Forum of Pathology

n° 31

11-10-2003

Differential Diagnosis of Splenic Lymphomas

Pr Jacques Diebold (Paris)

ForPath asbl
Avenue J. Wybran, 45A
1070 Bruxelles
Tél: 02 524 33 84
Fax:02 524 36 45

Workshop, Brussels, October 11th, 2003
Differential Diagnosis of Splenic Lymphomas
Pr Jacques Diebold (Paris)

Program

9:00	Registration
9:30	Slide Seminar (Part I)
11:00	Coffee break
11:30	Slide Seminar (Part II)
13:00	End of the Workshop

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List of Participants

CHAIKH	Ali
COUVREUR	Yves
de LEVAL	Laurence
DEHOU	Marie-Françoise
DELHOVE	Olivier
DIEBOLD	Jacques
FAVERLY	Daniel
GOOVAERTS	Gerda
INDERADJAJA	Nirwan
LIPCSEI	Györgyi
MICHEL	Pierrette
NGENDAHAYO	Placide
OANA	Michaela
ORIGER	Inès
RAHIER	Isabelle
SCAGNOL	Irène
THEATE	Ivan
VAN DEN HEULE	Bernard
VAN WING	Jacques
VANDE WALLE	Hilde
VANSTAPEL	Marie-José
VERBEECK	Guy
VIVARIO	Manuela

CLASSIC HODGKIN'S LYMPHOMA

J. DIEBOLD, J. AUDOUIN, A. LE TOURNEAU
(Hôtel Dieu, Paris, France)

Definition

Splenic involvement in classic Hodgkin's lymphoma is always secondary to nodal localizations. The dissemination is only hematogeneous due to the absence of different lymphatics to the spleen. Involvement of the spleen is rapidly associated with liver involvement and bone marrow extension.
In our experience, primary Hodgkin's lymphoma doesn't occur or is extremely rare (Symmers 1978, Martinazzi and Palatini 1978, Re et al 1986). In all cases we have seen, a careful search disclosed a nodal involvement either in the abdomen or in the mediastinum.
The incidence of spleen localization in the past increased during the evolution. At necropsy, the spleen was involved in the majority of the cases. Today, splenic involvement can be disclosed mainly during relapse.

Morphology

Cytology

On imprints performed on tumorous nodules, typical Sternberg-Reed cells can be recognized associated with Hodgkin's cells and either small to medium-sized lymphocytes or a mixture of lymphocytes, plasma cells eosinophils and histiocytes. Nests of epithelioid cells may also be present.

Macroscopy

In a personal series of 250 splenectomies performed systematically (Delarue and Diebold 1971, Diebold and Temmim 1980) at first presentation, the spleen was unscathed by disease in 58,8% of the cases and involved in 41,2% of the cases. Our experience is that the involvement of the spleen by classic Hodgkin's lymphoma is disclosed at the macroscopic level. We have done in non-involved spleens,

systematically in different regions, many blocks. We never found classic Hodgkin's lymphoma lesions at the histologic level which have not been recognized at the macroscopic level.

The smallest lesion is represented by a small whitish nodule measuring 0,5 to 1cm. In most of the cases, the nodules is not alone but belongs to a group of four to ten other nodules. Sometimes they can realize a single nodule by confluence with a polycyclic outline. Around the nodules, there is a brown corona due to hemosiderin deposits.

In our series, 9% of the cases show only one nodule measuring less than 1cm in only one region of the spleen (unimicronodular type). In 27% of the cases, 2 to 5 groups of micronodules have been observed either in the same area or dispersed in different areas (paucinodular type). There is 38% of the cases, multiple small nodules have been easily recognized dispersed all through the spleen. This multimicronodular type resembles to localization of small B-cell lymphomas (see chapter …) but the nodules are more often confluent and show a more irregular size from one nodule to the other (from 1cm to 5cm).

