Prevalence of Hemochromatosis Gene (HFE) Mutations in Greek Patients with Myelodysplastic Syndromes

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The article by Varkonyi et al. \cite{1} regarding the incidence of hemochromatosis gene (HFE) mutations in patients with the myelodysplastic syndrome (MDS) was of great interest to us. MDS is a heterogeneous group of clonal hematopoietic disorders characterized by refractory cytopenias and a high rate of transformation to acute leukemia \cite{2, 3}. Owing to the refractory nature of their anemia, MDS patients need frequent blood transfusions entailing the accelerated development of secondary hemosiderosis \cite{2, 3}. Mutations in the \textit{HFE} gene cause increased intestinal absorption, and 50–100\% of patients with hereditary hemochromatosis (HH) are homozygous for the C282Y mutation \cite{4–6}. Furthermore, compound or sole heterozygosity for the mutations C282Y and H63D provide increased capability of iron absorption and in particular circumstances lead to an iron-replete state \cite{7–9}.

Interestingly, in the study of Varkonyi et al. \cite{1}, a high incidence of \textit{HFE} mutations was established among 50 Hungarian MDS patients \cite{1}, implying the possible need of such testing in MDS patients. However, completely different results were observed in Greek patients with MDS. In our study, 54 patients (40 males and 14 females) with MDS were analyzed. Twenty-three patients with RA, 6 with RARS, 12 with RAEB, 6 with RAEBt, and 7 with CMML, were screened for C282Y and H63D point mutations of the \textit{HFE} gene by PCR and enzyme digestion analysis, as described previously \cite{10}. Thirty-six out of 54 patients needed blood transfusions, 18 had received more than 10 blood units and 4 of them displayed an iron-replete state (characterized by elevated levels of plasma ferritin) and were treated by chelation therapy. After transformation to acute leukemia, one of them eventually developed secondary hemochromatosis (established by elevated levels of amino-transferases, and computer tomography imaging analysis of liver and heart).

Fifteen out of 54 patients (27.77\%) were H63D heterozygous, but none displayed a C282Y mutation or was H63D homozygous. Comparing the incidence of \textit{HFE} mutations between MDS patients and blood donor controls \cite{10}, we did not find a significant difference (p = 0.20, independent TTEST). From the patients displaying iron overload, only 1 was H63D heterozygous, while the other 3 (the patient displayed secondary hemochromatosis among them) were C282Y and H63D negative.

In conclusion, we did not find a marked chance of carrying a \textit{HFE} mutation in our sera nor did we find any relationship between \textit{HFE} mutations and iron overload. It was interesting that the absence of a relationship between \textit{HFE} mutations and iron overload was also established in the study of Varkonyi et al. \cite{1}. Moreover, the low prevalence of \textit{HFE} mutations in our sera is in concordance with previous studies from Southern Europe, where the incidence of \textit{HFE} mutations both in the normal population and in patients with HH is lower than elsewhere \cite{5, 6, 10}. It is obvious that the \textit{HFE} mutational analysis cannot predict iron overload in MDS patients, and a such extensive genetic testing is not justified for MDS patients when it is not clear how to predict which patients are likely to develop iron overload syndromes. Moreover, it is possible that mutated genes other than \textit{HFE} may contribute to iron homeostasis in Southern Europe.
References


