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CASE REPORT

Nutrition

Anemia secondary to copper deficiency in a child receiving gastrojejunal feeds: A case report

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Abstract

Pediatric macrocytic anemia has a varied etiology, including nutritional deficiencies, such as folate or B12 deficiency, hematological factors, and micronutrient deficiencies, such as copper deficiency. We present the case of a 9-year-old girl with a complex medical history and gastrojejunal tube (G-J tube)-dependent nutrition who developed macrocytic anemia due to copper deficiency. Despite receiving enteral nutrition, her dietary copper intake was insufficient, leading to hematological abnormalities. Copper supplementation resulted in the normalization of hematological indices, highlighting the importance of considering trace element deficiencies in patients reliant on enteral nutrition, particularly in those receiving jejunal feeds. This case underscores the necessity for vigilant monitoring and optimized micronutrient supplementation in such patients given the lack of standardized guidelines for copper supplementation.

KEYWORDS

complex past medical history, macrocytic anemia, pediatric nutrition, trace elements

1 | INTRODUCTION

Pediatric macrocytic anemias have a varied etiology, including nutritional factors such as folate or B12 deficiency, exposure to certain drugs including chemotherapeutic agents and antiepileptics, and hematological factors such as hemolysis or bleeding, liver diseases, hypothyroidism, and myelodysplasia.[1] Micronutrient deficiencies such as copper deficiency may also lead to cytopenias. Copper is primarily absorbed in the stomach and proximal duodenum as the rate of absorption in jejunum is relatively low, this puts patients at a higher risk of copper deficiency unless appropriately supplemented.[2] We describe the case of a 9-year-old girl with a complex medical history and gastro-jejunal tube (G-J tube)-dependent nutrition who was diagnosed with copper deficiency leading to macrocytic anemia.

2 | CASE PRESENTATION

A 9-year-old girl was admitted to the pediatric intensive care unit (PICU) for *Klebsiella pneumoniae*. She was born at 31 weeks of gestation and had a complex medical history—including hypoxic ischemic encephalopathy, cerebral palsy, recurrent urinary tract infections (UTIs), chronic lung disease, precocious puberty, and severe cognitive impairment but no known liver disease or intestinal mucosal disease. She was nonambulatory and nonverbal and appeared to have a short stature. The weight was at the 90th percentile, height at the 50–75th percentile and body mass index (BMI) at 75–90th percentile on tube fed, cerebral palsy growth curve for girls. She had a tracheostomy, was ventilator-dependent, and required gastrojejunal feeding for oral dysphagia and gastroesophageal reflux. Her diet consisted of Pediasure Reduced Calorie 165 mL four times a day and two scoops of beneprotein

daily. Her caloric intake was limited to 650 kCal/day—her calorie provision had been titrated over time to achieve weight control as calorie requirements were less than predictive equation. She was on antiepileptic medication such as clobazapam, levetiracetam, and phenobarbital, and nitrofurantoin for UTI prophylaxis, in addition to albuterol and budesonide for her chronic lung disease, and muscle relaxants such as baclofen and diazepam.

During her PICU stay, she was noted to have macrocytic anemia with low hemoglobin levels (6.6 g/dL) and an elevated mean corpuscular volume (MCV) of 111 fl. Upon further review of previous labs, her MCV gradually rose from 90 to 111 fl over the past 2 years. She received two units of packed red blood cells and was discharged with improved hemoglobin levels (9.5 g/dL) and MCV (102.5 fl). Hematology initiated a workup (Table 1) for macrocytosis, ruling out common causes such as B12 and folate deficiencies. Reticulocyte count was mildly elevated. Thyroid function test results were within normal limits, and the patient had mild transaminitis. A peripheral smear revealed hypochromic macrocytic cells. Further investigation revealed low serum levels of zinc and ceruloplasmin and low whole blood copper level (Table 2).

Her dietary copper intake was 0.39 mg/kg/day, which is well below the recommended daily allowance (RDA) of 0.7 mg/kg/day.[3] Hence, copper supplementation at 0.8 mg/kg/day was started via a gastrostomy tube. Genetic testing for Wilson's disease and aceruloplasminemia was negative. Her hemoglobin, MCV, and copper levels improved with copper supplementation. However, once copper supplementation was discontinued after 12 months, the patient's macrocytosis recurred as evidenced by elevated MCV and decreased copper and ceruloplasmin levels as seen on laboratory testing (Table 2). Copper supplementation was restarted, leading to the normalization of hematological indices and copper levels once again within 6 months (Table 2). She continued to remain zinc deficient during this time.

TABLE 1 Labs at the time of diagnosis of macrocytic anemia.

	Reference range and units	Patient values
Zinc	48–129 mcg/dL	36
Haptoglobin	43–212 mg/dL	197
Retic count	0.5%–2.5%	4.5
Vitamin B12	250–1205 pg/mL	1022
Folate, serum	>7.1 ng/mL	23.7
Folate, RBC	>280	1232
Methylmalonic acid	87–313 mmol/L	87
White blood cell	4.5–17.0 k/cmm	6.9
Absolute neutrophil count	1.8–8 k/cumm	3.3
Platelet	140–450 k/cmm	241

Abbreviation: RBC, red blood cells.

