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Night Sweats, Stress Activation and Coeliac Disease

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Introduction

Coeliac disease (CD) is a genetic, immunologically mediated small-bowel enteropathy that causes malabsorption. It occurs mainly in childhood, but it can also present in adulthood. The condition is characterized by a permanent sensitivity to gluten that results in inflammation and atrophy of the mucosa of the small intestine.[1] CD has a wide variety of clinical presentations: the "classical" form, in which an intestinal symptomatology is prevalent with symptoms such as diarrhea, steatorrhea, and nutritional and vitamin deficiencies; the "atypical" form with predominating extraintestinal clinical features; and the "silent" form with no clinical symptoms. Atypical forms of CD have been reported with conditions of autoimmune origin. Secondary immunological illnesses may be the primary presentation of the disease.[2]

Night sweats are episodes of nighttime sweating that result in soaking of nightclothes or even beddings, and in most cases, these are signs of different underlying medical conditions.[3]

In this article, we present a case of a child with night sweats as a symptom that not only resulted in the diagnosis of an atypical form of CD but also helped in detecting relapses of the disease.

Patient Presentation

A 3-year-old girl was followed-up in the outpatient clinic for recurrent episodes of wheezing during the previous 6 months. There was no history of atopy or severe febrile illnesses. Her growth was along the 10th percentile. There were no gastrointestinal symptoms, and she had normal bowel habits. The only other symptom reported by the parents was night sweats without fever, but this had not caused any obvious discomfort to the child or concern to the parents. The patient was not very cooperative during the physical examination, giving the impression of a miserable disposition. There were no signs of respiratory distress, and she was in a good clinical condition. She had a runny nose, and auscultation revealed a sparse audible wheeze. A mild abdominal distention was also noted, which had previously been considered to be a normal anatomical variation.

The wheezing episodes were related to viral infections of the lower respiratory tract, with no underlying pathology. She had exhibited good responses to treatments with short courses of bronchodilators. A routine investigation revealed mild anemia (hemoglobin = 10.7 g/dL), with anisocytosis, microcytosis, hypochromia (mean corpuscular volume = 70.6% fL, mean corpuscular hemoglobin = 21.8% pg), and white blood cell count 6490/μL (neutrophils = 50%, lymphocytes = 38%, monocytes = 8%, and eosinophils = 4%), platelets = 353 000 000/μL, and slight derangement of hepatic biochemistry, with SGOT = 59 and SGPT = 27. The levels of urea, creatinine, electrolytes, and fasting glucose were within the normal ranges.

At the latest appointment, although her respiratory sounds were normal with no audible wheeze, the abdominal protrusion was more obvious, and her disposition remained miserable. Some queries emerged after reviewing this case by going back over her history and medical notes before discharging her from the outpatient clinic. Even though the findings of the clinical examination were unremarkable, anemia with anisocytosis,

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microcytosis, and hypochromia remained. Also, the night sweats that had been mentioned by the parents had not resolved.

The above-mentioned medical issues prompted further investigations to be performed. A chest X-ray did not reveal any pathology. A repeated peripheral blood film confirmed normal leukocyte morphology, while ultrasonographic imaging of the abdomen was negative for any pathology. Further investigations of the anemia attributed this to a significant iron deficiency (ferritin = 5 mg/dL). Other causes of anemia such as hemolysis or blood loss were excluded.

Repeated biochemical testing revealed that transaminases remained slightly elevated. Considering iron-deficiency anemia, poor growth, elevated transaminases, abdominal protrusion, and her consistently miserable disposition, it was considered crucial to exclude the diagnosis of CD. Therefore, specific antibodies for CD were obtained. The patient exhibited positivity for anti-gliadin, antiendomysial, and tissue transglutaminase antibodies. A subsequent jejunal biopsy revealed flattening of the villi at the distal duodenum and an increased crypt depth, findings diagnostic for CD.

The patient was initiated on a gluten-free diet. This resulted in a gradual improvement in all symptoms and signs, including an improved disposition and eating well. It was very interesting that night sweats disappeared. She remained well during a 2-year follow-up, with improvement on the scale of the growth chart and with repeatedly negative CD-specific antibodies. The patient was very compliant in maintaining a strict gluten-free diet.

Nevertheless, recently her night sweats recurred and she became a bit agitated although she had no physical complaints. During a couple of these episodes blood glucose measured with a glucometer yielded blood glucose within the normal range (75 mg/dL and 85 mg/dL), as was the glycosylated hemoglobin level (4.5%). However, a routine investigation unexpectedly found positivity in CD-specific antibodies, while the other biochemistry levels were normal. A close evaluation of the child's diet identified a recently introduced chocolate bar that contained traces of gluten. Removing this specific food product from the child's diet had the expected result of normalizing blood test findings. Also, the parents reported that her night sweats had ceased and she was again in good spirits. This scenario was repeated a few more times when she consumed a food product containing gluten.

