厚生労働省科学研究費補助金
「難治性疾患等克服研究事業（免疫アレルギー疾患等予防・治療研究事業）：
生命予後に関わる重篤な食物アレルギーの実態調査・新規治療法の開発および治療指針の策定
(H24-難治等（免）-一般-005)」

平成24年度　第2回　班会議プログラム

日時：平成25年1月12日（土）10：00～15：00（予定）
場所：島根イン青山　多目的ホール　パインコートⅡ
住所：〒107-0062　東京都港区南青山７丁目１番５号
Tel：03-3797-3399

事務局：島根大学医学部皮膚科
担当：高橋　仁、板倉絹子
〒693-8501　出雲市塩冶町89-1
TEL 0853-20-2210
FAX 0853-21-8317
e-mail tkh4@med.shimane-u.ac.jp　（高橋）
kinitaku@med.shimane-u.ac.jp（板倉）

平成24年度　第2回　班会議プログラム

10:00～

開会の挨拶、本年度の研究内容について

研究代表者　森田栄伸　（島根大学医学部皮膚科）

10:05～

ケースカードの解析結果について

高橋　仁、千貫祐子、森田栄伸　（島根大学医学部皮膚科）

10:40～

重篤な食物アレルギーの実態調査

平郡真記子、三原祥嗣、横林ひとみ、秀　道広（広島大学医学部皮膚科）

11:00～

納豆による遅発性アナフィラキシーにおける、ポリガンマグルタミン酸のアレルゲン性についての検討

相原道子、猪又直子（横浜市立大学医学部皮膚科）

11:20～

食物アレルギーの病態に基づいた好塩基球を標的とした新規試験法の開発

宇賀神つかさ、横関博雄（東京医科歯科大学医学部皮膚科）

11:40～

原因食物スクリーニングのためのIgE診断アレルゲンパネル

福冨友馬（国立病院機構相模原病院臨床研究センター）

12:00～

休憩

12:40～

口腔アレルギー症候群（花粉―食物アレルギー症候群）に対する各種検査法の有用性についての検討

松井佐起，小野慧美、北場俊、木嶋晶子、室田浩之、片山一朗（大阪大学医学部皮膚科）

13:00～

口腔アレルギー症候群に関する疫学調査

大澤陽子、藤枝重治　（福井大学医学部耳鼻咽喉科）

13:20～

加水分解小麦アレルギーの診断基準の確立と症例集積

松永佳世子、矢上晶子　（藤田保健衛生大学医学部皮膚科）

13:50～

お茶のしずく石鹸使用後発症した小麦アレルギー症例の臨床とアスピリンの経皮感作に及ぼす研究

岸川禮子、杉山晃子、西江温子（国立病院機構福岡病院アレルギー科）、田辺創一（広島大学生物圏科学研究科）

14:10～

加水分解小麦によるWDEIAの抗原解析

松尾裕彰、横大路智治（広島大学大学院医歯薬保健学研究院病態解析治療学）、秀道広（広島大学医学部皮膚科）、森田栄伸（島根大学医学部皮膚科）

14:30～

食物アレルギー診療における好塩基球CD203c測定の有用性に関する研究

千貫祐子、高橋　仁、森田栄伸（島根大学医学部皮膚科）

14:50～

報告会への対応と今後の検討課題

事務連絡、次回会議日程について

高橋　仁、板倉絹子、藤井　愛（島根大学医学部皮膚科）

平成 24 年度　食物アレルギー研究班　第 2 回会議議事録
研究課題「生命予後に関わる重篤な食物アレルギーの実態調査・新規治療法の開発および治療指針の策定」

日時：平成 25 年 1 月 12 日（土）10：00〜15：00

場所：島根イン青山　多目的ホール　パインコートⅡ

住所：〒107-0062　東京都港区南青山７丁目１番 5 号

班会議プログラム

1. 開会の挨拶、本年度の研究内容について
   研究代表者　森田栄伸　（島根大学医学部皮膚科）
