progression to acute myeloid leukemia (AML). Next-generation sequencing (NGS) has contributed to elucidating the pathogenesis of MDS through the identification of molecular drivers and secondary genetic events. While approximately 50% of MDS patients present chromosomal alterations, over 90% have somatic mutations detected. Several studies have shown that somatic mutations are important prognostic biomarkers. The Revised International Scoring System (IPSS-R) is the most used tool for risk stratification in MDS. The treatment of MDS is based on stratifying patients into low-risk (IPSS-R ≤ 3.5, i.e., very low, low, or intermediate) versus high-risk MDS (IPSS-R ≥ 4.0, i.e., intermediate, high, or very high risk). The IPSS-R is based on hematological and cytogenetic features but does not include molecular data. In 2022, the Molecular IPSS (IPSS-M) was developed, considering hematological, cytogenetic, and somatic mutations parameters in 31 genes. In this context, this study compared the risk stratification results in 13 MDS patients using the IPSS-R and IPSS-M tools. All patients had karyotype and NGS (panel of 40 genes) results performed on bone marrow samples. The average age of the patients was 69 years, and the median survival was 18 months. Eight (61.5%) patients had a normal karyotype. The detected cytogenetic alterations were: complex karyotype, del (9q), and -Y. In 10 patients (76.9%), between 1 to 5 mutations (average of 2.1 mutations) in 12 genes were detected, with *TP53* and *TET2* genes being the most frequently mutated. The VAF (variant allele frequency) of the identified mutations was >5%. The IPSS-R classified eight patients (61.5%) as low risk (IPSS-R < 3.5), with three patients (37.5%) being reclassified by IPSS-M. In these cases, mutations were identified in at least two genes, with *ASXL1*, *BCOR*, and *IDH2* being prominent, which are associated with a worse prognosis. In one of these cases, an *SF3B1* mutation, associated with a good prognosis, was also identified but was co-occurring with *DNMT3A* and *JAK2* mutations. Five patients (38.5%) were classified as high risk by IPSS-R (IPSS-R > 4.0), and IPSS-M reclassified one high-risk patient to very high risk and one intermediate-risk patient to very high risk. In these cases, mutations were also identified in genes associated with adverse prognosis, such as *ASXL1*, *BCOR*, *RUNX1*, *STAG2*, and *U2AF1*. It should be emphasized that in cases reclassified by IPSS-M, mutations in genes frequently mutated in MDS were identified. The investigation of gene mutations is important in identifying patients at high risk of progression to AML, allowing for early aggressive therapy. Genomic tests are still costly tools and, therefore, limited to a small portion of MDS patients, limiting the applicability of IPSS-M.

https://doi.org/10.1016/j.htct.2023.09.815

MYELODYSPLASTIC SYNDROME AFTER CHEMOTHERAPY FOR SOLID TUMOR: RISK FACTORS

TF Dios [a], CF Dios [b], EM Franzotti [b]

[a] *Universidade de Brasília (UnB), Brasília, Brazil*
[b] *Centro Universitário Euroamericano (UNIEURO), Brasília, Brazil*

Introduction: Chemotherapy was one of the biggest life changing discoveries. It has prolonged the life expectancy of cancer patients. However, one of its complications is related to secondary neoplasm such as myelodysplastic syndrome (MDS). **Objective:** This review's objective is to inform the health professionals the risk factors of one complication of the chemotherapy: secondary MSD. Condition that, even being rare, must be emphasized for having a great impact on life expectancy. **Methods:** Literature revision. The databases used were PubMed, SciELO and Google Scholar. The terms used in the search were: "myelodysplastic syndrome", "solid tumor", "chemotherapy". **Results:** Chemotherapy is related to therapy acute myeloid leukemia (tAML) and therapy related myelodysplastic syndrome (tMDS), which form a concept called therapy related myeloid neoplasm (t-MN). The prognosis of t-MN has an overall survival from 8 to 10 months. The t-MDS has been described in 0,08-0,83% of adverse events of chemotherapy depending on the solid tumor type. Approximately three-quarters of the cases happen in the first 5 years after the chemotherapy. Anticancer agents associated with the disease are alkylating agents and topoisomerase inhibitors (TI), agents used in 21% and 12 % of initial cancer therapy, respectively. Patients who receive alkylating agents can present with t-MDS, which often progresses rapidly to t-AML, but patients who receive TI usually present directly with t-AML. The risk of t-MN is associated with the drug doses, for example the incidence of t-MN in breast cancer patients in protocols of intensified and standard doses of cyclophosphamide was 1.01% and 0.21 %, respectively. The prevalence of t-MN is higher in young people. Furthermore, a population-based cohort study indicated elevated risk of t-MN after chemotherapy in 22 of the 23 solid tumors, colon being the exception. The site of the tumors that have more risks are bone/soft tissue, testicular and ovarian. **Conclusion:** The risk factors of developing a tMDS must be evaluated after the treatment of a solid tumor. This information helps the physician to be more aware of some patients that have associated risk factors, like anticancer agents, chemotherapy doses, age and tumor site. In any patient postchemotherapy, it is needed to investigate when there is a clinical presentation of fatigue, infections, bruising or in the case of cytopenias, even in asymptomatic patients, a possible presentation of tMDS.

