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A 17-Year-Old Girl With Weight Loss and Anemia

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Case Report

A 17-year-old female presented with 1-month history of more noticeable weight loss and increased tiredness. Over the last 6 years since immigrating to the United States with her family from Burma and going through puberty, her body habitus has changed to a very thin appearance. This period of time began with menarche, which subsequently demonstrated intermittent oligomenorrhea occasionally alternating with amenorrhea. Apparently, workup by a gynecologist was negative and a yearlong period of oral contraceptive use did little to change the scant flow pattern. She discontinued these 6 months ago. The patient's diet history revealed 3 meals a day of normal type foods but always smaller portions than other members of her family. Mother agreed that she does not eat much fried or fast foods, usually what is prepared for the family at home. The patient eventually suggested after repetitive questions that there was an increase in early satiety over the last month and she clearly was overall more tired. Five months ago, she had an outpatient visit for viral syndrome with vomiting and diarrhea, which resolved in 48 hours. At that time, her weight was 42 kg and no fever noted. Review of systems was notable for fatigue, intermittent chills, hair loss with nonvigorous brushing, intermittent "shakiness" when getting up, and shortness of breath on exertion. She denied any fever, upper respiratory tract infection symptoms, coughing, nausea, vomiting, dysuria, abdominal pain other than associated with her menstrual cycle, rashes, easy bruising or bleeding. Her past medical history was notable for the oligomenorrhea and scoliosis, but prior testing for anemia reported negative 6 months ago, and all chronic diseases, including in other members of the family, was denied, including anemia, thalassemia, and tuberculosis. The patient reports feeling "sad sometimes" but denied any suicidal or homicidal ideation. In the emergency department, her physical exam (PE) was notable for a tired appearing but otherwise well teenage girl with a temperature of 101.6°F, heart rate 125, respiratory rate 16, pulse oxygenation saturation of 97% on room air, weight 40 kg, height 144.78 cm, body mass index 20.1, some hair loss with brushing, II/VI systolic murmur over LUSB, and mild nonpitting bilateral edema. The remainder of the PE was unremarkable. Laboratory values were remarkable for white blood cell count 4700/μL with neutrophilic predominance, hemoglobin 7.3 g/dL, hematocrit 24.8%, mean corpuscular volume 74.9 fL, red cell distribution width 18.4%. Chemistry panel was within normal limits except for low albumin 2.9 g/dL, and a slightly elevated aspartate transaminase 54 U/L. Thyroid studies demonstrated slightly elevated thyroid-stimulating hormone of 6.68 mIU/L (05-6.0) with normal free T4 of 1.08 ng/dL (0.7-1.9). C-reactive protein and erythrocyte sedimentation rate were elevated to 65.4 mg/L (normal 0-5) and 132 mm/h (normal 0-20), respectively. Urinalysis was unremarkable and urine pregnancy test was negative. Additional iron studies demonstrated levels of iron 29 μg/dL, ferritin 3 ng/mL, and a total iron binding capacity of 144 μg/dL. Given the severe anemia and elevated inflammatory markers, the decision was made to admit the patient for further workup.

Hospital Course

The typical consideration for severe anemia in an American adolescent female usually includes dietary iron deficiency, menorrhagia, and/or risk of hemoglobinopathy/thalassemic state. The differential diagnosis for this patient was broader and included gastrointestinal, infectious, rheumatologic, oncologic, psychiatric, and volitional etiologies. Her hematologic labs coupled with her inflammatory markers were most consistent with a mixed picture of iron deficiency anemia coupled

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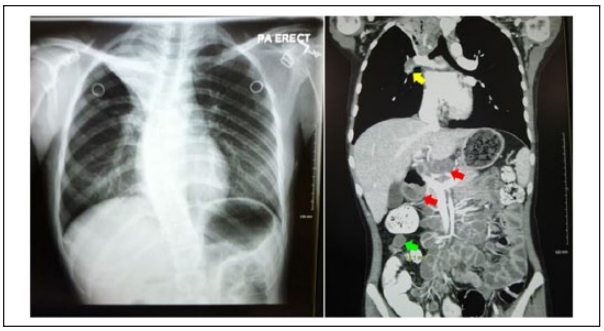

