Ocular Hypersensitivity and Bronchial Asthma in Children

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According to the classification by Swineford, many cases of the atopic type show allergic conditions among family members and, besides asthma, patients often have a past history of allergic rhinitis, atopic dermatitis, and urticaria. Many cases of vernal catarrh are assumed to be included in this atopic type in this study.

(Key words: Conjunctivitis, Asthma, Rhinitis and Allergy)

INTRODUCTION

Bronchial asthma has been classified by etiology, symptoms, and severities (1).

Among the classifications according to etiology, that by Rackemann (1) is introduced below:

I. Extrinsic Asthma: (Before 30 years old)

This is a condition in which respiratory or food allergens have been established. The conditions develop before patients become 30 years old. Many of the patients with vernal catarrh who visit the ophthalmology department have past histories of bronchial asthma and are believed to belong to this category.

II. Intrinsic Asthma: (After 40 years old)

This is a condition in which a putative allergen has not been established. It develops after the age of 40.

The classification by Swineford (1) includes atopic, infectious, and mixed types.

I. Atopic type:

Many instances in the atopic type show allergic conditions among family members and, in addition to asthma, patients often have a past history of allergic rhinitis, atopic dermatitis, and urticaria. Many cases of vernal catarrh are believed to be included in this category. The results of skin and inhalation tests are mostly positive and allergens are established; and the patients often have past histories of bronchial asthma.

II. Infectious type:

The infectious type, on the other hand, defines paroxysmal bronchial asthma which is incurred by respiratory tract infections.
There are paroxysmal and chronic types in the classification by asthmatic symptoms. The classifications by severity of the conditions include those proposed by Oshima and Adachi (1).

The present study describes in detail vernal catarrh, the most important ophthalmological condition related to bronchial asthma in children. The study also includes an outline of conjunctivitis incurred by pollinosis. Concerning palpebral conjunctivitis caused by contact hypersensitivity, refer to the section on allergic conditions of the conjunctiva by Kunitomo (1971) (15).

VERNAL CATARRH. CONJUNCTIVITIS VERNALIS

Vernal catarrh is a type of conjunctivitis which develops in spring and summer in Japan. It is believed to belong to the category of hypersensitivity type I (43) according to Coombs and Gell (1963) (4).

The condition is rare in Scandinavian countries but occurs frequently along the Mediterranean coast and in Mexico where 2% of all ambulatory patients are said to be affected. The incidence reaches as high as 30% in Pakistan (2) while in Japan it is 0.3%. The rate is higher in the eastern coastal region and in Kanto but lower in Hokkaido, Shikoku, and Kyushu (15, 34).

The age at which the initial symptoms develop ranges from 6 to 20. The sex ratio is 3:1 with young boys appearing to be most vulnerable. The condition lasts from 8 to 10 years on the average (43). A cyclic pattern of exacerbation in summer and remission in winter has been common in the past but, probably due to the prevalence of room air-conditioning, persistence of the condition throughout the year has recently been noted in Japan.

1. Etiology

In reviewing the literature, a report by Hayashi (7) is highly significant. In this study, Hayashi, while in Kurashiki, placed two patients affected with vernal conjunctivitis in an allergen-free room for a certain period and found that their ocular conditions rapidly improved. By placing two patients with vernal catarrh in a germ-free room of Tokai University Hospital, the author also noted improvement of the symptoms in one and complete recovery in 10 months in another (unpublished data).

Experimental data by Hayashi and Tazawa (8) naming fungi as the putative antigen for vernal catarrh should also be noted. In the same study, an intradermal test was conducted in patients with vernal catarrh using extracts of Penicillium and positive results were obtained in five out of eight patients tested.

House dust has been named as a putative antigen in the pathogenesis of respiratory hypersensitivities such as bronchial asthma and allergic rhinitis. It has been said that 50 to 80% of the patients in Japan and 60 to 90% of patients overseas are affected by this allergen. Many mites have been detected in this dust with Pyroglyphidae being the predominant strain. It
has recently been established that this mite is significant as the allergen contained in house dust (Ishii, 1975) (11).

