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Treatment of Keratomycosis

(keratomycosis/cryotherapy/antifungal agents)

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We treated a 44 year old Japanese woman who was diagnosed as having Keratomycosis following identification of Scopulariopsis as the related pathogen. Cryotherapy, oral 5-FC and amphotericin B and pimaricin proved to be effective treatment.

Keratomycosis was first reported in 1878. In Japan, Maki was the first to describe the case in 1909 (1).

Later there were several reports indicating that the pathogenesis was often Aspergillus, Candida and sometimes Cephalosporium. More recent were the findings of Fusarium. Indiscriminate use of corticoadrenal hormones and antibacterial antibiotics is considered to be related to fungal alternation and the impaired organic resistance of tissue.

We treated a patient with keratomycosis, and Scopulariopsis was detected. Pimaricin eye-drops and oral 5-Fluorocytosine (5-FC) in combination with cryotherapy proved to be effective treatment.

CASE REPORT

A 44 year old business woman was initially seen in our department on June 12, 1980 with the primary complaint of ophthalmalgia in the right eye and loss of right visual acuity. The familial history was non-contributory. This patient had had surgery for left paranasal sinus at the age of 20.

Clinical History

The patient had long before felt a sense of ocular strain and was habitually treating herself with commercial eye-drops. On the night of March 7, 1980, she felt as if a foreign matter was present in the right eye, possibly due to an injury by the nozzle of the eye drop bottle. The following day, she visited an ophthalmologist and was diagnosed as having a right corneal injury. There was a short interval of remittance, however, while repairing and cleaning refrigerators in the middle of March, dust entered the right eye, and ophthalmalgia returned. As eye-drops failed to alleviate the pain, she visited an ophthalmologic specialist who diagnosed keratitis of the right eye. She

did not experience relief and on April 16, she was hospitalized. Under a diagnosis of corneal herpes, IDU eye-drops and antibiotics were prescribed, but because of deterioration of the visual acuity, she was referred to our department. Findings by initial diagnosis :

V. D.=m. m./50cm (n. c.), V. S.= 1.5 (n. c.). The intraocular tension : Tod=immeasurable, Tos=13 mmHg. Slight swelling of the right eye-lid, congestion in bulbar and palpebral conjunctivae and edema were present. A whitish protuberant lesion with a relatively distinct border was noted in the central area of the cornea with an ulceration at the center surrounded by creamy turbidity. Peripheral corneal edema was evident (Fig. 1). Although

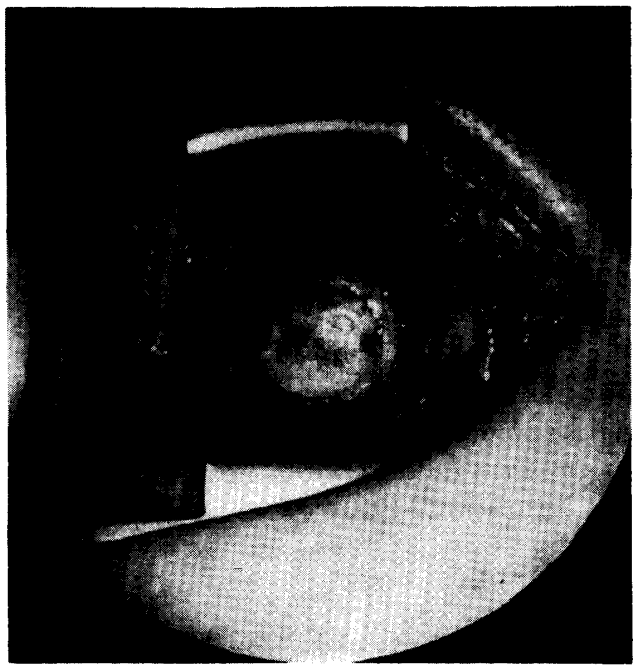

Fig. 1. Scopulariopsis fungal ulcer prior to treatment with antifungal agents (Amphotericin B, Pimaricin and 5-FC) and cryocurettage.

the anterior findings showed neither hypopyon nor posterior synechia of the iris and the lens was rather clear, the fundus was not clearly visible.