Discussion

The pathogenesis of CD is related to an immune response to gluten, which is the starting point of an immunological cascade.[4,5] Interactions between the stress system and immune reactions are undoubtedly complex and take place at multiple levels, and various immunomediators play crucial roles in the initiation and propagation of immune responses.[6] In addition, activation of the stress system leads to the stimulation of the systemic sympathetic and adrenomedullary nervous systems, and thus to the peripheral secretion of norepinephrine, epinephrine, and several neuropeptides.[7]

In the last decade, less than 50% of CD cases were found to have diarrhea as the main presenting symptom. The "atypical" forms of the disease are characterized by little or no gastrointestinal symptoms, and predominating extraintestinal features such as refractory iron-deficiency anemia, osteoporosis, short stature, pubertal delay, infertility, and recurrent spontaneous abortions. Other major extraintestinal manifestations include liver dysfunction and neurological, myoskeletal, and dermatological symptoms.[2]

Night sweats occur in the presence of many conditions. Also, it is well known that activation of the stress system via hormone secretion is a trigger for perspiration.[3] In our case, the night sweats were documented as occurring without fever or low blood sugar levels, and other possible causative conditions were excluded. The patient's night sweats subsided on a gluten-free diet and recurred when she consumed a chocolate bar or other food product that contained gluten. The observed sequence of events was in a vicious circle (Figure 1): night sweats, confirmed recurrence of CD, identification of the causative food product, subsequent removal of the food from the child's diet, subsidence of night sweats, and "smoothening" of the immune response with lowering the levels of specific antibodies. It is difficult to believe that this long series of events involving both clinical observations and laboratory findings and their occurrence in the same order is coincidental—this therefore needs to be explained. Moreover, in this child with CD, night sweats were a symptom that recurred also in many confirmed relapses of the disease.

Night sweats were first related to CD in the literature by Emery,[8] and although those findings were not consistent with hypoglycemia, the symptoms were attributed to some kind of disruption of carbohydrates metabolism. There has been no subsequent report in the literature of night sweats being associated with CD, even though many CD forums contain numerous reports of patients complaining about them nevertheless without medical explanation. In our case, blood glucose levels and glycosylated hemoglobin levels were within normal range.

The repeatability of this observation supports that night sweats could be a preliminary symptom of CD and

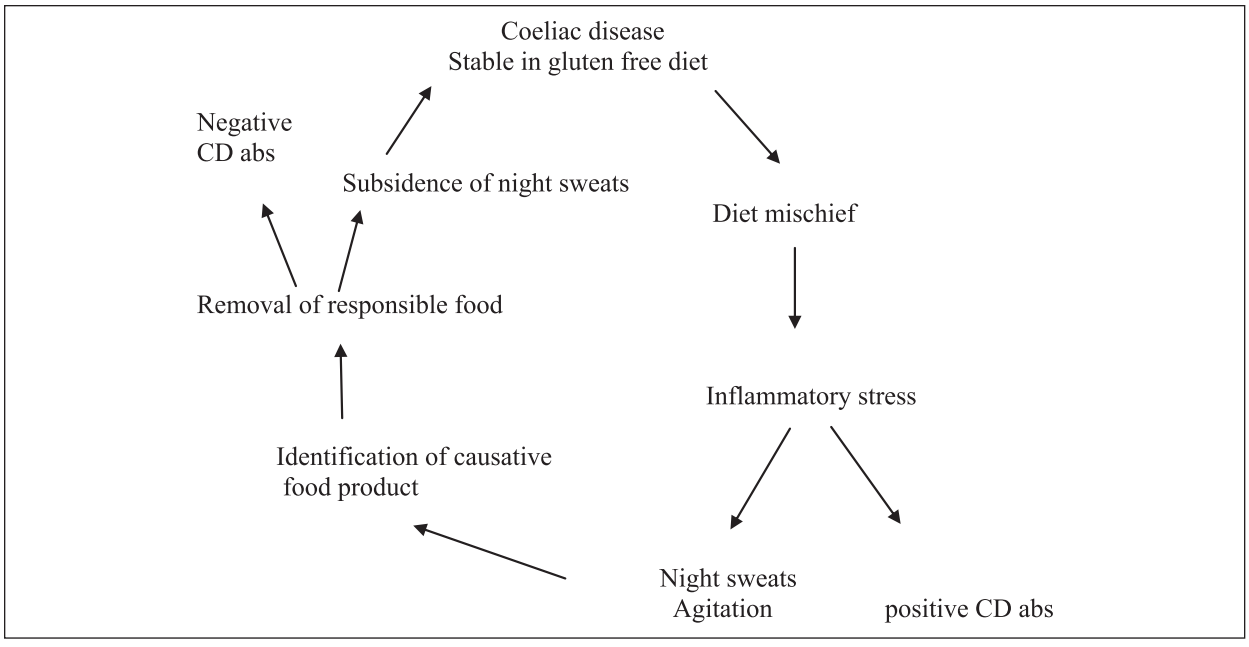

Figure 1. The vicious circle of night sweats in coeliac disease.
Abbreviation: CD abs, specific antibodies for coeliac disease.

even more a sign of a not-well-controlled diet. A possible hypothesis to explain how CD could be related to night sweats is the following: the exposure to gluten triggers an immune response; this is an ineffective alarm of an organism's stress system, with the subsequent production of catecholamines explaining the perspiration bouts. Exploration of this possible mechanism will require more detailed studies.

While it is difficult to draw any definitive conclusions based on a single case, the present findings support that night sweats can be a symptom of CD. Further studies are required in order to examine the consistency of night sweats as an indicator of dietary compliance in CD.

Author Contributions

DC: Contributed to conception and design; drafted manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
KK: Contributed to acquisition and analysis; drafted manuscript.
AM: Drafted manuscript; gave final approval.
IX: Contributed to conception; critically revised manuscript.
ST: Contributed to acquisition; drafted manuscript.
MA: Contributed to analysis; gave final approval.
SG: Contributed to conception and design; drafted manuscript; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
AC: Gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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