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SHORT COMMUNICATION

Is there a predictive significance of *ABO* blood group on chemotherapy-induced thrombocytopenia in patients with stage III colon cancer?

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Abstract Chemotherapy-induced thrombocytopenia (CIT) is the most important cause of thrombocytopenia in cancer patients. In this paper, I discussed the effect of ABO blood group on CIT in patients with stage III colon cancer. In a pilot study, a total of 131 (72 men, 55 %) eligible patients with stage III colon cancer were divided into two groups according to whether they had CIT. Both groups were compared using demographic, histopathological, and laboratory variables. CIT was detected in 51 (40 %) of 131 patients. The incidence of CIT had a significant increased in patients with 0 blood group compared to other blood groups. It was concluded that the relationship between blood group 0 and the presence of CIT in patients with stage III colon cancer is independent of other study variables ($P = 0.035$, OR 3.14, 95 % CI 1.16–7.01). In conclusion, I hypothesized that 0 blood group may predict to differentiate high-risk patients for CIT.

Keywords Blood group · Thrombocytopenia · Colon cancer

Introduction

Chemotherapy-induced myelosuppression includes anemia, neutropenia, and thrombocytopenia and is a common side effect of chemotherapy in cancer patients. However, the underlying etiopathogenic mechanisms of chemotherapy-related myelosuppression are not yet clear [1–3]. Additionally, chemotherapy-induced thrombocytopenia (CIT) is the most important cause of thrombocytopenia in patients with cancer [4]. Severe CIT not only has a risk of life-threatening hemorrhagic complications but also may necessitate dose reduction and/or delay in chemotherapy schedules [3, 5–8]. Previous studies have indicated that various factors, such as platinum-based regimen, multiple high-risk chemotherapy treatments, multiple primary tumors, patients with lung cancer, and baseline thrombocyte count, have a high predictive value for CIT (3). However, no valuable factor to identify which patient will develop CIT has been defined [9].

Previous studies have demonstrated a possible relationship between *ABO* blood group and risk of various malignant tumors such as colorectal, lung, and ovarian cancer [10–15]. Some studies have indicated an association between *ABO* blood group and cancer progression [16–20]. Additionally, experimental studies have shown that blood group A and B antigens are strongly expressed on platelets of some individuals [21, 22].

The results of a pilot study for future investigations

Based on this information, I hypothesized that *ABO* blood group may help to differentiate high-risk patients for CIT. The main objective in this study was to determine whether *ABO* blood group in eligible patients with stage III colon cancer had a relationship with CIT.

The study was planned as a retrospective cross-sectional study with diagnostic accuracy. The subjects of the present study were selected from 248 patients with stage III colon cancer who were treated with FOLFOX4 or mFOLFOX6 regimens between July 2011 and June 2014.

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A total of 131 (72 men, 55 %) eligible patients with stage III colon cancer who did not meet the exclusion criteria were enrolled in this study. The exclusion criteria were as follows: (1) patients with metastatic colon cancer in diagnosis; (2) patients diagnosed with deep vein thrombosis and/or pulmonary embolism by venous duplex/Doppler ultrasound and/or computerized tomography before first course of adjuvant chemotherapy; (3) patients previously diagnosed with chronic renal insufficiency, sepsis, diabetes mellitus, multiple primary malignancies, rheumatologic diseases, bone or bone marrow metastasis, chronic liver diseases, splenomegaly, hematological malignancies, or plasma electrolyte abnormalities; (4) patients still receiving acetylsalicylic acid and oral and/or parenteral antithrombotic or anticoagulant drugs; (5) patients receiving adjuvant chemotherapy or previously diagnosed with pseudothrombocytopenia, disseminated intravascular coagulation (DIC) or pre-DIC (with serum fibrinogen level, prothrombin and activated partial thromboplastin time, and peripheral blood smear), idiopathic thrombocytopenic purpura, heparin-induced thrombocytopenia, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, or autoimmune hemolytic thrombocytopenia; (6) patients who had increased splenic size and chemotherapy-associated hepatic sinusoidal obstructive syndrome; (7) patients with rectum cancer; and (8) blood or blood component transfusion within 6 weeks before first chemotherapy course.

