

oral terbinafine, the patient developed a generalized rash diagnosed as drug induced. Retrospectively, a so-called dermatophytid reaction (or 'id reaction') should also be considered. This is an often pruritic dermatitis based on sensitization to fungal antigens, reported in 4–5% of fungal infection. Although it may mimic an allergic reaction, it should not lead to discontinuation of antifungal treatment (10).

T. mentagrophytes is a zoophilic fungus that is usually found in rodents, like rabbits or guinea pigs (1). The patient had a guinea pig, which showed some skin symptoms suggestive of fungal infection. Unfortunately, this could not be confirmed by cultures, leaving only a label of 'most-likely culprit'. Human to human transmission in zoophilic fungi is often limited (1). In this case, however, there was a small outbreak of culture-proven fungal infection affecting five close contacts. Of these five, only three had had contact with the guinea pig. None of them developed kerion celsi.

In conclusion, tinea capitis is a common scalp condition in children that can present with a wide variety of signs and symptoms, including cervical lymphadenopathy. It is important to consider tinea capitis in all scalp lesions, as inappropriate and delayed treatment can lead to kerion celsi, a condition that can be devastating in an often young and school-going population. In this case, a 5-year-old girl, now 9 months after initiation of treatment, is left with large areas of alopecia. She is currently wearing a wig to school, and psychological support is ongoing.

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CONFLICT OF INTEREST

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The pendulum between food protein-induced enterocolitis syndrome and IgE-mediated milk allergy

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ABSTRACT

The transition from milk protein-induced enterocolitis syndrome to IgE-mediated milk allergy is uncommon. Herein, we describe three infants that suffered from recurrent vomiting and restlessness in response to cow's milk formula with negative skin prick to milk and therefore diagnosed as milk protein-induced enterocolitis syndrome. After recovering and reintroducing cow's milk formula, they developed disseminated urticaria and positive skin prick test to cow milk compatible with IgE-mediated milk allergy.

Conclusion: An infant that recovers from cow milk food-induced enterocolitis syndrome might develop afterward IgE-mediated cow milk allergy.

INTRODUCTION

Cow's milk is the most common food allergen in infants. The diagnosis in most cases is obvious after taking a careful history and performing skin prick test (SPT) or measurement of serum-specific IgE antibody levels to cow's milk in case of IgE-mediated reaction.

It is well accepted to divide patients with cow milk allergy (CMA) into three main groups according to the underline suspected immunologic mechanism: the classic IgE-mediated CMA, which comprises about 60% of all cases of CMA; the non-IgE-mediated CMA such as food protein-induced enterocolitis syndrome (FPIES) and the mixed cell-mediated as in atopic dermatitis and eosinophilic enteropathy. In the last years, we encounter in our outpatient allergy clinic, few infants who presented with milk FPIES who afterward developed full blown IgE-mediated milk allergy as described in these representatives' cases.

PATIENTS' PRESENTATIONS

Case 1

A 3-month-old boy was sent for allergic evaluation because of suspected cow's milk allergy. He was born after an uneventful pregnancy and delivery and was breastfed together with intermittent bottle supplement from birth. At the age of 10 days, he started to vomit within a few minutes after a bottle feeding. The mother was instructed to continue with exclusive breastfeeding. At the age of 3 months, he was evaluated for food allergy, and his SPT was positive (3-mm wheal/4-mm flare) for cow's milk and negative for soy, egg, peanut, sesame wheat and fish. The mother was told that she can give extensively hydrolysed cow's milk-based formula or alternatively soy-based formula as supplement for breastfeeding. At the age of 12 months, he was seen for re-evaluation and following a negative SPT for milk, an open oral challenge with incremental doses of dairy product resulted in recurrent vomiting and lethargy 4 h following the challenge. At the age of 2 years, the SPT was still negative, and an open oral challenge with dairy product was successful. However, 2 days after, following a bottle feeding, he became lethargic and cyanotic and recurrent vomiting within 5 min. A repeat SPT within a month was strongly positive (7-mm wheal/10-mm flare), and the mother was reinstructed to avoid any dairy products.

At the age of 3 years, the SPT was again negative and shortly after an oral challenge was carried out without any adverse reaction.

Case 2

A 2-year-old girl was sent for allergic evaluation because of suspected milk allergy. She was born as full term after normal pregnancy and delivery to parents with no allergic backgrounds. She was breast- and bottle fed soon after birth, and at the age of 2 weeks, her paediatrician recommended extensively hydrolysed cow's milk formula owing to edginess, perioral rash and infrequent vomiting in spite of normal weight gaining. Following the substitution, all these symptoms disappeared.

