Improving the care of infants with cow’s milk allergy

Cow’s milk allergy
Case studies

Skin and gastrointestinal symptoms caused by cow’s milk allergy

Severe eczema associated with multiple food allergies

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LUCY
Skin and gastrointestinal symptoms caused by cow’s milk allergy

Three-month old Lucy presented with chronic diarrhoea and mild-to-moderate eczema across her body and face. Her symptoms resolved after replacement of standard cow’s milk formula with Nutramigen* 1, an extensively hydrolysed formula. Food allergies are often temporary, and by age 2½ years, Lucy was able to return to a full, normal diet.

Presentation

Lucy first presented at the Allergy Centre at age 3 months with chronic diarrhoea and mild-to-moderate eczema across her body and face. Lucy’s weight was on the 25th centile and she had been formula fed from birth. Her history showed that she was born at full term, with a normal delivery. There was a maternal history of eczema, asthma and hay fever, but no paternal history of allergy.

Lucy first presented at age 3 months with chronic diarrhoea and mild-to-moderate eczema across her body and face

Lucy was seen by a paediatrician, an allergy nurse and an allergy/paediatric dietitian, who provided skin care advice and switched Lucy onto an extensively hydrolysed formula (eHF), Nutramigen 1, in line with current guidelines.1,2 Skin prick tests (SPTs) were not conducted at this stage, based on the presence of gastrointestinal symptoms, which suggested non-IgE-mediated allergy. Written and verbal advice on low-allergen weaning was provided, as Lucy’s mother wanted to start weaning her onto solid foods when she reached age 4–5 months.3

Lucy was switched onto an extensively hydrolysed formula, Nutramigen 1

Follow-up

When Lucy returned to the Allergy Centre at age 6 months, her diarrhoea had resolved and her eczema had cleared, with only the occasional flare. On examination, she was found to be well and thriving, with a normal physical examination. Her weight remained on the 25th centile, and her full blood count was within the normal range.

At age 6 months, Lucy’s diarrhoea had resolved and her eczema had cleared

Because Lucy was weaning, SPTs were performed to determine which foods could be safely introduced. The SPT for milk was positive (Box 1), which suggested that IgE-mediated hypersensitivity to cow’s milk may have played a role in her eczema flares in the past. Together with her improved symptoms since switching to Nutramigen 1, this allowed a diagnosis of cow’s milk allergy (CMA) to be made.

In consultation with the paediatrician and dietitian, Lucy’s mother was provided with advice, websites and recipes for dairy-free weaning. We also recommended that all other foods could be introduced one at a time, with the precautionary exception of soya and egg, because infants with CMA are commonly sensitized to these foods, and egg is a particularly common allergen in infants with atopic eczema.4 In addition, Lucy’s formula was switched to Nutramigen 2, which contains more calcium and other nutrients and is therefore suited to older babies.

Lucy’s formula was switched to Nutramigen 2, which contains more calcium and other nutrients and is therefore suited to older babies
At age 9 months, Lucy's weight gain had increased and she was now on the 50th centile. Her eczema was under control, and the diarrhoea had not returned. She was feeding on Nutramigen 2 and solid foods, excluding dairy, egg and soya. An oral challenge with one boiled egg was performed in hospital, with a negative result. Therefore we recommended that Lucy should be given a scrambled egg at home the next morning, returning to the children's ward if symptoms reappeared.

Lucy maintained her weight gain, remaining on the 50th centile at age 12 months. She was eating a varied diet and consuming 12–14 fluid ounces (355–414 ml) of Nutramigen 2 per day. SPTs gave negative results for cow's milk and soya (Box 1), so we performed oral challenges with these foods. The soya challenge, conducted over a period of a week at home, was negative. However, the cow's milk challenge, which was conducted in hospital, resulted in an immediate flare of Lucy's eczema (within 2 hours), getting progressively more itchy over the next 24 hours, with diarrhoea the following morning. Therefore, we recommended that soya yoghurts and puddings could be introduced to increase variety in Lucy's diet, but she should continue to avoid dairy.

