Peanut Agglutinin, a Marker for T-Cell Acute Lymphoblastic Leukemia with a Good Prognosis


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ABSTRACT

Peanut agglutinin (PNA) binding was studied in cells from 74 children with acute lymphoblastic leukemia (ALL). PNA positivity occurred in 50% of T-ALL (12 of 24) and was rare in other types of ALL. There was no clear relationship between PNA and initial white blood cell count, French-American-British classification, stage of differentiation of leukemic cells, hand mirror cells, and organomegaly at diagnosis. Prognosis, however, was significantly better (continuous complete remission, death) in the PNA-positive T-ALLs. It seems that PNA is a useful marker for a subgroup of T-ALL with a better prognosis.

INTRODUCTION

PNA is a plant lectin (Arachis hypogea) which specifically binds to terminal nonreducing galactose residues on the cellular membrane. Most mammalian cells do not bind PNA, because galactose is not the terminal sugar residue in the cell coat. PNA binding has been described in thymocytes, B-lymphocytes in germinal centers, and monocytes. Lymphocytes in peripheral blood, spleen, and tonsils do not bind PNA (3, 10, 11, 15, 17, 20, 21). PNA binding has also been described in lymphoma malignant disorders (1, 4, 9, 13, 16, 18, 19).

It appears that PNA is a marker for immature T-cells and possibly a marker for sessile, noncirculating cells (21). Levin et al. (9) suggest an unfavorable prognostic value of PNA positivity in childhood ALL. In this study, we determined PNA binding in childhood ALL, and we tried to determine whether PNA positivity was associated with immunological phenotype, initial WBC, maturity of the leukemic cells, HMCs (as index of cell motility), and clinical course.

MATERIALS AND METHODS

Cells. Blood and/or bone marrow were obtained from 74 children with ALL at diagnosis before treatment started. Bone marrow was suspended in Hanks' balanced salt solution containing heparin (50 units/ml). Blood and/or bone marrow were obtained from 74 children with acute lymphoblastic leukemia (ALL). PNA positivity occurred in 50% of T-ALL (12 of 24) and was rare in other types of ALL. There was no clear relationship between PNA and initial white blood cell count, French-American-British classification, stage of differentiation of leukemic cells, hand mirror cells, and organomegaly at diagnosis. Prognosis, however, was significantly better (continuous complete remission, death) in the PNA-positive T-ALLs. It seems that PNA is a useful marker for a subgroup of T-ALL with a better prognosis.

RESULTS

Immunological Phenotype (Table 2). Immunological phenotype was tested in 74 children with ALL. There were 39 cALLs, 15 B-ALLs, and 20 T-ALLs.
PEANUT AGGLUTININ IN ALL

9 null-ALLs, 24 T-ALLs, and 2 B-ALLs. From the cALL cases, only one child had PNA-positive cells. From the T-ALL group, however, 12 had PNA-positive cells. Because there was no significant difference between PNA positivity in cALL cases and null-ALL cases (Fisher's test), we compared PNA positivity between T-ALL cases and non-T-ALL cases. There was a considerable difference in PNA positivity between T-ALL and the other ALLs (χ² test, P < 0.001). For this reason, we studied the relevance of PNA positivity in the T-ALL group.

**Tumor Load and PNA (Table 3).** Twenty-one of the 24 children with T-ALL had a WBC above 50 × 10⁹/liter; 17 of them were above 100 × 10⁹/liter. There was no significant difference in WBC between the PNA-positive group and PNA-negative group (Wilcoxon's 2-sample test). Organomegaly was screened evaluating hepatomegaly, splenomegaly, lymphadenopathy, and enlargement of organs (thymus, kidneys, testes). There was no clear difference in organomegaly between the PNA-positive and the PNA-negative group. The French-American-British classification was known in only 15 cases; a relation between French-American-British classification and PNA positivity seems to be unlikely.

**HMCs and PNA (Table 3).** HMC percentage was used as an index of cell motility. Most T-ALL cases have a HMC count below 10%. In the PNA-positive group, all 12 cases were below 10%; in the PNA-negative group, 2 were above 10% (11 and 40%). Between these 2 subgroups, there was no significant difference (Wilcoxon's 2-sample test).

**PNA and Stage of Differentiation (Table 3).** The different T-ALL stages are described in "Materials and Methods." In 4 cases, staging was impossible because of lack of OKT-like monoclonal antibodies. Staging was possible in 10 PNA-positive cases and 10 PNA-negative cases. In the PNA-negative group, 6 Stages I and 4 Stages II were present. In the PNA-positive group, 4 Stages I, 2 Stages I/II, and 4 Stages II were present. There was no clear difference between both groups. Furthermore, there was no obvious relation between PNA and one of the used monoclonal OKT-like antibodies.

**Clinical Course.** From the 24 children with T-ALL, one child in the PNA-positive group was lost for follow-up because of emigration 1 month after diagnosis. Evaluable were 12 PNA-negative and 11 PNA-positive cases. In the PNA-negative group,
Thus, 21 children did achieve complete remission after 4 to 6 weeks of treatment.

In the PNA-negative group, the median duration of CCR was 4 months (range, 2 to 56 months); in this group, 2 children (2 of 10) are still in CCR 4 and 56 months after diagnosis. In the PNA-positive group, the median duration of CCR was 27 months (range, 2 to 62 months); in this group, 6 children are still in CCR 24, 45, 50, 52, 53, and 62 months after diagnosis.

For the PNA-positive and PNA-negative groups, we estimated the probability of CCR as a function of time according to the Kaplan-Meier method, and we tested whether these curves (Chart 1) differed by means of the log rank test. CCR was more frequent in the PNA-positive group \( (P < 0.05) \).

