

Case Report

Pica as a cause of iron deficiency anemia or the other way around? A look at the cause of iron deficiency anemia in young children.

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Abstract

We describe a young boy with the unusual habit of eating his own clothes and a severe form of iron deficiency anemia. Both phenomena have been mentioned in the same sentence for ages, but their exact relationship has never been shown. In this case report we will review the current literature on the etiology of pica and iron deficiency anemia and we will clarify the existing hypothesis. We want to raise awareness on the potential dangerous consequences of pica behavior because the diagnosis is still often missed.

Introduction

Pica is typically defined as an unusual craving for and ingestion of inedible substances (1). The term "pica" is derived from "pica pica" which is the Latin word for the brown-billed magpie. This bird is known for collecting and hoarding unusual objects to satisfy its hunger and curiosity (2). It is a complex behavior that can be classified according to the substance ingested (table 1) (2).

Table 1: Common subtypes of pica

Subtypes of pica	Substance ingested
Acuphagia	Sharp objects
Coniophagia	Dust
Coprohagia	Faeces
Emetophagia	Vomit
Geophagia	Clay
Hyalophagia	Glass
Lithophagia	Stones
Pagophagia	Ice
Plumbophagia	Lead
Tricophagia	Hair, wool, or other fibres
Xylophagia	Paper

Pica occurs worldwide but the frequency varies by location. Studies have shown that about 20 to 30% of children under the age of six have practiced pica (3). The prevalence might be even higher than documented because it is often overlooked by physicians or under-reported by patients or parents (2). Pica in children is mostly seen in children 18 months to 6 years and is more prevalent in lower socioeconomic classes (2).

Pica may be benign in children with normal intelligence but can also be associated with serious health problems such as electrolyte and metabolic disorders, lead and mercury poisoning, parasitic infections, destructed tooth enamel and various problems of the gastrointestinal tract (1). When associated with iron deficiency (ID), some believe that pica is a consequence rather than a cause. The discussion of this association has been of the chicken-or egg variety: which comes first?

Iron deficiency, with or without anemia, is a major health problem affecting more than 2 billion people around the world (4). Children and adolescents,

who have an increased requirement of iron during periods of rapid growth, have the highest risk to develop a shortage (5). Recent numbers from the United States estimates the prevalence of iron deficiency in toddlers at 9,2% and the prevalence of iron deficiency anemia (IDA) at 2,1% (6).

Anemia is defined as a hemoglobin level that is two standard deviations below the mean for age. In IDA there typically is hypochromia and microcytosis. The diagnosis of IDA is only certain when serum ferritin is low or the percent transferrin saturation is low with an elevated total iron binding capacity (4).

With this case report we want to raise awareness for IDA in children and its consequences. We will also try to shine a light on the association of pica with IDA.

Case report

A two and a half year old African boy without prior medical history was brought to our outpatient clinic by his mother with the complaint of her son "eating his clothes and diapers". This behavior began six months ago and escalated to the point of almost completely rejecting normal foods. He does drink large amounts of cow's milk, more than 1 liter a day. There were no other complaints. Especially no abdominal pain or extreme fatigue.

At consultation we saw an odd little boy who was actively playing but was not good at making social contact. He appeared pale and fatigued. Clinical examination revealed pale conjunctiva and gums. He was diagnosed with pica. Diagnostic work-up showed an important IDA with a hemoglobin level (Hb) of 6,2 g/dl (reference range 11,5-14,5), mean corpuscular volume (MCV) of 55 fl (reference range 75-87) and serum ferritin of 2,7 µg/L (reference range 15-150) He was started on oral iron therapy and we suggested limiting the amount of cow's milk.

Due to the COVID-19 pandemic he was lost to follow-up and we only saw him again after four months. We learned that the pica behavior almost resolved completely. Mama told us she kept giving the iron therapy daily and that the boy now only drinks 400ml of cow's milk a day. Control blood tests were performed. Hb was 11,5 g/dl, MCV 70,9 fl and serum ferritin 29.4 µg/l. Iron supplementation was continued.

After another four weeks we saw the boy again. Pica behavior had now completely resolved and he resumed normal eating habits. Blood control showed a normal Hb of 13.3 g/dl.

Discussion

Children mostly depend on their diet to provide around 30% of the daily iron need (7). These dietary factors play a major role in the development of IDA in children. Prolonged breastfeeding without iron supplementation, as well as a vegetarian diet, are risk factors. The ingestion of large volumes of unmodified cow's milk (CM) leads to IDA by either the low iron content of CM, the inhibition of iron absorption by components of CM or the risk of occult intestinal blood loss. Celiac disease, Crohn's disease and giardiasis are important etiologies as well because they influence the absorption of iron throughout the intestine. Inflammatory bowel disease and cow's milk protein induced colitis lead to increased gastrointestinal loss and are thereby also associated with ID (7,4,8).

