

Two Cases of Anaphylaxis After Laminaria Insertion

Anaphylaxis following laminaria insertion rarely occurs but may be a life-threatening condition. Laminaria tents, prepared from natural sea kelp, are commonly used prior to elective termination of pregnancy to achieve cervical dilatation. We report herein two cases of anaphylaxis caused by IgE-mediated hypersensitivity to laminaria. Two women, each of whom had undergone at least one previous abortion where a laminaria had been utilized, developed anaphylactic reaction following laminaria insertion. The reaction included urticaria, nausea, breathing difficulty, and hypotension. The patients subsequently underwent skin testing and measurement of serum specific IgE level to laminaria extract, and were shown to elicit positive responses to laminaria. The implication and impact of laminaria allergy on gynecologic procedures are significant and this allergy should be included in the list of differential diagnoses for hypersensitive reaction in gynecologic procedures.

Key Words : Laminaria; Anaphylaxis; Skin Tests

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INTRODUCTION

Repeated transvaginal exposure to antigen can cause anaphylactic reaction in obstetric and gynecologic procedures. These agents are latex, chemicals, and laminaria and in many cases have induced IgE-mediated hypersensitivities (1-4). Laminaria have been used for cervical dilatation prior to gynecologic procedures (5). Laminaria is composed of natural kelp and principally consists of a glucan carbohydrate called laminarin, which consists of about 92.5% β -D-glucose with 1; 3 linkages. Laminarin is thought to function as the active ingredient in dilatation by changing osmotic pressure or uterine prostaglandin metabolism (6). For use, the tent is inserted into the cervix several hours before the procedure. Although allergic reactions to laminaria are estimated to occur rarely, the cases are reportedly increasing. We describe two cases of anaphylaxis induced by laminaria insertion, which was subsequently confirmed by skin test and specific IgE measurement to laminaria.

CASES REPORT

Case 1

A 27-yr-old woman, with a history of one episode of abortion, was prepared for a second abortion procedure. Before the procedure, she had no abdominal discomfort. She had no history of atopic dermatitis, allergic rhinitis, or asthma, and had not experienced any side effects from the earlier procedure. The patient was not taking any medication. The laminaria tent was inserted into the cervix before the procedure. About 30 min later, she reported dizziness, sweating, and dyspnea. The blood pressure was 80/40 mmHg, but other physical findings were unremarkable. The laminaria was removed in the emergency room. The patient was treated with epinephrine, methylprednisolone and normal saline infusion, which promptly improved the symptoms.

Complete blood count, blood chemical values, and serologic tests were normal. Chest radiographs showed no abnormalities. Her serum total IgE level measured by RIA method was 140 IU/mL. Spirometry and methacholine bronchial provocation test showed normal responses. Skin prick test, which

was performed with 10 common inhalant allergens and latex extract, showed positive response to house dust mites (*Der-matophagoides farinae* and *D. pteronyssinus*) only.

Case 2

A 37-yr-old woman visited the outpatient clinic due to wheezing and dyspnea after ingestion of analgesics. She had a history of generalized urticaria and loss of consciousness after laminaria insertion 6 yr before. After this episode, she had been suffering from recurrent episodes of urticaria. There was no history consistent with food allergy, asthma, and allergic rhinitis. She had a history of aspirin idiosyncrasy.

Complete blood count, blood chemical values, C4, and CH50 values, and anti-nuclear antibodies were all within normal ranges. The serum total IgE level was 250 IU/mL and negative response on methacholine bronchial challenge test was noted. Skin prick test with 10 common inhalant allergens showed positive response to *D. farinae*.