2. ケースカードの解析結果について
   高橋　仁、千貫祐子、森田栄伸　（島根大学医学部皮膚科）
3. FDEIA、OAS の概念と診断基準についての検討
4. 重篤な食物アレルギーの実態調査
   平郡真記子、三原祥嗣、横林ひとみ、秀　道広 (広島大学医学部皮膚科)
5. 納豆による遅発性アナフィラキシーにおける、ポリガンマグルタミン酸のアレルゲン性についての検討
   相原道子、猪又直子 (横浜市立大学医学部皮膚科)
6. 食物アレルギーの病態に基づいた好塩基球を標的とした新規試験法の開発
   宇賀神つかさ、横関博雄 (東京医科歯科大学医学部皮膚科)
7. 原因食物スクリーニングのための IgE 診断アレルゲンパネル
   福冨友馬 (国立病院機構相模原病院臨床研究センター)
8. 口腔アレルギー症候群（花粉—食物アレルギー症候群）に対する各種検査法の有用性についての検討
   松井佐起, 小野慧美、北場俊、木嶋晶子、室田浩之、片山一朗 (大阪大学医学部皮膚科)
9. 口腔アレルギー症候群に関する疫学調査
   大澤陽子、藤枝重治　（福井大学医学部耳鼻咽喉科)
10. 加水分解小麦アレルギーの診断基準の確立と症例集積
    松永佳世子、矢上晶子　(藤田保健衛生大学医学部皮膚科)
11. お茶のしずく石鹸使用後発症した小麦アレルギー症例の臨床とアスピリンの経皮感作に及ぼす研究
    岸川禮子、杉山晃子、西江温子 (国立病院機構福岡病院アレルギー科)、田辺創一 (広島大学生物圏科学研究科)
12. 加水分解小麦による WDEIA の抗原解析

松尾裕彰、横大路智治 (広島大学大学院医歯薬保健学研究院病態解析治療学)、秀道広 (広島大学医学部皮膚科)、森田栄伸 (島根大学医学部皮膚科)

13. 食物アレルギー診療における好塩基球 CD203c 測定の有用性に関する研究

千貫祐子、高橋　仁、森田栄伸 (島根大学医学部皮膚科)

14. 事務連絡、次回会議日程について

高橋　仁（事務局長)、板倉絹子、藤井　愛（島根大学医学部皮膚科）

議事録

1．　本年度の研究計画と研究組織について

研究組織は、FDEIA 分科会、OAS 分科会、疫学分科会の３組織にて構成し、本研究を実施する。

加水分解コムギアレルギーの実態調査については、日本アレルギー学会化粧品中のタンパク質分解物の安全性に関する特別委員会と連携し、本研究をすすめる。

FDEIA、OAS の診断基準を作成するため、本年度は各施設における過去の症例を集積し、集計を行った。

2．　ケースカードの解析結果について

各機関から登録された FDEIA, OAS, その他の食物アレルギーのケースカード (917 症例) の解析結果について報告した。再度、ケースカードを確認した後、再解析することとした。

今後は保存血清を確認し、血清が保存されていれば、小麦関連抗原特異的 IgE および Bet v1 および、Lipid transfer protein 特異的 IgE 抗体価を測定し、診断基準やガイドライン作成の資料とする。

3．FDEIA, OAS の疾患概念について

FDEIA (Food-Dependent Exercise-Induced Anaphylaxis: FDEIA) の疾患概念は、「即時型食物アレルギーの特殊型で、特定の食物摂取と運動等の二次的要因の組み合わせで蕁麻疹等のアレルギー症状をきたすものをいい、重篤な場合はショックをきたす。」と定義した。

口腔アレルギー症候群 (Oral Allergy Syndrome: OAS) の疾患概念は、「即時型アレルギーの特殊型で、食物摂取時に口腔・咽頭粘膜の過敏症状をきたすものをいい、重篤な場合は、ショックをきたす。」と定義した。

