Abnormalities of Complement and Its Components in Patients with Acute Leukemia, Hodgkin's Disease, and Sarcoma

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SUMMARY

Whole complement and component titers were measured in patients with acute leukemia, Hodgkin's disease, and sarcoma. Serum samples were obtained from 42 consecutive patients and 11 healthy control subjects. Sera were frozen and maintained at -70° until analyzed by hemolytic assay. Titers were normalized using a titer obtained from a single source of pooled human serum analyzed simultaneously with each patient sample to correct for day-to-day variation inherent in the assay technique. Significant elevations (p < 0.05) of whole complement and C5, C8, and C9 were observed for each patient category, compared to controls. Forty-one of 42 patients had C9 titers 2 S.D. above the mean titer for controls. Mean C3 and C7 titers were not elevated or depressed in any group. No clinical factors that correlated with abnormal complement or component titers were identified.

INTRODUCTION

Abnormalities of complement and its components in patients with cancer have not been well defined, particularly in specific types of tumors. Most investigations have been limited to an analysis of whole complement or selected components, and we are not aware of any study in which whole complement and components have been evaluated simultaneously in patients with specific cancers.

We measured hemolytic titers for whole complement and components C1 to C9 in patients with acute leukemia, Hodgkin's disease, and sarcoma and found significant elevations of whole complement in all patient groups. The titers of most components were also increased.

MATERIALS AND METHODS

Patients. Pertinent characteristics of the patient population are presented in Table 1. Serum samples were obtained on admission prior to treatment from consecutive patients admitted to the Baltimore Cancer Research Center with the diagnoses of acute lymphocytic and nonlymphocytic leukemia, Hodgkin's disease, and sarcoma. None of the 19 patients with leukemia had received treatment prior to admission while 2 of 10 patients with Hodgkin's disease and 11 of 13 patients with sarcoma had been treated previously with radiation, surgery, chemotherapy, or combinations of these modalities. All previously treated patients were considered treatment failures with advancing disease at the time of evaluation. Eleven healthy employees served as control subjects.

Sample Collection. Blood was collected by venipuncture and allowed to clot for 30 min at room temperature. Clot retraction continued for an additional 2 hr on ice prior to centrifugation and serum separation. Serum samples were stored at -70° and maintained at that temperature until processed. Any sample that thawed during transportation or prior to processing was discarded.

Complement and Component Determinations. Whole serum complement and component (C1 to C9) titers were determined by hemolytic assays as previously described (8, 17). The titers for whole complement and C1 to C9 are expressed as CH₅₀ units/ml.

A limiting factor in the comparison of complement and component titers determined by hemolytic assay is the daily variation inherent in the assay technique. This consideration is particularly appropriate in the present study during which samples were analyzed on several different occasions. Therefore, the contribution of individual complement or component determinations to the mean titer can be made only in relative terms and requires a uniform standard to make such data meaningful.

A sample from a single source of pooled human serum was processed with each patient or normal sample to correct for this variation. Individual titers were subsequently normalized according to a formula similar to that described by Gaither et al. (5), except that the titers obtained according to a formula similar to that described by Gaither et al. (5), except that the titers obtained with the pooled serum sample were used instead of purified component titers as follows:

Normalized patient component titer

\[ \text{Normalized patient component titer} = \frac{\text{Observed patient component titer}}{\text{av. pooled component titer}} \times \frac{\text{observed pooled component titer}}{\text{av. pooled component titer}} \]

All data presented in this paper represent the normalized values for complement and C1 to C9.

Statistical evaluation. Values (p) were determined by the 2-tailed Student t test; p ≤ 0.05 was considered significant for this analysis.
RESULTS

Complement and component titers for the cancer patients and controls are presented in Table 2. Whole complement, C5, C8, and C9 were increased in each disease category compared to controls, while C3 and C7 were not significantly abnormal in any group. Fewer elevated titers were observed in acute leukemia patients, compared with those with Hodgkin’s disease or sarcomas.

The frequency of deviations of complement and component titers for individual cancer patients from the normal mean values obtained for control subjects is shown in Table 3. Deficiencies in components or complement were observed infrequently in contrast to numerous elevated titers. The increase in C9 was particularly striking, occurring in 41 of the 42 patients studied (Chart 1).

No correlation of abnormal complement or component titers with the patient’s course, presence or absence of infection, or altered hepatic or renal function was evident.

DISCUSSION

Although an early study of complement in cancer patients did not find significant abnormalities (15), other investigators have reported elevations of complement and selected components in patients with a variety of malignant tumors (1, 7, 11, 13, 18, 19). In the present study, elevations of whole complement titers were found in patients with acute leukemia, Hodgkin’s disease, and sarcoma. Increase in the titers of several individual components were also observed. This is in contrast to many acquired disease states in which complement titers tend to decrease (12, 14) and the depression of complement and C1 found in tumor-bearing animals (3, 6).

Little is known regarding complement in acute leukemia or sarcoma patients. Yoshikawa et al. (18) found no signifi-
cant increase of whole complement in patients with acute leukemia, while in the present study the mean complement titer was increased, compared with the control population. Similarly, few studies have explored individual component abnormalities in cancer patients. One study (16) found no significant increase in C2 titers in cancer patients, while another (7) reported increases in several components, especially C8 and C9. Our data confirm elevations of several individual components, particularly C9, while C3 and C7 were infrequently abnormal; the former is of interest because of its key role in the classic and alternate pathways.

These observations are not readily explained by present knowledge regarding the stimulation and synthesis of complement and its components (2). The role of tumor-associated antigens in this phenomenon (4, 9, 10), in addition to the contributions of increased synthesis, decreased utilization, and decreased metabolism, remains to be defined. The significance of these findings and potential application to understanding the mechanism of malignant disease require further study.

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REFERENCES


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