CIT was detected in 51 (40 %) of the 131 patients with colon cancer. The demographic, clinical, laboratory, and pathological characteristics of Group 1 with CIT ($n = 51$, 40 %) and Group 2 without CIT ($n = 80$, 60 %) are displayed in Table 1. A total of 1,490 chemotherapy cycles were administered (median 10.6 cycles, range 6–12). The median interval between cycles was 18 days (range 13–28). Twenty-one patients discontinued adjuvant treatments.

In this study, 41 % ($n = 54$) of all patients (Group 1 and Group 2) had blood group 0, 22 % ($n = 29$) blood group A, 22 % ($n = 29$) blood group B, and 15 % ($n = 19$) blood group AB. However, 61 % ($n = 31$) of patients with CIT had blood group 0 (Table 1). Additionally, patients with blood group 0 showed significantly higher incidence of CIT than did patients with blood group A, B, and AB (57, 28, 24, and 26 %, respectively) ($P = 0.034$). Blood group 0 had a significant correlation with gender (for men), positive lymphovascular invasion, and histological grade of tumor (for grade 2 and 3 tumors) ($r = 0.531$, $P = 0.041$; $r = 0.513$, $P = 0.043$; and $r = 0.547$, $P = 0.044$, respectively). It was concluded that the relationship between blood group 0 and the presence of CIT in stage III colon cancer is independent of other study variables (age, sex, BMI, smoking habits, treatment type, histopathological findings) ($P = 0.035$; OR = 3.14; 95 % CI 1.16–7.01).

Table 1 Comparison of the demographic, histopathological, clinical, and laboratory characteristics of patients with CIT (Group 1) and without CIT (Group 2)

Variables	Patients with CIT (Group 1)	Patients without CIT (Group 2)	*P**
Patients (*n*)	51 (40)	80 (60)	0.142
Age (year)	56 ± 16	59 ± 18	
Gender (*n*, %)			
Male	29 (57)	43 (54)	0.287
Female	22 (43)	37 (46)	
BMI (kg/m^2)(main ± std. dev.)			
All patients	30.6 ± 2.6	30.2 ± 2.4	0.218
Male	30.8 ± 2.1	30.6 ± 1.9	
Female	31.4 ± 2.2	31.5 ± 2.6	
Smoking (*n*, %)			
Present	36 (71)	56 (70)	0.304
Absent	15 (29)	24 (30)	
Tumor localization (*n*, %)			
Rectosigmoid and sigmoid colon	26 (51)	42 (52)	0.246
Transverse colon	8 (16)	11 (14)	
Ascending colon and cecum	17 (33)	27 (34)	
Operation type (*n*, %)			
Segmental resection	15 (29)	21 (26)	0.219
Right hemicolectomy	16 (31)	26 (32)	
Left hemicolectomy	20 (40)	33 (42)	
Nodal status, pN (*n*, %)			
N1a	17 (33)	26 (33)	0.213
N1b	8 (16)	17 (21)	
N2a	16 (31)	25 (31)	
N2b	10 (20)	12 (15)	
Tumor stage, pT (*n*, %)			
T1	9 (18)	15 (19)	0.274
T2	6 (12)	14 (18)	
T3	22 (43)	29 (36)	
T4a	8 (16)	14 (18)	
T4b	6 (11)	8 (9)	
Lymphovascular invasion (*n*, %)			
Presence	33 (65)	36 (45)	0.048*
Absence	14 (28)	37 (46)	
Unknown	4 (7)	7 (9)	
Tumor grades (*n*, %)			
Grade 1	15 (29)	19 (24)	0.294
Grade 2	27 (53)	46 (58)	
Grade 3	9 (18)	15 (18)	
Baseline hematological values (main ± std. dev.)			
Neutrophil count ($\times 10^9$)	5.6 ± 3.1	5.3 ± 2.8	0.242
Leukocyte count ($\times 10^9$)	10.6 ± 5.3	9.6 ± 4.2	0.239
Erythrocyte count ($\times 10^9$)	4.89 ± 1.42	4.41 ± 1.78	0.213
Hemoglobin level (g/dL)	10.1 ± 2.7	10.9 ± 2.6	0.202
Hct value (%)	36.3 ± 5.7	37.4 ± 4.1	0.186