4．FDEIA, OAS の診断基準（案）について

食物依存性運動誘発アナフィラキシー（Food-Dependent Exercise-Induced Anaphylaxis: FDEIA）

小麦の場合：

① 小麦製品の摂取後○時間以内に、運動などの二次的要因により蕁麻疹などのアナフィラキシー症状を生じる。

② 血清中に小麦蛋白質（ω-5 グリアジンを含む）特異的 IgE が証明される。

③ 小麦蛋白質のプリックテストが陽性を示す。

④ 経口小麦負荷試験（小麦摂取+運動負荷、アスピリン+小麦摂取あるいはアスピリン+小麦摂取+運動負荷）で即時型アレルギー症状が誘発される。

確定診断：①に加えて②、③、④のいずれか 1 つ以上を満たす。

口腔アレルギー症候群（Oral Allergy Syndrome: OAS）

バラ科果物関連の場合：

① バラ科の果物を摂取時に口腔・咽頭粘膜の過敏症状を示す。

② 血清中にバラ科の果物特異的 IgE が証明される。

③ バラ科の果物によるプリックテストが陽性を示す。

確定診断：①に加えて②、③のいずれか 1 つ以上を満たす。

ただし、非アレルギー性の血管性浮腫は除く。

などのようにまず個別に検討することとした。

5．各研究者から研究成果を上記プログラムの内容にて報告していただき、来年度も継続して研究を実施していただくこととした。

6．松永佳代子　教授より、化粧品中のタンパク質分解物の安全性に関する特別委員会の内容についてご説明頂き、特別委員会で得られた情報を本研究班で共有させていただくこととした。

7．平成 25 年度第 1 回班会議の日程は、平成 25 年 6 月 8 日、東京で開催することとした。

平成24年度第2回班会議名簿		
氏名	所属	出欠
森田 栄伸	島根大学医学部皮膚科　教授	出席
松永 佳世子	藤田保健衛生大学医学部皮膚科　教授	出席
秀 道広	広島大学大学院医歯薬保健学研究院皮膚科　教授	出席
岸川 禮子	国立病院機構福岡病院アレルギー科　医長	出席
福富 友馬	国立病院機構相模原病院臨床研究センター　診断・治療薬開発研究室長	出席
千貫 祐子	島根大学医学部皮膚科　助教	出席
片山 一朗	大阪大学大学院医学系研究科皮膚科　教授	出席
横関 博雄	東京医科歯科大学医学部皮膚科　教授	出席
相原 道子	横浜市立大学医学部皮膚科　教授	出席
藤枝 重治	福井大学医学部耳鼻咽喉科　教授	出席
塩飽 邦憲	島根大学　理事・副学長	出席
下条 直樹	千葉大学医学部小児科　准教授	欠席
松尾 裕彰	広島大学大学院医歯薬保健学研究院病態解析治療学 教授	出席
三原 祥嗣	広島大学大学院医歯薬保健学研究院皮膚科　准教授	欠席
平郡 真記子	広島大学大学院医歯薬保健学研究院皮膚科　大学院生	出席
足立 厚子	兵庫県立加古川医療センター皮膚科　部長	出席
棟方 充	福井県立医科大学医学部呼吸器内科　教授	欠席
矢上 晶子	藤田保健衛生大学医学部皮膚科　准教授	出席
堀川 達弥	西神戸医療センター皮膚科　部長	出席
高橋 仁	島根大学医学部皮膚科　助教	出席
北場 俊	公立学校共済組合　近畿中央病院皮膚科　医長	出席
松井 佐起	大阪大学大学院医学系研究科皮膚科	出席
小野 慧美	大阪大学大学院医学系研究科皮膚科	出席
宇賀神 つかさ	東京医科歯科大学医学部皮膚科　メディカルフェロー	出席
千葉 浩輝	千葉大学医学部小児科	出席
大澤 陽子	福井大学医学部耳鼻咽喉科	出席
板倉 絹子	島根大学医学部皮膚科	出席
藤井 愛	島根大学医学部皮膚科	出席