Clinical Course

The patient was admitted on June 12, 1980. Antibiotic eye-drops were prescribed but after 4 days were discontinued because the pain was not alleviated. Bacteriologic and mycologic examinations of the sebum and scrapings from the cornea were carried out on June 16. On the following day the first cryotherapy was performed for the purpose of alleviating the pain and for debridement. Microscopic examination of the sample of a partially excised lesion from the cornea demonstrated the presence of hyphae in the stroma. Hyphae were also confirmed on June 21 by smear examination. Frequent drops of amphotericin B was immediately prescribed. On June 24, a whitish moss on the cornea was obtained for culture in a Sabouraud medium, Malt

medium and Czapek medium, and a giant mycelial colony formed. On July 1, the ulcer disappeared, the turbidity and edema were reduced but hypopyon was evident. The frequency of administration of amphotericin B drops was reduced because of a strong irritation. An eye-drop solution and ointment of pimaricin were prepared and frequently applied from July 2. On July 15, the second cryotherapy was performed and oral administration of 5-FC was initiated. As a result, the hypopyon disappeared on July 20, subsequently with gradual decrease in conjunctival congestion and corneal turbidity. On August 5, the mycologic test was negative. The greyish white protuberant lesion had completely disappeared by August 19 and V. D. improved to 0.07 (n.c.). Only a thin cicatrization in the cornea could be observed (Fig. 2). The patient was discharged on September 6. Follow-up as an out-patient showed further improvement of V. D. to 0.08 (0.3×−1.0D) on December 6.

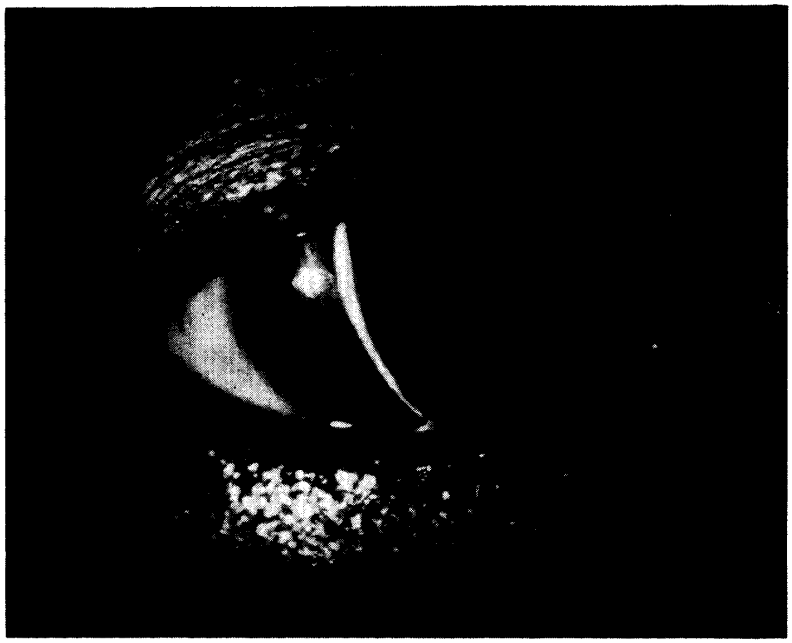

Fig. 2. Healed corneal scar after combined therapy.

Clinical Data

RBC 3.79-million/mm^3, WBC 3800/mm^3, Hb 12.0g/dl, Ht 34.3%, PLT 205-thousand, T-P 6.9g/dl, Alb 4.3g/dl, A/G 1.7, GOT 17, GPT 9, uric sugar (−), CRP (−), RA (−), ASLO (−) and TPHA (−). There were no other remarkable changes.