The nodules, in 22% of the cases were larger than 5cm. This macronodular type can be diffuse or localized in some part of the spleen. This represents the classic pattern described in the past in Hodgkin's lymphoma. A few number of cases (4%) present with massive tumours due to the confluence of small and large nodules, mimicking large B-cell lymphomas or carcinomatous metastasis. External deformation of the spleen due to large nodules or massive tumours has been observed only in 10% of the cases. The size and the weight of the spleen increase with the size and the number of nodules. So 20% of our cases had a weight superior to 300g up to 1000g or more. But, 34,9% of the cases had a normal weight, equal or inferior to 200g. So a small spleen can be involved by early lesions of classic Hodgkin's lymphoma.

On the other hand, if 60% of non-involved spleens had a weight less than 200g, 30% had a slight increase of the weight between 200 to 300g, and 10% had a abnormal weight comprises between 300 to 800g. So a large spleen is not always synonymous of tumourous involvement in classic Hodgkin's lymphoma. Other publications show the same results (Askergren et al 1981, Colby et al 1982, Maurer 1985).

In involved spleens between the tumour and in non-involved spleens whatever the weight, the pattern of the parenchyma is indentical to normal spleen. Regularly dispersed small white nodules are recognized, measuring about 0,2cm in diameter, and never more than 0,5cm , corresponding to normal white pulp.

Hilar lymphadenopathies have been disclosed in the majority of involved spleens. They were involved by classic Hodgkin's lymphoma in 72,5% of the cases. By contrast, lymph nodes of small size have been found in many cases of "uninvolved" spleens. They were never involved by classic Hodgkin's lymphoma which has been diagnosed in all patients on peripheral lymphadenopathies (Diebold and Temmim 1980).

Histology

Involved spleens

Large nodules and massive tumors are constituted by sheets of fibrosis rich in collagen fibres infiltrated by lymphocytes, plasma cells and eosinophils and showing larger areas with a more dense population in which typical Sternberg-Reed cells, lacunar cells and Hodgkin's cells are easily recognized. The difference between nodular sclerosing and diffuse mixed Hodgkin's lymphoma is not easy to draw. The presence of lacunar cells and of annular bands of fibrosis are in favor of nodular sclerosing type. In these large tumours, white pulp and red pulp are completely destroyed and the splenic parenchyma can be compressed by the expansion of the tumour.

The study of the smaller nodules is more interesting. The initial lesion of Hodgkin's lymphoma in our series develops always in the mantle or marginal zone of the follicles and is characterized by the presence of classic Sternberg-Reed cells and/or lacunar cells between mantle or marginal cells. Such follicles may have a normal size and it is quite possible that in the so-called not-involved spleens, histologic examination has missed a very early involvement of follicles without any macroscopic changes.

Enlarged follicles comprise numerous giant tumour cells surrounded by a corona of small lymphocytes and by eosinophils and plasma cells (Burke 1981, Butler 1983, Diebold and Temmim 1980). So the smallest lesions resemble to the so-called "cellular phase" of nodular sclerosing Hodgkin's lymphoma (Diebold et al 1995) which as be renamed intrafollicular Hodgkin'' disease (Ashton-Key et al 1995).

In groups of small nodules, in addition to the two types described, larger nodules are constituted by follicles completely replaced by Hodgkin's lymphoma. Intercellular collageneous fibrosis develop as well as in some cases complete or incomplete annular bans of fibrosis around one or a group of follicles.

At the periphery of the tumorous nodules, many hemosiderin-laden histiocytes are present, representing normal macrophages unable to leave the spleen, due to the

destruction of the initial efferent lymphatics present around the small arteries in the follicles.

Ischemic necrosis may be seen, particularly in lesions rich in eosinophils. Nests of epithelioid cells are not uncommon (Diebold et al 1977, Sacks et al 1978). The different histologic subtypes can be recognized (Diebold and Temmim 1980, Buttler 1983, Burke 1981, Falk et al 1987):

Lymphocyte rich, sometimes with epithelioid cells

- mixed cellularity
- nodular sclerosing with lacunar cells and annular fibrosis, sometimes with numerous Sternberg-Reed cells, sarcomatous cells as in grade 2
- lymphocyte depleted (Zellers et al 1990).

