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Monoclonal B-Cell Lymphocytosis

Guideline

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases

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DGHO Deutsche Gesellschaft für Hämatologie und
Medizinische Onkologie e.V.
Alexanderplatz 1
D-10178 Berlin

Executive chairman: Prof. Dr. med. Mathias Freund

Phone: +49 (0)30 27 87 60 89 - 0
Fax: +49 (0)30 27 87 60 89 - 18

info@dgho.de
www.dgho.de

Contact person

Prof. Dr. med. Bernhard Wörmann
Medical superintendent

Source

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Monoclonal B-Cell Lymphocytosis

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Authors: Karl-Anton Kreuzer, Monika Brüggemann, Alexander Egle, Michael Gregor, Clemens-Martin Wendtner

1 Definition and Basic Information

Monoclonal B-cell lymphocytosis (MBL) is defined by the presence of a monoclonal B-cell population in the peripheral blood, with [2]:

- light-chain restriction (kappa:lambda of <3:1 or <0.3:1), *or*
- monoclonal immunoglobulin heavy-chain gene rearrangement, *or*
- 25% B cells with low or absent expression of surface immunoglobulins, *or*
- B-cell population with an aberrant immunophenotype.

These findings must be reproducible and stable for at least 3 months.

However, MBL is ruled out by the following criteria:

- lymphadenopathy or organomegaly, *or*
- associated autoimmune disease (e.g. AIHA) or infectious complications, *or*
- B lymphocytes >5 G/l in the peripheral blood, *or*
- any other feature of manifested lymphoproliferative neoplasm.

In 80% of the cases MBL displays a CLL phenotype ("CLL-like MBL": light-chain restriction, $CD5^+/CD19^+/CD20^{low}/CD23^+/Ig^{low}$). The two most deviating phenotypes are MBL with the atypical CLL phenotype (light-chain restriction, $CD5^+/CD19^+/CD20^+/CD23^+/Ig^+$ or $CD5^+/CD19^+/CD20^{low}/CD23^-/Ig^+$) and MBL with the non-CLL phenotype (light-chain restriction, $CD5^-/CD19^+/CD20^+/Ig^+$) [3].

2 Incidence Rate

MBL is detectable in the general population at a rate of approx. 0.5-5% [4]. Prevalence depends on the diagnostic method and the age of the patient. It increases with increasing age and is also markedly higher in groups of first-degree relatives with a history of manifest lymphoproliferative disease.

3 Risk of Progression

The risk of MBL transforming into a therapy requiring CLL or any other malignant lymphoma amounts to rate of approx. 1-2% per year [7]. Epidemiological studies confirm individual variations in the likelihood of progression [5, 6]. Seminal stud-

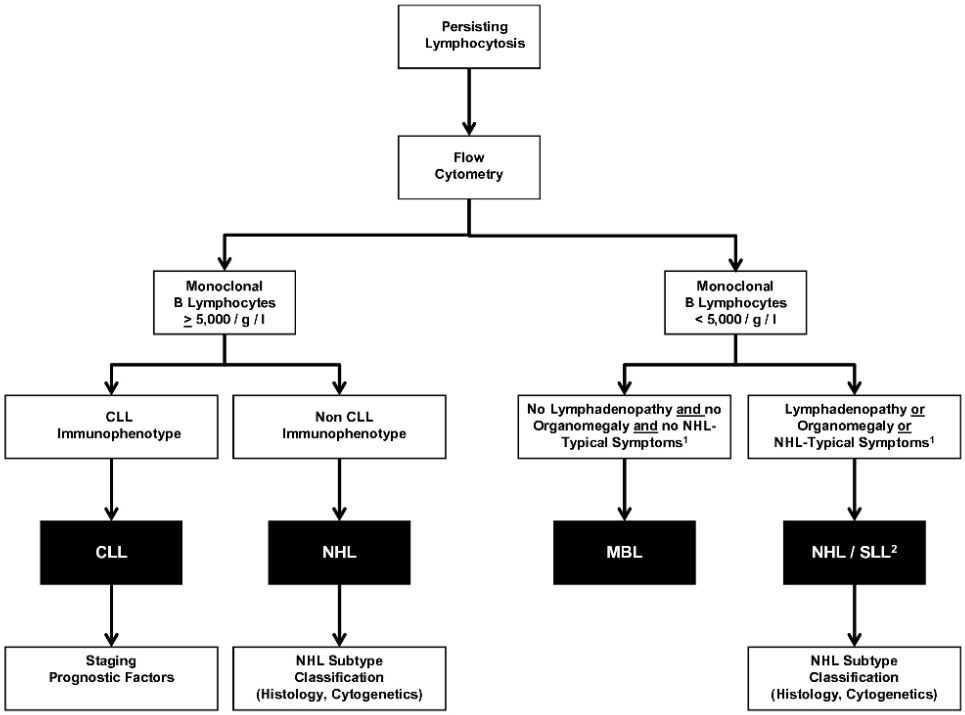
ies on the other hand, demonstrated that almost every CLL is preceded by MBL [1].