Figure 1. Left: Chest radiograph (PA) demonstrating right upper lobe wedge-shaped opacity with reticular changes suggesting possible consolidation and/or interstitial changes. Right: Computed tomography (coronal) view notable for (a) consolidation at right apex with extension to right hilum, (b) mediastinal/hilar adenopathy (yellow arrow), (c) low-density masses within and surrounding porta hepatis (red arrows) that were also well-visualized on additional slices, and (d) low-density mass in right lower quadrant near cecum suggestive of lymphadenopathy (18.1 mm, green arrow).

with anemia of chronic disease. Her description of increasing early satiety raised concerns for an inflammatory bowel disease or possible slow growing abdominal mass. Abdominal ultrasounds demonstrated complex solid and cystic masses in the region of the porta hepatis concerning for peritoneal lymphadenopathy. Follow-up abdominal computed tomography (CT) did not appear to be consistent with inflammatory bowel disease but several likely enlarged peritoneal and abdominal lymph nodes were present. Subsequent chest X-ray and thoracic CT were notable for a right apical consolidation and parabronchial masses, some with calcifications (see Figure 1). Therefore, pulmonary tuberculosis (TB) with abdominal involvement was considered. Gastric aspirates were negative for acid-fast bacilli. Induced sputum samples were attempted, but the patient was unable to produce sputum. Subsequent PPD (purified protein derivative) and T-Spot results were positive. Thus, she was taken for a bronchoscopy for sputum collection and a lymph node needle biopsy, both of which showed acid-fast stains positive for likely mycobacteria. These were only observed in combined samples enriched by centrifugation. The patient was started on RIPE therapy (rifampin, isoniazid, pyranizamide, ethambutol). An extensive infectious disease workup including HIV, viral hepatitis, RPR, *Helicobacter pylori* were all negative. Autoimmune workup including ANA, anti-dsDNA, RF, and thyroid peroxidase antibodies were negative. Of note, secondary review of the history directly with mother through an interpreter revealed that mother and maternal aunt were treated for TB upon arrival to the United states 6 years prior, but the mother thought patient was not positive to screening because she never received similar anti-TB treatment. It was unknown if patient had ever received BCG or PPD testing.

Throughout the hospital course, the patient had intermittent fevers to 104°F and hypothermia to 93°F, which self-resolved. On discharge, the appropriate communications with local health department officials were made for direct observed therapy and appropriate follow-up was arranged. *Mycobacterium tuberculosis* eventually was isolated from the cultures, sensitive to RIPE therapy.

Final Diagnosis

Activation of latent *Mycobacterium tuberculosis* with pulmonary and abdominal involvement.

Discussion

A history of weight loss, fatigue, chills, and shortness of breath necessitates considering a broad differential that must be approached systematically. Possible etiologies include infection, autoimmune disorders, hematologic/oncologic processes, and psychiatric and social/nutritional concerns. An accurate history is always mandated and in this case was not initially obtained because the teenager was allowed to answer the majority of the questions involved and in many cases answer for the mother, even with the interpreter present. Only specifically directed questions to the mother subsequently revealed what should now be considered an obvious set of clues, that of a teenager with a long history of weight loss immigrating from a TB endemic region of the world with prior exposure to TB and now presenting with severe anemia. There clearly was insufficient suspicion for activation of latent TB during that initial outpatient encounter.

We present a representative case of TB in a 17-year-old female whose initial presentation was quite concerning for an underlying hematologic process given her weight loss, anemia, and constitutional symptoms as well as a possible abdominal mass of oncologic origin given her increasing early satiety. However, her normal platelet and white blood cell counts made the diagnosis of leukemia or lymphoma unlikely. While the patient did endorse a decreased appetite, there was no evidence of overt nutritional deficiency nor eating disorder. Preliminary psychological evaluation was also reassuring. It is important to consider hyperthyroidism given the clinical presentation; however, the patient had only slightly elevated thyroid-stimulating hormone and normal free T4. Importantly, the patient also had a concurrent diagnosis of iron deficiency anemia as evident by the iron studies.

