

OCCURRENCE OF MALIGNANT NEOPLASMS IN PATIENTS WITH ATOPIC DERMATITIS

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Abstract. 326 patients with atopic dermatitis were followed for up to 42 years to ascertain development of cancer. In neither sex did the incidence of cancer differ significantly from the incidence of cancer in the general Danish population. This finding is discussed in relation to previous studies on the subject.

Key words: Atopic dermatitis; Neoplasm; Cellular immunity

Several recent studies have dealt with the relationship between atopic diseases and cancer. The results have been divergent, but most authors have found a negative association.

The study reported below concerned the incidence of cancer in a group of patients with atopic dermatitis followed for up to 42 years.

MATERIAL AND METHODS

The diagnostic criteria of atopic dermatitis were: Recurrent attacks of itching eczema affecting at least two of the following regions: cubital fossa, popliteal fossa, face, neck, and dorsum of hand, as a rule combined with positive scratch tests and a family history of atopy.

The material comprises all patients treated in the Department of Dermatology, Finsen Institute, Copenhagen, during the period 1930-1939 for atopic dermatitis. Seven patients were excluded, as they did not fulfil the diagnostic criteria. Of the remaining 338 patients, 11 were excluded because they were foreigners and information about the subsequent course was unobtainable. One patient could not be traced.

This leaves a material of 154 males and 172 females. The age at onset ranged from 0-27 years among the males and from 0-21 years among the females. All the patients were traced through public registers and classified as alive, dead, or emigrated. Death certificates were procured for all the deceased patients. Each patient's data were then sent to the Danish Cancer Registry who supplied information about cancer occurring in the ma-

terial. Owing to delay in notifying and recording cases, the analysis was closed on Dec. 31, 1971.

The follow-up period for each patient was calculated from the time of the first examination until the date of death or until cancer was diagnosed. Based upon the Cancer Registry data about the incidence of cancer in Denmark (2), the expected risk of developing cancer was calculated for each patient on the basis of birth date, sex, and follow-up period. The tables of the Cancer Registry were divided into 5-year periods from 1943 to 1967, giving the calculated incidence for males and females in 5-year age groups for each period. The calculations were based upon the incidence of cancer among the general Danish population.

The Finsen Institute admits patients from all over the country, so that a relatively large proportion of those investigated came from districts outside Copenhagen. As the incidence of cancer is higher in Copenhagen than in other parts of Denmark, the figures for the total population had to be used, since otherwise the expected number would be too high.

Concerning the follow-up period prior to 1943, the author used the incidence of cancer for the period 1943-47, and concerning follow-up after 1967, the period 1963-1967.

RESULTS

The results are set out in Table I which shows that within the follow-up period, cancer occurred in 1 male and 8 females, whereas the expected numbers are 4.34 and 6.04. When calculated on the basis of the Poisson distribution, using the expected value as a mean, neither of the observed values represents a significant deviation ($p > 0.05$).

The types of cancer were as shown in Table II.

DISCUSSION

In previous investigations the relationship between atopy and cancer has been studied in two fundamentally different ways.

Table I. Actual and expected numbers of malignant neoplasms

	Number	Died from cancer	Alive with cancer	Expected number of cancer cases (95% confidence limits)
Males	154	0	1 ^a	4.34 (0.026-5.5)
Females	172	6	2	6.04 (3.5-15.7)

^a One-sided significance test $p \approx 7\%$.

With one method, in-patients have been questioned concerning a history of atopic disease, and the occurrence of such diseases in cancer patients have been compared with that in a control group. Using this method, most authors have found a lower incidence of atopy among the cancer patients than among the controls (4, 5, 10, 12, 15). A few have found the same (11, 14) or even a higher incidence of atopic diseases among the cancer patients (9). In the last-mentioned material, however, the control group was not comparable with regard to age and sex.

The drawbacks of this method are the interviewing technique and the choice of control material. Besides, there are marked differences in defining atopic disease. McKee (11) included only asthma and rhinitis, Gabriel (5) also eczema, urticaria, and "food reactions". Shapiro (14) used the criteria: Hay fever, any allergic cutaneous manifestation, and/or reaction to serum or blood transfusion. On the other hand, he excluded asthma. Thus, the differences in the findings may be largely explained by the variation in the patient materials.

The other method of elucidating the problem has been that used by Alderson (1). In a large group

of asthmatics followed over a long period, he compared the mortality of cancer with that expected, calculated from mortality tables. There was a distinct reduction (about 30%) in cancer mortality among males as well as females, except for cancer of the lung which was of the same frequency.

In the present study, patients with atopic dermatitis displayed no reduction in cancer morbidity, but the expected number of cancer cases (Table I) could be reduced by 30% and still fall within the confidence limits.

This study concerns only atopic dermatitis, whereas Alderson (1) investigated the conditions in asthmatics and other investigators have elucidated the findings in "atopics", without strict diagnostic criteria. It is not inconceivable that within the group of atopic diseases there may be a difference in the tendency to develop cancer, as factors other than the atopic state may be operative. For instance, a reduced cell-mediated immunity has been demonstrated in patients with atopic dermatitis. This has been manifest partly in a reduced response to experimental Dinitrochlorobenzene sensitization and partly in a reduced cutaneous delayed hypersensitivity on antigen stimulation with tuberculin, parotid antigen, and candidin (8). Moreover, the percentage of T lymphocytes in the peripheral blood has proved less than that in a control group (6, 13). In other states of reduced cell-mediated immunity, the incidence of malignant neoplasms has been reported to be increased (3, 7).

Table II. The diagnoses of the occurred neoplasms

Malignant melanoma	1
Hodgkin's disease	1
Breast cancer	2
Hypernephroma	1
Thyroid cancer	1
Cancer of the rectum	1
Cancer of the colon ^a	1
Bowen's disease—gastric cancer	1

^a In 1939, before being treated here for atopic dermatitis, this patient had had irradiation for cervical carcinoma of the uterus. No subsequent signs of recurrence.

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