V. 研究成果の刊行に関する一覧表

著書

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
相原道子	3）蕁麻疹 ⑦蕁麻疹：食物アレルギーの関与. Ⅲ章 多彩な皮膚アレルギー疾患を理解する	塩原哲雄ゲスト編集, 宮地良樹, 清水宏常任編集	皮膚科サブスペシャリティーシリーズ 1冊でわかる皮膚アレルギー	文光堂	東京	2012	170-171

論文

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Shinoda J, Inomata N, Chinuki Y, Morita E, Ikezawa Z.	Case of allergy due to hydrolyzed wheat proteins in commercial boiled pork.	J Dermatol.	39	724-726	2012
Chang Y, Wang T, Gao S, Morita E.	Novel allergen from the freshwater clam and the related allergy.	J Dermatol.	39	672-674	2012
Morita E, Chinuki Y, Takahashi H, Nabika T, Yamasaki M, Shiwaku K.	Prevalence of wheat allergy in Japanese adults.	Allergol Int.	61	101-105	2012
Chinuki Y, Kaneko S, Dekio I, Takahashi H, Tokuda R, Nagao M, Fujisawa T, Morita E.	CD203c expression-based basophil activation test for diagnosis of wheat-dependent exercise-induced anaphylaxis.	J Allergy Clin Immunol.	129	1404-1406	2012
Takahashi H, Matsuo H, Chinuki Y, Kohno K, Tanaka A, Maruyama N, Morita E.	Recombinant high molecular weight-glutenin subunit-specific IgE detection is useful in identifying wheat-dependent exercise-induced anaphylaxis complementary to recombinant omega-5 gliadin-specific IgE test.	Clin Exp Allergy.	42	1293-1298	2012
Chinuki Y, Morita E.	Wheat-Dependent Exercise-Induced Anaphylaxis Sensitized with Hydrolyzed Wheat Protein in Soap.	Allergol Int.	61	529-537	2012
Chinuki Y, Takahashi H, Dekio I, Kaneko S, Tokuda R, Nagao M, Fujisawa T, Morita E.	Higher allergenicity of high molecular weight hydrolysed wheat protein in cosmetics for percutaneous sensitization.	Contact Dermatitis.	68	86-93	2013
Kohno K, Matsuo H, Takahashi H, Niihara H, Chinuki Y, Kaneko S, Honjoh T, Horikawa T, Mihara S, Morita E.	Serum gliadin monitoring extracts patients with false negative results in challenge tests for the diagnosis of wheat-dependent exercise-induced anaphylaxis.	Allergol Int.	62	229-238	2013
Inomata N, Morita A, Sawaki H, Aihara M	Case of rice allergy induced by epicutaneous sensitization to rice bran due to handling rice bran pickles	J Dermatol	39 (11)	1079-1080	2012
山川有子, 大砂博之, 相原道子, 池澤善郎	コチニール色素による即時型アレルギー患者におけるアレルギー検査の分析およびアレルゲン蛋白質の解析	臨皮	66	8-13	2012

