Thrombosis Research (2005) **115**, 59—64

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THROMBOSIS RESEARCH

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Regular Article

Symptomatic venous thromboembolism in acute leukemia. Incidence, risk factors, and impact on prognosis

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Received 27 May 2004; received in revised form 12 July 2004; accepted 28 July 2004
Available online 3 September 2004

KEYWORDS
Acute leukemia;
Venous thromboembolism;
Prognostic factors;
Survival

Abstract The association between malignant disorders and occurrence of venous thromboembolism is well established. Patients with cancer and venous thromboembolism have adverse prognosis. No systematic study on the incidence and prognostic impact of venous thromboembolism in acute leukemia has been performed as yet. We retrospectively evaluated the incidence of symptomatic venous thromboembolism before chemotherapy in 719 patients (371 males and 348 females, median age of 57.4 years), diagnosed with acute leukemia [534 with acute myelogenous leukemia, 185 with acute lymphoblastic leukemia]. Furthermore, the relationship of venous thromboembolism to clinical and laboratory parameters and its impact on prognosis was assessed. Fifteen patients (2.09%) had venous thromboembolism (objectively confirmed in 13 patients) in close temporal relationship to the onset of acute leukemia. The incidence of venous thromboembolism was the same in acute myelogenous and lymphoblastic leukemia. In five patients, pulmonary embolism was documented. Venous thromboembolism occurred in all subtypes of acute leukemia, but was most common in promyelocytic leukemia. All but one patient were treated with anticoagulants. No patient died from treatment-related bleedings or venous thromboembolism. Overall, survival, disease-free survival, and remission duration did not differ between the patient groups with

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0049-3848/$ - see front matter
doi:10.1016/j.thromres.2004.07.016

and without venous thromboembolism. In contrast to solid tumors, venous thromboembolism before or at diagnosis of acute leukemia is not associated with poor prognosis.

Introduction

Venous thromboembolism (VTE) is a common complication in patients with malignancies. It may precede malignancy [1—3], may be the presenting symptom, or may be a complication of chemotherapy. Recently, it has been shown that patients with solid tumors and VTE have an inferior prognosis [4]. VTE (at diagnosis or during therapy) is also common in high-grade non-Hodgkin lymphomas and is associated with an unsatisfactory response to chemotherapy [5]. In acute leukemia (AL), VTE was mainly reported as a complication of therapy. In acute lymphoblastic leukemia (ALL), a relatively high incidence of VTE was found in children [6] and adults [7] undergoing induction chemotherapy containing *Escherichia coli* asparaginase and prednisone. VTE, often on unusual sites [8—10], occurred in some cases after treatment of acute promyelocytic leukemia with tretinoin. Only a few cases of VTE have been reported in patients with AL before chemotherapy [11—17]. No systematic study on the incidence of VTE in acute leukemia before chemotherapy has been carried out as yet. We have retrospectively investigated the incidence of symptomatic VTE in a large cohort of consecutive, unselected patients with untreated acute myelogenous (AML) and ALL and studied the relationship to clinical and laboratory parameters and the impact on prognosis.

Patients and methods

Between 1979 and 2001, 719 patients with acute leukemia (534 AML, 185 ALL) have been admitted at our department. All patients were included in this analysis, irrespective of whether or not they were subsequently treated. Data on symptomatic VTE were retrieved from hospital charts. VTE was defined as "leukemia-associated", if an objectively documented VTE had occurred within the last 4 months before diagnosis or at the time of diagnosis, but before chemotherapy. The diagnosis of VTE was objectively confirmed in all but two cases either by sonography, phlebography, or helical computer tomography (CT). The demographic and haematological data of the patients without or with VTE are shown in Table 1. Results are expressed as absolute frequencies or median (inter-quartile range). The median follow-up time of survivors was 93 months.

Table 1 Patient data

		Patients without VTE (n=704)	Patients with VTE (n=15)	Significance (ns=nonsignificant)
Sex (males/females)		363/341	8/7	
Median age (year)		54.7 (IQR[a]: 34.9—68.8)	60.1 (IQR: 47.0—68.2)	ns (p=0.38)
Mean WBC (10^9/l)		39.5 (S.D.[b]: 64.0)	64.6 (S.D.: 161.0)	ns (p=0.5)
Mean platelet count (10^9/l)		67.8 (S.D.: 88.7)	95.7 (S.D.: 93.0)	ns (p=0.055)
Chemotherapy (yes/no)		598/106	14/1	
AML subtypes	M0, M1, M2	245	4	
	M3	46	3	ns (p=0.085)
	M4, M5	196	3	
	M6, M7	33	1	
	Mast cell leukaemia	1	0	
	Biphenotypic	2	0	
ALL subtypes	B-lineage	153	4[+]	
	T-lineage	26	0	
	Undifferentiated	2	0	

[a] IQR=Inter-quartile Range.
[b] S.D.=Standard Deviation.
[+] All c-ALL.