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637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Clinical Features of Myeloid Neoplasms with Germline GATA2 Mutations–a Systematic Review of Clinical Studies Retrieved through Extensive Searching

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Aims: Recent findings increasingly find individuals are being recognized as having germline predisposition to myeloid malignancies. GATA2 mutation is one of the most extensively studied germline mutations. However, until recently most of studies have focused on the mechanism of how GATA2 as one of the driver mutations causes malignancies. As regards the clinical features, such as the treatment and prognosis of myeloid neoplasms associated with germline GATA2 mutations, only small studies published, based on which they were insufficiently studied. Therefore, we did the systematic review to summarize the diagnosis, therapeutic methods and prognosis of myeloid malignant diseases associated with germline GATA2 mutations.
Methods: Two reviewers independently comprehensively searched Pubmed and hand searched the professional journals and the reference lists of related and included articles from Jan 1 st, 1990 until May 1 st, 2023. They also independently screened and evaluated the retrieved records and then extracted data of included studies. Studies reported clinical materials on the diagnosis, treatment and prognosis of myeloid malignant patients with germline GATA2 mutations will be included and the clinical data will be summarized. Searching strategies were as follows: #1 germline or predispo* or somat* or famil* or germ line or congenit* or altera* or non-tumor; #2 gene* or genom* or sequenc* or muta* or SNP or abnormal* or translocat* or chromosom* or frameshift* or exom* or GATA; #3 "acute myeloid leukemia" "Leukemia, Myeloid, Acute" "Myelodysplastic Syndromes" "refractory anemia" "myeloid or myeloblast*" or AML or MDS; #4 #1 and #2 and #3
Results: 2457 records were retrieved and 23 studies with 396 patients were included. Screening process was shown in Figure 1. Studies included were all small sample sized. The diagnosis age was from three to 78 years old, most of the median ages of included studies were less than 30 years indicated carriers would have symptoms in young age, on the other hand, there were also patients who began having symptoms in old age (the oldest 78 years) or remained asymptomatic carriers without getting sick in the whole life. There was no sex difference. Emberger syndrome which caused lymphedema and MonoMAC and/or DCML (dendritic cell, monocyte, B-lymphocyte and NK-lymphocyte) deficiency syndromes that caused cytopenia and infections were generally appeared earlier before myeloid malignancies. Myelodysplastic syndrome (MDS), acute myeloid leukemia (AML) and chronic myelomonocytic leukemia (CMML) are common malignant diseases for patients with germline GATA2 mutations predisposition. The morbidity was not able to be calculated based on the data available. MDS was the most common myeloid neoplasm compared with AML and CMML which were always transformed from MDS. Other hematologic malignancies were rare. The disease transformation was shown from refractory cytopenia to malignant clonal hematopoiesis that caused MDS, and then transformed into leukemia. In total, 311/396 (78.5%) patients developed malignant myeloid diseases. Nine studies had done the family pedigree analysis and there were 162 family members who had the germline GATA2 mutations predisposition, in which there were 32 asymptomatic carriers (19.7%). 128 patients were reported to receive allogeneic hematopoietic stem cell transplantation (allo-HSCT), 81 (63.3%) were alive and 44 (34.4%) died of relapse or transplantation related complications. Three patients' outcome was unknown. In study Michael A. Spinner et al, survival rate was 54% by 4 years after allo-HSCT (21 patients included). Nearly all patients (15/18) with myeloid malignancies who did not receive transplantation had died. The most common cytogenetic abnormalities were monosomy 7 and trisomy 8, and other abnormalities were also common.
Conclusions: Most of germline GATA2 mutation carriers will have symptoms in young age and many of them will progress into malignant myeloid diseases. Allo-HSCT was effective to treat symptomatic patients, especially for patients with malignant hematologic diseases, and furthermore that is the only curative treatment. Asymptomatic carriers are not rare and for them regular tests are essential. More clinical studies on germline GATA2 mutations for myeloid neoplasms are needed to clarify the clinical features in this setting and improve its treatment and prognosis.

Disclosures No relevant conflicts of interest to declare.

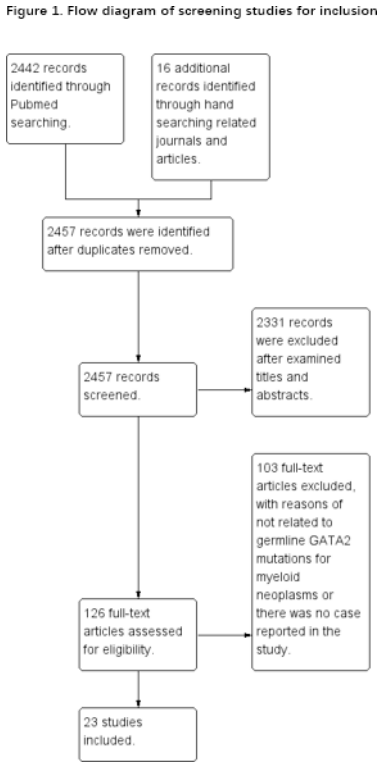

Figure 1

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