Best Practice & Research Clinical Haematology 32 (2019) 193–195

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/issn/15216926

Preface

Large granular lymphocytic and other rare lymphoid leukemias

This issue is dedicated to five rare lymphoid malignancies characterized by either B or T cell lineage clonal expansion including LGL leukemia, B and T cell prolymphocytic leukemia (PRL), monoclonal B-cell lymphocytosis (MBL), leukemic variants of cutaneous T-cell lymphoma (L- CTCL), and NK cell lymphoma. While chronic lymphocytic leukemia, follicular or diffuse large B cell lymphoma account for more than 70% of cases of lymphoproliferative disorders, LGL leukemia, PRL, L-CTCL, and NK cell lymphoma together represent less than 10% of cases. This special issue is an opportunity for the readers to have an overview of relatively unknown diseases having indolent or aggressive behaviour and presenting most often with abnormal lymphocytosis. In fact, LGL leukemia, B and T cell prolymphocytic leukemia, monoclonal B-cell lymphocytosis, and Sezary syndrome present systematically with abnormal lymphocytosis while NK cell lymphoma in its aggressive leukemic phase may display high levels of circulating cells. Conversely, in Mycosis Fungoides (MF), malignant cells are skin resident T cells. (see Table 1)

This review is focusing on clinico-biological features of these diseases, including phenotypic, cytogenetic and molecular features which have contributed over the recent years to a better understanding of physiopathology. A major emphasis is the importance of careful blood smear examination in patients presenting with lymphocytosis or cytopenia associated or not with skin lesions, lymphadenopathy and/or organomegaly. Phenotypic analysis routinely allows for rapid diagnosis. Important complementary tests in the diagnostic workup include karyotypic analysis, B or T cell clonality assessment using VH/JH or TRCR PCR rearrangement, and finally molecular analysis now routinely made using next generation sequencing (NGS). Specific biomarkers or mutated genes have been shown to be good surrogate markers of these diseases and should lead to innovative and targeted therapy in the next few years.

https://doi.org/10.1016/j.beha.2019.09.001
Received 2 September 2019; Accepted 2 September 2019

Table 1
Summarizes the clinicopathologic features of these lymphoid malignancies. It appears that these diseases share common characteristics, particularly acquired somatic mutations (ie Stat3, Jak 3, Stat5b …). This finding raises the possibility of including these patients in "umbrella" trials targeting the same mutation.

	Clinical characteristics	Biological features	Phenotyping	Cytogenetics	Molecular features	Innovative Therapy
LGL leukemia	Infections/ splenomegaly/ rheumatoid arthritis	Neutropenia and anemia Excess of LGL (> 0.5G/L)	T CD3+/CD5dim/CD8+/CD57+(terminal effector memory T lymphocyte) Or NK CD3-/CD16+/CD56+	< 10%, chromosome 5, 12, 14 abnormalities	Stat3 mutation (50%) Stat5b mutation (< 5%)	antiSTAT 3 antiJAK3 Bortezomib
MBL	nothing	Lymphocytosis	3 types - CLL-type MBL with < 5G/L lymphocytes - CLL-type High count lymphocytes > 5G/L - Atypical –CLL-type mbl	- Not to be done - Same as in CLL	- Not to be done - Same as in CLL	-No treatment - Same as in CLL
Leukemic phase of CTCL	Skin lesions	SS: presence of leukemic cells in blood	SS: Central memory T cells MF: effector memory T cells KIR3DL2+ (> 80%)	Losses involving 1p, 10q, 19, gains involving 4,18, 17	Numerous genes involved: CDKN2A, PTEN, RB1, genes having a role in epigenetic modification, T cell signaling and differentiation.	Mogamulizumab (antiCCR4) Durvalimab (antiPD1) antiKIR 3 DL2 Antogomir-155 (miRNA 155 inhibitor) TT1-621 (anti CD47).
T/B PRL	Splenomegaly B symptoms Lymphadenopathy	Significant lymphocytosis > 100 G/L Anemia/ thrombocytopenia	T-PRL: CD2+/CD4+/CD8- B-PRL:strong SmIG/CD19+/CD20+/CD22+/CD79a+/FMC7+/CD38+.	T-PRL; chromosome 6,8, 14, and 17 abnormalies B-PRL: del 11q, 13q, 17p	T-PRL: ATM/JAK3/STA5b/ TCL1/MTCP1 B-PRL: TP53/C-Myc	T-PRL: IV Alemtuzumab Bcl2 inhib, JAK2 inh, BTK inhib B-PRL: BTK inh, Bcl2 inhib
NK cell lymphoma	Nasal type: nasal cavity tumor Orbit, sinuses Non nasal type: skin, gastrointestinal tract, testis	EBV replication	Surface CD3 negative and cytoplasmic CD3€-, $CD56^{+}$ TCR germline configuration	Del 6q	HACE1, PRDM1, FOXO3, PTPRK, EZH2, RUNX3 Stat3, STAT5b, JAK3 mutation	Immunotherapy (*anti*-PD1, anti-CD30, anti-CD138)

Thierry Lamy
Head of Hematology Department, Microenvironnement & Cancers Unit (INSERM U 1236), Rennes University Hospital-France, France

Thomas P. Loughran*
University of Virginia Cancer Center, PO Box 800334, Charlottesville, VA, 22908-0334, USA
E-mail addresses: thierry.lamy@univ-rennes1.fr (T. Lamy), tploughran@virginia.edu (T.P. Loughran),

* Corresponding author.