Relapses occurred in 8 of the 10 PNA-negative cases. There were 4 bone marrow relapses and 4 meningeal relapses.

Relapses occurred in 5 of the 11 PNA-positive cases: 3 bone marrow relapses; 1 meningeal relapse; and 1 testicular relapse. Although it seems that in the PNA-negative group especially meningeal relapses occurred more frequently than in the PNA-positive group, this difference was not significant \( (\chi^2 \text{ test}) \).

Death occurred in 13 of the 23 evaluable cases (Chart 2): in the PNA-negative group in 10 of 12 cases; and in the PNA-positive group in 3 of 11 cases. According to the log rank test, there was a considerable difference \( (P < 0.001) \). Mortality was much higher in the PNA-negative group, while initial WBC and period of follow-up between both groups were comparable.

**DISCUSSION**

In this study on PNA positivity in childhood ALL, we found that PNA-binding properties of the cell membrane are common in T-ALL and rare in other ALLs, especially CALL. This finding is comparable to that of Newman and Delia (13), who found PNA positivity in 25% of T-ALL cases in childhood ALL and not in CALL, O-ALL, and B-ALL. The difference in percentage can be explained by the difference in criteria for PNA positivity. We use the 10% level; Newman and Delia use the 20% level. Levin et al. (9) found PNA positivity in T-ALL (2 of 4 cases) and a great part of O-ALLs, but in this study no monoclonal OKT-like antibodies were used. Bernard et al. (1) studied PNA in malignant lymphomas in childhood, and they found PNA positivity in a part of T-cell lymphomas but not in B-cell lymphomas. PNA positivity seems to be a marker for a subgroup of malignant T-cell lymphoid disorders.

In previous studies, it was clear that PNA binding is a property of immature thymocytes, while mature peripheral blood lymphocytes are negative for PNA (4, 5, 7). Within the T-ALL group, we found no correlation between PNA positivity and the different T-ALL Differentiation Stages I and II. This can be explained by the fact that these Stages I and II are closely related to each other. Newman et al. (13) suggest that PNA positivity in T-ALL is related to the "postprothymocyte but premedullary thymocyte stage," which corresponds with our Stages I and II.

In normal human beings, PNA positivity on lymphoid cells is not confined to thymocytes alone. It has already been described on B-lymphocytes in germinal centers (3, 20, 21). Rose (20) stated that these lymphoid cells are sessile and that PNA positivity possibly is correlated to noncirculating sessile cells. Another support for this thesis is the PNA positivity of plasmacytoma cells which also are sessile. In this study, HMCs are used as an index of cell motility as described by others (5, 14). There was no significant difference in HMCs between PNA-positive and PNA-negative T-ALLs. We already showed in an earlier study that most T-ALLs have a low HMC count, contrary to other phenotypes (6). Thus, our data do not support the presence of an association between PNA and lack of cell motility in T-ALL.

Another parameter for locomotive behavior of T-ALL cells would be evaluating organomegaly. Between PNA-positive and PNA-negative groups, no apparent difference in local tumor burden was present.

WBC at diagnosis, possibly lower in a more sessile cell population, was equal for both groups. These observations support our earlier conclusion that PNA positivity in T-ALL is not associated with a sessile leukemic T-cell population. Levin et al. (9) found in their study a possibly poor prognosis in childhood ALL with PNA-positive leukemic cells. However, in this study, no monoclonal OKT-like antibodies were used, resulting in a major group of undefined non-T-non-B-ALL. Furthermore, the follow-up period of the 16 children in CCR was significantly shorter than the follow-up period of the 8 children who relapsed (Wilcoxon's 2-sample test, \( P < 0.005 \)).

In a later study of Newman (13), PNA was not related to prognosis, but detailed clinical data were not mentioned. Newman used as definition for PNA positivity the presence of PNA binding on more than 20% of the cells. When we raise the cutoff point to 20% in our study, the difference in prognosis between PNA-positive and PNA-negative groups remains, 3 patients...
changing from PNA positive to "PNA negative," of whom 2 relapsed in the bone marrow.

The children with T-ALL in this study were treated in 5 different pediatric clinics. All received central nervous system prophylaxis including intrathecally given prednisolone and methotrexate and irradiation to the skull (2500 rads). In 4 centers, treatment included a superconsolidation therapy 3 to 6 months after remission-induction. In one clinic, treatment consisted of MOPP in a few patients. Separate analysis, however, of the patients of the 4 clinics gave comparable significant results with respect to prognosis. In our study, there was a remarkable difference in duration of CCR and in survival between the PNA-positive and the PNA-negative group. PNA-positive cases had a much better prognosis. We have no ready explanation for this difference in prognosis in the T-ALL group. It is possible that PNA-positive cells are more sensitive to cytostatic treatment. London et al. (10) showed in their study on thymocytes in mice that PNA-positive thymocytes were more sensitive to steroid treatment and irradiation than were PNA-negative thymocytes. Possibly the smaller (but not statistically significant) occurrence of meningeal relapses in the PNA-positive group is explained by a higher sensitivity to irradiation and corticosteroids, both used in central nervous system prophylaxis in all children with ALL in this study.

From this study, we conclude that PNA is a useful marker within the T-ALL group and is related to a better prognosis.

ACKNOWLEDGMENTS

We thank Dr. G. van Zanen, Dr. H. Behrendt, Dr. J. de Koning, and Dr. G. de Vaan, members of the Dutch Childhood Leukaemia Study Group, for their cooperation. We thank the department of Histology (head: Prof. Dr. H. L. Langevoort) for the hospitality in the laboratory.

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