Hypercoagulopathy Induced by
Chemotherapy in a Patient with
Lung Cancer*

A Possible Role for a Factor with
Thrombosis-Inducing Activity (TIA)

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We treated a patient with lung cancer in whom a hypercoagulopathy was induced acutely by chemotherapy. He received systemic chemotherapy twice and in both instances developed disseminated intravascular coagulopathy (DIC), accompanied by acute decrements of the peripheral platelet count and plasma fibrinogen, an increment of the fibrin degradation products (FDP), and bleeding tendency with the appearance of skin purpura. In each instance, the plasma thrombosis-inducing activity (TIA) appeared one to three days after chemotherapy and subsided subsequently. (Chest 1992; 101:277-78)

CDDP = cisplatin; DIC = disseminated intravascular coagulopathy; TIA = thrombosis-inducing activity

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Abnormalities of blood coagulation in malignant diseases have been noted repeatedly in clinical studies. Several mechanisms have been proposed by which malignant processes may induce altered hemostasis. Recently, we found that plasma from some patients with lung cancer contains a factor capable of inducing multiple thromboses in vivo. Herein, we present a patient with lung cancer who demonstrates that thrombosis-inducing activity (TIA) can be released into plasma by administering tumoricidal drugs and may cause disseminated intravascular coagulopathy (DIC).

CASE REPORT

A 73-year-old man was admitted to the hospital for a solitary coin lesion in the middle of the left lung field. The diagnosis of lung cancer (moderately differentiated adenocarcinoma) was achieved by transbronchial lung biopsy specimen. A chemotherapy regimen of cisplatin (CDDP) (100 mg/sqm), vindesine (3 mg/sqm), and tegafur (a precursor drug of fluorouracil; 600 mg orally, daily) was started. Two days later, peripheral platelet count fell suddenly to 4.8 × 10^9/cu mm from 23.7 × 10^9/cu mm, the pretreatment value. This was followed by a decrease in the plasma fibrinogen level and an increase in fibrin degradation products (FDP) (Fig 1). These laboratory values returned nearly to normal within one week with no specific management.

The second systemic chemotherapy with the same regimen was started at a two-month interval, and he developed more severe thrombocytopenia with skin purpura on the arms and chest wall. Continuous intravenous infusion of heparin (8,000 U/day) was

![Graph](image_url)

**Figure 1.** Effect of tumoricidal drugs on the peripheral platelet count (circles), plasma fibrinogen (squares), FDP (Xs), and TIA. TIA was measured on the indicated days. Plus sign = TIA positive in plasma; minus sign, TIA negative.
started, and the peripheral platelet count returned to normal level within a week. When plasma TIA was measured, as we reported previously, it was detected in plasma collected one to three days after the chemotherapy and then disappeared (Fig 1).

**DISCUSSION**

The frequency of hypercoagulability, which may lead patients to complications such as thromboembolism or DIC, is well known in malignant diseases.\(^1\)\(^-\)\(^2\) It has also been reported that antineoplastic drugs can induce hypercoagulability in patients with breast cancer.\(^3\)\(^-\)\(^4\) To our knowledge, there has been no study of the direct relationship between chemotherapy and hypercoagulability in lung cancer, although Ruiz et al.\(^5\) showed that fibrinopeptide A was elevated after chemotherapy in patients with lung cancer. We now report the case of a patient with advanced lung cancer complicated by DIC after chemotherapy.

Several mechanisms have been proposed to account for the pathogenesis of hypercoagulability in patients with malignant neoplasms. Tissue factor, the most potent initiator of the extrinsic coagulation cascade, was found to be present on various types of tumor cells.\(^6\) Furthermore, a cysteine protease capable of activating factor X directly was eluted from human cancer cell lines.\(^7\) Although factors in contact with peripheral blood or released into the circulation may be important in the pathogenesis of hypercoagulability, controversies remain.

Recently, we found that plasma from some patients with advanced lung cancer contains TIA that can induce DIC-like status in mice.\(^8\) An acute decrement of peripheral platelet count and the formation of numerous pulmonary thrombi was induced by the intravenous injection of plasma with TIA. The animal dies 3 to 10 min thereafter. A partial characterization of TIA reveals that it is a heat-labile glycosphospho-lipoprotein of high molecular weight. Although the origin of TIA is not yet defined, study of this patient with lung cancer indicates that TIA is induced in circulation by chemotherapeutic drugs. TIA may be responsible at least in part for alteration of blood coagulation activity seen after chemotherapy. Recent study showed that heparin could abolish the chemotherapy-induced increase in plasma fibrinopeptide A levels in patients with cancer.\(^9\) Heparin also inhibits TIA activity.\(^9\) Prophylactic use of heparin may be useful to prevent the chemotherapy-induced occurrence of hypercoagulopathy and also DIC.

**REFERENCES**

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**Long-term Follow-up of Tuberculoma of the Brain in an AIDS Patient**

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Human immunodeficiency virus infection and extrapulmonary TB are defined as AIDS. The clinical manifestations of the TB are related to the interplay of the organism and the host’s immune system. A seven-year follow-up of a woman successfully treated for biopsy- and culture-documented tuberculous brain abscess is described. Antibodies to HIV have been positive on repeated testing, yet CD counts remain over 500. Aggressive diagnostic and therapeutic maneuvers for all forms of TB in AIDS are warranted since long-term prognosis may be good.

(Chest 1992; 101:278-79)

**ARC** = AIDS-related complex; **HIV** = human immunodeficiency virus; **ELISA** = enzyme-linked immunoabsorbent assay

In 1987, the Centers for Disease Control broadened the definition of AIDS to include extrapulmonary TB in any HIV seropositive person. The immunosuppression caused by HIV infection predisposes individuals with prior *Mycobacterium tuberculosis* infection to develop active disease.\(^6\) The clinical presentation of TB tends to reflect the severity of the immunosuppression. The more "classic" primary and post-primary pulmonary manifestations (cavitary upper lobe infiltrates; noncavitary lower lobe infiltrates; mediastinal lymphadenopathy) are seen early on in HIV infection,\(^6\) often as the first "opportunistic" infection. Disseminated disease and extrapulmonary disease\(^6\) usually are associated with greater degrees of immunosuppression, as indicated by lower CD counts and the presence of oral thrush.\(^6\)

In 1986 our group presented the first report of central nervous system TB in patients diagnosed as having AIDS or ARC.\(^6\) We present here a more than seven-year follow-up of one of the patients in that report (case 6) who had docu-