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Who classification of tumors 5th edition

Redefining the biological basis of lineage-ambiguous leukemia through genomics: BCL11B deregulation in acute leukemias of ambiguous lineage. Therapy-related myelodysplastic syndromes deserve specific diagnostic sub-classification and risk-stratification-an approach to classification of patients with t-MDS. Indeed, the recent identification of BCL11B rearrangements in MPAL T/Myeloid, ETP-ALL, acute leukaemia of ambiguous lineage (ALAL) and a subset of AML with minimal differentiation suggests a biologic continuum across these entities, a finding with likely implications on future editions of the classification [58,59,60,61].Acute erythroid leukaemia (AEL) (previously pure erythroid leukaemia, an acceptable related term in this edition) is a distinct AML type characterized by neoplastic proliferation of erythroid cells with features of maturation arrest and high prevalence of biallelic TP53 alterations. Cytometry B Clin Cytom. AML transformation of MDS and MDS/MPN continues to be defined under AML-MR in view of the broader unifying biologic features. Khoury orcid.org/0000-0003-2621-35841, Eric Solary orcid.org/0000-0002-8629-13412, Oussama Abla3, Yassmine Akkari orcid.org/0000-0002-3072-73884, Rita Alaggio5, Jane F. Distinguishing AML with BCR::ABL1 from initial myeloid blast phase of CML can be challenging, and additional evidence continues to be needed to better characterize this AML type. 2015;29:1123–32.Article CAS PubMed Google Scholar Wang W, Cortes JE, Tang G, Khoury JD, Wang S, Bueso-Ramos CE, et al. Less frequent mutations involve genes such as PPM1D and DNA-damage response genes that may require additional work-up for germline predisposition.Myeloid neoplasms associated with germline predisposition: A novel scalable model is introducedMyeloid neoplasms associated with germline predisposition include AML, MDS, MPN, and MDS/MPN that arise in individuals with genetic conditions associated with increased risk of myeloid malignancies. Lymphoid blast transformation in an MPN with BCR-JAK2 treated with ruxolitinib: putative mechanisms of resistance. Indeed, neoplasms that arise from lymphoid stromal cells such as follicular dendritic cell sarcoma and fibroblastic reticular cell tumor are now appropriately classified under the new chapter of “stroma-derived neoplasms of lymphoid tissues” as detailed in the companion manuscript [4].Table 14 Dendritic cell and histiocytic neoplasms.Plasmacytoid dendritic cell neoplasms: recognition of clonal proliferations detected in association with myeloid neoplasms and refinement/update of the diagnostic criteria for blastic plasmacytoid dendritic cell neoplasmMature plasmacytoid dendritic cell proliferation (MPDCP) associated with myeloid neoplasm reflects recent data showing that these represent clonal proliferation of pDCs with low grade morphology identified in the context of a defined myeloid neoplasm. As indicated above, cytopenia definitions are adopted for consistency across CCUS, MDS, and MDS/MPN. TP53 mutation status divides myelodysplastic syndromes with complex karyotypes into distinct prognostic subgroups. These criteria improve the distinction between CEL and entities such as idiopathic hypereosinophilic syndrome and hypereosinophilia of unknown significance [22]. “Blasts” in myeloid neoplasms - how do we define blasts and how do we incorporate them into diagnostic schema moving forward? Long recognized as having distinctive features, MDS-h is associated with a T-cell mediated immune attack on haematopoietic stem and progenitor cells, along with oligoclonal expansion of CD8 + cytotoxic T-cells overproducing IFNγ and/or TNFα. A threshold of 10% for myeloperoxidase by flow cytometry is valid to classify acute leukemia of ambiguous and myeloid origin. 103SIHMDS, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, United Kingdom. 2015;125:3618–26.Article CAS PubMed PubMed Central Google Scholar Cargo C, Cullen M, Taylor J, Short M, Glover P, van Hoppe S, et al. Characteristics of RAS pathway mutations in juvenile myelomonocytic leukaemia: a single-institution study from Korea. 