FIBRIN AND FIBRINOGEN DEGRADATION PRODUCTS IN MALIGNANCY

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ABSTRACT

Sixty four patients of cancer, comprising of 39 leukaemia, 8 lymphomas and 17 cases of solid tumours were included in this study. Quantitative estimation of FDP, fibrinogen and platelets were done in all. Elevated levels of FDP ($\geq 10 \mu\text{gm/mL}$) were found in 29 patients. These patients were further categorised as decompensated, overcompensated and compensated intravascular coagulation and fibrinolytic syndrome on the basis of platelet counts and fibrinogen levels.

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KEY WORDS : Fibrin fibrinogen degradation product; Disseminated intravascular coagulation; Leukemia.

Introduction

Increased levels of fibrin and fibrinogen degradation products (FDP) are seen in malignancy, collagen disorders, infections and a variety of other conditions. It is generally believed that intravascular coagulation is usually, or perhaps always, associated with fibrinolysis which in turn is manifested by an increase in FDP. The prevalence of overt or subclinical intravascular coagulation has been noted to be very high (upto 92%) in patients with cancer [1,2]. Rickles et al [3] demonstrated elevated levels of fibrinopeptide-A in majority (60%) of patients with cancer, supporting the observation of others that patients with cancer have evidence of subclinical activation of blood coagulation. The definitive diagnosis of intravascular coagulation is rather difficult as it requires kinetic studies of platelets and other coagulation factors [4]. Such facilities are not available in most laboratories. In their absence Sun et al identified the key tests that might enable us to identify the patient with coagulation defects [1].

In this study, involving patients with various malignancies, we have estimated the levels of FDP and tried to identify different types of intravascular coagulation and fibrinolytic syndrome (ICF) in conjunction with other key tests such as platelet counts and fibrinogen levels [1].

Material and Methods

Sixty four patients admitted in the Malignant Diseases Treatment Centre at Army Hospital, Delhi with various types of malignancy were randomly included in this study. There were 39 cases of leukaemia (acute and chronic), 6 cases of lymphoma, 2 cases of multiple myeloma and 17 cases of solid cancers involving lung, breast, pancreas, and bone.

Blood samples were collected in 3.2% trisodium citrate (9 volumes blood in 1 volume citrate) for the fibrinogen estimation by Clause's method [6] using kits from Diagnostic Reagent Ltd. Blood was also taken into tubes containing epsilon aminocaproic acid (EACA) and trosylol for analysis of FDP. Blood in EACA tubes was clotted with thrombin and the serum was used to estimate FDP using Thrombo-well Cotest FDP kit (Wellcome, England) [7]. Two mL of blood was collected in a paraffin coated tube containing dried EDTA. Using criteria of Sun et al [1] coagulation defects in these patients were classified into three groups : patients with no ICF (normal FDP), those with compensated ICF (elevated FDP but normal platelet count and fibrinogen), and those with overcompensated ICF (elevated FDP, platelets, and fibrinogen).

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TABLE 1
Platelet count, fibrinogen and FDP levels in cancer patients

Test	Normal range	Low		Normal		High	
		No	%	No	%	No	%
Platelet count	150-400x10 ³ /cumm	34	53.0	30	47.0	—	—
Fibrinogen assay	200-400 mg/dL	7	11.0	47	73.5	10	15.5
FDP level	10 µgm/mL	—	—	35	54.5	29	45.5

TABLE 2
Showing various types of ICF syndromes

Type of ICF syndrome	Platelet count	Fibrinogen	FDP (µgm/mL)	No
Decompensated ICF syndrome	↓	↓	≥ 40	3
Overcompensated ICF syndrome	N	↑	≥ 40	6
Compensated ICF syndrome	N	N	10-40	20

Results

The average age of the patients included in this study was 29.1 years with a range of 5 to 70 years. There were 53 males and 11 females. Leukaemia and lymphoma together comprised the major group (47 out of total 64 patients).

A summary of results of platelet counts, fibrinogen assay and FDP level is shown in Table 1.

Increased FDP level (≥ 10 µgm/mL) was seen in 29 patients and thrombocytopenia was seen in 34 patients out of whom 21 were cases of acute leukaemia (AML 15 + ALL 6). Using modified criteria of Sun et al [1] these cases were divided into overcompensated, compensated and decompensated ICF as shown in Table 2. There were 3 cases of decompensated ICF, 6 cases of overcompensated and 20 cases of compensated ICF syndrome.

Discussion

Cancerous cells contain either a procoagulant substance or fibrinolysis promoting substance [8,9]. Therefore, the fibrinolysis in cancer patients may be some times primary and sometimes secondary with consumption coagulopathy. Alternatively, it may be a mixture of both due to a concurrent release of the fibrinolysis activators and the procoagulant substances as seen in acute

promyelocytic leukemia [10]. Therefore, elevated levels of FDP have been reported to be the most common abnormality in cancer patients. An incidence varying between 25 to 68% has been reported [1,10].

In the present study, FDP was found to be increased in 29 (45.5%) patients and it was the second most common abnormality after thrombocytopenia. The higher number of thrombocytopenic cases can be explained on the basis of inclusion of a large number of acute leukaemia cases where thrombocytopenia is commonly present. All 15 cases of AML and 6 out of 8 cases of ALL had thrombocytopenia. The increase in FDP in 20 cases of compensated ICF syndrome was moderate (10-40 µgm/mL in 3 cases of decompensated and 6 cases of overcompensated ICF syndrome. It is believed that this moderate increase in FDP is a result of slow primary or a very low grade secondary fibrinolysis [1-3]. The majority of patients with increased FDP belonged to the compensated and overcompensated groups and in this aspect our findings agree with those of Sun et al [1].

The present study indicates that elevated levels of FDP are common in cancer patients. This is as result of intravascular coagulation and secondary fibrinolysis which is not clearly defined, but it may be a slow and continuous introduction of either a

thromboplastin-like material or a plasminogen activator in circulation leading to consumption coagulopathy. The liver is capable of generating considerably more fibrinogen than it does normally and the bone marrow has the capability to produce upto 10 times the normal number of platelets. Therefore, the actual concentration of fibrinogen and number of platelets in blood reflects the balance between rates of synthesis and rates of destruction. In other words, the manifestations of the ICF syndrome depend on the degree of compensation afforded by the liver and marrow and this may not be the same for the two organs. This is proved by the findings of increased levels of fibrinogen and normal level of platelets in all the 6 cases of overcompensated ICF in this study.

In conclusion therefore, a combination of tests, i.e., quantitative estimation of fibrinogen, platelet, and FDP, may be useful in detection of different types of ICF syndromes and identification of cases of decompensated and overcompensated ICF which might require immediate therapeutic intervention to prevent further complications of haemorrhage and thrombosis.

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