serious health condition, such as an autoimmune disorder, human immunodeficiency virus, infection, and hematologic or oncologic conditions. Initially, the most important priority in caring for these patients is to obtain a complete history and physical examination to rule out systemic disease and lead to an accurate diagnosis and plan of care.

History of Present Illness

Briana states “my mouth hurts most of the time, especially when I eat foods I have to chew.” Both Briana and her mother state that Briana has had the mouth sores “several times” in the past 2 to 3 years, but they have gone away after about 2 weeks and have never bothered her enough to seek medical attention. She has never had to miss school before because of them. Briana describes the pain as “burning and aching,” identifies a pain level of 4 to 6 on a 10-point scale, and reports she has received relief from taking ibuprofen 400 mg three to four times a day for the past 2 weeks. She has also been sucking on zinc lozenges, which seem to help.

Briana is unable to associate any particular cause of the ulcers. She states that “they just seem to randomly appear.” She denies any allergies to food or medicines. The only medicines she takes are ibuprofen, zinc,

and a daily multivitamin. Both her mother and Briana agree that she has never suffered any oral trauma, toxic ingestion, or oral irritation from toothpastes or mouthwashes, and are not aware of any allergies.

Briana denies fever, nausea, vomiting, or headaches, although she recalls “feeling feverish” before starting the ibuprofen. She admits to intermittent, diffuse abdominal pain, but the ibuprofen usually relieves this discomfort. She also reveals she has had diarrhea for the past 2 weeks and admits this was the main reason she missed school. She was afraid she would not make it to the bathroom. She also adds she has been feeling fatigued most days.

Further investigation reveals that Briana has been having 5 to 10 loose, brown, and often watery stools a day. She recalls having “bouts of diarrhea” similar to this episode five or more times this past year. She admits to waking most nights, having to urgently “run to the bathroom” and stool. She denies ever seeing blood in her stool. Briana’s mother was unaware of her diarrhea symptoms.

Briana is unable to associate any particular foods with abdominal discomfort or diarrhea. She usually enjoys a varied diet. She has not been treated with antibiotics in the past year. Her mother denies any foreign travel. The family usually eats at a restaurant once every 2 weeks, and Briana eats lunch prepared by the school cafeteria.

The pediatric nurse practitioner (PNP) noted Briana lost 10 pounds since her annual well-visit 4 months ago, dropping one channel on the growth curve in weight, and two channels on the body mass index (BMI). Her BMI dropped from 17.6 (25th percentile) to 16 (5th percentile) in 4 months.

Birth, Development, and Growth History

Briana’s mother reports a healthy pregnancy and a vaginal delivery with no complications. She states she received prenatal care from about 8 weeks. Developmentally, Briana has progressed normally, sitting at 6 months, crawling at 9 months, and walking at 14 months. Her verbal development has always “seemed advanced.” She started verbalizing around 9 months and was singing the alphabet song at 16 months. She has always been a strong student in school.

Briana was in the 50th percentile for weight and height throughout childhood. At her well-visit (age 14 years, 2 months), she was at the 75th percentile for height and just under the 50th for weight.

Family and Social History

Briana lives with both her parents. She is the youngest of three siblings (sister age 20, brother age 17). Mom

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Statements of Disclosure: The author reported no actual or potential conflict of interest in relation to this continuing nursing education activity.

The Pediatric Nursing journal Editorial Board reported no actual or potential conflict of interest in relation to this continuing nursing education activity.

denies any family problems or significant family stress. They are a second generation Jewish family, attend their synagogue regularly, and report having a strong support system from friends and family.

Mom reports all immediate family members are healthy. Briana's paternal grandmother was diagnosed with Crohn's disease in her early 20s and died from intestinal cancer at age 63.

In a private interview with Briana, she states she is generally happy at home. She admits to being a "high achiever" and often worries about her grades. She adds that she knows she is a good student but worries about doing well anyway. She denies depression, substance use, use of tobacco products, and any current or prior sexual activity. She denies ever taking diet pills or laxatives, or intentionally vomiting her meals. She states she has never been concerned about her body weight until lately as she has noticed her clothes are very loose on her.