DISCUSSION

Keratomycosis is one of the very intractable diseases and there has been a tendency toward increase in recent years. Early detection and appropriate treatment is adamant (1−6).

Various clinical characteristics of keratomycosis were enumerated by Kaufman and Wood (7). They reported findings of a protuberant lesion with greyish white turbid ulcer, from the initial diagnostic stage, and the lesion assumed almost an typical development with emergence of greyish white hypopyon during the treatment. Tokoro (6) reported that cases which demonstrate all the 8 factors reported by Watanabe (5) are rare and that the presence of serpiginous corneal ulcer and corneal herpes supports the differential diagnosis. Uchida (8) reported that the determination of diagnosis of keratomycosis should be evidenced by the presence of myceleum in the lesion, stressing the importance particularly of examination of smears of scrapings from the cornea. Ishibashi (9) pointed out that an isolation culture, even if successful, is of little value, unless the result is positive, despite direct detection by microscopy, and further, that diagnosis is positive if the onset of the same lesion can be produced in animal experiments using the isolated fungus and identified by repeated (isolation) culture. All these mycologic procedures are not feasible for the average clinician.

Ishibashi (9) also pointed out that with respect to pathogenic fungi there is increasing incidence of infection with Fusarium and that there was a tendency toward diversification of phlogogenic fungi in keratomycosis. Infections with Monosporium (10) and Alternaria (11) are reportedly rare cases. In our patient, infection with genus Scopulariopsis ranks among the rare cases. Such was reported in 1957 in foreign countries and in the report of Takagi *et al.* (12) in 1958 in Japan. Scopulariopsis belongs to the genus with irregular asci, of which S. americana, S. brericaulis, S. blochii, etc. are the phlogogenic fungi known to infect man, causing blastomycosis-like dermatitis and onychomycosis. However, in most cases, such can be detected only as cultural contaminants (13). The fungus isolated from keratomycosis in the present study was identified as S. grisea. The identical fungi were detected in succession as a result of twice repeated direct microscopic examinations and culture processes of corneal scrapings collected after admission of the patient to our department. The above is considered, therefore, to validate S. grisea as the phlogogenic fungus in the present case.

The recent increase in the incidence of keratomycosis by invasion of fungi with an insignificant pathogen or those having inconfirmed toxicity seems to follow the induction of medication with antibiotics and steroids (14).

The latter in particular seems to contribute to the intensify of the toxicity of pathogenic fungi. The damage of the corneal epithelium, may be another significant factor where trauma is the most frequent cause. However, in the present case, in addition to these factors, IDU drops may have exerted side-effects in the form of tissue damage, and keratomycosis developed.

Chemotherapy and surgical procedures are required. The former may comprise the usual basic treatment with administration of cornea protective agents and vitamins, and application of iodine tincture and Povidone-Iodine after topical cauterization or curettage and special treatment with antifungal agents.

Pimaricin is the drug of first choice (5, 15). A combination of amphotericin

B and pimaricin was prescribed for our patient and side effects were minimal. Hakariya and Mishima (16) reported favourable results achieved with a combination of drops and the oral administration of 5-Fluorocytosine solution. Only oral administration of 5-FC was prescribed for our patient as this solution has a wide range of antibacterial properties against Candida, Aspergillus, etc.

Surgical procedures include curettage, kerectomy, covering of the cornea with conjunctival flaps, corneal transplatation, etc. However, cryotherapy was performed twice in our patient. The first approach was the cryocurettage (17), that is the mechanical detachment of the protuberant lesion with a frozen tip adhered to the lesion, in addition to the method employed for corneal herpes. This produced a favourable effect. Ishibashi and Tokoro (18) reported that the hypothermal therapy inhibited the fungal growth. It is estimated that application of cryotherapy in cases of keratomycosis when performed in combination with antibiotics may produce a greater effect, because epithelial detachment after cryotherapy allows for a greater penetration of the drug in question.

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