

—Reports on Experiments and Clinical Cases—

Fibroin allergy

IgE mediated hypersensitivity to silk suture materials

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Abstract

Delayed-type hypersensitivity with granulomatous lesions to silk sutures is rather rare. Yet, braided silk sutures often act as a non-immunologic foreign-body and cause a granulomatous inflammatory reaction years after surgery.

We report here a case of recurrent granulomas with remarkable infiltration of eosinophils that may have resulted from an IgE-mediated hypersensitivity reaction to silk fibroin, a component of the braided silk suture. Under normal circumstances exposure to fibroin is rather rare. Therefore, the present patient may have developed this reaction to the silk sutures used in a previous surgery. (J Nippon Med Sch 1999 ; 66 : 41—44)

Key words : silk suture, fibroin, type I allergy, IgE-mediated hypersensitivity, granuloma

Introduction

It is well known that silk acts as a potent allergen causing type I allergic diseases such as asthma^{1,2}, hypersensitivity pneumonitis³, and nasal allergy⁴. Silk is composed of two proteins, sericin and fibroin, with the former surrounding the latter. Sericin is considered to be the main inhalant allergen in silk-sensitive persons^{5,6}. Since it is reported that sericins from cocoon, silkworm moth, chrysalis, and butterfly share a common allergenicity, silk allergy may be caused not only by occupational but also by environmental exposure to the insects^{1,2,7,8}. Kino¹ reported that about one-third of patients with bronchial asthma in Japan showed an increase in the specific IgE to silkworm moth.

On the other hand, silk is being widely used as a suture material in various surgeries. Silk sutures are available in twisted and braided types. Twisted silk sutures contain sericin and are manufactured by reeling off raw silk from the cocoons. On the other hand, braided silk sutures are made from fibroin after removal of sericin from the raw silk. Recently, braided

silk sutures are widely used as suture materials, since sericin contained in the twisted silk sutures is known to exhibit strong antigenicity. However, braided silk sutures are known to cause a foreign-body reaction such as mononuclear cell infiltration, fibroblastic proliferation, and giant cell appearance⁹. It has also been reported that in rare cases, chronic inflammation with granulation can occur in the tissue around the braided silk suture years after surgery as a result of a T cell-mediated hypersensitivity response^{9,10}. However, there are no reports of a Type I allergic reaction caused by braided silk sutures. Under normal circumstances, it is rare for a person to be exposed to silk fibroin. However, atopic patients who have undergone surgery are likely candidates for this reaction due to continuous exposure to the braided silk sutures. This type of sensitization can cause a Type I allergic response in the case when the patient undergoes a second surgery in which the braided silk sutures are used.

We report here a case who had an inflammatory response associated with Type I allergy, probably as a result of a late-phase reaction to silk fibroin used as

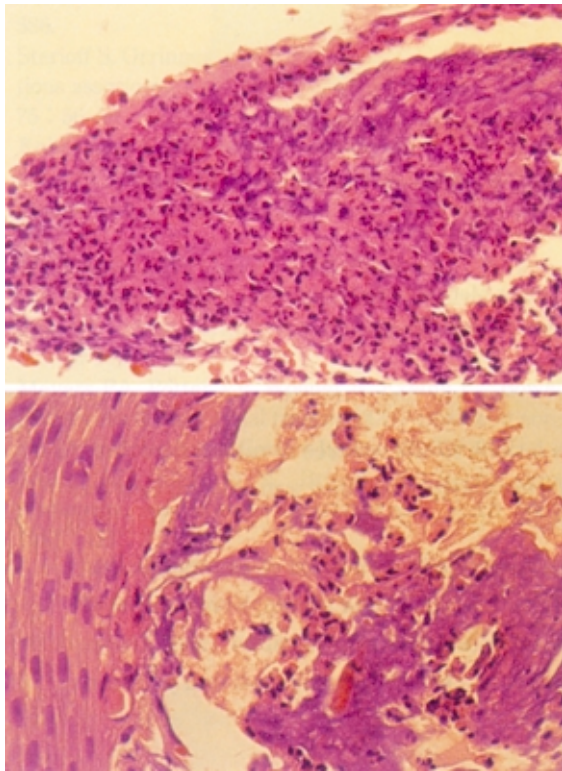


Fig. 1 An accumulation of eosinophils in recurrent granulomas

the suture material in his surgery.