Uchikoshi and Kimura (1980) (42) reported that incidences of hypersensitivity caused by mites have increased according to their statistics on 1,946 cases of allergic rhinitis collected at Wakayama Prefectural Medical University in the past 10 years. They suggested that changes in the structures and interiors of houses have provided favorable conditions for proliferation of the mite population (42). A need for investigation of other factors promoting sensitization and development of the allergic conditions was also emphasized in the same study (42). Therefore it appears inevitable that with westernization of life styles, the incidence of positive reactions to house dust as an antigen and that of vernal catarrh — a presumed chronic form of allergic conjunctivitis — will continue to increase.

In the field of ophthalmology, Yuasa, et al. (1978) (44) conducted RAST of sera using mites as the antigen and detected anti-mite IgE antibody in 53.2% of patients with vernal catarrh and 75.8% among patients with the same condition but with marked exacerbation. Furthermore, when conjunctival washing was used instead of sera, the same antibody was detected in 53.3% of the patient group and 80% in those with exacerbation. A house dust provocation test was conducted in patients with atopic deseases by Tada (1979) (37) and positive conjunctival reactions were noted in 71 to 88%.

The author also noted that 35% of the patients with allergic conjunctivitis reacting to house dust as the major antigen develop cobblestone-like papillary proliferation of the conjunctiva which is characteristic of vernal catarrh (21, 24). In these patients, a transient exacerbation of the symptoms provoked by house dust was noted (21, 24). Subsequently, it has been established that many of the cases with vernal catarrh react positively to dermal and provocation tests using house dust and mites as the antigens (21, 24).

The antigenicity of fungi has hardly been cited except in the study by Hayashi et al. Antifungal IgE antibody has been detected in the sera of 19% of the patients affected with vernal catarrh (44). It is presumed that the role of fungal antigens is significant in the pathogenesis of the desease (45).

Shimizu (1978) (36) states, based on his results of identification from cultures, that fungi are prevalent throughout the year in Japan due to its high humidity. He recognizes, however, the need for simultaneous slide glass isolation in the identification procedure for fungi. The same author points out that the recent popularity of modern room heating methods in winter has reduced the seasonal fluctuation in room temperature (36). Shimizu also reports that Alternaria is most frequently isolated in June and August in the analysis of air-borne fungal spores using a slide glass method (36), reflecting the regional variations and weather conditions each year as in the incidences of pollinosis (36). On the other hand, Nakayama (31) conducted skin tests using Aspergillus, Alternaria, Penicillium, Cladosporium, and Candida and found 54.9% of the patients to be positive to one or more of these fungi. Shimizu conducted immediate type intradermal
tests on 4,510 cases of allergic rhinitis or respiratory allergy with bronchial asthma and stated that 54.9% showed a positive reaction to Candida, 24.7% to Aspergillus, 16.3% to Trychophyton, 15.0% to Penicillium, 13.1% to Cladosporium, and 12.2% to Alternaria (36).

Judging by the above findings, the positive reaction to fugal antigens is quite probable in children with vernal catarrh often complicated with bronchial asthma. Future field work on this aspect is expected. Teramichi (39) and others have already adopted the analysis of anti-fungal antibodies in the routine diagnosis of bronchial asthma in children. Skin tests of Mucor and Broncasma Berna (R) should also be incorporated in routine ophthalmic diagnoses of vernal catarrh.

2. Symptoms and Classification

The most prominent subjective symptom is itchiness toward evening. Other symptoms include glaring, sensation of a foreign body, burning, and lacrimation. The condition can be classified according to its objective symptoms into palpebral, bulbar, and abortive types; or into the irritative type proposed by Alimuddin (1955) (2); or into an acute type proposed by Oguchi and Uchiki (1953) (32). According to Tsukahara, among the 70 cases he observed, 40% belonged to the bulbar, 39% to the abortive, and 20% to the palpebral type.

Kunitomo stated that the early stage of vernal catarrh is often associated with a varying degree of diffuse conjunctival hyperemia (15). Following sensitization of the conjunctiva with house dust, mites, fungi, and the general bacterial population for a prolonged period, together with exposure to allergens which exist in air in large quantities from spring to summer — such as cedar pollens — acute allergic conjunctivitis results. Some conditions are transient in nature taking a course to spontaneous recovery but recur at the next exposure. Others repeat the recurrence of symptoms of allergic conjunctivitis, and with insufficient therapeutic effects, result in accumulation of exudates in the subconjunctival tissues while inflammatory proliferation progresses. Such is the pathophysiology of vernal conjunctivitis observed by Kunitomo (15). Subsequently, development of steroid preparations and their clinical application served to reduce temporarily the number of cases of vernal catarrh seen in primary care; while the number of cases with more severe forms remain unchanged and, together with the increase of multiple sensitization, appear to cause a gradual increase of the incidence of vernal catarrh. Together with ophthalmic symptomatic therapy, a systemic approach to treatment — such as desensitization — should be the primary method of treatment for these cases. The classification of vernal catarrh is introduced as follows:

1. Palpebral Form (Figure 1).

The initial symptom is hyperemia involving a wide area of the conjunctiva, gradually followed by development of a milky coloration of the involved tissue. After a lapse of 2 to 3 weeks, a proliferative change is added to the symptoms causing hypertrophy of the conjunctiva and development of small papillae of the conjunctiva of the upper palpebral region. Later, these papillae rapidly increase in size and form a cobblestone-like
appearance covering the entire upper palpebral conjunctiva.

The lower palpebral conjunctiva also takes on a milky coloration but for some reason remains without proliferative changes although it often becomes characterized by follicular formation. In general, large papilae are limited to the upper palpebral region close to the palpebral rim or on the auricular side. In some instances, multiple, giant papilae fail to develop and only a few occur on the palpebral conjunctiva close to the palpebral rim. Advanced thickening of the palpebral conjunctiva tends to cause mild ptosis. Only a small amount of ocular discharge is seen in the early stage but it later becomes viscous. A thin pseudomembrane is formed in mild cases; but in severe cases formation of a thick pseudomembrane is seen together with a yield of viscous discharge and eventual development of corneal ulcers. The conjunctival pH, as in other inflammatory conditions, is alkaline (approximately 8.0) (33). The ocular discharge contains eosinophils and neutrophils. Mast cells may also be seen in severe cases.

II. Bulbar Form (Figure 2).

At the onset, the bulbar form is often characterized simply by hyperemia and opacity of the annular region, especially of the region near the palpebral fissure. For this reason the term, allergic conjunctivitis, rather than vernal catarrh, is more appropriate for this condition (15). Most of the clinical cases are suggestive of hypersensitivity Type I caused by house dust, mites, bacteria, pollen and fungi. Insufficient treatment is likely to cause progression of many of these cases to a bulbar form of vernal catarrh. The clinical course often undergoes exacerbation with repeated fluctuations. The presence of the antigens in the environment in excess of what the body can remove may explain this condition. The outpatient clinic of the Tokai University Hospital Ophthalmology Department has a health education program in which some of the patients who react positively to house dust and mite antigens are given educational pamphlets to aid them in reducing their exposure to the putative antigens in their daily environment.

During exacerbation of the symptoms, a milky coloration of the conjunctiva gradually intensifies and the discharge begins to accumulate under the conjunctiva. Development of a gelatin-like ridge of the bulbar conjunctiva adjacent to the annule and white spots the sizes of pinholes and pinheads (Horner-Trantas spots) of the bulbar conjunctiva at the fissure are also observed during this period. These spots are identical in these conditions, a fact which strongly suggests that the two disease entities are similar (15).

Mixed form.

The mixed form includes changes in both palpebral and bulbar forms.

III. Abortive form.

The symptoms at the onset are quite similar to those of the aforementioned three forms but papilla formation of the palpebral conjunctiva and the conjunctival symptoms of palpebral fissures do not become evident; or rather the proliferative changes succeeding the exudative inflammation are incomplete. Among the abortive forms, some are said to retain black or brown melanin pigment deposits in the palpebral and bulbar conjunctiva.
This form is also considered to be a manifestation of chronic allergic conjunctivitis with varied exposure to the antigens and undergoing sequential changes due to this exposure.

3. Changes of the Cornea

Approximately one half of the patients undergo some changes of the cornea during the clinical course. The bulbar form is usually characterized by ridge-like elevation of the annular cornea, pathological involvement of the peripheral cornea continuous toward the interior, and thin gelatin-like or pannus-like opacity (vernal keratitis). Rarely, opacity of the entire cornea with destruction of Bowman's membrane may occur in some cases (15). The bulbar form of vernal catarrh sometimes shows a fine-speckled surface layer infiltration of the upper half of the cornea (which can be stained by fluorescein). This is interpreted to be a secondary change of the cornea caused by changes of the palpebral conjunctivitis. Such lesions are often eradicated by treating the papilla of the palpebral conjunctivitis. When the papillae of the palpebral region have grown excessively large, they may form corneal ulcers. For treatment of such corneal ulcers, a detailed report with case studies by Hori et al. (10) may be found helpful. Ulceration around the cornea is sometimes observed in cases exhibiting the bulbar form (15).

