Acute vitamin A toxicity: A report of three paediatric cases

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Abstract: The following report describes three paediatric cases of vitamin A toxicity secondary to carnivorous fish liver ingestion. Further discussion of vitamin A toxicity and management of toxicity is included.

Key words: fish oil; hypervitaminosis A; poisoning; vitamin A.

Case Report

Case 1
A 23-month-old Chinese girl presented to the emergency department with vomiting, irritability, sore eyes and a red, peeling rash on the face. She had consumed four pieces of fish liver the night before. Her grandfather, who also ate the fish liver, had similar symptoms.

Case 2
An 11-year-old Chinese boy presented with a 2-day history of abdominal pain, vomiting, headache, a red, peeling rash over his body, blistering on his fingers and tongue and perioral tingling. He and his family had eaten fish livers 8 h prior to the onset of symptoms.

Case 3
A 14-year-old Chinese boy presented with a 12-h history of vomiting, severe headache and sore red eyes after ingestion of 8–10 pieces of Polyprion oxygeneios (Hapuka) fish liver. His mother and sibling also had similar symptoms after ingestion of the same fish livers. He was also taking a regular vitamin supplement that contained vitamin A.

Key Points
1. Vitamin A toxicity should be considered in the differential of acute food poisoning, particularly when symptoms such as erythema, skin peeling, red eyes and headache are present.
2. Vitamin A toxicity can lead to raised intracranial pressure and serious sequelae.
3. Vitamin A/retinol levels are not helpful in determining vitamin A toxicity. The metabolite retinoic acid is a more accurate marker of toxicity.

The above cases are unrelated and presented to the Children’s Emergency Department, Starship Hospital, over a 3-year period. All children had normal serum electrolytes, liver function and full blood counts. They were rehydrated and discharged home with a diagnosis of food poisoning.

Case 2 re-presented at 48 h and was admitted for 2 days with ongoing symptoms, predominately vomiting, headache and peeling red skin. Case 3 re-presented daily for 3 days and was admitted after developing intermittent blurred vision and a left-sided ptosis on day 3 of illness. Further investigation included a normal head computerised tomography scan. A lumbar puncture revealed an opening pressure of 41 cm. Ophthalmology review on day 7 of the illness confirmed bilateral sixth nerve palsy and early right optic disc changes. He was diagnosed with benign intracranial hypertension, secondary to vitamin A toxicity from consumption of fish livers in addition to vitamin supplements containing vitamin A, and commenced on acetazolamide 500 mg mane, 250 mg midi, 250 mg nocte with improvement in symptoms. Follow-up 6 weeks later showed ongoing headache and a right lateral rectus palsy.

Discussion
These three cases illustrate acute vitamin A toxicity secondary to fish liver consumption.

Vitamin A, and its two main metabolites, retinol and retinoic acid, are fat-soluble vitamins. They are utilised in the body for retinal function, epithelial proliferation and keratinisation. Dietary vitamin A undergoes intestinal hydrolysis, is transported via chylomicrons and is stored as retinyl esters in the liver.1 Excretion occurs at a constant rate in the bile; thus, vitamin A will accumulate in the liver and other tissues.2 Acute toxicity presents with dry, scaly skin with areas of desquamation and fissuring of the lips. Other symptoms include headache, fatigue, anorexia, nausea, vomiting, blurred vision, pseudotumor cerebri, myalgias and arthralgias.1 Vitamin A is known to efficiently enter the central nervous system and bind to retinoic acid receptors which are responsible for the regulation of development and gene expression.1

Recommended daily intake of Vitamin A is between 1000 and 5000 IU.1,4 Acute toxicity can occur in children at intakes as low
as 1500 IU/kg/day or at 20 times the recommended daily intake. A fatal intake dose of Vitamin A has not been established.3

Animal liver contains approximately 80% of the total body reserve of vitamin A. In carnivorous animals, vitamin A will move up the food chain and bioaccumulate, explaining the high levels of vitamin A in animals such as polar bears. The polar bear liver can contain up to 6285 ± 2228 IU/g (mean ± standard deviation) of vitamin A.4 Hence, consumption of animal liver, particularly carnivorous animal livers, can result in vitamin A toxicity. Currently, the risk of acute vitamin A toxicity with individual species is not known. Furthermore, it is unknown if seasonal variation in the liver concentration of vitamin A in carnivorous fish species occurs based on seasonal variations in diet, although this is reported in arctic seals.6

As early as 1842, reports from the New Zealand Gazette and Wellington Spectator warned against consumption of P. oxygene- cis or Hapuka liver after a family developed vomiting, headache and a red, peeling rash.7 Similar symptoms were described by Australian Antarctic explorer Douglas Mawson 70 years later.8 Starving, he and his companion, Mertz, were forced to consume dog livers. Both developed symptoms and Mertz died, presumably from acute vitamin A toxicity. Lonie in 1950 described vomiting, headache and peeling skin in Immigrant New Zealand fishermen of Chinese descent after eating fish livers and attributed this to acute vitamin A toxicity.9

The symptoms described in the cases are consistent with acute vitamin A toxicity. Vitamin A toxicity can result in raised intracranial pressure leading to headache, visual changes and, in extreme cases, visual loss. Acute vitamin A ingestion in infants is observed to cause a bulging fontanelle and vomiting.10 Cases 2 and 3 had normal serum retinol levels at the time of hospital admission. This is not inconsistent with the diagnosis as serum retinol in acute vitamin A toxicity has been shown to initially rise and then return quickly to normal levels at the onset of symptoms and around 12 h post-ingestion.11 As serum retinol is rapidly metabolised and stored in the liver, a more accurate marker of toxicity in a symptomatic patient is retinoic acid.4

Vitamin A in plants is found as provitamin A carotenoids, which are not as efficiently absorbed as preformed vitamin A, the form found in animal liver and pharmaceutical supplements. Supplementation with fish liver oil or fortified foods in the present era is the most common cause of acute vitamin A toxicity.4 A distinction should be made between fish liver oil and omega-3 fatty acid without any vitamin A. Although polar bear liver would contain the highest level of vitamin A, it is not commonly seen as a cause of toxicity. Carrot ingestion is unlikely to lead to vitamin A toxicity, as the available form of vitamin A is not as well absorbed as the vitamin A in animal liver. Vitamin A supplementation with fish liver oil or in addition to fortified foods or iatrogenic administration is the most common cause of vitamin A toxicity. Correct answer is c, vitamin A supplementation.

Vitamin A or retinol levels (same thing) are rapidly metabolised. Thus, at the time of presentation, retinol levels will be within the normal range. Vitamin E is not a marker of vitamin A. Isoretinoin is a form of retinol that is used in acne preparations. Retinol is metabolised to retinoic acid. Correct answer is b, retinoic acid levels.

What is the most common cause of vitamin A toxicity?
a Ingestion of 50 g of polar bear liver
b Ingestion of 50 g of carnivorous fish liver
c Vitamin A supplementation
d Excess ingestion of carrots
e Ingestion of 50 g of Huskie dog liver

Although polar bear liver would contain the highest level of vitamin A compared to fish and dog liver, it is not commonly seen as a cause of toxicity. Carrot ingestion is unlikely to lead to vitamin A toxicity, as the available form of vitamin A is not as well absorbed as the vitamin A in animal liver. Vitamin A supplementation with fish liver oil or in addition to fortified foods or iatrogenic administration is the most common cause of vitamin A toxicity. Correct answer is c, vitamin A supplementation.

References

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