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

screening bone marrow aspirate samples. **Results/Discussion:** In the intent-to-treat (ITT) population (n = 120), EFS trended longer with pevonedistat+azacitidine vs azacitidine (median 21.0 vs 16.6 months; hazard ratio [HR] 0.67; 95% confidence interval [CI], 0.42–1.05; *P* =.076) and was longer in higher-risk MDS (median 20.2 vs 14.8 months; HR 0.54; 95% CI, 0.29–1.00; *P* =.045). Median OS was 21.8 vs 19.0 months (HR 0.80; 95% CI, 0.51–1.26; *P* =.334) in the ITT population, 23.9 vs 19.1 months (HR 0.70; 95% CI, 0.39–1.27; *P* =.240) in higher-risk MDS (n = 67), and 23.6 vs 16.0 months (HR 0.49; 95% CI, 0.22–1.11; *P* =.081) in LB-AML (n = 36) with pevonedistat+azacitidine vs azacitidine, respectively. In response-evaluable patients (n = 108), ORR with pevonedistat+azacitidine vs azacitidine was 71% vs 60%; in higher-risk MDS (n = 59), ORR was 79% vs 57%, and CR rate was 52% vs 27%. Median azacitidine dose intensity was 97% (pevonedistat+azacitidine) vs 98% (azacitidine). Grade ≥3 adverse events occurred in 90% (pevonedistat+azacitidine) vs 87% (azacitidine) of patients (most common: neutropenia [33% vs 27%], febrile neutropenia [26% vs 29%], anemia [19% vs 27%], thrombocytopenia [19% vs 23%]). No difference was observed in patient-reported HRQoL between arms, with similar mean scores maintained from study entry to end of treatment. Clinical activity was observed in patients with higher-risk MDS or LB-AML harboring poor prognostic mutations. **Conclusions:** Pevonedistat+azacitidine led to longer EFS vs azacitidine in higher-risk MDS, had a comparable safety profile to azacitidine alone, and azacitidine dose intensity was maintained. A randomized phase 3 trial (NCT03268954) is ongoing to evaluate further.

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SÍNDROME MIELODISPLÁSICA ASSOCIADA A TUMOR DE SACO VITELÍNICO PRIMÁRIO DE MEDIASTINO: RELATO DE CASO

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Introdução: As síndromes mielodisplásicas (SMD) compreendem um grupo de neoplasias hematológicas caracterizadas por hematopoiese clonal, uma ou mais citopenias, maturação mieloide anormal e risco aumentado de leucemia mieloide aguda. Os tumores de células germinativas primários do mediastino (TCGM) correspondem a 10 a 20% das neoplasias mediastinais. O tumor de saco vitelínico mediastinal é um subtipo de TCGM e acomete, sobretudo, homens jovens. A associação destes tumores com cânceres hematológicos é muito rara. **Objetivo:** Relatar caso de rara associação entre TCGM e SMD. Material e métodos: Coleta de dados de prontuário clínico e revisão bibliográfica. Relato de caso: Homem, 20 anos, previamente hígido, foi internado com queixa de astenia há 2 semanas e síncope, sem sintomas B. Ao exame físico, constatou-se palidez e esplenomegalia discreta. Em avaliação laboratorial havia anemia grave (Hb 3,8 g/dL VCM 84,6 fL HCM 30,6 g/dL), ferritina elevada (10733 ng/dL) e desidrogenase láctica sérica (186 U/L). Dosagem sérica de alfa feto proteína (AFP) revelou-se elevada (231 ng/mL - VR 0,9-8,8). Sorologias para HIV e hepatites virais eram não reagentes. Iniciado suporte transfusional com concentrado de hemácias. Todavia, houve progressão para pancitopenia em intervalo de 14 dias. Mielograma evidenciou medula óssea (MO) hipocelular, com displasias eritroide e granulocítica e hipoplasia megacariocítica, sem sinais de infiltração por câncer. Biópsia de MO foi compatível com SMD. Análise por tomografia computadorizada (TC) de tórax, complementar a alergamento de mediastino detectado em radiografia de tórax, evidenciou massa mediastinal (8,6 x 6,8 cm). Estudo de abdome por TC documentou esplenomegalia moderada e estrutura ovoide inguinal direita (análise por ultrassonografia testicular revelou criptorquidia à direita com diminuição do volume testicular). Análise de biópsia transtorácica de massa mediastinal foi compatível com tumor de saco vitelínico por positividade em análise imunohistoquímica para AFP e negatividade para os marcadores CD57, Citoceratina 7 e 20, p63, PAX8, fosfatase alcalina placentária e TdT. Em cenário de falência medular e elevada dependência transfusional, quimioterapia (QT) com idarrubicina, citarabina, etoposídeo e cisplatina foi iniciada. Paciente morreu após 9 dias devido sepse. Discussão: Os TCGM são cânceres raros, de prognóstico desfavorável, decorrentes da transformação maligna de elementos germinativos sem foco gonadal primário. O tratamento consiste em QT com esquemas baseados em bleomicina, etoposide e cisplatina, complementado por ressecção cirúrgica. O prognóstico ruim dos TCGM relaciona-se à irressecabilidade tumoral. Um em cada 17 pacientes com TCGM apresenta associação com câncer hematológico com sobrevida média de 5 meses, mais comumente leucemia mieloide aguda e SMD. No presente caso, o principal desafio foi a associação com SMD com grave disfunção de MO. As leucemias agudas associadas a TGCM carregam alterações genômicas características (isocromossomo 12p, mutações de ativação da via RAS-PI3K-AKT ou inativação da via TP53), sendo os desfechos ruins mesmo após QT agressiva. **Conclusão:** A associação de TCGM com cânceres hematológicos apresenta curso clínico extremamente agressivo, sendo o tratamento ineficaz. O reconhecimento desta associação para diagnóstico precoce pode permitir a inclusão destes pacientes em ensaios clínicos, para definição de melhor tratamento.

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SÍNDROME MIELODISPLÁSICA COM DEL(5Q) ISOLADA: RELATO DE EXPERIÊNCIA COM USO DE LENALIDOMIDA

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Introdução: A Síndrome Mielodisplásica (SMD) corresponde à um grupo de doenças clonais das células tronco