SIRIRAJ MEDICAL LIBRARY

Food Allergy of Infancy: Approaches to Diagnosis

Pipop Jirapinyo, M.D.

Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Siriraj Med J 2010;62:257-258

E-journal: http://www.sirirajmedj.com

From the previous chapter, the signs and symptoms of FAI are nonspecific and are often difficult to objectify. Most of these symptoms can be treated with medications which almost always result in remission. However, within a short period, the symptoms recur. Making a wrong diagnosis of FAI or over diagnosis of FAI may not only result in somatisation, but also fear for the introduction of solid foods to the infants. Furthermore, long-term elimination of cow's milk protein without cow's milk protein allergy (CMA). may result in inadequate intake of calcium. Therefore, careful diagnosis of FAI in an infant is of utmost importance.

FAI can present with a broad diversity of symptoms, mainly cutaneous (atopic dermatitis, urticaria), respiratory (rhinitis, asthma) and gastrointestinal (vomiting, diarrhea, colic, GE reflex) symptoms. Other general symptoms include food refusal, failure to thrive and irritability which can be part of FAI. There are many tests that are used for the diagnosis of FAI. Some tests are specific to food proteins, but some are nonspecific.

Eosinophilia

The eosinophil count in blood of over 700/mm^3 is considered eosinophilia as a predictor of FAI. Noh et al[1] reported in their study about 303 infants with cow milk allergy who manifested as atopic dermatitis. In their report, 44.9% had high eosinophil levels. An elimination diet improved clinical severity and decreased blood eosinophil levels. In this study, eosinophilia appeared to be a significant predictor of food allergy in atopic dermatitis and an indicating factor for diet manipulation, including an elimination diet.

Specific IgE to Cow Milk Protein

CMA, as a part of FAI, is classified as IgE-and non-IgE mediated. Less than 50% of infants with CMA are reported with elevated specific IgE due to cow milk protein in their serum.[2] Children with non-IgE mediated CMA have been shown to develop tolerance to cow's milk earlier and more frequently than those with IgE-mediated CMA.[3] Therefore those infants who are IgE-mediated tend to have a more prolonged course of CMA than those which are non-IgE mediated.

Skin Prick Test (SPT)

A SPT is performed by using a 1-mm single peak lancet with histamine dihydrochloride (10 mg/ml) and isotonic saline solution as positive and negative control, respectively. Reactions are recorded on the basis of the largest diameter (mm) of the wheal and flare at 15 minutes. The SPT result is considered "positive" if the wheal is 3 mm or larger, without reaction of the negative control.[4]

Less then 50% of infants with CMA show a positive skin prick test to cow's milk protein. However, a higher maximum wheal diameter on skin prick test to cow's milk and a higher maximum level of specific IgE to CM were associated with reduced likelihood of acquiring tolerance in the subgroup of children with IgE-mediated CMA.[5]

Atopy Patch Test (APT)

APT is performed in all children using freeze-dried purified food extracts contained in a commercial kit. The commercial APT is performed according to the manufacturer's instructions. The freeze-dried purified extracts are put on filter paper and applied with adhesive tape to the unaffected skin of the child's back, using 12-mm aluminum cups. Isotonic saline solution is the negative control. Seventy-two hours after the start of the test, reactions are classified as follows: negative, doubtful, weak positive, strong positive and very strong positive.[6] Canani et al[7] demonstrated that APT is a reliable, safe, and useful diagnostic tool with which to evaluate suspected food allergy related gastrointestinal symptoms in childhood and infancy. Keskin et al[8] reported that the combined use of APT and SPT had a sensitivity of 100% and a negative predictive value of 76%. The addition of milk specific assays to APT and SPT did not improve these values. However, double-blind, placebo-controlled food challenges (DRPCFCs) are still necessary in the presences of positive test results.

Double-Blind, Placebo-Controlled Food Challenges (DBPCFCs)

To date, the DBPCFCs is used as a standard method for diagnosis of food protein allergy including CMA.

