Endocrinology, Diabetes & Metabolism CASE REPORTS

K Hamid and others | Abdominal pain caused by hypothyroidism

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My tummy hurts – a case report of abdominal pain and macrocytic anemia caused by hypothyroidism

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Summary

A 6-year-old female presented with chronic intermittent abdominal pain for 1 year. She underwent extensive investigation, imaging and invasive procedures with multiple emergency room visits. It caused a significant distress to the patient and the family with multiple missing days at school in addition to financial burden and emotional stress the child endured. When clinical picture was combined with laboratory finding of macrocytic anemia, a diagnosis of hypothyroidism was made. Although chronic abdominal pain in pediatric population is usually due to functional causes such as irritable bowel syndrome, abdominal migraine and functional abdominal pain. Hypothyroidism can have unusual presentation including abdominal pain. The literature on abdominal pain as the main presentation of thyroid disorder is limited. Pediatricians should exclude hypothyroidism in a patient who presents with chronic abdominal pain. Contrast to its treatment, clinical presentation of hypothyroidism can be diverse and challenging, leading to a delay in diagnosis and causing significant morbidity.

Learning points:

- Hypothyroidism can have a wide range of clinical presentations that are often nonspecific, which can cause difficulty in diagnosis.
- In pediatric patients presenting with chronic abdominal pain as only symptom, hypothyroidism should be considered by the pediatricians and ruled out.
- In pediatric population, treatment of hypothyroidism varies depending on patients' weight and age.
- Delay in diagnosis of hypothyroidism can cause significant morbidity and distress in pediatrics population.

Background

Regardless of the site, pain is one of the main reasons patients seek medical attention (1, 2). Chronic abdominal pain is common and can be caused by a myriad of pathological processes involving gastrointestinal and other organs such as severe constipation, gastroesophageal reflux disease or pancreatitis. However, abdominal pain in pediatric population is usually due to functional causes such as irritable bowel syndrome, abdominal migraine and functional abdominal pain (3). Absence of organic causes often means lack of objective clinical finding, as a result extensive and invasive investigations are often conducted (4). Hypothyroidism can have unusual presentation including abdominal pain. Also, macrocytic anemia can be present in up to 55% of cases of hypothyroidism, it could be due thyroid hormone deficiency rather than secondary to nutritional causes such as B12 and folate

deficiency (5). The literature on abdominal pain as the main presentation of thyroid disorder is limited. Pediatricians should exclude hypothyroidism in a patient who presents with chronic abdominal pain, especially if other evidence of hypothyroidism such as macrocytic anemia is present.

Case presentation

A 6-year-old female presented to the emergency department complaining of 4-day history of fever, cough and nasal congestion. Additionally, she has been complaining of a chronic abdominal pain for the past year. Her abdominal pain was described by her mother as intermittent periumbilical pain that starts immediately after eating solids, per her mother the patient 'curl up into a ball' due to the pain, leading to avoiding solid foods and poor weight gain. No nausea, vomiting. Over the course of the past year, patient has undergone extensive investigation and imaging, including abdominal X-ray, ultrasound and CT scan, which were inconclusive except for increased fecal matter concerning for mild constipation on plain abdominal film; however, no increased fecal material was found on CT scan of abdomen. One week prior to current hospital admission, patient underwent elective upper and lower gastrointestinal endoscopy that were within normal limits. Patient was empirically treated with polyetheleneglycol and cyproheptadine with no observed benefit. Family history was positive for maternal cutaneous Lupus, leukemia in a cousin and unclear thyroid diseases in maternal grandmother and aunt. Patient had an episode of lower UTI 2 weeks prior to presentation which was treated with trimethoprim-sulfamethoxasole. During this episode a complete blood count revealed macrocytic anemia that was overlooked. Her immunization is documented as up to date for her age. Patient's newborn screen which included screening for congenital hypothyroidism was within normal limits. Rest of history and review of systems were unremarkable.2

Physical examination revealed heart rate of 132, respiratory rate of 20, blood pressure of 112/61 and temperature of 38.8 C (Oral). Auxological data were notable for poor growth rate with weight 19.5 kg at 4.02 percentile ($Z=-1.75$), height 114.7 cm at 1.53 percentile ($Z=-2.16$) and BMI 17.14 kg/m^2 at 74.52 percentile ($Z=0.66$) (Figs 3 and 4). Right upper quadrant and epigastric tenderness was elicited without guarding and rigidity on abdominal palpation, extremities were cold to touch. Rest of examination was within normal limits.

