um alto risco de conversão para leucemia mieloide aguda (LMA). O diagnóstico advém da suspeita, principalmente entre idosos, de anemia refratária, leucopenia ou trombocitopenia, sendo a comprovação definitiva advinda dos achados de alterações citogenéticas específicas e mutações somáticas. A análise socioepidemiológica da SMD ainda é rasa, pois conta com poucos estudos para um consenso mundial. Porém, estudos realizados em países europeus e nos Estados Unidos, com grandes populações, demonstram que a média da idade, de diagnóstico da doença, é acima dos 60 anos, chegando, nos Estados Unidos, a 76 anos. Além disso, em estudo realizado no Brasil, pôde-se perceber maior número de casos na cor de pele branca. **Conclusão:** Apesar de poucos estudos, nota-se que as pesquisas vigentes convergem para um perfil socioeconômico-cultural semelhante. Dessa forma, mais estudos epidemiológicos devem ser desenvolvidos para aumentar a precisão do perfil dos pacientes que possuem SMD e, assim, desenvolver manobras de contenção e cura da doença.

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NEOPLASIA MIELÓIDE ASSOCIADA A MUTAÇÃO GERMINATIVA DO GATA2

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Introdução: O GATA2 é um fator de transcrição com dois domínios de Zinco que é importante para a hematopoese, incluindo manutenção do *pool* de células progenitoras hematopoéticas (CPH), maturação de linfócitos B, Nk e monócitos. A deficiência do GATA2, causada por mutação germinativa neste gene, está associada a um amplo espectro de manifestações clínicas, incluindo anemia aplástica, síndrome mielodisplásica (SMD), leucemia mielóide aguda (LMA) infecção pulmonar por micobactérias, proteinólise alveolar, aumento do risco de trombose venosa profunda, fenômenos autoimunes, surdez neurossensorial e maior suscetibilidade a infecções por HSV e HPV. Os pacientes com deficiência do GATA2 possuem maior risco de evolução para SMD e LMA. Diferentes trabalhos tem demonstrado que aproximadamente 20% dos pacientes pediátricos com diagnóstico de SMD apresentam deficiência de GATA2. Em pacientes com monossomia do 7 esta prevalência aumenta para aproximadamente 30%. Contudo, a idade de apresentação do primeiro sintoma, o espectro de manifestações clínicas e a evolução para SMD e LMA é muito variável. **Objetivo:** Relato de neoplasia mielóide associada a mutação germinativa do GATA2, com progressão para SMD com excesso de blastos 2. **Relato de caso:** Mulher, 81 anos, estava em acompanhamento ambulatorial trimestral no HC-FMRP-USP devido ao diagnóstico de deficiência de GATA2, com história prévia de síndrome mielodisplásica hipoplásica e duas meningoencefalites por EBV em 2019. Cariótipo de 2018, demonstrava 46,XX,der(7)t(1;7)(q10;p10)[20]. Há 15 dias da data de admissão hospitalar, apresentou queda do estado geral, associado a astenia e dispneia. Hemograma evidenciava pancitopenia, sendo que o esfregaço do sangue demonstrava 11% de blastos. Realizado mielograma que demonstrou série granulocítica hipocelular, com atraso de maturação. A contagem diferencial demonstrava a presença de 14% de blastos de tamanho intermediário, com relação núcleo/citoplasma intermediária, núcleo com cromatina frouxa e 1 nucléolo visível, citoplasma basofílico, com poucos grânulos, sem vacúolos. O cariótipo referente a esta puncão evidenciou 46?2,XXX,der(7)t(1;7)(q10;p10),+8,+16,+18,+21+mar,inc[cp10]. Dessa forma, foi comprovada morfologicamente e citogeneticamente a evolução para SMD com excesso de blastos 2. **Discussão:** O gene GATA 2, localizado no cromossomo 3, tem função essencial na regulação e transcrição de genes envolvidos na hematopoese e manutenção das CPH. Sua deficiência causa interferência nas vias de diferenciação, com destaque para monocitopoese e linfopoese B e NK. Devido a ampla variedade de apresentação clínica, incluindo manifestações pulmonares, hematológicas, infecciosas, neurológicas e autoimunes, e a grande variação na data do início dos primeiros sintomas é necessário o reconhecimento precoce desta entidade com intuito de minimizar as complicações relacionadas a esta patologia. **Conclusão:** A capacidade oncogênica da deficiência de GATA2 encontra-se bem estabelecida na literatura, estando incluída na última classificação da OMS de malignidades hematológicas como entidade na leucemia mieloide aguda. Destaca-se o conhecimento desta alteração genética pelos hematologistas, ainda que se apresente em indivíduos adultos com quadro de falência medular, pois impacta no seguimento e tratamento singular desses pacientes e no rastreio familiar muitas vezes necessário.

