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Increase in natural killer cell activity during diethylcarbamazine treatment of patients with filariasis

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Summary

Two patients, one with Bancroftian filariasis and the other with onchocerciasis, and two healthy controls were treated with diethylcarbamazine (DEC). The natural killer (NK) cell activity of the two patients increased during DEC treatment to 2.5 and 2.8 times, respectively, while that of the controls remained unchanged. We conclude that the augmentation of baseline NK cell activity, as well as interferon- and interleukin-2-enhanced NK cell activity seen in the patients, is not a direct effect of DEC, but is related to the reaction to DEC in lymphatic filariasis and onchocerciasis.

Key words: natural killer cells; microfilariasis; diethylcarbamazine.

Introduction

Diethylcarbamazine (DEC) is widely used in the treatment of onchocerciasis. The well-known reaction to treatment consists of pruritis, increased rash, aggravation of keratitis and iritis, tender lymph node enlargement, arthralgia and fever (Bryceson et al., 1977). This anaphylactic reaction may even be dangerous (Fuglsang and Anderson, 1974). When DEC is given to healthy controls, without any history of worm infections, no side effects occur. Natural killer (NK) cells are morphologically identified as large granular lymphocytes (LGL). Their role in the defense against filariae is not known; furthermore, NK cell activity has not previously been studied in relation to anaphylactic reactions. In this study, NK cell activity before and during treatment with DEC was studied in two patients with mild chronic filarial infections (lymphatic filariasis and onchocerciasis) and in two healthy controls.

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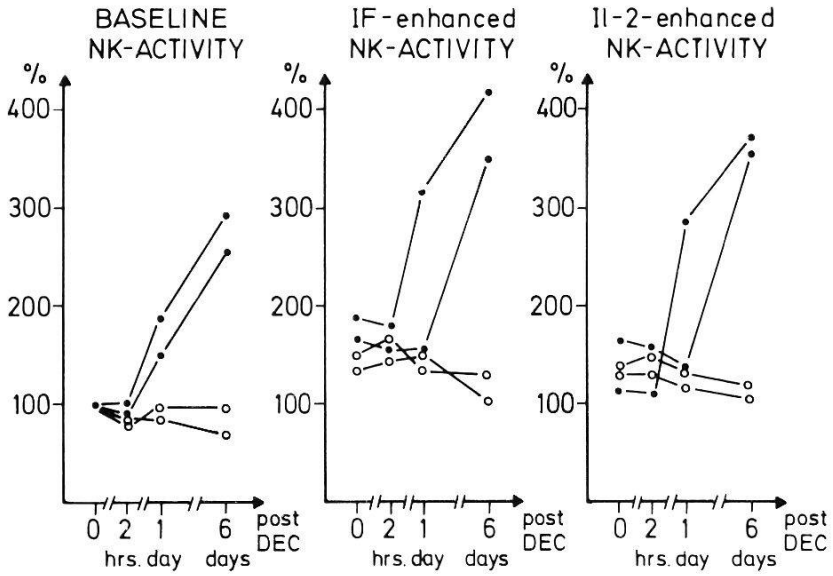

Fig. 1. Baseline NK cell activity (a), interferon (IF)-enhanced NK cell activity (b) and interleukin-2 (Il-2)-enhanced NK cell activity (c) measured against K 562 target cells in a Cr-release assay before and during DEC treatment of two patients (●), with onchocerciasis and lymphatic filariasis respectively, and in two healthy controls (o).

Patients and Methods

Patient 1 was a 33-year-old female, born on the island of Zanzibar. For 6 years she had recurrent lymphatic filariasis in the groin and right lower limb, gradually developing into slight elephantiasis. Patient 2 was a 52-year-old male, born in Denmark, who had worked for 8 years in areas of Africa with high endemicity of onchocerciasis. By the end of the stay, scanty microfilariae of *Onchocerca volvulus* were found in skin snips, and in the anterior chamber of the eye on one occasion, and after returning to Denmark a nodule developed on the right arm. Two healthy males without history of worm infections served as controls. One was 34 years old, the other 40. Patients and controls were given DEC 50 mg by mouth on the first day, after the initial blood sample for NK testing had been obtained; the next day 150 mg of the drug was given, then 200 mg daily for another 5 days. Blood samples were obtained immediately before the first DEC dose was given, and two hours, 24 h and 6 days later.

NK cell activity against K562 target cells was measured in a Cr-release assay and large granular lymphocytes identified as previously described (Pedersen et al., 1986).

Results

Baseline NK cell activity, interferon (IF)- and interleukin-2 (Il-2)-enhanced NK cell activity during DEC treatment are shown for patients and controls in Fig. 1. Treatment of the patients with DEC resulted in a considerable rise in baseline NK cell activity. Six days after DEC treatment was started, the NK cell activities of the two patients were increased with 2.5 and 2.8 times, respectively. The IF- and Il-2-enhanced NK cell activities were similarly increased. Treatment of the controls, however, had no influence on baseline or IF- and Il-2-enhanced NK cell activities. The proportion of LGL did not change during DEC treatment neither in patients nor controls. In vitro DEC had no effect on the NK cell function (data not shown).

Discussion

Our results showed a marked increase in baseline, IF- and Il-2-enhanced NK cell activities during DEC treatment of one patient with lymphatic filariasis and one with onchocerciasis. The augmentation of NK cell activities was not due to a quantitative rise in NK cells, as the percentages of LGLs and total lymphocyte counts did not fluctuate during DEC treatment. The stimulatory effect of DEC on the NK cell function is not a direct effect of DEC, since treatment of controls with DEC had no effect and as DEC did not influence the NK cell activity in vitro. Thus the increase in NK cell activity is probably related to the reaction to DEC, i.e. to the drug's antiparasitic effect. The studies of immunological changes after DEC, as well as the well-known general and local reactions following DEC administration, indicate activation of the immune system by DEC in filarial patients. Whether the augmentation of NK cell activity observed by us is part of such activation, and whether the NK cells play a role in killing the parasites, are unknown.

Acknowledgments

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