At distance of the localizations, red and white pulp are normal. Follicles show a more or less active germinal centre and a marginal zone of variable importance. In the cords, plasma cells are often numerous around terminal arteries.

Uninvolved spleens

Red and white pulp are normal. The size and the degree of activation varie greatly from case to case. Often due to the young age of the patients, germinal centres were active and marginal zone broad. Many plasma cells may be present around the arteries in the cords. Three points have to be stressed:

1. As mentionned before, the earliest lesion of classic Hodgkin's lymphoma being present in follicles of normal size, and these early lesion being very rare, it is quite possible to imagine that despite the study of at least ten blocks for one spleen, the diagnosis of such initial lesions have been missed. So what we called uninvolved spleen are in fact spleens without minimal macroscopic involvement.
2. These "uninvolved" spleens had in 10% of the cases a weight comprised between 300 and 800g. In these spleens, a follicular hyperplasia has been always observed. So it is possible that a huge spleen in classic Hodgkin's lymphoma may only reflect a lymphoid stimulation.
3. Epithelioid cell nests or even granulomas without necrosis have been recognized in the red pulp at the periphery of the follicles or in the mantle zone, without any histologic localization of Hodgkin's disease. The same has been observed in the

liver. So it is possible that a granulomatous inflammatory reaction develops at distance of the lymphoma (Diebold et al 1977).

Immunohistochemistry

Identical to nodal classic Hodgkin's lymphoma (see chapter …).

Differential Diagnosis

Multimicronodular lesions can mimick small B-cell lymphomas or some types of tuberculosis or sarcoidosis. Macronodular and massive lesions mimick large B-cell lymphomas, metastasis or various malignant soft tissue tumours. At the histologic level, the presence of typical Sternberg-Reed cells is the hallmark for the diagnosis associated with the typical immunophenotype.

Clinical Presentation

At first presentation the majority of the patients has no splenomegaly. The results of series of patients treated by initial systematic splenectomy show that:

1. absence of splenomegaly is not synonymous of absence of involvement,
2. presence of splenomegaly is not synonymous of presence of involvement.

It has been shown that initial splenectomy doesn't improved the survival and that polychemotherapy (MOPP for ex.) is able to destroy splenic localization. The incidence of liver and bone marrow involvement seems to increase in patients with multiples micro or macronodular or massive involvement.

Splenomegaly can only be disclosed in many cases during relapses.

HODGKIN'S LYMPHOMA, LYMPHOCYTE PREDOMINENT NODULAR

Definition

This type of Hodgkin's lymphoma is now regarded as a peculiar B-cell lymphoma different from classic Hodgkin's lymphoma (see chapter …). Splenic involvement occurs very rarely.

Morphology

Macroscopy

The very few cases we have seen present small whitish nodules measuring from 1 to 5cm in diameter in one or different part of a spleen which is otherwise macroscopically normal. The size of the spleen was normal or slightly increased.

Histopathology

The initial lesions begin in the follicles which are homogeneized, and expansile. Large histiocytes, some epithelioid cells, hypertrophic follicular dendritic cells may be present. The diagnosis is based on the presence of large cells with a typical L and H morphology particularly a multilobated nucleus with a popcorn like appearance. A group of follicles present this pattern but at distance the other follicles have a normal more or less active morphology. The red pulp is normal. In one case, homogeneized follicles were confluent and a very high number of L and H cells were present, realizing a pattern resembling T-cell rich B-cell lymphoma. This case was interpreted as a case transforming in a large B-cell lymphoma.

Immunohistochemistry

Identical to nodal localization (see chapter …).

Differential Diagnosis

Due to the localization to a few number of follicles, the only differential diagnosis to discuss is the cellular phase of early classic Hodgkin's lymphoma. The morphology and immunophenotype of the giant cells, the immunophenotype of the lymphoid cells around them allow an easy distinction (see chapter …).