3 | DISCUSSION

Copper deficiency is linked to macrocytosis and can result from malabsorption exacerbated by factors such as dietary limitations, food intolerance, and anorexia. It is crucial to exclude inherited disorders, such as Menkes disease and aceruloplasminemia, as potential causes. While acquired copper deficiency causing cytopenias has been extensively documented in adults with impaired intestinal absorption, particularly in conditions such as short bowel syndrome postbariatric surgery,[4–6] there are limited case reports in pediatric patients receiving jejunal nutrition.[6–9]

Pediatric case reports have discussed the development of anemia in patients with micronutrient deficiencies. These case reports highlight the significance of copper deficiency in causing hematological abnormalities, such as macrocytic anemia and pancytopenia, in patients reliant on total parenteral nutrition (TPN) or long-term enteral feeds. In one case, a 9-month-old infant with short bowel syndrome and TPN dependence exhibited anemia and pancytopenia, which was resolved with copper supplementation. Another case involved a 4-year-old male on enteral feeding, who developed macrocytic anemia likely due to dietary copper deficiency exacerbated by excessive zinc supplementation.[8] These cases emphasize the importance of balanced micronutrient supplementation and vigilant monitoring to prevent and manage hematological complications in such patients. Long-term enteral feeding poses a heightened risk of micronutrient deficiencies, especially in patients receiving jejunal feeds rather than gastric feeds.[9] With jejunal feeding, copper absorption sites in the stomach and duodenum are bypassed. This contributes to macrocytic anemia and leukopenia. This in addition to the low-calorie copper deficient diet contributed to the copper deficiency seen in this patient.

Copper deficiency can manifest through various symptoms, such as fragile hair, muscle weakness, bone weakness, and neurological abnormalities, such as ataxia and impaired cognition. However, evaluating these manifestations in our case posed challenges because of the underlying cerebral palsy. Furthermore, severe copper deficiency has been associated with late onset hypogammaglobulinemia and decreased mean platelet volume.[10] Prompt evaluation and management in our case prevented the worsening of the copper deficiency.

TABLE 2 Lab values in chronological order since presentation.

Date	Hemoglobin (11.2–14.5 g/dL)	Hematocrit (35%–44%)	MCV (78–91 fL)	Copper (117–181 µg/dL)	Ceruloplasmin (23–48 mg/dL)	Copper supplementationmg/kg/day	Zinc (48–129 mcg/dL)
April 26, 2021	6.8	20.8	111.5	5	6	0	3
May 01, 2021	9.5	28.7	102.5	-	-	0.8	-
May 27, 2021	14.5	43.6	99.4	0.84	30.5	0.8	-
July 22, 2021	15.1	45.2	95.4	1.02	32.8	0.8	-
April 10, 2022	15.0	42.5	91	-	37.2	0	-
July 14, 2022	14.3	43	95.8	-	5.3	0	-
November 14, 2022	13.9	42	98.4	-	4.6	0.8	-
June 20, 2023	-	-	-	1.35	41.9	-	6.9

Abbreviations: MCV, mean corpuscular volume; N/A, not available.

Careful monitoring and collaboration between the registered dietitian nutritionist and the patient or caregiver are recommended for patients receiving transpyloric enteral nutrition. This need is further emphasized in those with medical complexity, including low-calorie requirements, because meeting micronutrient needs can take time.

The literature reports hematological abnormalities associated with antiepileptic medications. While older studies suggest a link between nitrofurantoin and antiepileptics, such as phenobarbital and megaloblastic anemia,[11] evidence for causation remains unclear. In our case, the reversal of macrocytosis with copper supplementation corresponded to increasing copper and ceruloplasmin levels. The positive correlation with copper replenishment along with negative workup effectively ruled out other causes of anemia, solidifying copper deficiency as the underlying cause.

Although copper deficiency is readily reversible, there are currently no standardized guidelines regarding the formulation, route, or dosage of copper supplementation. Some case reports have proposed initial intravenous cupric oxide administration for swift resolution, followed by oral therapy for maintenance.[8] American Society for Parenteral and Enteral Nutrition recommends active intravenous repletion with doses four to eight times the usual nutrition recommendations.[12] However, it does not specify whether it includes pediatric population. According to American Academy of Pediatrics, there is no standard supplementation but current practices are to supplement with a recommended daily dose amount of 40–50 µg/kg of elemental copper.[13]

4 | CONCLUSION

This case highlights the impact of inadequate dietary copper intake and malabsorption in jejunal feeding, leading to copper deficiency and subsequent macrocytic anemia, which was successfully reversed by copper supplementation. This emphasizes the necessity of considering trace element deficiencies, particularly copper deficiencies, as a potential cause in patients receiving enteral nutrition. Optimizing the micronutrient levels in enteral feed formulations is crucial. However, the absence of clear guidelines for the formulation, dosing, and duration of copper supplements concerning macrocytosis indices emphasizes the importance of ongoing follow-up, even after supplement discontinuation.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

The parents of the patient provided informed consent for publication of this case report. Informed patient consent was obtained for publication of the case details.

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