Case report

A 52 year-old male patient presented with hoarseness of 3 months duration and was diagnosed as a case of a squamous cell carcinoma of the larynx by clinical and histopathological examination. Total laryngectomy was performed in March 1994, after pre-operative radiotherapy. Dexson[®] sutures were used for suturing the fascia, muscle, and pharyngeal mucosa. Interrupted nylon sutures were taken for the closure of the skin. Braided silk sutures were used to prepare a permanent tracheostoma and to ligate the vessels. While extubating the patient post-operatively, he suffered from fits of dry cough and difficulty in breathing, followed by congestion of the skin around the neck. No abnormal findings were detected on chest X ray and electrocardiogram. Intravenous administration of steroids was used to treat him, after which his symptoms subsided. Seven days post-operatively, he developed ulcerations in the skin around the silk suture sites. The following day, granulomatous lesions were detected. After removing the

silk sutures, the congestion and the granulations disappeared. The ulcerations also healed after several days. However, he developed stenosis of the tracheostoma.

Fifteen days after surgery, a vesicle appeared in the neck away from the line of incision, and ruptured spontaneously. The wound was cleaned with saline and debrided, and a week later the ulceration had healed. The skin ulcerations occurred repeatedly at different sites of the neck for almost five times over a period of 3 months. Although antibiotics were ineffective in healing the ulcerations, dressing with a steroid ointment was effective.

In October 1994, a lateral skin flap technique was performed for the correction of the tracheostomal stenosis using silk sutures. Nylon sutures were used for the closure of the skin. Just after the surgery, we observed redness around the braided silk suture sites but not around the nylon suture sites. Five days post-operatively, serous discharge was detected at the silk suture sites. This was followed by ulceration and granuloma formation. The nylon suture sites didn't cause such ulcerations. Seven days after the second surgery no signs of bacterial infection were detected in his peripheral blood examinations.

The pathological findings around the silk sutures are as shown in **Fig. 1**. The histopathological findings of the lesion were characterized by a remarkable infiltration of eosinophils with prominent exudative reaction under the epithelium. Epithelial cells had enlarged hyperchromatic nuclei and basal cells were stratified.

We evaluated the change in count and percentage of his peripheral blood eosinophils before and after each surgery (**Fig. 2**). In addition, levels of serum total and specific IgE antibodies were measured by the Pharmacia CAP-RAST[®] system. Serum total IgE was 70.7 U/ml. No increase was detected in the levels of specific IgE to house dust, house dust mite, orchard grass, ragweed, or silk. However intradermal skin test to the silk extract (Torii Pharmaceuticals Co Ltd, Tokyo, Japan) showed an immediate type reaction (**Fig. 3**).

The patient had no history of a type I allergic disease, but had undergone a partial gastrectomy, using silk sutures, seven years before his visit.