Investigation

Pertinent laboratory investigations included CBC with differential which revealed mild pancytopenia with macrocytosis (Table 1), peripheral blood microscopy showed white blood cell dysplasia. Nasopharyngeal swab detected Influenza A Antigen. Rest of initial investigations including comprehensive metabolic panel, serum lipase and urinalysis were within normal limits. Imaging with abdominal X-ray (Fig. 1), ultrasound and abdominal CT (Fig. 2) were done and were unremarkable. Patient was started on supportive care and oseltamivir for acute viral illness dehydration with admission to pediatric care unit.

Differential diagnosis

With available lab results and clinical picture, differential diagnosis was expanded to assess for hypothyroidism, Vitamin B12, folate and iron deficiency in addition to further assessing for possible underlying bone marrow disease such as myelodysplastic syndrome or hypoplastic anemia secondary to combination of recent antibiotic use and viral infection. A plan for bone marrow biopsy

Table 1 Initial complete blood count results.

Investigations	Patient range	Ref. range for age 2–9 years
WBC	**3.1 (L)**	**4.0–12 K/mL**
RBC	**3.65 (L)**	**3.88–4.72 m/L**
Hemoglobin	**10.8 (L)**	**11.5–14.5 g/dL**
Hematocrit	33.8	33.0–43.0%
MCV	**92.6 (H)**	**76–90 fL**
MCH, POC	29.5	25–31 pg
MCHC	31.9	32.0–36.0 g/dL
Red cell distribution width	13.5	12.8–13.9%
MPV	7.7	7.4–8.1 fL
Platelets	**142 (L)**	**150–400 K/mL**
Neutrophil	56	54–62%
Lymphocyte absolute	**0.7 (L)**	**1.5–3.0 K/µL**
Lymphocyte	22	25–33%
Monocyte	5	3–7%
Monocyte absolute	0.2	0.4–0.9 K/µL
Band absolute	0.5	0.0–1.2 K/µL
Bands	**16 (H)**	**3–5%**
Meta	**1 (H)**	**0%**
Seg absolute	1.7	1.6–7.8 K/µL

H, high; L, low; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; RBC, red blood cell; WBC, white blood cell.

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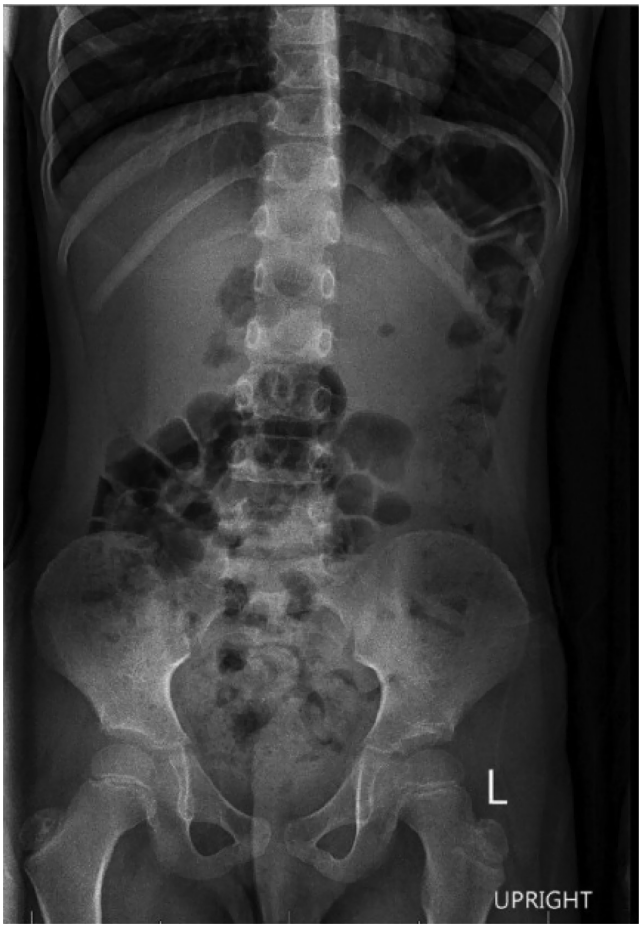

Figure 1
Abdominal X-Ray showing no acute abdominal pathology.

