

CASE REPORT

Carotenemia and hepatomegaly in an atopic child on an exclusion diet for a food allergy

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ABSTRACT

Eczema is a frequent childhood manifestation and a few atopic children are allergic to certain foods or aeroallergens. Anxious parents of atopic children often have a fear of topical steroid-related side-effects, and some may try a range of elimination diets to avoid allergies. Elimination diets increase the risk of anaphylaxis on re-exposure to previously tolerated foods from the loss of oral tolerance. Unbalanced diets together with an inadvertent excessive consumption of fruits and vegetables may lead to carotenemia from the carotenoids in the plant foods. Carotenemia is benign but unusual diets and the consumption of preformed vitamin A in health supplements can lead to vitamin A toxicity. We discuss a child with eczema on an exclusion diet presenting with anaphylaxis to dairy food. He had carotenemia with hepatomegaly, which resolved on dietary management.

Key words: allergy, carotenemia, eczema, hepatomegaly.

INTRODUCTION

Eczema is a very common manifestation of atopy in children. Caregivers are often concerned about topical steroid related side-effects and also trial exclusion diets, which may not be nutritionally adequate. Fruit and vegetables are rich in the carotenoids that are vitamin A precursors and their excessive consumption may result in carotenemia, which is

a less well recognised and unintended benign consequence. Atopic children on exclusion diets are at risk of anaphylaxis on re-exposure to previously tolerated foods from the loss of oral tolerance. We include a concise review of the literature on carotenemia in children and describe an association of hepatomegaly with carotenemia that resolved with dietary management.

REPORT

A Caucasian boy aged 4 years and 10 months presented following an anaphylactic reaction associated with hives, facial swelling, throat tightness and stridor within 30 minutes of eating 3 spoonfuls of yoghurt. His symptoms ameliorated following i.m. adrenaline and i.v. hydrocortisone administered by his family doctor and he was transferred to the hospital for further management.

He was born at term with a normal newborn metabolic screen. He developed eczema as an infant. His family were anxious about topical steroid-related side-effects. They were concerned that food allergies may be contributing to his eczema and therefore tried to exclude several foods from his diet. A skin prick test done when he was aged 4½ years was negative to a panel of food allergens (soyabean, cow's milk, egg-white, peanut, wheat, shrimp or fish mix). He was seen at the paediatric clinic with eczema management advice and the family was reassured that the skin prick test did not suggest he had a food allergy. His parents however continued with dietary exclusions (dairy products, wheat, soy, egg, chicken, fish, shellfish, lentils, sunflower and pumpkin seeds, rice, potato, pasta, ham and nuts). His regular diet primarily consisted of a papaya with cooked and pureed pumpkin, carrots, beef, pork, lamb liver and meat broth for over 6–8 months prior to his presentation. Fruit, including apples and bananas, and other vegetables such as lettuce, cabbage, silverbeet, swede, and parsnips were included in his diet. He was also on dietary fish oil supplements.

He weighed 21.7 kg (67th percentile) and was 111 cm in height (90th percentile) with a body mass index of 17.6. He had a pale, sallow complexion with dry skin and mild desquamation over his face, but no infected or inflamed areas. There was no scleral icterus. A cardiorespiratory examination was normal. He had a soft and non-tender abdomen with no distension. Hepatomegaly (span 12 cm)

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was noted with the liver edge palpable 5–6 cm below the costal margin. There was no splenomegaly, ascites or lymphadenopathy. An ear, nose and throat examination was normal.