Clinical Presentation

The few cases we have seen were patients with first nodal localization of Hodgkin's lymphoma, lymphocyte predominance nodular type and relapsing with discovery of a splenomegaly. Patients had clinical stage III disease.

SPLENIC LYMPHOMA

Either primarely or secondarely involvement (hematogenous dissemination, absence of afferent lymphatics). Mostly in the white pulp. Rarely in the red pulp. Dissemination from the spleen to the liver and bone marrow thru portal vein.

Macroscopy

Splenomegaly (400g to 4.000g or more).
Great value of the macroscopic pattern.
Precise protocol of dissection (slices not thicker than 0.5cm). Careful search and study of hilar adenopathy.
Same patterns seen whatever the splenic ML is primary or secondary.

1. Multimicronodular pattern

- small nodules (0.5-1cm in diameter) : enlarge follicles and nodules in the cords
- **Mature small B-cell ML** :
  . B-CLL
  . Follicular ML
  . Mantle cell ML
  . Lymphoplasmacytic ML (?)
- **Differential diagnosis** :
  . sarcoidosis
  . tuberculosis
  . reactive follicular hyperplasia (autoimmune or viral diseases)
  . early phase of splenic involvement by classical Hodgkin's lymphoma

2. Multimacronodular pattern

- nodules often polycyclic (1 to 5cm in diameter),localized in one or in multiple different areas
- **Different types of ML**:
  . Burkitt's ML
  . Peripheral NK/T-cell ML (unspecified, or angioimmunoblastic type or Lennert's lymphoma)

. Anaplastic large B-cell ML

- **Differential diagnosis** :

. Caseo-follicular tuberculosis

. Classic Hodgkin's lymphoma

. Splenoma (splenic hamartoma)

. Metastasis of carcinoma

3. Polycyclic masses

- More than 5cm in diameter up to 10 or 20cm
- **Large B-cell lymphomas**
- **Differential diagnosis** :

. Classical Hodgkin's lymphoma

. Histiocytic sarcoma

. Non hematopoietic tumors

4. Diffuse pattern

- No nodules. No masses
- **Different types of ML:**

. hairy cell leukaemia

. a few B-CLL and leukaemic variant of mantle cell ML

. peripheral NK/T-cell ML, unspecified

. hepatosplenic ML

. lymphoblastic ML/acute leukaemia of precursor B or T cells

- Differential diagnosis : chronic and acute myeloproliferative diseases

LIST OF ENTITIES

Primary splenic ML

Definition of primary splenic lymphoma: predominance of the splenic localization without any other organ involvement which can be clinically disclosed.

Less frequent than secondary (2 to 4% of ML)

Most frequent type:

Small B-cell ML

Hairy cell leukaemia

Splenic marginal zone ML

Lymphoplasmacytic ML

Plasmacytoma

B-prolymphocytic leukaemia

Follicular ML (very rarely)

Large B-cell ML

Peripheral NK/T cell ML

Hepatosplenic ML

T-cell leukaemia with large granular lymphocyte

Peripheral NK/T-cell ML, unspecified (very rarely)

Secondary splenic ML

Small B-cell lymphoma

B-CLL

Follicular ML

Mantle cell ML

Large B-cell lymphoma

Peripheral NK/T cell lymphoma

Peripheral NK/T-cell ML, leukaemic/disseminated

T-prolymphocytic leukaemia

Agressive NK/T-cell leukaemia

T-cell lymphoma/leukaemia, HTLV1 associated

Peripheral NK /T-cell ML, nodal

AILD type

Unspecified

Anaplastic large cell ML

Extra-nodal NK/T-cell lymphoma

Primary intestinal T-cell lymphoma

Precursor cell lymphoblastic lymphoma/leukaemia of T or B-cell

SPLENIC LYMPHOMA

Description of theprimary and secondary splenic lymphomas according to the WHO classification.