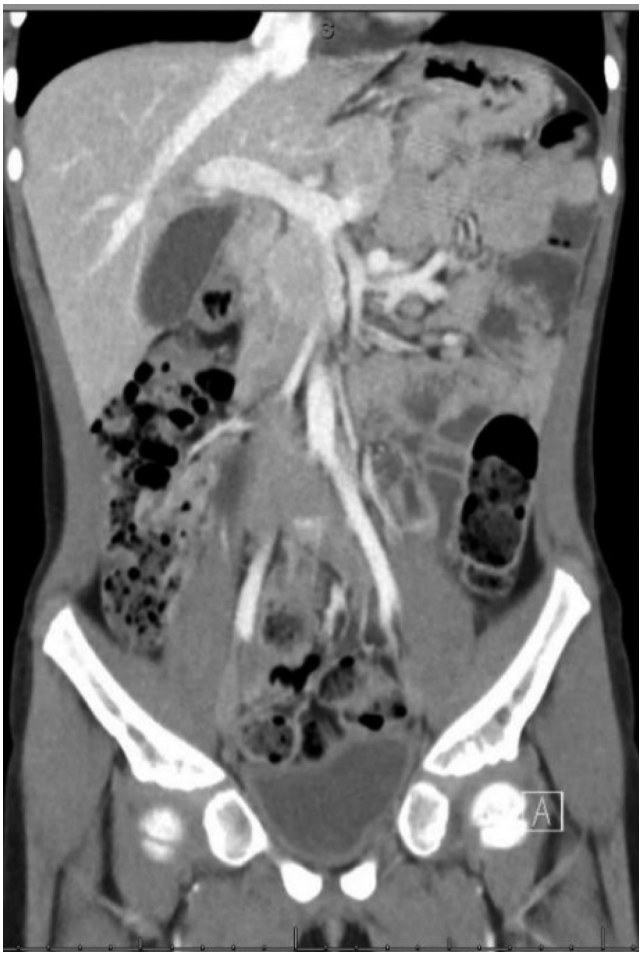

Figure 2
CT abdomen, pelvis with IV contrast showing no abdominal pathology.

was aborted when investigations revealed elevated thyroid-stimulating hormone (TSH). A diagnosis of primary hypothyroidism was made with further work up for a potential etiology of thyroid disease including thyroid antibodies (Table 2) and ultrasound of thyroid, which were within normal limits. Although no exact etiology was revealed – because thyroid antibody levels could normalize in longstanding overt hypothyroidism – autoimmune thyroiditis continued to be the most likely underlining etiology (6). Work up for possible adrenal insufficiency that could accompany hypothyroidism with early morning serum cortisol was obtained and was negative (Table 2).

Treatment

Patient was started on levothyroxine tablets at a dose of 2.5 µg/kg with close monitoring of her vitals and general condition. With plan to reach the full dose within 6–9 weeks by gradually increasing the dose of her levothyroxine every 2–3 weeks.

Outcome and follow-up

Patient remained stable, abdominal pain improved and she was discharged from the hospital. At 3-week follow-up with our pediatric specialty clinic, family reported improved appetite and complete resolution of her symptoms. Repeat thyroid function test showed normalization of thyroid parameters (TSH = 3.33, T4 = 1.6, total T3 = 181). She was continued on her initial dose of levothyroxine without any adjustment.

Discussion

Hypothyroidism is one of the most common endocrine disorders worldwide. Overt hypothyroidism has a prevalence of between 0.3% and 3.7% in the United

Table 2 Additional laboratory investigations obtained.