Parameters of progression in CLL patients are not applicable for a reliable estimation of the likelihood of progression of a "CLL-type MBL". It can merely be stated that the prevalence of CLL-typical cytogenetic (e.g. del(13q)) or molecular genetic lesions (e.g. IgHV mutation status) increases with increasing lymphocyte counts [4, 8]. Despite the fact that larger studies on this subject are still unavailable a monoclonal B-cell lymphocytosis of ≥1.9 G/l may be currently regarded as a practically relevant threshold limit value (see below).

4 Diagnosis

The diagnosis of MBL is often incidental. However, if there are specific suspicious facts which indicate a lymphoproliferative disease, particularly a persisting lymphocytosis, the diagnosis of MBL usually results from the according diagnostics by exclusion. A diagnostic algorithm is presented in the overview below, see Figure 1.

Figure 1: Differential Diagnostics of B-Cell Lymphocytosis



Legend:
[1] NHL-typical symptoms: B symptoms (fever, night sweats, weight loss), autoimmune cytopenias, opportunistic infections
[2] The aleukemic form of CLL is classified as small-cell lymphocytic lymphoma (SLL).

5 Follow-Up

The objects pursued by follow-up examinations consist first of all in the exclusion of a treatment requiring lymphoproliferative disease at an early stage, and the as

early as possible identification of a development which is directed toward a prognostically unfavorable or treatment requiring disease.

As 90% of the individuals who have MBL and a stable lymphocytosis of <1.9 G/l do not display progression over a period of five years, a single follow-up examination appears to be sufficient for this group, by means of immunophenotyping 6-12 months after the initial diagnosis [5], see Tab 1.

Individuals with a lymphocytosis of ≥1.9 G/l display a high risk of progression, wherefore regular examinations in intervals of 6-12 months appear to be indicated for this group. In addition to immunophenotyping, a physical examination should also proceed in these cases, perhaps supplemented by sonography of the abdomen inclusive of lymph-node sonography, in order to identify a lymphadenopathy or organomegaly [5].

Time	Group	Interval	Method
Initial diagnosis	All	once	Immunophenotyping, clinical examination
Course	< 1.9 G B cells	once after 6-12 months	Differential blood cell count, perhaps immunophenotyping
	≥ 1.9 G/l B cells	regularly, every 6-12 months	Differential blood cell count, perhaps immunophenotyping, clinical examination

In case the number of B cells exceeds a value of ≥5.0 G/l, or should symptoms typical of a lymphoma appear additionally (e.g. lymphadenopathy, splenomegaly, autoimmune cytopenia), a manifest lymphoproliferative disease (CLL etc.) will have to be diagnosed. See elsewhere other Onkopedia Guidelines for further diagnostics.

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7 Affiliations

PD Dr. med. Karl-Anton Kreuzer
Klink I für Innere Medizin
Klinikum der Universität zu Köln
Kerpener Straße 62
D-50937 Köln
Phone: +49 / 221 / 478-97626
karl-anton.kreuzer@uni-koeln.de

PD Dr. med. Monika Brüggemann
II. Medizinische Klinik und Poliklinik
Universitätsklinikum Schleswig-Holstein, Campus Kiel
Chemnitzstraße 33
D-24116 Kiel
Phone: +49 / 431 / 1697-5235
m.brueggemann@med2.uni-kiel.de

PD Dr. med. Alexander Egle
3. Medizinische Universitätsklinik für Hämatologie, internistische Onkologie, Hämostaseologie, Infektiologie und Rheumatologie
Universititätsklinikum Salzburg
Müllnerhauptstraße 48
A-5020 Salzburg, Österreich
Phone: +43 / 662 / 4482- 57700
a.egle@salk.at

Dr. med. Michael Gregor
Hämatologische Abteilung
Luzerner Kantonsspital
Ch-6000 Luzern 16
Phone: +41 / 41 / 205-5313
michael.gregor@ksl.ch

Prof. Dr. med. Clemens-Martin Wendtner

Klinik für Hämatologie, Onkologie, Immunologie, Palliativmedizin, Infektiologie und Tropenmedizin
Klinikum Schwabing
Kölner Platz 1
D-80804 München
Phone: +49 / 89 / 3068-2228
clemens.wendtner@klinikum-muenchen.de