67Clinical Research Division, Fred Hutchinson Cancer Center, Department of Medicine, Division of Medical Oncology, University of Washington, Seattle, WA, USA. Novel genetic findings are listed as subtypes under ALAL with other defined genetic alterations as additional data accrues. ApperleyMoores Cancer Center, University of California San Diego, La Jolla, CA, USARafael BejarUniversity of Milan, Fondazione Cà Granda, IRCCS, Ospedale Maggiore Policlinico, Milano, ItalyEmilio BertiService d’hématologie, oncologie et transplantation, Hôpital Maisonneuve-Rosemont, Université de Montréal, Montréal, QC, CanadaLambert BusqueDepartment of Pathology, Queen Elizabeth Hospital, Kowloon, Hong KongJohn K. The classification introduces the term myelodysplastic neoplasms (abbreviated MDS) to replace myelodysplastic syndromes, underscoring their neoplastic nature and harmonizing terminology with MPN. 2006;81:484–91.Article PubMed Google Scholar Kowal-Vern A, Cotelingam J, Schumacher HR. The natural history of untreated CML before the introduction of targeted tyrosine kinase inhibitors (TKI) was biphasic or triphasic: an initial indolent CP followed by a blast phase (BP), with or without an intervening accelerated phase (AP). Thoracic Tumours is the fifth volume in the 5th edition of the World Health Organization (WHO) series on the classification of human tumours. 2022;139:323–32.Article CAS PubMed PubMed Central Google Scholar DiNardo CD, Garcia-Manero G, Kantarjian HM. 2021;21:e66–e75.Article PubMed Google Scholar Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, Ki M, et al. 2019;567:521–4.Article CAS PubMed PubMed Central Google Scholar Chakraborty R, Abdel-Wahab O, Durham BH. Rearrangements, a broad term that encompasses a range of structural genomic alterations leading to gene fusions, are part of the nomenclature of types/subtypes when there are multiple possible fusion partner genes of a biologically dominant gene (e.g., KMT2A). 85Department of Medical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, India. 2019;20:2976.Reiter A, George TI, Gotlib J. Prospective assessment of NGS-detectable mutations in CML patients with nonoptimal response: the NEXT-in-CML study. Nat Commun. Biallelic TP53 (biTP53) alterations may consist of multiple mutations or mutation with concurrent deletion of the other allele. With TKI therapy and careful disease monitoring, the incidence of progression to advanced phase disease has decreased, and the 10-year overall survival rate for CML is 80–90% [10, 11]. WHO Classification of Tumours Online is indispensable for pathologists and cancer specialists worldwide. A third component of the new structure is the introduction of a section on AML with other defined genetic alterations, a landing spot for new and/or uncommon AML subtypes that may (or may not) become defined types in future editions of the classification. Plasmacytoid dendritic cells proliferation associated with acute myeloid leukemia: phenotype profile and mutation landscape. 117Faculdade de Medicina, Universidade de São Paulo, Departamento de Patologia, São Paulo, Brazil.Open Access funding enabled and organized by Projekt DEAL.Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USAJoseph D. This change underscores the MDS/MPN nature of the disease and avoids potential confusion with CML. 2022;128:1568–70.Article PubMed Google Scholar Chen X, Fromm JR, Naresh KN. The presence of one or more cytogenetic or molecular abnormalities listed in Table 8 and/or history of MDS or MDS/MPN are required for diagnosing AML-MR.Table 8 Cytogenetic and molecular abnormalities defining acute myeloid leukaemia, myelodysplasia-related.AML with other defined genetic alterations represents a landing spot for new, often rare, emerging entities whose recognition is desirable to determine whether they might constitute distinct types in future editions. This is envisioned as a landing spot in the classification to incorporate new/rare entities whose recognition is increasing as high-throughput molecular diagnostic tools become more available. 57Department of Cellular Pathology, the Royal London Hospital, Barts Health NHS Trust, London, United Kingdom. Notwithstanding, there was broad agreement that MDS-IB2 may be regarded as AML-equivalent for therapeutic considerations and from a clinical trial design perspective when appropriate.Childhood myelodysplastic neoplasms: Enhanced specificity of disease terminology introducedChildhood MDS is a clonal haematopoietic stem cell neoplasm arising in children and adolescents (10% for myeloperoxidase positivity seems to improve specificity [81], but no consensus cutoff has been established. Genomic patterns associated with hypoplastic compared to hyperplastic myelodysplastic syndromes. An additional modification is a clarified terminology to distinguish between MDS with low blasts (MDS-LB) and MDS with increased blasts (MDS-IB), while retaining longstanding cutoffs.Table 3 Classification and defining features of myelodysplastic neoplasms (MDS).MDS with defining genetic abnormalitiesMyelodysplastic neoplasms with defining genetic abnormalities are grouped together and include: MDS with low blasts and isolated 5q deletion (MDS-5q), MDS with low blasts and SF3B1 mutation (MDS-SF3B1), and MDS with biallelic TP53 inactivation (MDS-biTP53). 