Skin testing

Laminaria was obtained from the Gynecology department and Laminaria extracts were prepared as previously described (7). The extract was used for the skin prick test at a concentration of 1:10 w/v. Extracts of laminarin from *L. digitata* (Sigma Chemical Company, St. Louis, MO, U.S.A.) were also included in skin test. After obtaining informed consent, we tested the patients and five healthy non-atopic subjects. Skin prick test with 10 common aeroallergens (*D. pteronyssinus*, *D. farinae*, *Aspergillus* spp, *Alternaria* spp, tree pollen mixture I and II, grass pollen mixture, mugwort, ragweed pollen, animal epithelium, and cockroach, Allergopharma Co, Hamburg, Germany), latex, laminarin (1 mg/mL), laminaria extract, histamine, and normal saline was performed on the volar side of both forearm. After 15 min, the mean diameter of a wheal formed by allergen was measured. If the diameter of the wheal was 3 mm or more, it was considered positive. All control subjects were negative on test but the patients showed positive responses to laminaria as shown in Table 1.

ELISA for specific IgE to laminaria extract

The specific IgE antibody to laminaria extract was measured using ELISA, as previously described (7). In brief, microtiter plates (Dynatech, U.S.A.) were coated with 50 μ L of laminaria extract (1:10 w/v), and then incubated with 50 μ L of either the patient's sera, or undiluted sera from five controls for 2 hr. After washing three times with 0.05% Tween phosphate buffered saline (PBS-T), 50 μ L of the 1:1,000 vol/vol biotin-labeled goat anti-human IgE antibody (Vector Co, U.S.A.) were added to the wells and incubated for 2 hr. The color reaction was developed by adding 100 μ L of ABTS (2,2'-azino-bis-3-ethyl-benzthiazoline in a citrate phosphate buffer) for 10 min

Table 1. Results of the skin prick test in the patients

Substance tested	Case 1		Case 2	
	Wheal (mm)	Flare (mm)	Wheal (mm)	Flare (mm)
Laminaria extract	4 \times 3	6 \times 5	7 \times 6	10 \times 9
Laminarin	–	–	2 \times 2	3 \times 3
Histamine	7 \times 6	10 \times 8	3 \times 3	4 \times 3
Saline	–	–	–	–

*The reaction was assessed after 15 min. Results were considered positive if the diameter of the wheal was 3 mm or more.

at room temperature. The reaction was stopped by adding 100 μ L of 2.5 N sulfuric acid and the absorbance was read at 490 nm by an automated microplate reader. All assays were performed in duplicate. IgE activity of case 1 and 2 to laminaria allergen was 0.201 (O.D.) and 0.645 (O.D.), respectively. The cut-off value (0.198) of the positive IgE binding was determined from two-fold of the mean absorbance from 5 unexposed controls.

DISCUSSION

These cases are consistent with anaphylaxis caused by the intracervical application of the laminaria tent. On the basis of history, response to skin test, and specific IgE antibody to laminaria, the patients were diagnosed as anaphylaxis to laminaria. Five previous cases of anaphylaxis following insertion of laminaria have been reported (4, 8-11). In one patient, RAST studies subsequently demonstrated specific IgE binding of 7.8% to the whole kelp extract and 6.3% to the purified carbohydrate (4). All of our cases also showed the specific IgE response to laminaria. This supports the diagnosis of IgE-mediated anaphylaxis to laminaria. The allergenic component of laminaria tent has not been identified. Laminaria consists mainly of glucan carbohydrate called laminin and a trace amount of protein (4). Unlike protein, polysaccharides have not been found to bind to and be presented by MHC molecules to T cells, and in general, T cells do not recognize carbohydrates. Polysaccharides should be attached to a carrier protein to act as an allergen. Therefore the activity may result from the carrier protein-bound polysaccharides. But it is also possible that the trace amount of protein present in the laminaria may act as an allergen.

Vaginal mucosa is also able to show an allergic response similarly to the nose, eyes, lungs, and skin. A great variety of allergens are able to provoke allergic reactions in the female genital tract. Human seminal fluid and latex applied intracervically are well recognized antigens and may develop clinically significant IgE-mediated reactions (2, 3). These reports show the potential risks of repeated exposure to allergic substances by this route.

Allergic reactions to laminaria have been recognized very rarely but the number of reported cases is increasing. There-

fore, gynecologists should counsel patients with histories of multiple previous laminaria insertions about this possibility, have alternative methods of cervical dilatation available, and be able to recognize and treat the reactions promptly when necessary.

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