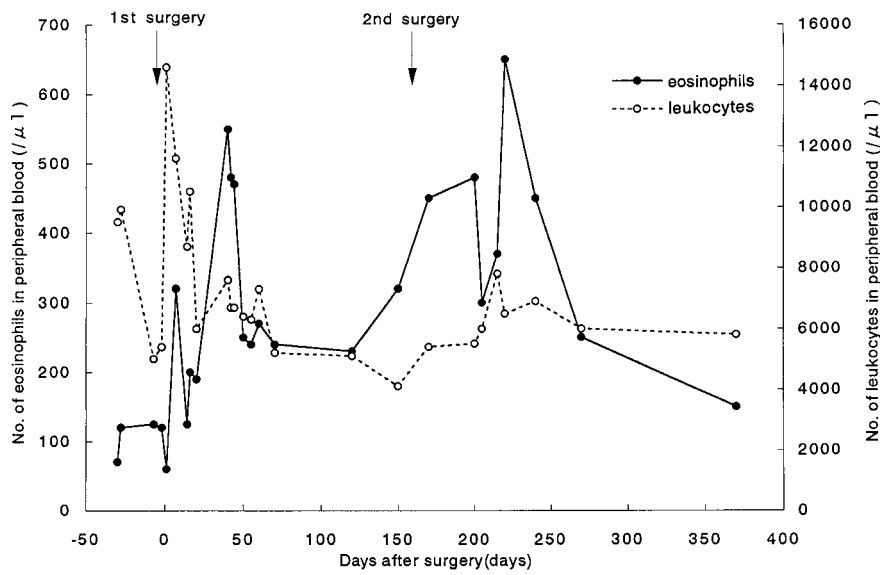


Fig. 2 No. of eosinophils and leukocytes in the patient blood after each surgery



Fig. 3 Immediate type reaction to an intradermal skin test to 1 : 100 diluted silk extract which contained both sericin and fibroin

Discussion

Silk from cocoons is composed of two proteins, sericin and fibroin. Each protein has a separate phase

structure. Fibroin, which is a fibrous protein present in the center of the silk thread, is linked and surrounded by sericin as an adhesive agent. Sericin which comprises the outer layer of the silk is relatively fragile, and is composed of a lower molecular weight substance as compared to fibroin¹¹. Sericin is a soluble protein, whereas fibroin is insoluble, and these silk proteins can be easily separated by boiling. These characteristics of sericin suggest its susceptibility to be one of the main inhalant allergens in silk that can cause an IgE-mediated allergic reaction. In a comparison of four kinds of batches of silk, by Dewair and his colleagues⁵, the silk sample containing the maximum quantity of sericin induced the highest level of specific IgE as well as degree of positive reaction to the skin test in silk sensitive subjects. By analysing the immunoblots of the silk extract using sera from silk allergy patients, Zaoming et al⁶ reported a single protein band with a molecular weight between 35.1 and 50 kD that was the specific allergen. Sprague¹¹ described that silk sericin consisted of polypeptides with molecular weights between 20 and 220 kD, whereas fibroin was composed mainly of two polypeptides with molecular weights of about 350 kD. These reports suggest that the main allergen in silk which causes an IgE-mediated allergy in silk sensitive patients is not fibroin, but sericin.

Although suture materials used in surgery are being made of silk for over a long time, braided silk sutures composed of pure fibroin which was manufac-

tured by eliminating the sericin from the cocoons are now being generally used. Therefore, the use of braided silk sutures in silk sensitive patients such as asthma never causes an IgE-mediated allergic reaction during or after the surgery. In a retrospective review, we were unable to find any reports of the induction of type I allergy after an operation using braided silk sutures. However braided silk sutures incidentally react in the skin site as a foreign-body. Although foreign-body induced granulomatous inflammation is usually characterized by an accumulation of macrophages, it is induced by a T cell-mediated immune reaction in rare cases^{9,10}. It has not been determined whether T cells are stimulated directly by a braided silk suture antigen, or indirectly by the collagen which the suture material replaces¹². In this case, recurrent granulomas can occur at the sites where braided silk sutures are used for ligating vessels or for closure of the skin. Pathological findings of these granuloma showed a remarkable infiltration of eosinophils in this case. The patient also underwent anaphylaxis just after the first surgery. The redness around braided silk suture sites were observed just after both surgeries and disappeared after removing of the braided silk sutures. These findings suggested that silk fibroin induced not foreign-body reaction but the IgE-mediated allergic reaction and that the recurrent granulomas were the result of a late-phase reaction of type I allergy. Although no increase of specific IgE to silk was detected by Pharmacia CAP-RAST[®] system which made use of both sericin and fibroin as silk antigens, an intradermal skin test to silk extract which contained sericin and fibroin showed an immediate type reaction. These differences may be concerned with specificity of each examination to detect specific IgE.

It is unclear when and how the patient was sensitized to silk fibroin. It is difficult to inhale fibroin naturally, and there was no chance of exposure to silk fibroin at his house or during his work. He had a history of surgery using silk sutures seven years before his visit. It is possible that he developed allergy due to

the continuously exposure to the silk fibroin in the suture material.

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