CASE REPORT

Angioneurotic oedema secondary to oral thiamine

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SUMMARY

Although allergic side effects due to parenteral thiamine are well-documented, they are extremely rare when thiamine is used orally. We report a case of a 47-year-old woman who developed angioneurotic oedema secondary to oral ingestion of thiamine at a therapeutic dose. The incident occurred twice with a clear temporal relationship to the initiation on thiamine.

BACKGROUND

Thiamine, vitamin B₁, is an essential cofactor for a number of enzymes involved in the metabolism of glucose and amino acids. Thiamine is indicated in the treatment of thiamine deficiency syndromes (beriberi and Wernicke-Korsakoff syndrome) and a variety of genetic metabolic disorders. Oral thiamine hydrochloride is absorbed rapidly into the circulation.¹ Thiamine supplementation is best practice in treatment of alcohol dependency syndrome to prevent selective cerebral neurodegeneration that leads eventually to Wernicke-Korsakoff syndrome.^{2,3}

With this case report we attempt to raise awareness among practicing clinicians about the potential for allergic reaction with seemingly safe medications such as thiamine, even if taken orally. This case report describes a patient developing angioneurotic oedema twice following intake of oral thiamine.

CASE PRESENTATION

A 47-year-old woman was hospitalised for inpatient treatment of alcohol dependency syndrome. No remarkable medical or surgical history was uncovered. She was started on thiamine supplementation as an important biological component of the overall biopsychosocial management plan. The use of thiamine was for prophylaxis against Wernicke-Korsakoff encephalopathy. She was entirely compliant with the 200 mg oral thiamine hydrochloride dose she was prescribed. Seven days later, she developed sudden onset bilateral lower limb swelling, more remarkable below the skin surface of the left leg. Oedema was mildly painful, but spread out rapidly to the upper two-thirds of the leg. Erythema was evident. The patient found it 'difficult to put her shoes on', and she 'had to drag her left leg as it was heavy'. Doppler Ultrasonographic imaging confirmed the absence of deep vein thrombosis. Swelling was relieved by the simple measure of elevating the legs. Full resolution of symptoms was attained in 4 days after thiamine was discontinued.

After 18 months, she sustained a relapse into alcohol dependency syndrome presenting with high intake of alcohol, and thiamine 300 mg was prescribed during the process of detoxification. By the

fourth day, she developed a bilateral lower limb swelling, more noticeable on the left leg. She noted that the left leg was 'coloured' and 'rockhard'. The oedema was associated with minimum pain, marked redness and inability to walk. Recognising it as an allergic reaction, the patient self-discontinued thiamine, and symptoms resolved over a period of 2 days.

DISCUSSION

Although unusual as a consequence to thiamine treatment, oedema is clearly documented and described in thiamine deficiency.⁴⁻⁶ Anaphylactic reactions to parenteral thiamine are well known from as early as the 1930s^{7,8} and specific immunoglobulins involved in thiamine allergy were identified in the mid-1990s.⁹ These allergic reactions are extremely rare, with an estimated incidence of 1 per 5 million pairs of ampoules of Pabrinex.³ Anaphylaxis to parenteral thiamine was reported recently presenting as a hypotensive crisis when a patient developed low blood pressure after she was given a combination of thiamine, pyridoxine and cyanocobalamin intravenously.¹⁰ In another case report, symptoms of systemic pruritus, generalised erythema and hypotension were reported as an allergic reaction to parenteral administration of thiamine, cyanocobalamin, lidocaine and dexamethasone to a middle-aged female patient in whom specific antithiamine IgE antibodies were detected.¹¹

In this case, symptoms were clearly related to oral thiamine initiation. The constellation of symptoms cannot be explained on the basis of known pharmacological or idiosyncratic effects of thiamine. The temporal relationship is apparent especially following the second attempt at trying thiamine, where a similar presentation occurred. Full resolution of oedema on self withdrawal of thiamine, supports the diagnosis of allergic reaction.

However, it is compellingly arguable that this allergic reaction may have occurred due to the fillers rather than to thiamine. Any of the pharmacologically inactive substances used for colouration can be responsible. Specifically the Food and Drug Administration-approved commonly used colouring additive called tartrazine, and is also known as E102 or "FD&C yellow No. 5", which was reported to be responsible for allergic reactions in almost 4% of psychiatric patients.^{12,13} Tartrazine is also implicated in possible causation of aspirin intolerance syndrome.¹⁴ The patient took Sona Thiamine, a brand that did not contain tartrazine. Furthermore, she reported no allergy to any medication in the past, apart from penicillin. She has no history of aspirin insensitivity. Other fillers and diluents that are ingredients in Sona Thiamine and

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may be responsible for this allergic reaction are plant cellulose, vegetable stearic acid and vegetable magnesium stearate. Plant cellulose was reported to produce local tissue reactions following surgical interventions.^{15 16} Vegetable stearic acid was also reported to cause contact dermatitis.^{17 18} A recent case report of vegetable magnesium stearate associated urticarial allergic reaction carries many similarities to our patient's presentation.¹⁹ Our case, as far as we know, is unique in being the first to report such reaction occurring in the context of oral thiamine treatment.

Learning points

- ▶ Allergic reactions can be caused by any medication taken through any route, including oral vitamin B₁.
- ▶ Allergic reactions can be caused by unrelated fillers as well as pharmacologically active substances. Still they are of equivalent seriousness and clinical significance.
- ▶ The possibility of allergy has to be always kept in the mind, and must be communicated clearly to the patient prior to starting of thiamine treatment.
- ▶ Clear documentation of allergy is crucial in preventing future prescription of the same medication.

Competing interests None.

Patient consent Obtained.

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