猪又直子, 相原道子	成人の食物アレルギーの特徴, 原因食物, 自然史	Visual Dermatology 最新！食物アレルギーの診断と治療	11	272-279	2012
松倉節子, 板垣康治, 相原道子	パパイン酵素入り洗顔料による経皮感作とワサビのアナフィラキシー合併例	Visual Dermatology 最新！食物アレルギーの診断と治療	11	292-294	2012
松倉節子, 相原道子, 池澤善郎	食物アレルギーと経皮感作	小児科	53	347-357	2012
松倉節子, 相原道子, 池澤善郎	話題の疾患と治療 経皮感作による食物アレルギー	感染 炎症 免疫	42	75-78	2012
長島真由美, 猪又直子, 相原道子	「茶のしずくＲ石鹸」使用者に発症した小麦依存性運動誘発アナフィラキシー	治療	94	1872-1879	2012
長島真由美, 相原道子	これが口腔アレルギー症候群だ！	皮膚アレルギーフロンティア	10	201	2012
岡田里佳, 猪又直子, 相原道子	加水分解コムギの経皮感作による小麦依存性運動誘発アナフィラキシー	臨床免疫・アレルギー	58	85-93	2012
岡田里佳, 澤木晴名, 相原道子	クロモグリク酸ナトリウム内服で症状が増強されたエビアレルギーの1例	日小児皮会誌			in press 2013
Kijima A, Murota H, Takahashi A, Arase N, Yang L, Nishioka M, Yamaoka T, Kitaba S, Yamauchi-Takihara K, Katayama I.	Prevalence and Impact of Past History of Food Allergy in Atopic Dermatitis.	Allergol Int.	62(1)	105-12	2012
Yamaoka T, Azukizawa H, Tanemura A, Murota H, Hirose T, Hayakawa K, Shimazu T, Wada N, Morii E, Katayama I.	Toxic epidermal necrolysis complicated by sepsis, haemophagocytic syndrome, and severe liver dysfunction associated with elevated interleukin-10 production.	Eur J Dermatol.	22(6)	815-7	2012
Hanafusa T, Igawa K, Kotobuki Y, Kitaba S, Tani M, Katayama I.	Systemic lymphadenopathy with systemic sclerosis and Sjögren's syndrome: A case report.	J Dermatol.	40(2)	124-5	2013
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ORIGINAL ARTICLE

Prevalence of Wheat Allergy in Japanese Adults

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ABSTRACT

Background: Wheat is one of the most common causes of food allergies. The exact prevalence of wheat allergy has not been well delineated in Japanese adults.

Methods: We enrolled 935 adults in a cohort study established by Shimane University in order to examine the determinants of lifestyle-related diseases. A screening was conducted by a questionnaire-based examination and a detection of serum omega-5 gliadin-specific IgE. Subjects who tested positive in the questionnaire-based examination and/or the serum omega-5 gliadin-specific IgE test were further examined by detailed interviews and skin prick tests.

Results: A total of 22 subjects were picked up by the screening process, and 17 of these were further examined by secondary testing. Only two subjects were conclusively identified as having wheat allergy.

Conclusions: The prevalence of wheat allergy in Japanese adults was found to be 0.21% by using a combination of questionnaire-based examination, skin prick test and serum omega-5 gliadin-specific IgE test.

KEY WORDS

ImmunoCAP, omega-5 gliadin, skin prick test, wheat allergy

INTRODUCTION

Wheat allergy is one of the most widespread food allergies, because wheat is the most widely consumed food grain in the world. Acute IgE-mediated responses to wheat are common in children, whereas wheat-dependent exercise-induced anaphylaxis (WDEIA) is more common in adolescents and adults. Many studies have investigated the prevalence of wheat allergies in the European countries and the USA.[1-11] The prevalence of wheat allergies was found to be 0.2-0.9% in adults and 0.4-1.3% in children, by using questionnaire-based studies.[1-6] Wheat sensitization was assessed by the detection of a serum IgE specific to wheat, which indicated non-specific binding of IgE in the IgE detection system; the prevalence was found to be fairly high in adults (0.4-4%).[7-11] A few surveys of wheat allergies have been reported from Asian countries.

Study of wheat allergens indicated that water/salt-insoluble gluten is responsible for WDEIA whereas acute IgE-mediated responses and atopic dermatitis in children are related to a wide range of wheat proteins. Among the water/salt-insoluble proteins, omega-5 gliadin was identified as the major allergen in WDEIA.[12-14] The detection of omega-5 gliadin-specific IgE was also found to be useful for identifying acute IgE-mediated wheat allergy and WDEIA in adolescents and adults.[15] The aim of the present study was to determine the prevalence of wheat allergy in Japanese adults by using the omega-5 gliadin-specific IgE detection system.