Easty (12) reports that vernal catarrh progresses to keratoconjunctivitis in 42% of the affected patients. Takeuchi et al. (38) state, on the other hand, that 30% among 34 cases of keratoconjunctivitis have past histories of atopic diseases. Pseudogerontoxon due to degeneration of the periphery of the cornea may remain and cause permanent opacity, which may be a hindrance in the diagnosis of a past history of vernal catarrh (15).

Dermatitis of the eyelid region is often associated with severe cases of vernal catarrh. Many of the children affected with vernal catarrh are also suffering from atopic dermatitis. In the treatment of eczema herpeticum in these children, particular care must be taken because ointments normally used for the treatment of palpebritis are contraindicated in dermatitis caused by herpes virus.

4. Eczema Herpeticum, Kaposi’s Varicelliform Eruption, Pustulosis Acuta Varioliform (Juliusberg) (9)

The condition occurs mainly in children with atopic dermatitis or diseases of a refractory nature. After a latency of approximately 10 days sudden high fever and discomfort develop, followed by swelling of the focal eczematous lesions and development of broad bean-sized or smaller vesicles and blisters with accentuated redness and indentations in clusters or scattered on the surface of eczematous foci and their peripheries, with further accentuation of the swelling. The vesicles eventually become pustulated or desiccated leaving slight scarifications. The lesions heal within 10 to 20 days from onset. During the clinical course, old and new skin eruptions coexist. The head, face, and neck regions are often affected. The condition may be complicated with such clinical entities as ulceration of the oral mucosa, herpetic keratitis, corneal ulcer, painful swelling of local
Fig. 1  Palpebral form. A cobblestone-like appearance on the upper palpebral conjunctiva.

Fig. 2  Bulbar form. A gelatin-like ridge of the bulbar conjunctiva.
lymph nodes, anuria, bloody diarrhea, otitis media, conjunctivitis, and cerebral symptoms. Mortality is approximately 25% but a fair number of patients recover completely. The disease is often caused by initial infection of herpes simplex virus (HSV) but, as in most viral infections, prior exposure to HSV patients is hard to prove. Therapeutic measures are injections of gamma-globulin and sera of patients recovering from HSV infection, administration of VIBRAMYCIN, (R) MINOMYCIN, (R) and ACHRO-MYCIN (R) and, if the systemic condition warrants it, fluid infusion or blood transfusion is applied. Local lesions are treated to prevent secondary infections. As a rule, systemic treatment constitutes the basis of the therapy and local treatment is applied as an adjunct. The mortality is relatively high among young patients and their hospitalization or frequent ambulatory care is desirable.

5. Allergic Shiner (40)

The lower eyelid region sometimes assumes a light brown coloration as if a woman's eye shadow was applied. It may become pronounced as a sign prior to an attack of bronchial asthma in children and in cases of vernal catarrh particular attention must be paid. Hyperemia caused by nasal allergy is said to be responsible for this condition.

6. Atopic Cataracts

Review of the literature reveals little on the interrelationship between bronchial asthma in children and atopic cataracts. However, if we shift the focus to atopic dermatitis, a disease entity closely related to bronchial asthma in children, atopic cataracts which are often associated with this dermatitis must be included in the present discussion. A brief outline is given below.

Among atopic dermatitis cases, frequent association of Andogsky's syndrome with cataracts was first reported by N. Andogsky (1914) (3) of St. Petersburg. The cataracts are usually bilateral and the pathological process becomes complete in 30 to 50 years (3). It has been reported that retinal detachment occurs regardless of cataract extraction (5). Prior to cataract surgery, systemic administration of steroids should be performed to minimize the allergic state. If this is not possible, the surgical procedure should be postponed until the hypersensitivity subsides. Intracapsular extraction is recommended. Otherwise lenticular opacity or atopic keratosis is likely to develop following surgery resulting in complications such as reductions in visual acuity (5).