Investigations	Patient range	Reference range
Cortisol, free	0.18 µg/dL	
Cortisol, total	7.2 µg/dL	5–23 µg/dL
CK total	**160**	**5–130 U/L**
Ferritin	**189 (H)**	**10–60 ng/mL**
Folate	12.41	4–20 ng/mL
Free T4	**0.3 (L)**	**0.7–2 ng/dL**
Iron, serum	52	22–184 µg/dL
TIBC	309	250–400 µg/dL
Iron saturation	**17 (L)**	**27–44%**
T3 total	**46 (L)**	**90–230 ng/dL**
Triglycerides	131	28–129 mg/dL
TSH	**449.44**	**0.5–4.5 mIU/mL**
LDH	283	150–500 U/L
G6PD Quant	10.5	8.8–13.4 U/g Hgb
Vitamin B-12	761	200–835 pg/mL
Vitamin D 25-hydroxy	**20.7 (insufficiency)**	**≥20 ng/mL**
Hemoglobin A	98%	Latest units: %
Hemoglobin A2	2%	Latest units: %
HGB electrophoresis	Normal pattern	
ANA	Negative	
Antithyroglobulin Ab	<20	≤40 IU/mL
TPO Ab	<10	≤40 IU/mL

Ab, antibody; ANA, antinuclear antibodies; CK, creatinine kinase; G6PD, glucose 6-phospate dehydrogenase; H, high; HGB, hemoglobin; L, low; LDH, lactate dehydrogenase; TIBC, total iron-binding capacity; TPO, thyroid peroxidase; TSH, thyroid-stimulating hormone.

States (7). Female: male ratio is 6:1 (4, 8). It is a pathological condition of thyroid hormone deficiency, which if not treated, can lead to serious adverse events and is potentially fatal. The clinical presentation of hypothyroidism is variable and lacks specificity, adding to physicians' frustration (7).

Hypothyroidism can be classified as primary (defect in thyroid gland), secondary (decreased TSH hormone release) or tertiary (due to deficiency in thyrotropin-releasing hormone). It is also classified as peripheral or central (includes secondary and tertiary) (7, 8). Hypothyroidism could also be congenital (present at birth) or acquired (after a period of normal thyroid function) (9).The most common cause of hypothyroidism in developed countries is autoimmune thyroiditis (Hashimotos thyroiditis). It is also important to mention that hypothyroidism secondary to iodine deficiency still affects specific subpopulations, particularly among pregnant women in the United States (7).

Clinical manifestation of hypothyroidism in pediatric populations is broad, and it also presents differently based on the age of the child, making the diagnosis more challenging. Signs and symptoms might include goiter, global developmental delay, poor statural growth with delay in osseous maturation, fluid retention and generalized edema causing increased weight, tiredness and excessive sleepiness, poor school performance, cold intolerance, dry skin and pallor, coarse voice, constipation, menstrual irregularity, delayed puberty or occasionally precocious puberty. One should keep in mind that hypothyroidism is not associated with mental retardation beyond 3 years of age (10, 4, 11).

Abdominal pain as the presenting symptom has been reported in patients as the only presenting symptom in few case reports at adult literature (4); however, to the best of our knowledge, this is the first reported case of hypothyroidism presenting only as abdominal pain in a pediatric patient. Although patient had radiological features of probable constipation, patient was never symptomatic, and did not respond to treatment given for constipation. The observed poor growth rate is better explained by the overt hypothyroidism plus decreased tolerance to solid foods rather than poor oral intake alone (11). Especially since patient's height is also affected (Figs 3 and 4).

An important factor aided in the diagnosis of this case was the macrocytic anemia observed on her hematological investigation. Macrocytic anemia can be seen in up to 55% of patients with hypothyroidism without comorbid nutrition deficiency (5). Our patient had mild pancytopenia, which could have been partially explained by her recent antibiotic treatment and her current viral influenza A infection. However, presence

