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Persistent Fevers and Abdominal Pain in a 13-Year-Old Neutropenic Patient

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EDITORS NOTE

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AUTHOR DISCLOSURE Drs Ross, Lee-Miller, Bagrosky, and Rogers have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

CASE 1 PRESENTATION

A 13-year-old girl who is receiving oral maintenance chemotherapy for acute lymphoblastic leukemia that is in remission is admitted with acute-onset abdominal pain and fever. She was well until the evening before admission, when she developed periumbilical and pelvic pain with fever. She had one episode of emesis. She denies constipation, diarrhea, dysuria, vaginal discharge, or sexual activity. She currently has a central venous catheter. Her onset of menses was at age 12 years with regular monthly periods; her last period was approximately 2 weeks before the onset of pain.

Vital signs are as follows: temperature, 102.9°F (39.4°C); heart rate, 132 beats per minute; respiratory rate, 20 breaths per minute; and blood pressure, 98/53 mm Hg. Physical examination is notable for present bowel sounds and a soft and nondistended abdomen without organomegaly but with diffuse abdominal tenderness. The central venous catheter site is clean. The remainder of her physical examination findings are unremarkable. Pelvic and rectal examinations are not performed because of the patient's history of neutropenia.

Laboratory evaluation reveals the following: white blood cell count, $0.6 \times 10^3/\mu\text{L}$ with an absolute neutrophil count (ANC) of $480/\mu\text{L}$ ($0.48 \times 10^9/\text{L}$) (reference range, $3,000\text{--}5,000/\mu\text{L}$ [$3.0\text{--}5.0 \times 10^9/\text{L}$]); hemoglobin, 9.5 g/dL (95 g/L); and platelets, $70 \times 10^3/\mu\text{L}$ ($70 \times 10^9/\text{L}$). Urinalysis reveals moderate bacteria and trace leukocytes. Urine pregnancy test result is negative. She is admitted and empirically administered intravenous cefepime and gentamicin. Initial blood culture from her central venous catheter yields *Escherichia coli*; thus, gentamicin therapy is discontinued. Abdominal ultrasonography reveals a fluid-filled right adnexal cyst that measures 6.5 cm in diameter. Computed tomography (CT) confirms the cyst; no other abnormalities are noted. However, the appendix is not visualized on either ultrasonography or CT. Her abdominal pain worsens and localizes to the right lower quadrant and pelvis. Subsequent pelvic ultrasonography reveals a stable cyst size.

She continues to have daily fevers and pain for 19 days despite treatment with broad-spectrum antibiotics and subsequent negative blood culture results. An imaging study suggests a diagnosis.

CASE 1 DISCUSSION

On the basis of persistent fevers, positron emission tomography (PET)–CT is performed to look for areas of high glucose metabolism suggestive of infection, inflammation, or oncologic disease. PET-CT revealed a right adnexal hypodensity with a surrounding area of intense hypermetabolism consistent with an abscess. Because of these findings, the patient was diagnosed as having tubo-ovarian abscess (TOA). Antibiotics were changed to ampicillin, gentamicin, and clindamycin, and fevers resolved within 48 hours after initiation of this regimen and increase in the patient's ANC. Abdominal pain was well controlled with acetaminophen and oxycodone as needed.

The Condition

Typically, TOAs occur as complications of pelvic inflammatory disease and ascending infection from the lower genital tract. They may also occur as a complication of gynecologic surgery. Often, TOAs are polymicrobial and can be facilitated by sexually transmitted bacteria, such as *Neisseria gonorrhoea* and *Chlamydia trachomatis*. Adjacent gastrointestinal infection or underlying immunodeficiency may predispose a patient to TOA. Hematogenous spread with seeding of the ovarian tissues is described in the literature but occurs rarely. Because this patient denies sexual activity and is severely immunosuppressed because of chemotherapy, she may have been predisposed to this infection and therefore spontaneously developed the abscess.