METHODS

STUDY POPULATION

The study population comprised 935 adults (female : male, 523 : 412; median age, 68.6 years; age range, 24-93 years) who were enrolled in a cohort study established by Shimane University that was designed to examine the determinants of lifestyle-related diseases. This study was carried out from July 2009 to March 2010.

This study was approved by the ethics committee of the Shimane University Faculty of Medicine (ap-

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Table 1 Background of the subjects who were picked up by the screening, and the results of the secondary tests

case	age	gender	screening			second tests			
						interview	prick test		
			history	Frequency of episode	ω-5 gliadin-ImmunoCAP		wheat	bread	ω-5 gliadin
1	40	male	+	2	1.15	confirmed	+	+	+
2	72	female	-	0	0.46	excluded	-	-	-
3	74	male	-	0	0.59	excluded	-	-	-
4	74	female	-	0	0.51	nd	nd	nd	nd
5	75	male	-	0	2.07	excluded	-	-	-
6	77	male	-	0	0.91	excluded	-	-	-
7	82	male	-	0	2.35	excluded	-	-	-
8	67	male	+	>30	4.47	confirmed	+	+	+
9	78	male	-	0	0.97	nd	nd	nd	nd
10	72	female	-	0	0.77	excluded	-	-	-
11	69	female	-	0	0.92	nd	nd	nd	nd
12	85	male	-	0	9.53	excluded	-	-	-
13	73	male	-	0	0.45	excluded	-	-	-
14	77	male	+	10	<0.35	nd	nd	nd	nd
15	77	female	+	2	<0.35	excluded	-	-	-
16	73	female	+	unclear	<0.35	excluded	-	-	-
17	74	female	+	unclear	<0.35	nd	nd	nd	nd
18	67	female	+	unclear	<0.35	excluded	-	-	-
19	74	female	+	3	<0.35	excluded	-	-	-
20	67	male	+	4	<0.35	excluded	-	-	-
21	79	female	+	2	<0.35	excluded	-	-	-
22	75	female	+	1	<0.35	excluded	-	-	-

+, positive; -, negative; nd, not done.

proval No. 199), and written informed consent was obtained from all participants.

DIAGNOSTIC PROCEDURES

The subjects were screened for wheat allergy by a questionnaire-based examination and a serum omega-5 gliadin-specific IgE detection test. Unusual reactions that occurred within 4 h of ingestion of wheat products, including urticaria, angioedema of the face, discomfort sensation of mucosa, dyspnea, and unconsciousness, were recorded by the questionnaire-based examination. Serum omega-5 gliadin-specific IgE was detected using an enzymatic immunoassay system (ImmunoCAP; Phadia, Uppsala, Sweden), as described previously.[16] A measurable specific IgE response was classified as a positive test result (i.e. CAP >0.35 kUA/L).

Wheat allergy was diagnosed using an in-depth interview to identify any allergic symptoms after ingesting wheat products, and a skin test. The skin prick tests were conducted with steel lancets by using purified omega-5 gliadin (1 mg/mL in saline) prepared as previously described,[13] wheat extract (Torii Pharmaceutical Co., Tokyo, Japan) and bread extract (Torii). Histamine dihydrochloride solution (10 mg/mL) was used as a positive control, and saline was used as a negative control. The wheals were evaluated after 15 min[4]; their sizes were measured using the formula, (D + d)/2, where D was the maximum diameter, and d, the perpendicular diameter. A positive test was defined as a wheal size of ≥3 mm greater than the negative control.[17]

WESTERN BLOTTING

Purified omega-5 gliadin (1 μg/lane) was electrophoresed by SDS-PAGE and transferred to a polyvinylidene difluoride membrane (PVDF, Immobilon-P; Millipore Corp., Bedford, MA, USA). The PVDF membrane with sample from each patient was blocked with tris-buffered saline (TBS; pH 7.4), containing 5% skim milk, and was incubated with TBS containing 10% serum, at room temperature for 8 h. The membrane was washed 3 times with TBS containing 0.1% Tween 20 (TBST), and incubated at room temperature for 1 h with 20,000× diluted horseradish peroxidase-labeled anti-human IgE polyclonal antibody (BioSource Int., Camarillo, CA, USA). The membrane was washed 3 times with TBST, and the IgE bound to