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OUTCOME OF PATIENT WITH POLYCYTHEMIA VERA WITH PSYCHIATRIC SYMPTOMS

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Introduction: Polycythemia Vera (PV) is a chronic myeloproliferative neoplasia generatingan accumulation of erythrocytes in the peripheral blood (polyglobulia). Reportedprevalence is close to 2 cases per 100 thousand inhabitants/year worldwide. The disease is described as polysymptomatic but with unspecificmanifestations, such as plethora, itching and splenomegaly. Thus, a diagnosis of polycythemia is usually suspected when it is found in casual blood tests and suchfinding cannot be explained by secondary causes. Psychiatric symptoms have been described for the disease, mostly in papersfrom the beginning of the 20th century, but are rare in current clinical practice. **Case report:** Male patient, 54 years old, was admitted to the emergency room withpsychiatric symptoms which started one month prior. An organic origin wassuspected, due to the patient's age and healthy condition, and was hospitalized forclinical control and

investigation. Investigation showed polycythemia and on the thirdday of hospitalization, he was discharged with psychiatric medication. After four days, the patient returned with the same symptoms. He wastransferred to another hospital, where he was discharged with more psychiatricdrugs. He maintained an outpatient follow-up with the psychiatric team, oligosymptomatic, reducing the dose of medications. Six months after the second hospitalization, the patient was taken to thehospital again and new tests were requested. Due to hyperviscosity a phlebotomywas performed. After four phlebotomies and reintroduction of psychiatric medication, there was an improvement in the symptoms and laboratory stabilization, and thepatient was discharged. He started an follow-up with hematology and psychiatry. The patient gatheredcriterias for starting PV treatment with hydroxyurea and phlebotomies, leading to acomplete improvement of the condition. The psychiatric team suspended themedications after one year due to adverse reactions to the treatment and absence ofsymptoms. **Discussion:** Initial studies from the 1920's described the diseases as variablesymptomatology with mainly neurologic and eventually psychiatric symptoms. Reports of such symptoms became more scarce as the years went by. Thepopularization of hemograms, allowing for earlier diagnosis, and more effectivetreatment protocols may have contributed for a reduction of complicated cases, making the psychiatric symptoms rarer. When they appear, psychiatric symptoms are referred as being resistant topsychiatric treatment but responsive to the hematological one. Literature shows thatthese symptoms remain uncontrolled with the use of antipsychotics, but disappearwith cytoreduction even without the usage of psychiatric drugs. **Conclusion:** The case stands out for its exceptionality: psychiatric and neurological manifestations are rare and were already considered such in older studies. Despitethis, the case behaved consistently with the literature. The patient had polyglobuliasince the onset of the condition, was refractory to psychiatric treatment, even havingside effects from it, and was responsive to hematological treatment. Lastly, the case warns of the importance of cautious and complete analysis of complementary exams. As this did not happen, the patient stayed a greater periodwith uncontrolled mental status and increased thromboembolic risk, the main causeof death in these patients.

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PHASE 2 STUDY OF PEVONEDISTAT + AZACITIDINE VERSUS AZACITIDINE IN PATIENTS WITH HIGHER-RISK MYELODYSPLASTIC SYNDROMES/CHRONIC MYELOMONOCYTIC LEUKEMIA OR LOW-BLAST ACUTE MYELOGENOUS LEUKEMIA (NCT02610777)

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Goals: Pevonedistat, the first small-molecule inhibitor of the NEDD8-activating enzyme, disrupts proteasomal degradation of select proteins and has shown encouraging clinical activity in combination with azacitidine in acute myelogenous leukemia (AML). This phase 2, randomized, open-label trial evaluated the efficacy and safety of pevonedistat+azacitidine vs azacitidine in patients with higher-risk myelodysplastic syndromes (MDS)/chronic myelomonocytic leukemia (CMML) or low-blast (LB) AML. **Materials and methods:** Patients with higher-risk MDS/CMML (Revised International Prognostic Scoring System risk >3, including intermediate [≥5% blasts], high, or very high risk) or LB-AML who were naïve to hypomethylating agents were randomized 1:1 to receive pevonedistat intravenously (IV) (20 mg/m^2 days 1, 3, 5) + azacitidine IV/subcutaneous (75 mg/m^2 days 1–5, 8, 9) (n = 58), or azacitidine alone (n = 62), in 28-day cycles until unacceptable toxicity, relapse, transformation to AML, or progression. The study was powered on an endpoint of event-free survival (EFS; time from randomization to death/transformation to AML). Overall survival (OS), overall response rate (ORR; complete remission [CR] + partial remission [PR] + hematologic improvement [HI] in higher-risk MDS/CMML, or CR + CR with incomplete blood count recovery [CRi] + PR in LB-AML) and safety also were assessed. Patient-reported health-related quality of life (HRQoL) was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30. Mutational profiling was performed on