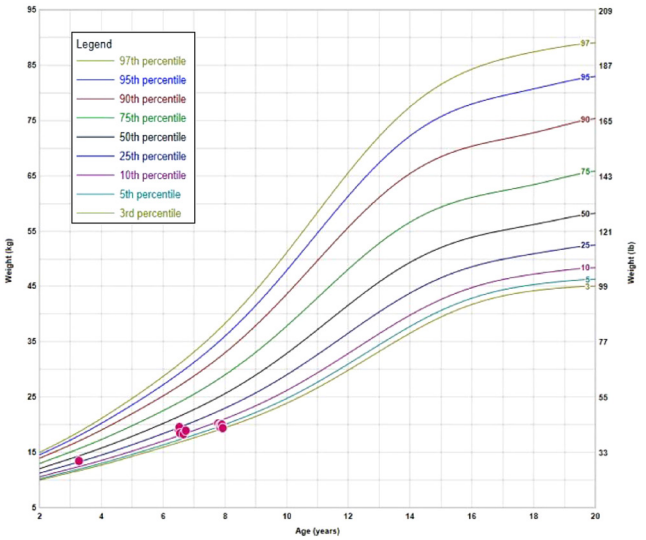

Figure 3
Patient growth chart showing weight for age poor weight gain.

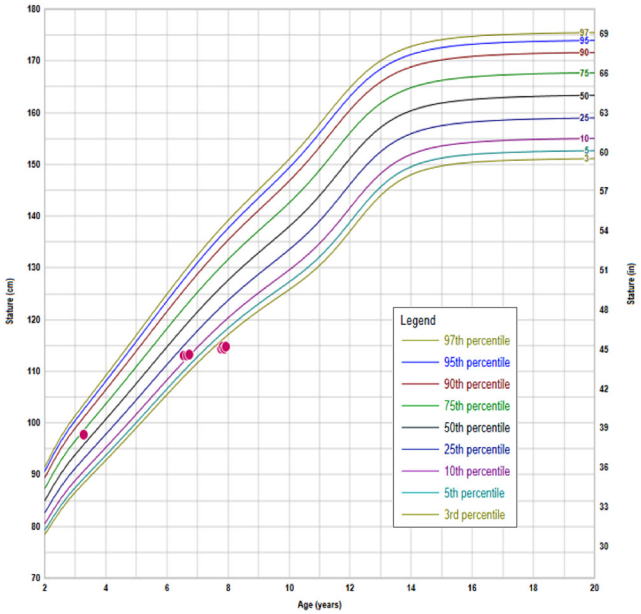

Figure 4
Patient's growth chart showing height for age showing lack of appropriate gain of height.

of her macrocytosis few weeks prior to her hospital admission and duration of her abdominal pain was a clue that a systemic pathological process is more likely, ultimately aiding in the diagnosis. However, the use of adult reference range by the laboratory initially caused some delay.

Once hypothyroidism is diagnosed, treatment is straightforward with levothyroxine. The goal is resolution of symptoms and keeping serum TSH level within normal reference range (7, 11). Levothyroxine dose varies based on patients age: During infancy the dose is 6–8 µg/kg/day from 1 to 3 years, adjusted to 4–6 µg/kg/day from 3 to 10 years, adjusted to 3–5 µg/kg/day for 3–10 years; and from 10 to 16 years 2–4 µg/kg/day is recommended. It is important to start at a lower dose and gradually increase every 3–6 weeks to reach the full recommended dose. The rationale is to decrease deterioration in school performance, restlessness and behavioral issues often associated with starting thyroid replacement therapy at full dose. Single daily dose on empty stomach is recommended to enhance absorption (11, 12). Adequacy of thyroid replacement is done by checking TSH hormone and monitoring growth and development of the child (11). In case of central hypothyroidism, treatment is attuned to keep serum T4 level at upper half of normal range (12).

Patient's perspective
When the nature of the condition and treatment plan was explained, the family expressed relief, because they finally had an answer and treatment is safe and easy to administer, in addition to the fact that they did not have to expose their daughter to further expensive and invasive investigations.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this case report.

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Patient consent
The authors of this article confirm that a written consent from thepatient's motherwas obtained for publication of the article and accompanying images. She willingly signed the consent after she saw and read the included material needed to be submitted.

Author contribution statement
Kewan Hamid: Primary Team Resident (gathered information, performed literature search and wrote the initial manuscript of the case report); Neha Dayalani: Primary Team Resident (obtained informed consent, performed literature search, assisted in preparing the initial manuscript); Muhammad Jabbar: Consulting pediatric endocrinology,. involved in editing and revision of the manuscript; Elna Saah, Consultant pediatric hemato-oncologist, involved in editing and revision of the final draft of the case.

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