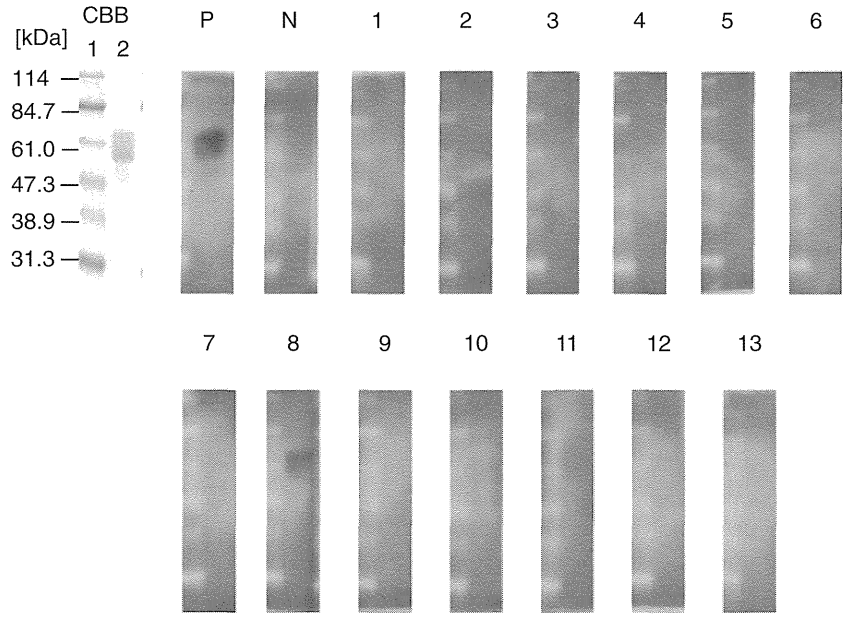

Fig. 1 Western Blotting of 13 subjects who were positive in the serum omega-5 gliadin-specific IgE test. P: positive control, N: negative control, 1-13: subjects who were positive in omega-5 gliadin-ImmunoCAP corresponding to Table 1.

the membrane was detected using an ECL-plus western blot detection reagent (GE Healthcare UK Ltd., Buckinghamshire, UK) and RX-U Fuji medical X-ray film (FUJIFILM Co., Tokyo, Japan).

RESULTS

The first screening using the questionnaire and the serum omega-5 gliadin-specific IgE test, identified 22 subjects (Table 1). The questionnaire showed that a history of unusual reactions after ingestion of wheat products was noted in 11 of the 935 subjects. Serum omega-5 gliadin-specific IgE screening detected 13 positive subjects, and 2 of these were positive in the questionnaire-based examination also, whereas the remaining 11 subjects were negative.

Of the 22 subjects, 17 (questionnaire-positive = 9; serum omega-5 gliadin-specific IgE test-positive = 10; both tests positive = 2) were accepted to enter secondary tests, namely, a detailed interview and skin prick tests. In the detailed interview, the responses to the questions regarding to the allergic symptoms after ingestion of wheat products confirmed that 2 of 17 subjects (cases 1 and 8) were allergic to wheat (Table 1). The skin prick test with wheat, bread, and omega-5 gliadin confirmed that both the subjects (cases 1 and 8) were sensitive to wheat products (Table 1). The remaining 15 subjects, who tested positive in the questionnaire-based examination and/or the omega-5 gliadin-specific IgE test were excluded after the detailed interview and the skin prick test.

Western blotting of the serum samples of the 13 subjects who tested positive in the omega-5 gliadin-specific IgE test showed that the serum sample from only case 8 was positive, whereas the serum samples from the remaining 12 subjects showed no reaction (Fig. 1).