An SPT for milk at age 2 years produced a 2 mm wheal. On analysing Lucy's diet, her nutritional intake was found to be adequate. As a result, we recommended continuation of the dairy-free diet, and suggested that a calcium-enriched soya milk could be introduced.

Four months later, Lucy accidentally drank a cup of milk at nursery, without an adverse reaction. Consequently, we performed an oral challenge in hospital, which continued at home for a week. As Lucy showed no allergic symptoms, we advised that dairy could be gradually reintroduced. Subsequently, Lucy occasionally experienced eczematous symptoms, which were treated with emollients, antihistamines and a topical hydrocortisone. SPTs at age 3 years were negative for all allergens tested, and Lucy was tolerating all foods.

**SPTs at age 3 years were negative for all allergens tested, and Lucy was tolerating all foods**

<table>
<thead>
<tr>
<th>Test</th>
<th>Wheal size at 6 months (mm)†</th>
<th>Wheal size at 12 months (mm)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Egg</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Wheat</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Soya</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Peanut</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Positive control</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Negative control</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

†SPTs are considered positive if the wheal is ≥3 mm larger than the negative control.5,6
Box 2. Key learnings from Lucy’s case.

1. **Recognising patterns of symptoms can be a crucial first step for diagnosing CMA.**
   CMA may present as generalised systemic reactions (anaphylaxis), gastrointestinal, cutaneous, and/or respiratory reactions. This variation arises because CMA can be driven by two distinct immune pathologies: IgE- and non-IgE-mediated allergy, or indeed a mix of the two as in Lucy’s case.\(^1,6\) For non-IgE-mediated allergy, establishing the cause–effect relationship can be difficult, making the diagnosis challenging. Lucy presented with a combination of cutaneous and gastrointestinal symptoms, and had a maternal history of eczema. Recognising this symptom overlap and familial history helped to diagnose CMA.

2. **Formula-fed infants with CMA should receive an extensively hydrolysed formula as a first-line management measure.**\(^1\)
   In line with European and international guidelines, Lucy was offered a hypoallergenic formula based on extensively hydrolysed protein for management of her CMA.\(^1,5\) By contrast, soya formulas are not recommended for infants with CMA during the first 6 months of life, and should not be the first choice thereafter.\(^4,7\)

3. **Resolution of allergy can be detected through careful follow-up.**
   Careful follow-up at regular intervals (6–12 months) with oral challenges and SPTs when appropriate, helped identify when Lucy’s hypersensitivity to cow’s milk resolved, thus avoiding an unnecessarily prolonged exclusion diet. This case also illustrates that a record of accidental ingestion can provide important indicators for allergy resolution.

4. **The SPT is a useful tool, but must be interpreted with caution.**
   SPTs are only helpful for detecting IgE-mediated allergy and may produce false negative or false positive results. Therefore, a negative SPT does not conclusively exclude an allergy and a positive SPT does not conclusively identify an allergy. It is important to confirm a negative or a positive SPT where there is a good clinical history of immediate reactivity, especially in a very young infant, by conducting an oral challenge under medical supervision. Lucy’s history of GI symptoms with a delayed onset suggested additional involvement of non-IgE-mediated allergy; consequently her symptoms were carefully monitored at home for a week following each oral challenge.

5. **Diets should be monitored and adjusted to meet the needs of the growing infant.**
   As infants wean onto solid foods, their milk intake drops; as a result, children on restricted diets require careful support and advice from a dietitian to ensure adequate nutritional intake. The paediatrician and dietitian advised that all foods excluding milk, egg and soya be introduced one at a time, to help provide variety, and gave allergen-free recipes as support. In addition, Lucy’s switch at age 6 months from Nutramigen 1 to Nutramigen 2 helped provide higher levels of key nutrients like calcium and other nutrients, thus addressing the specific nutritional needs of older babies.
JACK
Severe eczema associated with multiple food allergies

Three-month old Jack presented with severe eczema over his face and body. At age 6 months, skin prick tests indicated that Jack was sensitized to milk, egg and soya. As Jack was breast fed, we advised his mother to exclude these foods from her diet, and when she wanted to introduce formula feeds, the paediatrician prescribed Nutramigen® AA. These steps resulted in substantial improvement in Jack’s symptoms, and by age 12 months he was consuming a varied diet of solid foods, breast milk and Nutramigen AA. This careful and methodical approach identified multiple food hypersensitivities and allowed for ongoing evaluation of Jack’s progress.