At the age of 6 months, she was seen for allergic evaluation. Her physical examination was normal with normal percentile and with signs for atopic dermatitis. SPT was positive for histamine but negative for cow's milk, soy, egg, peanut, sesame, wheat and fish. The mother was instructed to reintroduce cow's milk formula, which she did without any problems for a week. However, after 10 days, the mother stopped the cow's milk formula because of non-specific complaints, such as impression of abdominal discomfort and loose stool. Upon refusal of soy-based formula, the extensively hydrolysed formula was reintroduced, and according to the mother's report, all the symptoms disappeared within few days.

At the age of 12 months, she was seen again in the Allergy Clinic for re-evaluation, and at that time, her SPT was positive (3-mm wheal/5-mm flare) for milk and negative for soy, and an open oral challenge with cow's milk formula was made. Within 10 min, she developed disseminated urticaria that subsided following antihistamine treatment. The parents were instructed to avoid any dairy products in her diet, appropriate antihistamine was prescribed, and she was invited for re-evaluation in 6-month intervals. Her last SPT is strongly positive (7-mm wheal/12-mm flare) for cow's milk.

Case 3

A 2-year-old boy was sent for allergic evaluation because of suspected milk allergy. He was born as full term after normal pregnancy and delivery to parents with no allergic backgrounds. He was exclusively breastfed for 2 months when he reacted to the first trial of cow's milk formula. Symptoms occurred after 2 h, including abdominal discomfort, recurrent vomiting, diarrhoea and lethargy that subsided within a few hours without any treatment. At the age of 3 months, his SPT was borderline positive for cow's milk (2-mm wheal/3-mm flare) and negative for soy.

At the age of 12 months, his SPT for milk was negative, and a successful open oral challenge was carried out with dairy product in the clinic. In the next few days, the mother tried other dairy products which he tolerated with on apparent reactions although the mother reported that he suffered from abdominal discomfort. However, a week after, he was bottle fed, and within minutes, he developed disseminated urticaria and facial angioedema without respiratory symptoms that disappeared only after oral antihistamine administration. His SPT at 13 months of age became strongly positive (8-mm wheal/10-mm flare), and the mother was instructed to avoid every milk products.

These three infants suffered from recurrent vomiting, diarrhoea and restlessness, and their SPT was negative at the time of open oral challenge and therefore diagnosed as cow milk FPIES. The appearance of urticaria, facial oedema, respiratory distress, vomiting or anaphylaxis with a positive SPT to cow milk suggested the development of IgE-mediated CMA.

DISCUSSION

The transfer from FPIES to IgE milk protein allergy is very rare, and the clinical manifestations are different in most cases. In FPIES, initial symptoms occur during the first months of life as repeated vomiting episodes appear within 4 h after ingestion of cow milk. Occasionally accompanied by diarrhoea leading to dehydration, lethargy and in severe cases resemble sepsis with hypotension and elevated polymorphonuclear cells count (1–3).

In these infants, measurements of food allergen-specific IgE antibodies or SPT are typically negative (4). In IgE-mediated CMA, approximately 30–70% infants manifest dermatological symptoms such as urticaria, flushing and angioedema, 50–60% manifest gastrointestinal symptoms such as abdominal pain and vomiting, and 20–30% manifest respiratory symptoms such as dyspnoea, wheezing or cyanosis (5,6). The majority of patients manifest symptoms involving more than one system and in some cases develop a severe, potentially fatal, systemic allergic reaction.

The mechanism underling FPIES is not clear. From previous studies, it was suggested that the immune response in this phenomena is primarily a TH1/TH2 cell mediated. An elevation of the cytokines IFN- γ , interleukin 10 (IL-10), tumour necrosis factor- α and IL-5 was found in the blood of individuals after exposure to the offending food (7). In an interesting case report, a challenge with rice that caused gastrointestinal as well as systemic symptoms induced an increase in IL-4 and a decrease in IFN- γ expression in peripheral T cells, suggesting that an acute FPIES reaction is associated with a Th2 skewing of the T cells cytokine profile (8).

One can speculate that a Th2-skewed lymphocyte reaction probably IL-4 and IL-5 might predispose some individual to develop specific IgE to food which can eventually lead to a classic IgE-mediated reaction. In addition, the inflammation in the intestinal tract caused by FPIES might increase the penetrability of milk proteins and their presentation to the immune system. Interestingly, Sicherer et al. (1) suggested the presence of specific IgE to the involved

antigen in patients with FPIES, which are usually negative, predicting a prolonged sensitivity to the antigen.

In conclusion, further investigation should be performed to better characterize these patients and to understand the pathogenesis of this phenomenon. In addition, paediatricians should be aware of this uncommon condition; therefore, in case of symptoms suggesting of IgE-mediated CMA in infants who recovered from FPIES, an allergic re-evaluation including SPT or specific serum IgE should be performed.

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