Constitutional symptoms such as fever should always trigger a workup for infectious etiologies. The history of immigration from an endemic region, coupled with exposure from her mother and aunt who had been previously treated for TB, pointed to the underlying infectious process. Anemia without iron deficiency has been associated with a 4-fold increased risk of TB recurrence. Iron deficiency and anemia, with or without co-presentation in a patient with TB, are associated with a 2- to 3-fold increase in the risk of death.[1] The patient had an unclear history of PPD testing. Thus, TB screening tests including a chest radiograph and either PPD or interferon-γ release assays (IGRA) should be performed during the early evaluation of possible infectious causes. While chest X-ray or PPD findings may be nonspecific, it could prompt—as in this case—further serological and radiographic workup.

With a rising immigrant population in the United States, TB—the second most common infectious cause of mortality worldwide—should be included in the differential for a patient with generalized symptoms, weight loss, and anemia. Contracted through airborne droplets, pulmonary TB classically presents with fever, long history of cough, hemoptysis, and several constitutional symptoms including weight loss, diaphoresis, and malaise. Typical risk factors include recent contact with infected individual, immunocompromised state, homelessness, and incarceration. Laboratory analysis can include PPD, usually now referred as tuberculin skin test (TST), as well as IGRA, such as the QuantiFERON-TB Gold or T-SPOT TB Test. It is also important to consider prior history of BCG vaccination in immigrant populations, as this may lead to positive PPD testing with no evidence of concurrent infection. IGRAs are unaffected by prior BCG vaccination.[2,3] The current recommendation by many infectious disease experts is that all persons with a positive PPD, irrespective of prior BCG vaccine, be further tested with IGRAs to ensure that there is not latent, if not active, TB.[4] Both IGRA tests available in the United States, QuantiFERON-TB Gold In-Tube Test (QFT-GIT) and the T-SPOT TB Test (T-Spot), are approximately similar in turnaround time, cost, and accuracy. However, the T-Spot assay may be slightly more accurate than QFT-GIT when comparing both assays to tuberculin skin testing.[3]

Extrapulmonary tuberculosis (EPTB) constitutes 15% to 20% of all cases of TB in immunocompetent patients in some areas, but accounts for more than 50% of the cases in HIV-positive individuals.[5] The exact frequency in immunocompetent patients varies among studies from different sites, but it has been suggested that, overall, approximately 10% of HIV-negative patients present with EPTB. In contrast, in HIV-positive patients, 33% present with EPTB alone and 33% present with both pulmonary and extrapulmonary disease, although many will have negative initial chest X-ray. Therefore, it is important for all pediatric patients that test positive by IGRA to have their HIV status determined.[6] Our patient tested HIV-negative.

Conclusion

While multiple processes could create the clinical presentation herein (eg, autoimmune, hematological, infectious), our case is unique in that the final diagnosis of TB lacked some typical features (eg, cough, hemoptysis). Given the social history, it is important to remember that foreign-born patients have a case rate approximately 13 times higher than US-born patients.[2] Even with initial presentation suggesting other underlying causes of the clinical presentation, TB must remain on the differential. The final diagnosis was established taking into account the clinical history as well as social history. Early detection and adequate knowledge of the appropriate serologic and radiographic workup for TB infections can improve patient outcomes, and TB should remain high on the differential for severe anemia in any for any immigrant child.[7] Considering the current heterogeneity of the US pediatric population, the association between anemia and *Mycobacterium tuberculosis* needs to be better kept in mind during all pediatric clinical encounters.

Author Contributions

ZOE: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JC: Contributed to acquisition, analysis, and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

LAM: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JMC: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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