DISCUSSION

This study identified 2 adults with wheat allergy out of 935 adult subjects, which indicates that the prevalence of wheat allergy in the adults residing in Shimane Prefecture is 0.21%. The population tested in the present study was not large, but the diagnosis was reliable, because it was confirmed by the detailed interview conducted by the dermatologists, skin prick tests, and serum omega-5 gliadin-specific IgE tests, although a provocation test was not performed. This prevalence is comparable to that found in the European countries,[1-6] but it is remarkably higher than the prevalence of food-dependent exercise-induced anaphylaxis reported in Japanese children, in which case, the prevalence is 0.017%.[18] The large difference may be attributed to the type of population being studied and the methods being used. This study screened adult subjects with questionnaire-based examination, skin prick test, and serum omega-5 gliadin-specific IgE test, whereas the previous study administered questionnaires to junior high school nurses. If the prevalence of 0.21% in the study population was to be generalized to estimate the prevalence of wheat allergy in all Japanese adults (approximately 100,000,000), then there could be 210,000 individuals with wheat allergy in Japan. The 2 subjects diagnosed with wheat allergy in this study had not been previ-

ously diagnosed; this indicates that the number of undiagnosed wheat allergy patients could be higher than that estimated by routine patient examinations.

We have previously demonstrated that detection of serum omega-5 gliadin-specific IgE is a highly useful method for identifying WDEIA patients and children with wheat allergy,[13-16,19] and the omega-5 gliadin-ImmunoCAP system using recombinant omega-5 gliadin is now widely utilized in the diagnosis of wheat allergy. In the present study, 13 subjects were identified after screening 935 adults using the omega-5 gliadin-ImmunoCAP (class 1, 4; class 2, 7; class 3, 2); thus the proportion of Japanese adults testing positive in the omega-5 gliadin-ImmunoCAP test was 1.4%. The ImmunoCAP system usually considers class 2 as positive, so the positive percentage was calculated to be 0.96% (9 out of 935). This percentage is rather low compared with the levels previously determined in the adults in the European countries, by using methods for detecting serum IgE specific to wheat,[7-11] although approximately 80% of the positive reactions in our subjects are false-positives. The present study diagnosed wheat allergy in only 2 of 9 subjects, which indicates that the test yields false-positive results at a relatively high rate in healthy adults. This false-positive reaction was also confirmed by western blotting with native omega-5 gliadin, where only 1 subject (case 8) was found to have specific IgE (Fig. 1). The lack of reactivity of case 1 may be attributed to lower sensitivity of the western blotting.

On the other hand, 9 subjects were picked up by questionnair-based examination, although omega-5 gliadin-ImmunoCAP test was negative in these subjects. Of these 9 subjects, 7 were excluded from wheat allergy by the detailed interview and skin prick testing. There remain 2 subjects (cases 14 and 17) who have not accepted the secondary tests. More recently, an increase of wheat allergy patients who were possibly sensitized with hydrolyzed wheat products have been reported.[20] These patients have been known to have low or negative score of omega-5 gliadin-ImmunoCAP test, thus these 2 subjects have still possibility to have wheat allergy. This might be a limitation of the study. Upon the questionnair-based examination, none of these 9 subjects had angioedema of the face, which is a characteristic symptom of the patients sensitized with hydrolyzed wheat products, thus it is unlikely that these 9 subjects were sensitized with hydrolyzed wheat products.

The present cohort study was performed in Daito-cho and Kamo-cho in Shimane Prefecture, both of which locate rural area. Since most subjects enrolled in the study were relatively aged, the result might not directly indicate a prevalence of wheat allergy in adults of whole Japan.

This study reports that the prevalence of wheat allergy is at least 0.21% in the Japanese adults, which was determined by using a combination of questionnaire-based examination, skin prick test, and serum omega-5 gliadin-specific IgE test.

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