Briana started her menses 2 months after her 13th birthday. She has had regular periods for the past 4 months, which last about 5 to 7 days and have been coming about every 26 to 28 days. She denies excessive pain or bleeding with menses. Her last menses was 3 weeks ago.

Past Medical History

Briana has been a patient in this clinic since age 8. She has had no major illnesses. She had an appendectomy at age 7 with no complications and has suffered two sprained ankles in the past 2 years while playing tennis. She has no history of chronic illness. Briana received all required childhood immunizations. Additionally, she has received the human papilloma virus vaccine series, meningococcal vaccine, and both doses of hepatitis A vaccine.

Nutritional History

Briana states she likes most foods but for the past few weeks has been ingesting small amounts of soft foods. Her mother states Briana has always been a healthy eater. Her 24-hour diet recall includes two containers of yogurt, 1 cup of plain non-fat milk, 2 cups of milk mixed with instant breakfast additive for calories, 1 cup apple juice, ½ cup applesauce, one bowl of chicken noodle soup, and a cup of buttered pasta noodles. She drinks 4 to 5 cups of water daily. This intake is typical for Briana over past 2 to 3 weeks.

Physical Examination Findings

Briana presents alert and cooperative, although with a slumped posture. She appears pale, fatigued, and proportionally thin in relation to her height. Vital signs consist of temperature, 100.8; pulse, 110; respirations, 22; blood pressure, 92/58; and pulse oximetry, 98%.

HEENT: Head normocephalic, scalp intact; PERRLA; EOMI; visual acuity 20/20 ou; conjunctivae pale; sclerae and corneas clear; red reflex ou. TMs translucent with sharp cone of light. Throat benign; lips dry, peeling; multiple, shallow, erythematous, round, and ovoid ulcers measuring 3 to 8 mm noted on buccal mucosa, dorsal tongue, and inner lower lip. Mild, submaxillary lymphadenopathy.

Chest: Clear bilaterally.

Cardiac: Mildly tachycardic, regular rhythm, no murmurs. Capillary refill is under 2 seconds.

Abdomen: Non-distended, bowel sounds hyperactive all four quadrants, diffuse pain of 4/10 on pain scale with light-to-moderate palpation; no rebound tenderness; no masses; no hepatosplenomegaly.

Musculo/Skeletal: Full range of motion of all limbs. No tenderness to joints on palpation.

Neurological: No deficits appreciated.

Genitourinary: Breasts and genitalia Tanner stage four. No ulcers or lesions noted on genitalia. Two erythematous, perianal skin tags noted. No masses or stool appreciated on rectal exam.

Skin: No rashes, no finger clubbing.

Laboratory Testing

Guaiac test positive for blood in stool. CBC results indicate a normal WBC; low Hgb/Hct: Hgb 10.8; Hct 32; low MCV 74,000; elevated platelets 470,000; elevated erythrocyte sedimentation rate 32 mm; elevated C-reactive protein (CRP) 1.6; low serum albumin 3.3; normal thyroid function tests; normal complete metabolic panel; stool for leukocytes and stool cultures for ova, parasites, *Clostridium difficile*, *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia* were negative. Urinalysis was negative for bacteria and ketones. A referral was made with a gastroenterologist, and an endoscopy and colonoscopy were scheduled after stool cultures were negative and initial lab work results were consistent with an inflammatory process. A Mantoux test (result negative) and an anti-tissue

transglutaminase (aTTG) level (celiac marker, result negative) were both drawn at the request of the gastroenterologist. Endoscopy revealed inflammation, granulomatous appearance, and multiple areas of aphthous ulcers throughout the small intestine, most notably in the terminal ileum. A biopsy was collected, and the diagnosis of Crohn's disease was made.

