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Tissue expression of cytokines (IL-1α, IL-2, IL-6, IL-12, TNF-α) in B-cell lymphomas in children

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In most malignant tumours disturbed production of cytokines and of their receptors can be noted. The main immune system cells engaged in tumour regression with the involvement of cytokines include helper lymphocytes (Th1), cytotoxic lymphocytes (Tc) and dendritic cells. It has been noted that cytokines are also produced by the cells of a tumour. The present study aimed at immunocytochemical localisation of cytokines (IL-1α, IL-2, IL-6, IL-12, TNF-α) in B-cell lymphomas in children (n = 10). The studies were performed on surgical material following formalin fixation and embedding in paraffin. The control material involved human reactive lymph nodes (n = 5). IL-2, IL-6, IL-12 were detected in 4//10 examined cases. Expression of IL-1α was highly pronounced, as in the control, and was detected in 6/9 examined patients. No TNF-α could be demonstrated in tumours even if lymph node expression of the cytokine was demonstrated in the control. The studies pointed to a decreased production of antitumour cytokines in B-cell lymphomas in children, which might correspond to the progression of the tumour.

key words: non-Hodgkin's B-cell lymphomas, children, IL-1α, IL-2, IL-6, IL-12, TNF-α, immunocytochemistry

INTRODUCTION

Cytokines play an important role in the pathogenesis of non-Hodgkin's lymphomas in children [1, 3]. Apart from participation in immune responses, they may induce tumour regression by direct interaction with tumour cells [3, 4]. In normal or reactive conditions the production of cytokines by cells of the immune system corresponds to current needs [3]. In cells of a lymphoma regulatory mechanisms are disturbed, which results in abnormal expression of cytokines [4]. Currently, cytokines may be identified by any of four potential approaches. These include measurement of serum cytokine level, studies on mRNA in tissue isolates, *in vitro* studies and detection of proteins and mRNA in tissue sections. The most reliable data on expression of cytokines in tumours are obtained in studies on cytokines directly in the tissue [3].

MATERIAL AND METHODS

The group studied consisted of children with non-Hodgkin's high-grade lymphoma consisting of B-cells (n = 10), confirmed by the expression of several B-cell antigens, including CD19 and CD20 antigens, treated in the Department of Haematology and Paediatric Oncology, University of Medical Sciences in Poznań. The studies were performed on surgical material, fixed in formalin and embed-

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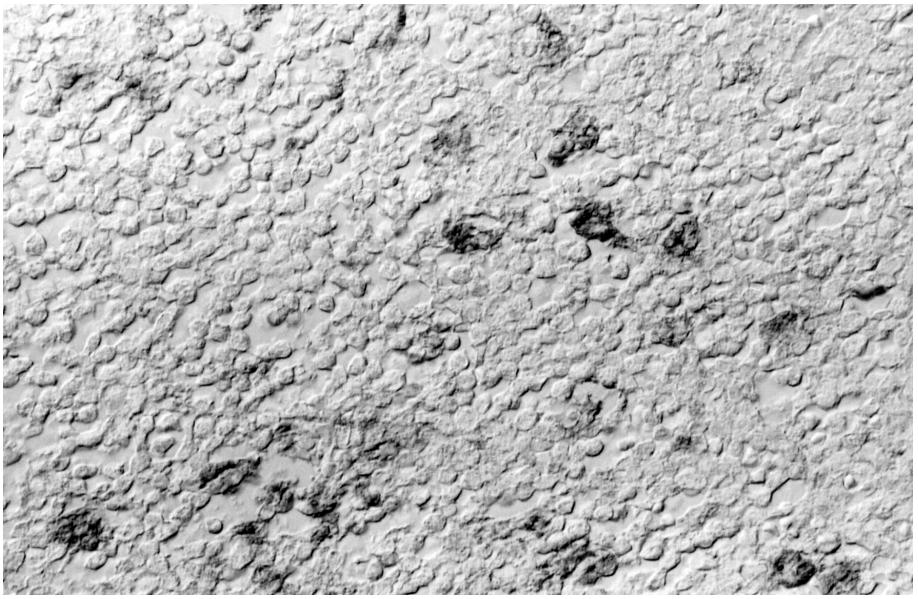

Figure 1. Immunocytochemical localisation of IL-2 in non-Hodgkin's lymphoma cells. ABC method; × 400.

ded in paraffin. Immunocytochemical reactions were performed using ABC technique [2]. The following monoclonal antibodies were used: (a) goat anti-human IL-1α, b) mouse anti-human IL-2, (c) mouse anti-human IL-6, (d) mouse anti-human IL-12 and (e) mouse anti-human TNF-α (all originating from R&D Systems). The control material involved reactive lymph nodes (n = 5) without inflammatory infiltrations obtained from adult patients with colitis ulcerosa after receiving the informed consent of the patients.

RESULTS AND DISCUSSION

Studies on cytokines *in situ* yield a reliable appraisal of their expression in tumours and of their potential role in the pathogenesis of these most frequent and most malignant lymphomas in children [3]. The presence of all the cytokines studied (IL-1α, IL-2, IL-6, IL-12 and TNF-α) was demonstrated in reactive lymph nodes (positive control). In the preparations of B-cell lymphomas the most pronounced expression was documented in the case of IL-1α (6/9 examined cases). The intensity of the reaction for the cytokine was high in most cases and the reaction developed in a cell number comparable to that in the control. As compared to the remaining cytokines, expression of IL-1α was noted in a markedly higher number of cells. Only in 4 out of 10 patients examined could expression of IL-2, IL-6 and IL-12 be detected. In most of the children the intensity of the reactions was lower than that in the control and the expression pertained to individual cells only or their groups (Fig. 1). Expression of TNF-α could not be detected in any of B-cell lymphomas in our patients. Basically, our results are consistent with the literature data and supplement them with information on additional cytokines [3]. They are also derived from a more uniform clinical material. The results have shown that lymphomas of high grade clinical malignancy, consisting of B cells, exhibit in children pronounced inhibition of cytokine production and of anti-tumour cytokines in particular (IL-2 and IL-12), which may promote tumour progression. The conclusions, however, require confirmation on the basis of a larger group of cases, accompanied by analysis of cytokine expression using *in situ* hybridisation.

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