THE CLONAL HEMATOPOIESIS OF INDETERMINATE POTENTIAL IS A RISK FACTOR OF CARDIOVASCULAR COMPLICATION IN PATIENTS OF OLDER AGE

6th Kaunas / Lithuania International
Hematology / Oncology Colloquium
28 May 2021

O. Mishchenuk 1, O. Kostiukevych 1, B. Klimyk 2, S.Klymenko 2,3

Workplace of the author(s):

1. State Institution of Sciences “Research and Practical Center of Preventive and Clinical Medicine”, State Administrative Department,
2. Feofaniya Clinical Hospital
3. Shupyk National Medical Academy of Postgraduate Education

Objective

Despite controversial values of different new thrombosis predictors, the “classical” triggers of them, such as diabetes mellitus, hyperlipidemia or dyslipidemia, smoking, obesity and family anamnesis, are still most powerful risk factors. However, according to the last data, the clonal hematopoiesis of indeterminate potential (CHIP) is an independent risk factor of cardiovascular complications (CVC) such as myocardial infarction or coronary stenosis (CS).

Methods

In the study we included 243 patients with median age of 67.0 (25-percentile and 75-percentile (PL) = 57.0 and 76.0, accordingly). The main group included 157 patients, who had CVC and who were performed percutaneous coronary intervention (PCI) because of CS, the comparison group created 86 subjects, who had CVD without CVC and whom PCI was not performed. In the main group the median age was higher (67.0; 25 and 75- PL = 49.0 and 88.0 accordingly), than in the control group (65.0; 25 and 75-PL = 48.0 and 78.0 accordingly) (Z = 3.0; p = 0.002). To assess CHIP we tested DNMTA3A (R882), IDH1 (R132), IDH2 (R140 and R172), SRSF2 (P95) by real-time polymerase chain reaction (PCR) with melting curve analysis and NPM1 in exon 12 (4 bp insertion), JAK2 V617F was determined by PCR and gel electrophoresis. DNA was obtained from peripheral blood mononuclear cells. Comparison between categorical indices was made using two-tiled Fisher’s test. The degree of correlation between categorical indices was expressed as relative risk (RR) with corresponding confident intervals (CI). The presence of significant discrepancies was assumed in cases of the error probability below 0.05.

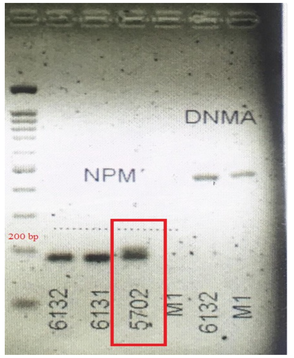

Image 1. The results of PCR reaction with next gel electrophoresis with detection of NPM1 in exon 12 (4 bp insertion) mutation and DNMTA3A (R882) ampliphicat.

Results

In the general cohort of patients, the CHIP was found in 30 of 243 patients (12.24%). The DNMTA3A (R882) mutation was detected in 20 (64.51 %), JAK2 V617F – in 6 (19.35 %), NPM1 in exon 12 – in 3 (9.67 %), IDH2 (R140 and R172) – in 2 (6.45 %) subjects. The SRSF2 (P95) mutation was not detected in any case. The frequency of DNMTA3A (R882) mutation was higher, than JAK2 V617F (p=0.007), NPM1 in exon 12 (p=0.004) and IDH2 (R140 and R172) (p=0.001) mutations. In patients 60 years of age and older CHIP was detected in 15.11 % (26 from 172) cases, and in persons, who were younger, than this age’s limit – in 5.63 % (4 from 71) (p=0.052). The age of 60 years increased the risk of CHIP by factor of 1.2 (95 % CI = 1.0-1.5). In the main group, one of the markers of CHIP was found in 16.02 % of patients (25 out of 156 cases), in the control group – in 6.97 % of cases (6 from 86) (p = 0.046). It was estimated, that the relative risk of CVC associated with CHIP was equal 1.3 (95 % CI = 1.0-1.6). The DNMTA3A (R882) mutation was found more frequent in the group with CVC on the level of statistical significance (17 out of 165 vs 3 out of 86; p=0.051), compared to the control group. The difference of the frequency of JAK2 V617F mutation (5 from 156 vs 1 from 86; p = 0.426), NPM1 mutation in exon 12 (3 from 156 vs 0 from 86; p = 0.554) and IDH2 (R140 and R172) (2 from 156 vs 0 from 86; p = 0.539) mutation was not detected between the main and control groups.

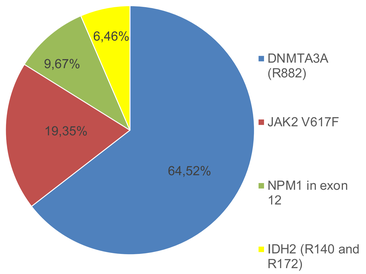

Image 2.. The frequency of DNMTA3A (R882), IDH1 (R132), IDH2 (R140 and R172), NPM1 in exon 12 (4 bp insertion) mutation in cochort of patients with CHIP.

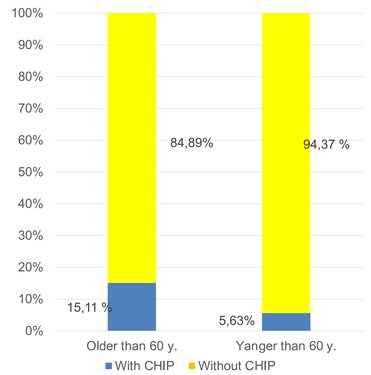

Image 3. The frequency CHIP in the cochort of patients older and younger than 60 .

Conclusions

The most often mutation in patients with CHIP was DNMTA3A (R882) which was found in 64.51 % of cases. The JAK2 V617F mutation was detected in 19.35 %, NPM1 in exon 12 – in 9.67 %, and IDH2 (R140 and R172) – in 6.45 % subjects. The CHIP more often was found in the group with CVC (16.02 % vs 6.97 %). CHIP carriers are characterized by 1.2 times increased CVC risk in persons older than 60.

Key words:

the clonal hematopoiesis of indeterminate potential, cardiovascular complication, older age.