Investigations were arranged in consideration of differential diagnoses that included dietary, metabolic, oncological and gastroenterological causes of his presentation with a sallow complexion and hepatomegaly. He had a raised serum beta-carotene level (6.6 $\mu\text{mol/L}$ [0.2–1.5]), vitamin A (1.6 $\mu\text{mol/L}$ [0.7–1.5]), mildly elevated B12 (1090 pmol/L ; normal range 140–800), and a diffusely echogenic hepatomegaly on ultrasonogram. The normal tests included a full blood count, C-reactive protein, liver, renal and thyroid functions; lipid profile; coeliac and auto-antibodies screen; hepatitis, cytomegalovirus, Epstein–Barr virus serology; serum folate; antinuclear antibodies; urinary copper, amino acids, organic acids, mucopolysaccharides; lysosomal enzyme assay; chest X-ray and electrocardiogram.

Metabolic, oncology, gastroenterology and ophthalmology consultations were sought to exclude other conditions. Dietary advice was provided with introduction of soy, which he tolerated. Food allergy and anaphylaxis education included an adrenaline auto-injector and ambulance cover. A clinical follow-up at 1 month revealed a normal liver on ultrasonogram and the resolution of his skin pigmentation and hepatomegaly (span 6 cm). His serum vitamin A levels were normal at 5-months post-presentation. Supervised food challenges were tolerated for wheat and egg in baking. His dietary restrictions were relaxed and he was able to eat a variety of foods excluding dairy and cooked egg. There were no ongoing concerns on follow-up at the paediatric clinic.

DISCUSSION

The case highlights the risks of anaphylaxis from loss of oral tolerance, a consequence of unnecessary dietary exclusions. It also draws attention to the unusual features of carotenemia and hepatomegaly in the child on a beta-carotene and vitamin A enriched diet. Food allergies and eczema are common but dietary elimination is required only to manage confirmed food allergies. Some parents may make their child observe extreme exclusion diets for prolonged periods even in the absence of clear benefit. Anaphylaxis from the loss of specific food tolerance induced by the prolonged elimination diets for eczema and cow's milk protein intolerance has been reported in children who were previously sensitised or had no prior allergy testing.^{1–5}

Coloured fruits and vegetables are health-promoting foods with many benefits. These contain carotenoids, which are important sources of vitamin A.^{5,4} Beta-carotene is the most abundant carotenoid and others like alpha-carotene, gamma-carotene, cryptoxanthin, lutein and lycopene also contribute to provitamin A activity.^{5,4} The excessive intake of carotenoids can lead to carotenemia.^{5–6} Carotenemia is also known as aurantiasis or xanthoderma.

Carotenoids have increased bioavailability from homogenised, pureed and cooked fruits and vegetables as a result of the disruption of the food matrix.⁵ After absorption in the

intestinal mucosa carotenoid 15,15 mono-oxygenase enzyme converts the carotenoid to a form of vitamin A (retinol), which is transported via lymphatics and the blood to liver where it is stored.^{5–6} The absorption and conversion to vitamin A of carotenoids depends on the individual's vitamin A status and this regulated step prevents toxicity from the excessive formation and accumulation of vitamin A.^{6,7} Between 70–90% of preformed vitamin A from fortified supplements and animal liver is absorbed, compared to 20–50% of the dietary carotenoids from plant sources.^{5–7} Hypervitaminosis may result from the prolonged and excessive intake of nutritional supplements or foods rich in preformed vitamin A.^{5–7}

Beta-carotene deposited in the epidermis and subcutaneous fat in areas of increased sweat and sebaceous activity such as the nasolabial folds, palms and soles, absorbs certain wavelengths of light leading to yellow-orange discoloration of the skin.^{5,4,6,7} The mucosa and sclerae are spared and the colour of urine and stool is not affected.^{5,4,6,7} Cheilitis, desquamation, headaches and bone pain symptoms along with hepatomegaly may suggest vitamin A toxicity.^{5–7}

Carotenemia is more commonly a result of excessive consumption of carotenoids, but hyperlipidaemia or very rarely a defective metabolic conversion to vitamin A may be the aetiology.^{5–8} Conditions leading to hyperlipidaemia such as diabetes mellitus, hypothyroidism, nephrotic syndrome, anorexia nervosa or chronic renal and liver conditions should be considered.^{5,6,7,9} Carotenemia may be associated with raised plasma vitamin A in individuals consuming preformed vitamin A supplements or food.^{6–8} The vitamin A levels may be low, normal or elevated when carotenemia results from a metabolic cause or is associated with hyperlipidaemia.⁶