Diagnosis

This neutropenic patient's fever and abdominal pain were concerning for urinary or gastrointestinal tract infection, in particular typhlitis (neutropenic colitis). The differential diagnosis also included appendicitis, pyelonephritis, abscess, and central catheter infection. This case illustrates that a broad differential diagnosis should be maintained in the immunocompromised population. During this patient's hospitalization, TOA was discussed but thought to be unlikely in this young teenage patient with no history of sexual activity and lack of ultrasonographic evidence of infection. Ultimately, the diagnosis was made with the assistance of PET-CT intended to search for other occult sources of infection because it is an unconventional imaging modality for TOA. Fevers resolved after administration of the appropriate antibiotics. Surgical drainage or biopsy was not necessary in our patient, although they would have been useful in confirming the microbiology of the infection.

TOA can be diagnosed with ultrasonography alone, which typically reveals fluid collections with a thick hyperechoic

rim. Signs of surrounding inflammation are often noted, and free fluid is frequently observed in the pelvis. Magnetic resonance imaging or CT may be useful in further characterizing a mass and excluding other causes of fever and abdominal pain, including appendicitis. In this patient's case, the surrounding inflammatory reaction was visible neither on ultrasonography nor CT, likely because of neutropenia, and the adnexal TOA appeared to be a simple hemorrhagic cyst. Neutropenic patients lack the ability to mount a visible infectious and inflammatory response to infection (including edema, exudate, and fluctuance), often presenting with only fever and pain.

Treatment and Prognosis

Neutropenia in pediatrics is defined as an ANC below $500/\mu\text{L}$ ($0.50 \times 10^9/\text{L}$) or less than $1,000/\mu\text{L}$ ($1.0 \times 10^9/\text{L}$) with anticipation to decrease in the next 48 hours. Blood cultures are obtained in patients with indwelling central venous catheters because this is a likely source of infection. Empiric broad-spectrum antibiotics with antipseudomonal activity, such as cefepime, ceftazidime, or levofloxacin, are administered. Antibiotics therapy is continued until the ANC is greater than $100/\mu\text{L}$ ($0.10 \times 10^9/\text{L}$) and increasing and blood culture results are negative after 48 hours. Patients with proven infection require antibiotic treatment of appropriate duration.

Treatment of TOA begins with medical management with intravenous antibiotics. Surgery is not typically the preferred initial method of treatment because there is risk of loss of the ovary and fallopian tube during drainage of the mass. Because these infections are often polymicrobial, empiric parenteral treatment is broad spectrum and directed at gram-negative, gram-positive, and anaerobic microbes. Typical regimens include a third- or fourth-generation cephalosporin plus doxycycline and should include at least one agent able to penetrate an abscess cavity. If the patient has persistent fever, increased abscess size after 48 to 72 hours of antibiotic therapy, or concern for rupture at any point, surgical exploration should be pursued. In fact, in approximately one-third of patients, surgical intervention is required to achieve cure because of severity of illness. For most pediatric patients, conservative management is sufficient, and duration of antibiotic therapy is typically 14 days. Patients should be followed up closely by a gynecologist, and ultrasonography screening may be indicated after antibiotic treatment is complete to ensure resolution.

Lessons for the Clinician

- Female patients with few or no risk factors for pelvic inflammatory disease are still at risk for

developing a tubo-ovarian abscess, particularly if they are immunosuppressed.

- Conservative management is preferred, particularly in young patients. This management avoids significant surgery and risk of loss of the affected ovary and fallopian tube.

- Serious bacterial infection can be difficult to diagnose in neutropenic patients given their lack of typical symptoms at presentation.

View the Suggested Reading list for this case at http://pedsinreview.aappublications.org/content/36/3/127/suppl/DCSupplementary_Data.

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Pediatric Movement Disorders: 1. D; 2. A; 3. D; 4. D; 5. C.

Nephrotic Syndrome: 1. E; 2. E; 3. C; 4. D; 5. E.

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