Presentation
Jack presented at the Allergy Centre at age 3 months with severe eczema covering a large area of his body and face. A detailed history revealed that he had been born at full term, with a normal delivery. Jack was exclusively breast fed and his weight was between the 25th and 50th centile. His family history included asthma and hay fever in both parents.

Jack presented at age 3 months with severe eczema covering a large area of his body and face

Following consultation with a paediatrician and a dietitian, Jack’s mother was given information on skin care for eczema, in line with NICE guidelines.² Although she did not want him to have skin prick tests (SPTs) at this stage, we advised her on avoidance of foods that commonly cause allergic reactions in breast-fed infants, and she agreed to begin a diet excluding cow’s milk and egg. In addition, we provided advice on low-allergen weaning, as Jack’s mother wanted to start introducing solid foods in the coming months.

Follow-up
When Jack returned to the clinic at age 6 months, his mother was successfully avoiding dairy and egg. She had read advice that rice milk should be avoided for babies and toddlers,⁶ so she was drinking soya milk instead, consuming more than 500 ml each day. Jack’s eczema was improving but not completely cleared, and his weight had dropped below the 25th centile. His mother also felt that he was irritable and not keen on feeding. Jack was otherwise well, with a normal physical examination and full blood count.

Jack had begun weaning at age 17 weeks, with baby rice, fruit and vegetables. He had accidentally been given fromage frais by a relative and had experienced a severe immediate reaction, involving swelling of his lips and tongue, red facial flush, hives on his chest and wheezing. Indeed, SPTs at age 6 months confirmed that Jack was sensitized to a number of foods, including milk (Box 3).
Given Jack’s ongoing symptoms and his positive SPT to soya (Box 3), the paediatrician advised his mother to begin excluding soya from her diet, while continuing to avoid egg and dairy. Jack’s mother was feeling worn out by the constant effort of checking food labels and managing Jack’s eczema and irritability. Consequently, she wanted to introduce a formula feed at bedtime, so the amino acid-based formula, Nutramigen AA, was prescribed. We provided written information explaining that it could be expected to taste and smell different from other formulas, and also that the change in diet may alter stool colour and consistency. If required, to aid introduction we advised that it could be mixed with breast milk, pointing out that mixed feeds must be used immediately to avoid possible digestion by enzymes in the breast milk.\(^9\) Additionally, we recommended that all foods, excluding dairy, egg, soya and peanut, could be introduced into Jack’s diet, one at a time.\(^1,3\)

**Box 3. Skin prick tests: results at ages 6 months and 12 months.\(^6\)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Wheat size (mm)(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 months</td>
</tr>
<tr>
<td>Milk</td>
<td>9</td>
</tr>
<tr>
<td>Egg</td>
<td>3</td>
</tr>
<tr>
<td>Soya</td>
<td>3</td>
</tr>
<tr>
<td>House dust mite</td>
<td>4</td>
</tr>
<tr>
<td>Dog</td>
<td>2</td>
</tr>
<tr>
<td>Sesame</td>
<td>–</td>
</tr>
<tr>
<td>Wheat</td>
<td>–</td>
</tr>
<tr>
<td>Grass</td>
<td>–</td>
</tr>
<tr>
<td>Cod</td>
<td>–</td>
</tr>
<tr>
<td>Peanut</td>
<td>–</td>
</tr>
<tr>
<td>Cat</td>
<td>–</td>
</tr>
<tr>
<td><strong>Positive control</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>Negative control</strong></td>
<td>0</td>
</tr>
</tbody>
</table>

\(^5\)Tests not conducted at a given timepoint are indicated by a dash.