ID is not just anemia. Anemia is only one of the manifestations of ID. It is the most known clinical feature and is mostly asymptomatic. Pallor is used to estimate the grade of anemia but is often an unreliable sign. Consequences of the anemic state are lethargy, fatigability, tachycardia, irritability and poor appetite (9).

ID at a young age can result in impaired psychomotor and mental development. Iron is required for proper myelination of neurons, neurogenesis, and differentiation of brain cells that can affect learning, memory and behavior. It's also a cofactor for enzymes that synthesize neurotransmitters. Some of these effects may not be reversible which makes ID a really important topic in pediatrics (10).

And what about pica and IDA? There are a lot of articles written on their possible association. A recent meta-analysis of 83 studies from Miao et al. including more than 6.000 individuals with pica stated that pica was associated with a 2.35 times greater odds of anemia and lower zinc concentrations (11). But how are these two related? Is pica responsible for iron deficiency or is iron deficiency responsible for pica? Despite the knowledge about this phenomenon for centuries, there is still no explanation of the pathophysiology of it. There do exist a number of hypotheses that we will try to clarify.

Some authors suggest that pica could induce iron deficiency by the binding of pica materials on the mucosal layer of the gut and thereby preventing the absorption of micronutrients. This is described in the literature as the first adaptive hypothesis or the 'protection hypothesis'. These materials may also absorb micronutrients in ingested food, which prevents them from being metabolized (12). In a recent study, Seim et al. refuted this hypothesis, stating that geophagic substances do not bind to bioavailable iron and are therefore not responsible for reduced iron absorption. With their study they proposed an in vivo model for assessing the impact of geophagic earth on iron status. A group of broiler chickens were force-fed daily with varying dosages of geophagic material or pure clay mineral. At the end of a 4 weeks period they detected only a minimal impact on the iron status and on the transcript levels of divalent metal transporter 1 (DMT1) of the animals (13). The protection hypothesis suggests that pica-materials are ingested as medication. Pica may be protective by either reducing the permeability of the gut wall to toxins and pathogens or by binding directly to the toxins (12). In this hypothesis questions about the strong association between pica and anemia continue to exist. Pentice et al. suggest in their interpretation of the protective hypothesis that anemia might be a response to infections, whereby the sequestration of certain nutrients can protect against pathogenic agents. Many bacteria need iron to reproduce and so iron sequestration would reduce bacterial growth rates. By accepting this hypothesis, the relationship between anemia and pica would rather be correlational than causal (14,15).

More often it is said that iron deficiency itself induces pica. Young et al. explain this in their second adaptive hypothesis, claiming that consuming micronutrients like calcium, sodium, zinc, and iron is an attempt to compensate for their shortage. They actually rejected this hypothesis in their 2016 paper about geophagy when they said that the timing of geophagy does not parallel the timing of changes in nutrient needs through the lifespan. Furthermore, the irregular presence and low bioavailability of iron in geophagic earth, as well as experimental data indicating that micronutrient absorption is limited after earth consumption, raises doubts on their hypothesis (15).

The last and most plausible explanation is the neurological based or non-adaptive one. Pica cravings could be an epiphenomenon of nutrient deficiencies that affect appetite-regulating brain enzymes or taste sensitivity (15). Recent experiments in rats have shown that iron deficiency can modify olfactory behavior and that DMT1 levels are significantly higher in the olfactory bulbs of iron-deficient rats. The gustatory function might also involve DMT1 and therefore be influenced by body iron repletion. It is possible that the iron content of the hippocampus influences the expression of pica in humans (12). Another possible explanation is that iron deficiency is responsible for a decrease in dopaminergic transmission, leading to pica. This is suggested because of a clear exacerbation of pica behavior under therapy with neuroleptics (8). The decreased iron levels in the central nervous system would therefore be the pathophysiological basis of pica (12).

Conclusion

Pica and its association with IDA have been known for centuries but its precise pathophysiology remains a mystery. Its cause keeps being the source of speculation and no study results have been unanimous. Even in this case, it is not sure whether the pica behavior disappeared because of the oral iron treatment or because of the dietary changes and how big the impact of his autistic behavior was. It is important to treat the possible underlying ID and therefore oral iron therapy is the first choice because it is readily available, inexpensive, effective and safe.

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