Table 1 continued

Variables	Patients with CIT (Group 1)	Patients without CIT (Group 2)	*P**
MCV (fL)	88 ± 11	89 ± 13	0.251
MCHC (pg)	35 ± 7	36 ± 4	0.297
MPV (fL)	9.4 ± 1.3	9.1 ± 1.2	0.237
Thrombocyte count ($\times 10^9$)	349 ± 102	345 ± 93	0.194
Serum iron level (μg/dL) (main ± std. dev.)	77 ± 26	76 ± 23	0.243
Total iron-binding capacity (μg/dL) (main ± std. dev.)	397.4 ± 108.4	387.9 ± 111.2	0.238
Serum ferritin level (ng/mL) (main ± std. dev.)	118.3 ± 67.9	129.4 ± 72.8	0.193
Iron deficiency anemia (*n*, %)			
Presence	21(41)	39 (49)	0.307
Absence	26 (51)	34 (42)	
Unknown	4 (8)	7 (9)	
CIA (*n*, %)	24 (47)	32 (40)	0.214
CIN (*n*, %)	16 (31)	29 (36)	0.241
Treatment or/and prophylaxis with GCSF (*n*,%)			
Yes	11(22)	29 (36)	0.205
No	36 (71)	46 (58)	
Unknown	4 (7)	5 (6)	
Type of GCSF treatment (*n*, %)			
Filgrastim 30 million unit/day	3 (37)	6 (42)	0.274
Filgrastim 48 million unit/day	2 (26)	4 (29)	
Lenograstim 34 million unit/day	3 (37)	4 (29)	
Treatment regimens (*n*, %)			
FOLFOX4	29 (57)	41(51)	0.239
mFOLFOX6	22 (43)	39 (49)	
Blood group (*n*, %)			
O	31 (61)	23 (29)	0.037*
A	8 (16)	21 (26)	
B	7 (14)	22 (28)	
AB	5 (9)	14 (17)	

std.dev. standard deviation, *BMI* body mass index, *Hb* hemoglobin, *Hct* hematocrit, *MCV* mean corpuscular volume, *MCHC* mean corpuscular hemoglobin concentration, *MPV* mean platelet volume, *GCSF* granulocyte colony stimulating factor, *CIA* chemotherapy-induced anemia, *CIN* chemotherapy-induced neutropenia, *CIT* chemotherapy-induced thrombocytopenia

* A two-tailed *P* value of < 0.05 was considered statistically significant

Conclusion and recommendation

According to these results, blood group 0 might be noted to negatively affect the precursors of circulating platelet through DIC or pure myelosuppression. Therefore, it can be hypothesized that blood group 0 is associated with CIT in stage III colon cancer patients.

The most important limitation of this study is the similar number of selected patients. In this study, the preliminary conclusion is that blood group 0 might affect the platelets in cancer patients who had received chemotherapy. Additionally, in this hypothesis, blood group 0 may play a considerable role in thrombocytopenia, in addition to drug-related myelotoxicity, and it might be considered to be a cofactor in patients with CIT. However, these results should be explained by larger clinical or molecular studies that include sufficient number of patients. Future well-designed studies that address the relationship between *ABO* blood group and CIT should be molecular and prospective.

Conflict of interest I certify that all of my affiliations with or without financial involvement, within the past 5 years and foreseeable future and any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, and royalties).

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