https://doi.org/10.1016/j.htct.2023.09.816

MYELODYSPLASIA/MYELOPROLIFERATIVE WITH RING SIDEROBLAST AND THROMBOCYTOSIS OR UNCLASSIFIABLE (MDS/MPNI)

MM Garcia, SLBG Oliveira, ACP Silva, CM Freitas, JPB Júnior, JOR Cassiano, RDA Conserva, ERM Neri, VM Sthel, VLP Figueiredo

Hospital do Servidor Público do Estado de São Paulo (HSPE), Instituto de Assistência Médica ao Servidor Público Estadual (IAMSPE), São Paulo, Brazil

Introduction: Myelodysplasia/ myeloproliferative with ring sideroblasts and thrombocytosis (MDS/MPNRST) presents with anemia and platelets greater than ≥450,000 /mm^3, >15% RS, or >5% with the SF3B1 mutation in the absence of the 5q deletion and blasts <1% in peripheral blood and <5% in bone marrow. Megakaryocytes are atypical resembling myelofibrosis and essential thrombocythemia. The most frequent mutations are SF3B1 (93%), JAK2 (57%), TET2 (25%), DNMT3A (15%), ASXL1 (15%). Mean age 71-75 years with an annual acute myelogenous leukemia (AML) transformation rate of 1-2%. The difference for myelodysplasia/ myeloproliferative unclassifiableMDS/MPNU is that the latter has a greater number of blasts and a greater risk of transformation to AML. Anemia is important with need for transfusion and risk of arterial and/or venous thrombosis in around 20% of cases and can be fatal. There are reports of vasomotor symptoms such as headache, palpitations, paresthesia, atypical chest pain and erythromelalgia. Some patients have acquired von Willebrand disease, particularly in the presence of extreme thrombocytosis (>1000×109/L) and risk of bleeding with antiplatelet therapy. Currently, there are no general guidelines for the treatment of this pathology, the use of hydroxyurea, alpha interferon, anagrelide and busulfan has been described. Anemia is treated with red blood cell transfusion or erythropoietin. Median survival was around 70 months for MDS/MPNRST and 21.8 months for MDS/MPNU. The AZAVIT+ABCDEF protocol, linked to the Plataforma Brasil CAAE: 53015421.0.0000.5463, consists of azacytidine associated with high doses of vitamins (B1, C and D) with erythropoietin and filgrastim, started after signing the consent form. Goal: Report a clinical case of a patient in a reference service. Method: data collection in HSPE's digital system. **Clinical case:** Male, 73 years old, with asthenia, weight loss of 15 kg, night sweats and recent herpes zoster. Hb: 7.1 g/dL, leukocytes: 4680/mm^3, platelets: 819,000/mm^3, Myelogram: Dysplastic alterations in the 3 lineages with 15.6% of blasts. Medullary iron with 25% ringed sideroblasts, positive blast immunophenotyping for: CD13, CD34, CD117, CD45, HLA-DR, CD38, CD105, partial CD7 and Bone marrow biopsy: hypercellular with dysplastic alterations in the 3 lineages with increased shapes precursors, moderate dysmegakaryocytopoiesis and dense reticulin tissue. Karyotype: 46, XY. Initially classified as (MDS/MPNRST) and reclassified to MDS/MPNU due to having 15.6% blasts in the bone marrow. The patient received 8 cycles of the protocol. Initially, maintenance of anemia with an increase in platelets, reaching 1,266,000/mm^3. After the 2nd cycle, there was a drop in platelets and normalization of hemoglobin. Currently: Hb: 12.2 g/dL, leukocytes: 3630/mm^3, platelets: 162,000/mm^3 in July/23. Myelogram and immunophenotyping: hypercellular with dysplastic alterations and without blasts. The observed toxicity was mild joint pain. Discussion: We believe that the protocol can promote differentiation by increasing the transcription of factors related to differentiation, improving aerobic metabolism and promoting immunomodulation. **Conclusion:** The hematological response was important with an improvement in the patient's quality of life and possibly in the gain of survival. the AZAVIT-ABCDEF protocol should be analyzed in a prospective cohort in future studies.