Differential Diagnoses

The differential diagnoses for Briana comprises a long list. Briana's chief complaint compels the PNP to consider a differential diagnosis for aphthous ulcers: RUA, benign, cause unknown; herpes virus; HIV; Behcet's syndrome; reactive arthritis; Sweet's syndrome; erythema multiforme; cyclic neutropenia; cancer; leukemias; celiac disease; inflammatory bowel disease (IBD) including ulcerative colitis and Crohn's disease; periodic fever syndromes (FAPA: fever, aphthous ulcers, pharyngitis, adenitis); and Stevens-Johnson syndrome (Scully, 2006; Weston, Lane, & Morelli, 2007).

The presence of chronic and persistent diarrhea, weight loss, mild abdominal pain, and perianal tags expanded the differential and suggests a gastrointestinal etiology. This provider anticipated the abdominal pain and fever would have been more predominant symptoms but were likely masked by frequent intake of ibuprofen. Primary differential diagnoses are infectious colitis (including *Clostridium difficile*), gastroenteritis, irritable bowel syndrome (IBS/IBD), Crohn's disease, ulcerative colitis, celiac disease, cystic fibrosis, anorexia nervosa, hyperthyroidism, diabetes, food/medication allergy, lactose intolerance, constipation with encopresis, and laxative use (Hyams, 2005; Yamada, Hasler, Inadomi, Anderson, & Brown, 2005). Appendicitis must always be included in the differential with a patient presenting with symptoms of fever and abdominal pain; however, this patient had an appendectomy. The possibility of concurrent conditions must also be recognized.

Primary Differential Diagnoses

After completing a thorough history and physical, the primary differential diagnoses for Briana are a) IBS, b) infectious colitis, c) celiac disease, d) ulcerative colitis, and e) Crohn's disease.

Irritable bowel syndrome (IBS) is a functional disorder characterized by abdominal pain and altered bowel pattern (often diarrhea and frequency of stooling), which commonly presents in childhood (American Academy of Pediatrics [AAP] Subcommittee on Chronic Abdominal Pain, 2005; Holten, Wetherington, & Bankston, 2003). When no organic disease is found, IBS is often the diagnosis of exclusion (Holten et al., 2003). The AAP (2005) and Holten et al. (2003) identify alarm symptoms, including weight loss, fever, gastrointestinal bleeding, right lower quadrant pain, anemia, night-time symptoms, deceleration in linear growth, and family history of IBD. If present, these should immediately prompt further testing and evaluation by a gastroenterologist (AAP, 2005; Boyle, 2008; Holten et al., 2003).

Infectious colitis can be caused by bacteria, parasites, ova, and viruses; it can often cause abdominal pain, bloody diarrhea, weight loss, and electrolyte imbalance (Yamada et al., 2005). The PNP should screen for these causes prior to referral to gastroenterology by obtaining stool for ova, parasites, giardiasis, and leukocytes; and obtain stool culture for *Campylobacter*, *Salmonella*, *Yersinia*, *Shigella*, and *Clostridium difficile* (Yamada et al., 2005).

Celiac disease, also known as gluten-sensitive enteropathy, is a chronic lifelong, auto-immune condition that causes damage to small intestine mucosa (Rashid et al., 2005; Yamada et al., 2005). It affects "as many as 1 in 104 children in the United States" (Rashid et al., 2005, p. e754), making it one of the most common chronic childhood diseases. While celiac disease peaks commonly at age 3, with the ingestion of cereal and exposure to wheat, rye, barley, and oats (gluten containing foods) and again in the third and fourth decade of life, it can present at anytime (Rashid et al., 2005; Yamada, 2005). Early diagnosis is essential to preventing further damage and serious complications. According to Rashid et al. (2005) in their study of 168 children, "After [sic] starting the gluten-free diet, 89% noted a significant improvement in health" (p. e756). Excellent screening tests for celiac disease are available to the PNP and include IgA tissue transglutaminase or IgA endomysial antibody tests.