2019;33:415–25.Article CAS PubMed Google Scholar Wang SA, Hasserjian RP, Tam W, Tsai AG, Geyer JT, George TI, et al. Lowering the blast cutoff to define AML was felt to suffer from the same challenges listed above and would merely replace one cutoff with another. Mutational landscape in children with myelodysplastic syndromes is distinct from adults: specific somatic drivers and novel germline variants. Classical B-findings (‘burden of disease’) and C-findings (‘cytoreduction-requiring’) have undergone minor refinements. The term MDS/MPN with neutrophilia replaces the term atypical CML. Relevant gene mutations are detected in a subset of patients with morphologically normal-appearing bone marrow, suggesting low-level clonal myeloid disease or CH in the bone marrow [68, 70]. Fanconi anaemia is a heterogeneous disorder caused by germline variants in the BRCA-Fanconi DNA repair pathway (≥21 genes) resulting in chromosomal breakage and hypersensitivity to crosslinking agents used for diagnosis. Thoracic Tumours WHO Classification of Tumours, 5th Edition, Volume 5 Edited by the WHO Classification of Tumours Editorial Board See WHO Classification of Tumours: Thoracic Tumours Read more about the WHO Classification of Tumours The 2021 WHO classification of tumors of the central nervous system (CNS), 5th edition (WHO CNS 5) [24] is built on the previous, revised 4th edition, published in 2016 (WHO2016CNS) [14], … The WHO Classification of Tumours is a series of authoritative and concise reference books, previously based on histological and molecular classification but now increasingly … This series is a synthesis of the published evidence and the practice of cytopathology, linked to the WHO Classification of Tumours, now in their 5th Edition. Erratum in Blood. Where possible, a triad of attributes was systematically applied and included: lineage + dominant clinical attribute + dominant biologic attribute. MDS/MPN with ring sideroblasts and thrombocytosis redefined based on SF3B1 mutation and renamed MDS/MPN with SF3B1 mutation and thrombocytosis. Morphological differentiation of severe aplastic anaemia from hypocellular refractory cytopenia of childhood: reproducibility of histopathological diagnostic criteria. 61Georgia Cancer Center, Augusta, GA, USA. ZNF384-rearranged B/myeloid MPAL and B-ALL have similar transcriptional profile, suggesting a biological continuum [79]. The multisystem systemic form that typically occurs in infants, with involvement of liver, spleen and/or bone marrow, runs a protracted course but often resolves slowly, either spontaneously or with chemotherapy. Time to blur the blast boundaries. Furthermore, the histiocytic neoplasm and associated lymphoma/leukaemia often show additional genetic alterations exclusive to each component, suggesting that divergent differentiation or transdifferentiation occurs from a common lymphoid progenitor clone [100, 102, 103]. The latter factor is gaining increased recognition as cancer survival is prolonged and the incidence of late complications of therapy such as secondary myeloid neoplasia increases. ALK-positive histiocytosis: a new clinicopathologic spectrum highlighting neurologic involvement and responses to ALK inhibition. Leuk Res. 2021;34:101329.Article CAS PubMed Google Scholar van den Ancker W, Westers TM, de Leeuw DC, van der Veeken YF, Loonen A, van Beckhoven E, et al. Kratz orcid.org/0000-0003-4120-587332, Xiao-Qiu Li33, Megan S. This series (also known as the WHO Blue Books) is regarded as the gold standard for the diagnosis of tumours and comprises a unique synthesis of histopathological diagnosis with digital and molecular pathology. More information here. AML-MR replaces the former term AML “with myelodysplasia-related changes”, and its diagnostic criteria are