https://doi.org/10.1016/j.htct.2023.09.817

PROPOSTA DE REALIZAÇÃO DE PAINEL GENÉTICO REDUZIDO PARA AVALIAÇÃO DE VARIANTES GENÉTICAS EM NEOPLASIAS MIELODISPLÁSICAS

MP Pinto, JHS Maués, FS Niemann, FV Pericole, MP Colella, PM Campos, STO Saad

Centro de Hematologia e Hemoterapia (Hemocentro), Universidade Estadual de Campinas (UNICAMP), Campinas, DP, Brasil

Introdução: As Neoplasias Mielodisplásicas (NM) surgem de alterações clonais nas células tronco hematopoiéticas, causando citopenias e risco de desenvolver leucemia mieloide aguda (LMA). Mutações genéticas patogênicas têm impacto terapêutico e prognóstico, mas exomas e painéis genéticos tradicionais geram dados complexos, de interpretação incerta e de alto custo. Estudos de NGS indicam poucos genes com potencial prognóstico e terapêutico, mas a validação desses dados em populações brasileiras ainda não ocorreu. **Objetivo:** Avaliar a incidência das mutações mais prevalentes e de significado clínico relevante em pacientes brasileiros com NM e propor um painel genético reduzido. **Métodos:** O estudo incluiu pacientes com NM acompanhados no Hemocentro da Unicamp de 2020-23. Dados clínico-laboratoriais foram coletados de prontuário. As mutações foram identificadas por sequenciamento de DNA com o painel TruSight Myeloid, abrangendo 54 genes. Foram usados para análise dos dados os softwares DRAGEN Amplicon, VarAFT, CancerVar e Maftools. O estudo foi aprovado pelo CEP e todos os pacientes assinaram o TCLE. **Resultados:** Foram incluídos no estudo 31 pacientes: sexo 12F/19M, idade mediana 68 anos (27-89). A classificação OMS 2016 foi: MDS-SLD (n = 4), MDS-MLD (n = 13), MDS-EB1 (n = 4), MDS-RS-SLD (n = 1), MDS-RS-MLD (n = 8), MDS-del(5q) (n = 1). Quanto ao IPSS-R, as categorias de risco foram: muito baixo (n = 6), baixo (n = 11), intermediário (n = 4), alto (n = 8), muito alto (n = 1), NA (n = 1). Parâmetros hematimétricos: Hb 10,05 g/dL (6,7 – 14,1), neutrófilos 1650 cél./mm^3 (268-5534) e plaquetas 164 mil cél./mm^3 (130 – 854). A análise genética revelou mutações em: TET2 (48%, n = 15), principalmente missense, patológico em 4; SF3B1 (29%, n = 9, sendo 8 com sideroblastos em anel), todas missense, patológico em 3; U2AF1 (16%, n = 5), todas missense, patogênica em 3. SRSF2, ZRSR2 e STAG2 mutadas (13%, n = 4 cada), com padrões frameshift, inframe e nonsense, respectivamente. ASXL1, EZH2 e ETV6 apresentaram mutações (10%, n = 3 cada). Outras mutações patogênicas de menor prevalência (<5%): SH2B3, ASXL1, FLT3, DNMT3A, NF1, JAK2, EZH2. **Discussão:** Na população estudada, há alta prevalência de mutações em 8 genes, corroborando com estudos anteriores que mostram um grupo restrito de genes frequentemente mutados em NM. As mutações em TET2 são associadas a maior progressão da NM e maior risco de evolução para LMA, enquanto mutações em SF3B1 conferem melhor prognóstico e terapia alvo específica. Mutações em U2AF1 e STAG2 relacionam-se ao aumento do risco de progressão para LMA, e SRSF2 e ZRSR2, apesar de citadas em outras fontes, ainda não possuem impacto patogênico bem estabelecido. Ressalta-se que as mutações patogênicas mais frequentes foram missense em genes que codificam proteínas que atuam na clivagem do