7. Treatment of Vernal Catarrh

The efficacy of conventional local ophthalmic treatment is limited to about 60% (17, 41). To improve the therapeutic efficiency, two areas of therapeutic modalities must be investigated: 1) development of more effective local therapeutic agents; and 2) application of systemic treatment as the basis of the therapy supplemented by adjuvant local treatment. A recent development, DSCG (INTAL) ophthalmic preparation, a steroid ophthalmic solution, offers some help for conditions amenable to 1).
The systemic treatment mentioned in 2) is discussed in detail below.

I. Eradication of antigens

If the putative antigen is identified, the first step in radical treatment is to prevent the contact with this antigen. However, eradication of most of these antigens is often impossible and the effort is only likely to result in their reduction at best. Examples of measures to reduce the levels of antigens in the environment are: thorough cleaning of the indoor space; avoidance of the use of floor coverings and furniture which catch dust easily; use of synthetic fibers for bedding; covering the blanket with white cotton; removal of house pets from the family; and installation of a dust collector in rooms. In addition, if a humidifier is used, the water in the reservoir should be changed daily to inhibit proliferation of microorganisms such as fungi. It is often overlooked but hanging of washing, bedding, and sheets outdoors during the season of high pollen count results in attachment of pollen to these items. Use of a dryer is recommended instead. Relocation to another area and the use of a mask and eyepieces to keep dust out are also effective. For severe cases, a short term stay in a germ-free room is helpful.

II. Desensitization

Methods of desensitization are identical to those applied in cases of bronchial asthma and nasal allergies. Details are omitted in the present study.

III Non-specific therapy

Non-specific therapy is indicated when the allergen is not established or the effect of desensitization is insufficient. HISTAGLOBIN,(R) a combination of gamma globulin prepared from human serum and histamine chloride, has a capacity to bind histamine which is absent in the sera of patients with hypersensitivity and is an effective agent in the treatment of these patients. Other therapeutic agents include BRONCASMA BERNA (R) and PASPAT.(R)

IV. Chemotherapy

Principal agents are steroids (17) and DSCG (INTAL). (R) (41) Anti-histamine (KETOTIFEN) (R) is also known to be effective. (29, 47)

INTAL (R) and KETOTIFEN (R) are also used as prophylactic agents. Special care must be taken in long-term application (over 4 weeks) of steroid preparations (13). Oriental herbal medicine may also be applied (16).

V. Surgical treatment

Freeze-coagulation of the cobblestone-like follicular formation by cryogenic surgery has been described (14).

POLLEN CONJUNCTIVITIS (28, 41)

If antigenicity of the pollen is proven, theoretically the pollen count should be proportional to the incidence of pollinosis. The relationship is,
however, not at all simple because such elements as the genetic background called the atopic factor and environmental factors other than the pollen count are involved in the development of pollinosis (46).

The incidence of pollinosis in the United States is computed to be 2 to 3% of the entire population and, with cases of sensitization added, the incidence is believed to be as high as 10%. Accurate statistical surveys have not been conducted in Japan (46).

Pollen conjunctivitis discussed in the present study includes cedar pollen conjunctivitis, Gramineae pollen conjunctivitis, and Asteraceae pollen conjunctivitis. Cedar pollen conjunctivitis is defined as an allergic conjunctivitis which develops in cedar pollen-positive patients during the season when cedar pollens disperse from February to May; (21, 28, 46, 30, 18, 20) while Gramineae pollen conjunctivitis (19) and Asteraceae pollen conjunctivitis (19, 21) are defined as allergic conjunctivitis developing in patients reacting positively to Gramineae or Asteraceae pollens during the seasons when the respective pollens disperse (from April to November for Gramineae pollens and from August to November for Asteraceae pollens).

The subjective symptoms are itchiness of the eye, lacrimation, and a sensation of having a foreign body in the eye. The objective symptoms include conjunctival hyperemia associated with nasal allergy. Diagnosis is made with such procedures as skin reaction (21), provocation tests (22, 26), conjunctival smears, analysis of peripheral eosinophils, RIST, and RAST. Ocular instillation of steroids (28), INTAL, (22, 27) KETOTIFEN (29), and antihistamines are cited as the topical therapy. In severe cases, oral administration of non-steroid agents, steroids, and histamine is recommended. Application of Oriental herbal medicine and desensitization are also recommended (23, 25).

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