updated. OA, JFA, RB, EB, LB, WC, XC, JKC, IC, NCPC, MTE, ET, JFE, LF, MF, UG, TH, CH, SH, JHJ, RKS, CPK, XQL, KL, SL, AM, SM, PM, YN, RN, EP, KPP, NP, JP, UP, IR, PT, JT, SV, WW, WX, and CY contributed as responsible authors in the book. MDS genetic types updated to include MDS-5q, MDS-SF3B1 and MDS-biTP53 Hypoplastic MDS (MDS-h) is recognized as a distinct disease type. Histiocytoses are also sometimes associated with myeloproliferative neoplasms [104], sharing mutations with CD34+ myeloid progenitors [105], and with CH [106]. Individuals with germline pathogenic variants in GATA2, DDX41, Fanconi anaemia (FA) or telomerase complex genes can have hypoplastic bone marrow and evolve to MDS and/or AML and do not respond to immunosuppressive treatment.As the number of dysplastic lineages is usually dynamic and often represents clinical and phenotypic manifestation of clonal evolution – rather than per se defining a specific MDS type, the distinction between single lineage and multilineage dysplasia is now considered optional. 2019;11:1951.Wang W, Beird H, Kroll CJ, Hu S, Bueso-Ramos CE, Fang H, et al. Please click here to access the online beta versions. Khoury, Eric Solary or Andreas Hochhaus. Hodge29, Shimin Hu orcid.org/0000-0001-7110-38141, Joop H. 2012;26:1537–46.Article CAS PubMed PubMed Central Google Scholar Wen XM, Hu JB, Yang J, Qian W, Yao DM, Deng ZQ, et al. Additionally, the recommended threshold for dysplasia is set at 10% for all lineages. 2021;5:3492–6.Article CAS PubMed PubMed Central Google Scholar Carll T, Patel A, Derman B, Hyjek E, Lager A, Wanjari P, et al. MDS with low blasts (MDS-LB) is a new term that enhances clarity. CouplandFaculty of Medicine, University of Southampton, Southampton, UKNicholas C. Thus, it is recommended that ALK immunostaining be performed for histiocytic proliferations not conforming to defined entities, to screen for possible ALK-positive histiocytosis.In most circumstances, classification of a dendritic cell/macrophage neoplasm as Langerhans cell histiocytosis/sarcoma, indeterminate dendritic cell tumor, interdigitating dendritic cell sarcoma or histiocytic sarcoma is straightforward. The incidence of CH increases with age [6]. Myeloid/lymphoid neoplasms with eosinophilia/ basophilia and ETV6-ABL1 fusion: cell-of-origin and response to tyrosine kinase inhibition. 2008;112:2965–8.Article CAS PubMed Google Scholar Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, et al. Cases of de novo myeloid sarcoma should be investigated comprehensively, including cytogenetic and molecular studies, for appropriate classification and planning therapy. 65Department of Pediatrics, Center for Cancer Cellular Therapy, Cancer Correlative Sciences Unit, Stanford University School of Medicine, Stanford, CA, USA. N Engl J Med. Expert consensus, systematic reviews or both? KratzDepartments of Pathology and Oncology, Fudan University, Shanghai, ChinaXiao-Qiu LiDepartment of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, USAMegan S. Nat Med. Specifically, MDS, unclassifiable, which was present in the prior edition, is removed.The boundary between MDS and AML is softened, but the 20% blast cutoff to define AML is retainedReassessment of the bone marrow blast percentage defining the boundary of MDS-IB2 and AML has been advocated for several cogent reasons and in view of novel therapeutic approaches that show efficacy in patients currently classified as MDS or AML with 10-30% myeloid blasts [37,38,39]. 2016;127:2672–81.Article CAS PubMed PubMed Central Google Scholar Feldman AL, Arber DA, Pittaluga S, Martinez A, Burke JS, Raffeld M, et al. 2017;376:917–27.Article CAS PubMed PubMed Central Google Scholar Kalmanti L, Saussele S, Lauseker M, Müller MC, Dietz CT, Heinrich L, et al. Most AML with defining genetic abnormalities may be diagnosed with 60% of cases [17, 18].Chronic eosinophilic leukaemia (CEL) is a multi-system disorder characterized by a sustained clonal proliferation of morphologically abnormal eosinophils and eosinophil precursors resulting in persistent hypereosinophilia in blood and bone marrow [19,20,21]. Additional studies are needed to determine the optimal approach to classifying individuals with unexplained clonal monocytosis [50] who do not fit the new diagnostic criteria of CMML.Table 6 Diagnostic criteria of chronic myelomonocytic leukaemia.Two disease subtypes with salient clinical and genetic features are now formally recognized based on WBC: myelodysplastic CMML (MD-CMML) (WBC