\(^6\)SPTs are considered positive if the wheal is ≥ 3 mm larger than the negative control.\(^5,6\)

**Jack’s mother wanted to introduce a formula feed at bedtime, so the amino acid-based formula, Nutramigen AA, was prescribed**

Jack’s mother initially introduced Nutramigen AA in a 30:70 mix with breast milk. The proportion of formula was gradually increased and within a few days, Jack was taking full Nutramigen AA feeds.

At age 9 months, Jack’s weight had increased to just below the 50th centile and he had a varied diet of solid foods, with breast milk and night-time feeds of Nutramigen AA. Jack’s mother was also adhering well to the exclusion diet and was taking calcium and vitamin D supplements. At age 12 months, his weight was on the 75th centile. Two days prior to the appointment, he had a reaction after eating hummus, despite the fact that his mother was eating hummus regularly and he was still receiving breast milk. The symptoms included swollen lips and a red facial flush, though there was no wheezing this time. SPTs at age 12 months confirmed that he was sensitized to sesame, among other foods (Box 3).

**At 9 months, Jack was gaining weight and had a varied diet of solids, breast milk and night-time feeds of Nutramigen AA**

We advised that Jack and his mother should exclude sesame from their diets, while continuing to avoid dairy, egg and soya. We decided not to recommend exclusion of wheat at this stage, despite the positive SPT. This is because wheat and grass are often cross-reactive, and only a small proportion of patients sensitized to wheat actually report clinical reactivity to it.\(^10\) We also recommended that peanut could be introduced, due to the negative SPT result and the lack of a history of reactivity to peanut.
We will continue to monitor Jack’s progress at 6- to 12-monthly intervals, as appropriate. At each follow-up visit, SPTs and records of accidental ingestion will be used to determine whether oral challenges should take place. Deciding when to challenge can be difficult, and should take into account both the clinical factors discussed here, and the family’s readiness, as the process can cause anxiety and emotional distress. A negative oral challenge for a given food will then enable us to recommend its introduction to Jack’s diet.

References:

Box 4. Key learnings from Jack’s case.

1. **Taking a detailed patient and family history can help identify food allergy.**

A family history of atopic disorders, such as eczema, food allergy, allergic rhinitis and asthma, is a risk factor for development of food allergy. In addition, an infant with one atopic condition has a significant risk of developing another, and approximately a third of children with moderate to severe atopic eczema have a food allergy. Therefore, Jack’s family history of atopy and his extensive eczema were risk factors for food allergy.

2. **An amino acid-based formula should be used if multiple or severe food allergy is suspected.**

Up to 23% of infants with CMA develop the allergy during exclusive breast feeding. However, the severe adverse reactions displayed by Jack and the positive SPTs to several foods are thought to be uncommon both in breast-fed babies, and in infants of his young age. Although extensively hydrolysed formula is the first choice for most infants with cow’s milk allergy, international guidelines recommend that infants with severe or multiple allergies should receive an amino acid-based formula. Consequently, it was appropriate to offer Jack an amino acid-based formula, and Nutramigen AA was well tolerated for his formula feeds.

3. **Exclusion diets require substantial dietetic support.**

Children with food allergies need dietetic support to prevent growth problems or inadequate nutrient intake, and children with multiple food allergies are at greater risk than those with only one allergy. Accordingly, detailed practical advice was provided for Jack and his mother, including low-allergen weaning foods and dairy-, egg- and soya-free recipes. It was also helpful to give advice on initial introduction of hypoallergenic formulas, as they taste different from other formulas, and may be difficult to introduce to older babies like Jack.

4. **Food allergy has a profound impact on quality of life for patients and their families.**

The impact arises in part from the distress of the symptoms, such as Jack’s extensive, severe eczema, but also from the constant vigilance to avoid allergens. For instance, grocery shopping for a child with food allergy may take on average 39% longer and incur 11% greater expense than for a non-allergic child. Indeed, Jack’s mother reported feeling worn out by the continual effort of checking food labels. Compounded, these effects can seriously impair the everyday functioning of families affected by food allergy.
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