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Missed or delayed diagnosis of Kawasaki disease during the 2019 novel coronavirus disease (COVID-19) pandemic

To the Editor:

Due to "stay-at-home" orders and the risk of novel coronavirus disease 2019 (COVID-19), many parents now hesitate or fear seeking in-person consultations for their children. This has led to reductions in emergency department visits and hospital admissions for other critical illnesses. In addition, healthcare providers have focused on COVID-19 management during the pandemic. Because of Bayesian thinking, other diseases may be underdiagnosed or undergo delayed treatment.

Because COVID-19 now leads as the probable diagnosis for first-line providers encountering febrile patients, the potential for missed or late diagnosis and treatment of Kawasaki disease in children is particularly concerning.[1] Prompt diagnosis of Kawasaki disease and treatment with intravenous immunoglobulin (IVIG) prevents coronary artery aneurysms (CAA).[2,3] Without timely treatment, CAAs could occur in up to 25% of children with Kawasaki disease.[3]

We respectfully remind caregivers of the following principles for the care of children with suspected or definite Kawasaki disease: (1) Keep a high suspicion for Kawasaki disease in all children with prolonged fever, but especially in those younger than 1 year of age. (2) Administer IVIG within 10 days, and ideally within 7 days, from onset of fever. (3) In the presence of ongoing systemic inflammation, children with Kawasaki disease presenting with greater than 10 days of fever and/or CAA may warrant IVIG treatment. (4) Continue to obtain recommended echocardiograms according to published guidelines.[3] (5) Watch for late manifestations of Kawasaki disease, review the clinical history, and seek pediatric cardiology consultation.[4,5] (6) In the case of delayed diagnosis, refer to the American Heart Association management guidelines or contact an expert in Kawasaki disease.[3] (7) Offer telemedicine services, remote echocardiogram, and direct-to-consumer visits that allow for nonverbal communication when evaluating children with confirmed or suspected Kawasaki disease.[6-8]

With this, we hope to avoid a future surge in the prevalence of CAAs in patients due to missed or delayed diagnosis of Kawasaki disease.

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Iron, ketone bodies, and brain development

To the Editor:

Iron deficiency is deleterious in early life brain development and a risk for short- and long-term cognitive, motor, and socioemotional impairment.[1,2] Parkin et al recently reported that increasing serum ferritin values, up to a level of 17 μg/L, were correlated with higher cognitive function in infants of 1-3 years of age.[3] Here, we address another aspect of the role of iron deficiency in brain development in relation to ketone bodies as an energy source for brain metabolism.

In the starved state, ketone bodies are synthesized from free fatty acids produced by breakdown of body fat, and cross the blood-brain barrier for use in brain metabolism. Ketone bodies may have neuroprotective effects and a ketogenic diet is used in treatment of neurological diseases such as refractory epilepsy, Parkinson disease, Alzheimer disease, and traumatic brain injury.[4,5]

Kuzawa and Blair hypothesized that body fat is a critical brain energy source, especially during infancy and early childhood.[6] In this period, the brain consumes about 40% of daily energy expenditure (20% for adults). Glucose alone cannot supply this energy, and ketone bodies are used. Thus, brain energy expenditure is inversely related to body fat gain (increased body mass index) during early childhood, and thus, decreases the risk of obesity.[6,7]

In an iron-deficient state, ketogenesis is impaired, citrate synthase and succinate dehydrogenase activities are decreased, and production of free fatty acids and ketone bodies is limited.[8,9] Therefore, iron deficiency may not only have a direct effect on brain function and development, but may also decrease the availability of ketone bodies as an energy source.[3] This possibility that the brain is deprived of ketone bodies as an energy source in iron deficiency indicates a need for further research into how iron is involved in brain development during early childhood.

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