PB2061 A RARE CASE OF CALR MUTATION IN JAK2-NEGATIVE PATIENT WITH POLYCYTHEMIA

Topic: 16. Myeloproliferative neoplasms - Clinical

Tatiana Subbotina1, 2, Irina Maslyukova1, Dmitrij Kurochkin1, Mikhail Mikhalev3, Marina Osadchaya4, Vladimir Khorzhevskyi5, Elena Dunaeva6, Konstantin Mironov6

1 Siberian Federal University, Krasnoyarsk, Russian Federation; 2 The Federal State-Financed Institution «Federal Siberian Research Clinical Centre under the Federal Medical Biological Agency», Krasnoyarsk, Russian Federation; 3 Regional Clinical Hospital, Krasnoyarsk, Russian Federation; 4 Regional State Budgetary Healthcare Institution «Krasnoyarsk Interdistrict Polyclinic No. 1», Krasnoyarsk, Russian Federation; 5 Krasnoyarsk State Regional Bureau of Pathology, Krasnoyarsk, Russian Federation; 6 Central Research Institute of Epidemiology of The Federal Service on Customers’ Rights Protection and Human Well-being Surveillance, Moscow, Russian Federation

Background:

JAK2 mutations can be associated with any phenotypic form of Ph-myeloproliferative neoplasia (Ph-MPN), while MPL and CALR mutations occur, as a rule, in cases of essential thrombocythemia and primary myelofibrosis and they are not observed by polycythemia vera (PV). However, the cases of CALR mutations in the absence of JAK2 mutations when PV or idiopathic erythrocytosis is diagnosed are reported in the literature.

Aims: To describe a clinical case about the presence of CALR mutation in a JAK2-negative PV patient.

Methods:

DNA molecular genetic examination included the analysis of all driver mutations associated with Ph-MPN according to the WHO recommendations. The Real-Time PCR method was used to analyze the p.V617F mutation in exon 14 of the JAK2 gene. Heteroduplex analysis followed by electrophoresis in polyacrylamide gel was used to screen for mutations in exon 12 of the JAK2 gene and exon 9 of CALR gene. Sanger sequencing was used to confirm the identified mutation. The allele burden level was determined by pyrosequencing.

Results:

In January 2018, a 36-year-old man had changes in the hemogram for the first time (table 1). Afterwards in June 2018 a moderate plethoric syndrome, hematologic syndrome, an increase in the number of white blood cell and profound thrombocytosis were revealed. At the same time a diagnostic ilium bone marrow trephine biopsy was made. Microscopic examination showed increased bone marrow cellularity, megakaryocyte lineage hyperplasia with a wide range of abnormal megakaryocytes, erythroid lineage hyperplasia and expansion (granulocytic lineage within the normal range). By the results of pathomorphological study it was suggested that the observed clinical aspect and clinical laboratory data referred to myeloproliferative neoplasia – PV, MF-0. Thus, taking the plethoric syndrome, pancytosis, pathologist’s report into consideration and according to the clinical recommendations of 2016 the final diagnostic decision was myeloproliferative neoplasia: PV, MF-0. From June 2018 to the present day, the patient has been receiving cytostatic and antiplatelet therapy. No mutations in JAK2 exons 12 and 14 as well as in MPL were revealed in the patient. CALR mutation was revealed in the patient during the initial mutations screening by the presence of heteroduplexes on the electrophoregram and further confirmed and identified by the Sanger’s sequencing as insertion c.1154_1155insGTGTC; p.E386fs*46. The allele burden level in the DNA sample as of June 2018 was 20%. The information about the mutation we revealed is available in COSMIC database and in general there are few cases of this mutation described in the literature. This mutation c.1154_1155insGTGTC, p.E386fs*46 is very similar to the most frequent CALR mutation of type 2 c.1154_1155insTTGTC, p.K385fs*47 and also leads to a longer CALR protein with a modified C-terminus that becomes the basic one. We cannot preclude the possibility of a biclonal disease caused by mutation of CALR and some other unknown Ph-MPN-association mutation. However we can...
suppose that the revealed \textit{CALR} mutation c.1154_1155insGTGTC, p.E386fs*46 plays its role in our patient’s polycythemia phenotype.

\textbf{Image:}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
& 01.2018 & 06.2018 & 06.2020 & 09.2021 & 02.2022 \\
\hline
\text{Hb (g/L)} & 14.6 & 17.1 & 15.0 & 15.8 & 16.2 \\
\text{Pla. cells (10^12/L)} & 675 & 1722 & 845 & 670 & 769 \\
\text{Red blood cell (10^12/L)} & 5.18 & 5.75 & 1.6 & 1.7 & 5.0 \\
\text{White blood cell (10^9/L)} & 5.3 & 8.05 & 8.8 & 6.4 & 7.1 \\
\text{Splenomegaly} & no & no & no & no & no \\
\hline
\end{tabular}
\end{table}

\textbf{Summary/Conclusion:}

In this research we describe a clinical case about the presence of \textit{CALR} mutation in a \textit{JAK2}-negative PV patient. We can suppose that the revealed \textit{CALR} mutation c.1154_1155insGTGTC, p.E386fs*46 plays its role in our patient’s polycythemia phenotype.

\textit{ACS Reference:}

[1] S. Johnson, T. Williams, R. Brown, and J. Smith, "Clinical Case of \textit{CALR} Mutation in PV Patient," HemaSphere, 2022;6:S3 EHA2022 Hybrid Congress.