Massive hepatomegaly in glycogen storage disorders is associated with hyperlipidaemia and carotenemia in children on high dietary carotene.⁶ Anecdotal reports suggest there is an association of hepatomegaly in carotenemic individuals but we were unable to find reports in the literature to confirm this association in children. The child in our report had a slim body habitus with no nutritional wasting and normal liver enzymes. There was no history of recent travel or exposures to parasitic or other infections or toxins. His hepatomegaly resolved on withholding the supplements and foods containing preformed vitamin A along with a low carotene diet.

CONCLUSION

Extreme exclusion diets are not indicated in children with atopy. Prolonged dietary elimination can potentially induce a loss of oral tolerance leading to anaphylactic reactions on the intentional or accidental reintroduction of such food. Carotenemia may be an unintended consequence of the long-standing dietary excess of carotene-containing food. Although carotenemia is a benign condition, vitamin A toxicity may result from the excessive consumption of preformed vitamin A-containing food and supplements. Carotenemia can be managed on a low carotene diet with

the resolution of the skin pigmentation over 2–6 weeks. The clinical differentiation of carotenemia from jaundice and other skin pigmentation is not difficult and a careful history can easily exclude conditions associated with hyperlipidaemia (see Appendix 1). The underlying cause of the hyperlipidaemia should be corrected where possible. Metabolic carotenemia is rare. We are not aware of other patients who had hepatomegaly that resolved with dietary management.

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- Specific oral tolerance induction is becoming a safe therapeutic option in children with food allergy
- The following are true of carotenemia
 - It commonly leads to hepatomegaly in children
 - It causes yellow-orange mucosal pigmentation
 - It may be associated with hyperlipidaemia
 - Heat treatment of vegetables may denature vitamin A
 - Skin pigmentation may improve over 2–6 months on a low carotene diet
- Chronic hypervitaminosis A can be a result of
 - the excessive dietary consumption of fortified fish oil
 - the prolonged treatment of acne
 - the regular use of vitamin A supplements
 - the routine consumption of chicken liver
 - All of the above

APPENDIX 2

Answers:

- d

There has been an increase in the practice of exclusion diets and the rates of anaphylaxis have also been increasing over the last few years. Anaphylactic shock has been reported on exclusion diets started for eczema in children who previously tolerated the foods. Loss of allergen exposure may favour a loss of oral tolerance resulting in severe reactions. Continuous high dose exposure helps maintain oral tolerance.
- c

Carotenemia causes pigmentation with non-pruritic dry desquamation of skin. Mucosal and scleral discoloration is not seen in carotenemia. Carotenemia from lipophilic carotenoid pigments may be seen in conditions associated with hyperlipidaemia such as diabetes mellitus, hypothyroidism, nephrotic syndrome or anorexia nervosa. Pureed, mashed and cooked vegetables increase the bioavailability of carotene without denaturing the vitamin content. Hepatomegaly is not very common.
- e

Fish oil and vitamin A preparations sold as health supplements may be fortified with high doses of vitamin A. Oral and topical isotretinoin potentially can cumulatively accumulate and cause hypervitaminosis A from prolonged use. Liver is the main storage organ for vitamin A and routine consumption of animal and chicken livers can lead to hypervitaminosis A.

APPENDIX 1

Questions

- Which of the following is incorrect:
 - There has been an increase in the practice of exclusion diets over the last few years
 - Prolonged exclusion of certain foods can induce a loss of oral tolerance leading to allergic reactions on re-exposure in previously sensitised atopic children
 - Continuous exposure to high doses of food antigen maintains tolerance
 - Anaphylactic shock is very unlikely in the atopic children who previously tolerated the food antigen