Ulcerative colitis (UC) is a chronic, inflammatory, systemic, autoimmune disease that affects the colon. Crohn's disease and UC present similarly, are frequently mistaken for each other, are

considered by some experts as different manifestations of the same condition, and are medically managed very much the same way (Hyams, 2005; Yamada et al., 2005). These conditions are different in their location in and the type of damage they do to the bowel (Hyams, 2005). Ulcerative colitis can involve the rectum to the proximal colon, presenting with mucosal inflammation and crypt-like ulcerations (Hyams, 2005). The patient presents with frequent bloody diarrhea (Hyams, 2005). Colonoscopy is necessary to evaluate for UC (Yamada et al., 2005). When UC has too dramatic an impact on the patient's quality of life, it can be cured through colectomy. Crohn's disease can be managed but it cannot be cured.

Crohn's disease is also a chronic, systemic, inflammatory, autoimmune disease that can affect any part of the gastrointestinal tract from mouth to anus (Hyams, 2005). The disease process affects all four layers of the intestine and is characterized by "skip areas" where inflamed bowel is interspersed with healthy bowel (Yamada et al., 2005). The strongest risk factor for developing "IBD is having a first-degree relative who has the disease, with the estimated risk being 30 to 100 times greater than in the general population" (Hyams, 2005, p. 309). This risk is greater with Crohn's disease than UC. Additionally, the risk of IBS is significantly greater in persons of Jewish descent, especially Ashkenazi Jews (Yamada et al., 2005).

Crohn's disease can present with subtle extra-intestinal symptoms, such as aphthous ulcers; arthritic complaints (especially knee joint pain); growth failure or deceleration; delayed puberty; eye problems (blurred vision, painful and red eyes) including uveitis, iritis, and episcleritis; erythema nodosum; pyoderma gangrenosum; and finger clubbing (Haas-Beckert & Heyman, 2004; Hyams, 2005; Rose, Vogiatzi, & Copeland, 2005; Wine et al., 2004). Two of the most common early presentations of Crohn's disease are mucocutaneous lesions (namely, aphthous ulcers) and linear growth failure (Galbraith, Drolet, Kugathasan, Paller, & Esterly, 2005; Rose et al., 2005; Scully, 2006).

Crohn's Disease Diagnosis Confirmed

Endoscopy and biopsy confirmed Crohn's disease. Colonoscopy ruled out UC. Negative IgA aTTG ruled out celiac. Stool was negative for ova, parasites, and common pathogens.

History and physical findings support the diagnosis. To summarize: persistent and recurring aphthous ulcers; chronic, persistent, and frequent diarrhea; abdominal pain (likely masked by use of ibuprofen); weight loss (especially crossing of growth channels); decreased appetite; positive hemocult test; elevated inflammatory markers (ESR, platelets, CRP); decreased serum albumin (decreased protein); low Hct and Hgb; and a low MCV (indicating chronic blood loss); Jewish ancestry; and a positive family history.

Most Reliable Laboratory Tests in Screening for IBS

Primary care providers need to know which tests are reliable and necessary when a child presents with typical or atypical symptoms of IBS (Wong & Bass, 2008). Sabery and Bass (2007) determined Hgb and ESR were more cost-effective and accurate for predicting IBS in the general population compared to more expensive serologic testing. Mack et al. (2007) determined negative screening results do not eliminate the possibility of IBS, and symptomatic patients should be referred for endoscopy and colonoscopy.

The Guaiac test is important to confirm the presence of occult blood in stool (Boyle, 2008). Patients with Crohn's disease can present with grossly bloody stools, especially if the terminal ileum or proximal colon is involved (Hyams, 2005). They can also present with no occult blood in their stool (Hyams, 2005). Abdominal pain with bloody stools is always grounds for immediate referral to gastroenterology (Boyle, 2008; Holten et al., 2003).

Often, the patient has to wait for a month or more to see the gastroenterologist. The PNP should collaborate with the specialist to determine if there are additional screening tests that can be done in advance and to discuss medical management of symptoms and pain in the interim.