257-258Pipop-Approaches.indd 257 12/23/10 11:41:05 AM

Bachler et al[9] demonstrated that using prolonged DBPCFCs, the infants with CMA had either immediate-type IgE dependent or delayed-type IgE-independent allergy.

The major problem in doing this test is to switch the current infant's cow milk formula to a very low hypoallergenic formula. However, the infants who are affected by this disease (FAI) are most likely to be allergic to soy bean, goat milk and cow milk protein hydrolysates. Now an amino-acid-based (AAF) formula is recommended for DBPCFCs in suspected infants of FAI.

When an infant's symptoms subside within 2-weeks of intake of AAF, then, small amounts of cow's milk formula are gradually re-introduced to the infant. If within 2 weeks of cow's milk challenge, the symptoms recur, then it is proved that the infant is CMA.

There are 2 possibilities to occur when the infant is switched to AAF. First, the infant's symptom does not resolve or the infant develops a new symptom that is suggestive to be allergic. Secondly, the infant's symptoms subside completely. The second option means that the infant is most likely to be CMA and responses well to the AAF. After 2 weeks of AAF, the infant is then fit to go through the DBPCFCs test. In case, the first option occurs, it can be interpreted that the infant might still be allergic to AAF or the infant's symptom is not related to CMA. To differentiate this, we suggest that the infant should be starved for a 3-days period. If the infant's symptom subsides, then it is most likely that the infant is allergic to cow's milk protein and AAF.

In conclusion, the DBPCFCs is a standard test for diagnosis of CMA and FAI. Using other tests are most likely to confirm the diagnosis. The negative results of other tests do not rule out FAI. A positive test for specific IgE to cow's milk most likely will predict the duration of CMA in the infant.

REFERENCES

1. Noh G, Jin H, Lee J, Lee WM, Lee S. Eosinophilia as a predictor of food allergy in atopic dermatitis. Allergy Asthma Proc. 2010;31:e18-24.
2. Skripak JM, Matsui EC, Mudd K, Wood RA. The natural history of IgE-mediated cow's milk allergy. J Allergy Clin Immunol. 2007 Nov;120 (5):1172-7.
3. Saarinen KM, Pelkonen AS, Makela MJ, Savilahti E. Clinical course and prognosis of cow's milk allergy are dependent on milk-specific IgE status. J Allergy Clin Immunol. 2005 Oct;116(4):869-75.
4. Lee LA, Burks W. Food allergies: prevalence, molecular characterization, treatment/prevention strategies. Annu Rev Nutr. 2006;26:539-65.
5. Santos A, Dias A, Pinheiro JA. Predictive factors for persistence of cow's milk allergy. Pediatr Allergy Immunol 2010; (epub ahead of print).
6. Niggemann B, Reibel S, Wahn U. The atopy patch test (APT)-a useful tool for the diagnosis of food allergy in children with atopic dermatitis. Allergy. 2000 Mar;55(3):281-5.
7. Canani RB, Ruotolo S, Auricchio L, Caldore M, Porcaro F, Manguso G, et al. Diagnostic accuracy of the atopy patch test in children with food allergy-related gastrointestinal symptoms. Allergy. 2007 Jul;62(7):738-43.
8. Keskin O, Tuncer A, Adalioglu G, Sekerel BE, Sackesen C, Kalayci O. Evaluation of the utility of atopy patch test, skin prick test, and total and specific IgE assays in the diagnosis of cow's milk allergy. Ann Allergy Asthma Immunol. 2005 May;94(5):553-60.
9. Bachler P, Chad Z, Gurbindo C, Bonin AP, Bouthillier L, Seidman EG. Distinct patterns of cow's milk allergy in infancy defined by prolonged, two-stage double-blind, placebo-controlled food challenges. Clin Exp Allergy. 1996 Mar;26(3):254-61.

257-258Pipop-Approaches.indd 258 12/23/10 11:41:06 AM