Persistent polyclonal B-cell lymphocytosis (PPBL)

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Here you can inform yourself about characteristics, diagnostics and prognosis of persistent polyclonal B-cell lymphocytosis.

Diagnostic recommendation

Method	Anticoagulant	Recommendation
Cytomorphology	EDTA	mandatory
Immunophenotyping	EDTA or Heparin	mandatory
Chromosome analysis	Heparin	optional
FISH	EDTA or Heparin	optional
Molecular genetics	EDTA or Heparin	no

Definition and characteristics

Persistent polyclonal B-cell lymphocytosis (PPBL) is a rare benign disease with chronic lymphocytosis of polyclonal origin, first described in 1982, which occurs more frequently in middle-aged female smokers. These are mostly mild lymphocytosis and are mostly symptom-free or show unspecific symptoms such as fatigue. Often, therefore, the findings are random and no other underlying diseases are found, but an association with EBV infections has been discussed (Delage et al. 2001). Typical for the disease are bilobulated, mostly even binuclear B-lymphocytes in peripheral blood as well as a polyclonal increase of IgM in serum. In some cases splenomegaly has been described (Cornet et al. 2009, Del Giudice et al. 2009). Lymphomas and secondary solid tumours seem to occur more frequently over the years, but this is still controversially discussed (Cornet et al. 2009, Cornet et al. 2016).

The actual cause of the disease and the associated mechanism are unknown and probably represent a step-by-step process. In addition to the external factor "smoking", a genetic predisposition to PPBL is very likely due to the gender-dependent and familial occurrence (Carr et al. 1997, Delage et al. 2001).

Diagnostics

Cytomorphology

The lymphocyte count in peripheral blood can vary greatly. Morphologically characteristic in the blood picture are binuclear, cytoplasmic-rich B-lymphocytes, which after immunophenotyping are of polyclonal origin (Mossafa et al. 1999).

Immunophenotyping

The immunophenotype of B lymphocytes in PBBL is similar to that of lymphocytes in the splenic marginal zone ($CD27^{+}$, $CD21^{high}$, IgM^{high}, $CD5^{low}$, $CD23^{low}$) or B memory cells, which suggests that the disease originates in the marginal zone (Salcedo et al. 2002). According to the polyclonality of the disease a normal kappa/lambda light chain quotient is shown (Cornet et al. 2009). Often there is an association with a specific HLA haplotype. Most frequently an *HLA-DR7* expression has been described (Troussard & Flandrin 1996, Cornet et al. 2016).

Chromosome analysis

Despite the polyclonality of the disease, recurrent genetic abnormalities can be found. For example, patients with PPBL have an above-average number of polyclonal IGH-*BCL2* rearrangements with different break points, whereby the type and occurrence of the rearrangements often correlate with the HLA type (Delage et al. 2001). Typical is also the addition of an isochromosome 3q (Cornet et al. 2009). Additionally, trisomy 3 or duplications of the long arm of chromosome 3 (Callet-Bauchu et al. 1999) as well as abnormalities of further chromosomes and independent clones have been described (Mossafa et al. 1999, Mossafa et al. 2004, Cornet et al. 2016). Another special feature of PPBL is the so-called "Premature Chromosome Condensation (PCC)" (Mossafa et al. 1999). This is a premature condensation of the DNA in the interphase, probably due to the binuclear nature of the cells.

FISH

If it is not possible to carry out a chromosome analysis, the chromosomal abnormalities occurring in PPBL (see above) can also be detected using FISH.

Molecular genetics

While molecular genetics plays no role in the routine diagnostics of PPBL, the molecular genetic characterisation of the disease is the subject of current research. In two studies, **whole genome and whole exome sequencing** was used to detect mutations associated with tumours and particularly lymphomas, such as *MYD88*, *ATM*, *NOTCH2* and *TRAF1* (Tesson et al. 2017, Stengel et al. 2018). However, characteristic driver mutations as described for other hematological diseases are missing (Tesson et al. 2017). However, due to the rarity of the disease, the data available to date on the incidence of mutations in PPBL are difficult to compare. A **gene expression analysis** also indicates that, among other things, lymphoma-associated genes such as *BCL11B* and *MYC* are overexpressed (Stengel et al. 2018).

Prognosis

Persistent polyclonal B-cell lymphocytosis has several characteristics associated with malignant tumors. These include the occurrence of cytogenetic abnormalities and the frequently observed chromosomal instability (Mossafa et al. 2004, Cornet et al. 2016) as well as the detectability of various tumor-associated mutations (Stengel et al. 2018). Nevertheless, PPBL often shows an indolent, stable course over many years or slight progress with continued cigarette consumption. Only in isolated cases of PPBL has the occurrence of a malignant disease, e.g. lymphoma, been described and an association discussed (Del Giudice et al. 2009, Cornet et al. 2009, Cornet et al. 2016). The achievement of cytomorphological remission by stopping cigarette consumption is controversially discussed but observed (Mossafa et al. 1999, Cornet et al. 2009), the cytogenetic abnormalities seem to persist. A clear separation of malignant lymphomas is important, because due to the indolent course and the lack of malignancy, a therapy is generally not indicated. Regular follow-ups are recommended.

References

You can find the corresponding references here:
https://www.mll.com/en/diagnostic-offer/others/persistent-polyclonal-b-cell-lymphocytosis-ppbl.html#references