The Management Plan

After collaboration with the gastroenterologist, Briana will be put on mesalamine 800 mg po tid and prednisone 40 mg po qd, with the primary goal of reducing inflammation and inducing remission (Colombo, Roberts, & Friesen, 2006; Hyams, 2005). Once the inflammation is under control, Briana should be able to absorb nutrients normally and gain

her weight back. Additionally, control of the inflammation should result in elimination of other symptoms, such as aphthous ulcers, diarrhea, and perianal tags. Briana and her parents will be informed about her medications and instructed never to discontinue the prednisone abruptly. The complex medical management is beyond the scope of this article.

Briana will be placed on a daily iron supplement of ferrous sulfate 60 mg (elemental iron) po bid for 3 months to correct anemia. She will be given a prescription for "magic mouthwash," which consists of one part viscous lidocaine to one part liquid diphenhydramine hydrochloride to one part aluminum hydroxide; 5 to 10 ml are swished in the mouth and spit out four times a day for 7 days to sooth the pain of her mouth ulcers (Lawrence, Gootman, & Sim, 2009). Briana and her parents will be scheduled to see a dietician to help plan a tolerable, high-calorie diet. A follow-up appointment will be scheduled for 1 to 2 weeks to review laboratory results and monitor Briana's status, including the healing of her mouth ulcers. At the fourth week follow-up, more detailed education on Crohn's disease will be discussed. Briana and her parents will be provided with educational brochures on Crohn's disease, introduced to the local chapter of the Crohn's and Colitis Foundation of America (CCFA), encouraged to consider family and individual counseling to help adjust to the diagnosis of a chronic condition, and encouraged to visit the Web site for CCFA (www.ccfa.org). If symptoms do not improve or worsen, the gastroenterology appointment would be changed to an earlier date. In severe cases, Briana would be hospitalized.

Discussion

The goal of medical management of Crohn's disease is to induce remission and prevent relapse of the disease with as few side effects from medications as possible (Colombo et al., 2006; Hass-Beckert & Heyman, 2004). This is done through daily maintenance medications and multiple medication management during exacerbations (Colombo et al., 2006). Medications used in managing Crohn's disease are 5-aminosalicylates, corticosteroids, immunomodulators, probiotics, and antibiotics (Colombo et al., 2006; Hass-Beckert & Heyman, 2004). Once stable, the patient will usually follow up with the gastroenterologist once or twice a year.

Although Crohn's disease is characterized by exacerbations and remissions, many children have a good quality of life (Colombo et al., 2006; Cunningham, Drotar, Palermo, McGowan, & Arendt, 2007). Parents and families benefit by participating in support groups (Cunningham et al., 2007). Disease management and optimal health are achieved through use of medication, nutritional therapy, and psychosocial support (Cunningham et al., 2007; Haas-Beckert & Heyman, 2004).

Children with Crohn's disease will be managed in primary care for the majority of their health needs. Accuracy in taking growth measurements and plotting them on the growth curve remains a critical skill in recognizing growth delay or failure (Rose et al., 2005). Special attention should be given to yearly eye exams and bone density screening (Haas-Beckert & Heyman, 2004). Awareness of extraintestinal as well as gastrointestinal symptoms will result in earlier diagnosis of disease exacerbation and limit or eliminate serious complications (Hyams, 2005).

Scheduled immunizations are given unless the child is taking immunosuppressants, in which case live vaccines could not be given (killed vaccine [the flu shot] should be given). Additionally, immunosuppressed patients who are exposed to chicken pox should be given VZIG (immunoglobulin for varicella) within 48 hours of exposure (Haas-Beckert & Heyman, 2004).

Depression and anxiety are more prevalent in children with chronic illnesses, with reports of decreased quality of life correlated with more severe disease presentations (Cunningham et al., 2007). If school performance is affected, the PNP can assist in addressing these issues. The prognosis for Crohn's disease is usually good, and in most cases, the child can take part in all activities in which children without Crohn's disease participate. ■

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