

学位論文の要旨

氏名 新原 (河野) 邦江

学位論文名 Serum Gliadin Monitoring Extracts Patients With False Negative Results in Challenge Tests for the Diagnosis of Wheat-Dependent Exercise-Induced Anaphylaxis

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著者名 Kunie Kohno, Hiroaki Matsuo, Hitoshi Takahashi,
Hiroyuki Niihara, Yuko Chinuki, Sakae Kaneko,
Tsutomu Honjoh, Tatsuya Horikawa, Shoji Mihara,
Eishin Morita

論文内容の要旨

INTRODUCTION

Wheat dependent exercise-induced anaphylaxis (WDEIA), a specific form of wheat allergy, is typically induced by physical exercise as secondary factor after the ingestion of wheat containing foods. Aspirin is also a triggering factor of WDEIA. Challenge testing with wheat plus exercise and/or aspirin is a gold standard for the diagnosis of WDEIA; however, the test may often yield false-negative results. In a previous study, we found that gliadin concentrations markedly increased in the sera of patients with WDEIA in parallel with allergic symptoms during positive challenge testing. This observation indicated that both exercise and aspirin intake causes absorption of non-digested gliadin from the intestine into the blood circulation. In addition, we found that the increase in serum gliadin also occurred in healthy subjects. Taken together, we consider that the amount of allergen-absorbed via the intestine is critical for eliciting the allergic symptoms of WDEIA seen after wheat ingestion. Based on this knowledge, we sought to extract the patients with false negative results in the challenge tests of WDEIA.

MATERIALS AND METHODS

Thirty-six patients (17 female and 19 male; mean age, 34.9 years; range, 9–71 years), who experienced allergic symptoms after ingesting wheat-containing foods in combination

with exercise and/or NSAIDs were enrolled in this study. All the patient went through the wheat plus exercise and/or aspirin challenge testing and serum gliadin concentration during the tests are measured. Serum gliadin concentrations were determined using an ELISA kit for wheat gliadin. Briefly, gliadin in serum was extracted by 70% ethanol and dried. The dried residue was dissolved in sample buffer and the gliadin concentration in each sample was calculated using a gliadin standard.

According to the challenge tests and serum gliadin concentration, group categorizations were given as follows; Group I, challenge tests were positive; Group II, challenge tests were negative and serum gliadin were undetectable; Group III, challenge tests were negative and serum gliadin were detectable. The Grope I patients are diagnosed as definite WDEIA. The Group II patients were considered insufficiently challenged and were required to undergo retesting. Patient with positive retests were considered as definite WDEIA. Patients with a negative retest, with undetectable serum gliadin, were considered as a failure of retesting and followed with a diet management. Those who declined retests also followed with a diet management. The diagnostic endpoint of the diet management was the clinical outcomes during a 1-year follow-up of wheat elimination diet or exercise-restriction after their meals. If the patient did not experience symptoms during the 1-year follow-up, a diagnosis of probable WDEIA was given. If a patient in this group had recurrent symptoms without wheat plus exercise and/or NSAIDs, a diagnosis of non-WDEIA was given. The Group III patients maintained a normal diet for a year, and during this time their allergic symptoms were carefully monitored. If a patient in this group had no symptoms during the year, a diagnosis of non-WDEIA was given. If a patient in this group had recurrent symptoms with wheat plus exercise and/or NSAIDs, a diagnosis of probable WDEIA or other food allergy was considered.

RESULTS AND DISCUSSION

All 36 patients had a negative reaction to a single challenge with wheat, exercise or aspirin. Of the 36 patients, 17 had a positive reaction with either wheat plus exercise, aspirin plus wheat or aspirin plus wheat plus exercise. However, 19 patients had a negative reaction even in the combination challenge of wheat and exercised and/or aspirin. A diagnosis of definite WDEIA was made in 17 patients and they were categorized into Group I. Ten patients who were negative to wheat plus exercise and/or aspirin challenge with undetectable serum gliadin were categorized into Group II. Nine patients who had negative challenge testing with detectable serum gliadin concentration were categorized into Group III. The patients in Group II were proceeded to either retest and/or follow a diet management. In this group, definite WDEIA was diagnosed in three patients by retesting, probable WDEIA was diagnosed in six patients, and non-WDEIA was

diagnosed in one patient. In Group III, a final diagnosis of non-WDEIA was given for 7/9 patients who experienced no symptoms after a normal diet for more than 1 year. In the rest two patients, one was considered as probable WDEIA because this patient has specific IgE to ω -5 gliadin, a major allergen of WDEIA. Another patient did not have specific IgEs to ω -5 gliadin nor HMW-glutenin. Thus there is still the possibility that this patient has another food allergy.

In the present study, we provided evidence that serum gliadin monitoring is a good tool to use in checking the efficacy of challenge tests for the diagnosis of WDEIA, since a lack of increased serum gliadin can prove an insufficient challenge test. We focused on an extraction of WDEIA-suspected patients who had negative results of the challenge test, because it was believed that an elevation of serum gliadin is required to develop allergic symptoms in WDEIA. As with our previous study, increased serum gliadin levels were observed in the patients with positive challenge testing, supporting research that gliadin levels in the sera correlate with allergic symptoms in WDEIA. The patients who had shown negative challenge testing were divided into two groups based on their serum gliadin levels; patients who had been tested by an efficient challenge with increased serum gliadin level (Group III) and patients who had not been tested efficiently without serum gliadin-increase (Group II). The false-negative challenge performed in Group II was confirmed by the retesting or diet management and the result showed that 9 out of 10 in Group II patients were definite/probable WDEIA, whereas the result of normal diet treatment showed that 8 out of 9 Group III patients were non-WDEIA. Thus, the detection of serum gliadin and classification of patients by its level during the challenge testing is of importance for interpreting the negative challenge test result.

For the further prospects, the feasibility of serum gliadin monitoring is required to be examined because of the difficulty in its measurement methods.

CONCLUSION

Serum gliadin monitoring during challenge testing for WDEIA is helpful to extract the patients with false negative results. However further study is needed for the practical application of this method.