1. B-CLL

- **Multimicronodular pattern:** homogeneous follicles, cords and sinuses are still recognizable but are infiltrated by a variable number of small lymphocytes (round or bilobated nucleus with clumped chromatin, unconscupious nucleolus, small cytoplasm)
- rarely **diffuse pattern** (more advanced cases), with heavy infiltration of red and white pulp, masquing the normal architecture
- in dense areas, *proliferative centres* with prolymphocytes and paraimmunoblasts
- **Immunophenotype**:

positive	CD20 (often faint, rarely negative)
	CD5, CD23, IgD
	monotypic intracytoplasmic Ig defining the *plasmacytoid variant*
negative	CD10

- **Richter's syndrome**: association with sheets of immunoblasts and plasmablasts, with sometimes larger nodules (≥ 1cm in diameter).

2. B-prolymphocytic leukaemia

- Exceptionaly seen by pathologists because of chemotherapy without splenectomy
- Multimicr**onodular or diffuse pattern**
- Homogeneous cell population: medium-sized, round nucleus, prominent central nucleolus, cytoplasm more abundant than in B-CLL. *No proliferative centre.*
- **Immunohistochemistry**

positive:	CD20
negative:	CD5, CD10, CD23

- **Differential diagnosis**

. B-CLL with large proliferative centers or transforming in B-prolymphocytic leukaemia

. blastic transformation of mantle cell lymphoma

. lymphoblastic lymphoma/leukaemia of precursor B or T-cell

. acute myeloid leukaemia

3. Follicular ML

- **Multimicronodular patterrn** or rarely polycyclic masses.
- The nodules are expanding follicles with small and medium centrocytes replacing the reactive germinal centre. Variable number of large cells (centroblasts, immunoblasts). WHO grading system can be used. Sometimes marginal zone differentiation.
- **Immunohistochemistry**

  positive: CD20, CD10, bcl-2 (75%)

  negative: CD5, CD23, bcl-2 (25%)
- **Differential diagnosis**

  . All the other small B-cell ML with a multimicronodular pattern

  . Follicular hyperplasia

4. Mantle cell ML

- **Multimicronodular pattern:** homogeneized follicles with remnants of germinal centre and/or reactive germinal centre with a thick mantle cell area.
- **Rarely**, in advanced and/or leukaemic form, **diffuse pattern** due to heavy infiltration of the red pulp.
- Medium-sized cells either with a round nucleus (resembling a B-CLL cell) or irregular, cleaved (resembling a centrocyte). No centroblasts++. No immunoblasts++.
- Blastic transformation ressembling lymphoblastic ML or centroblastic ML
- **Immunohistochemistry**

  positive: CD20, CD5, IgD, bcl-2, cyclin D1++

  negative: CD10, CD23

  blastic transformation (↗ Ki67> 10%).
- **Differential diagnosis**

  . all the other small B-cell ML with multimicronodular pattern

. in cases of blastic transformation, lymphoblastic lymphoma/leukaemia of B and T precursor cells, acute myeloid leukaemia or even diffuse large B-cell ML.

5. Splenic marginal zone ML

- **Multimicronodular pattern**
- Enlarged follicle with a pale corona surrounding the follicles which are homogeneous, darker, sometimes with a remnant of a germinal centre more or less colonized, sometimes with a Castleman's like pattern or a reactive germinal centre. In the marginal zone: monocytoid B-cells and a few immunoblasts. In the centre: small lymphoid cells with either a round or an irregular nucleus (centrocyte-like cells).

  Red pulp: variable number of these small cells in the cords and sinuses (particularly in patients with a preipheral blood lymphocytosis, with or without villous lymphocytes).

  In about 40 to 50% of the cases, numerous plasma cells and lymphoplasmacytoid cells (sometimes with a PAS positive intranuclear vacuole) in the marginal zone, in the centre of the follicles and in the cords (periarteriolar nodules).

- **Clinical presentation :** all cases with a monotypic plasma cells component may present a peripheral blood monoclonal gammapathy. Sometimes leading to the diagnosis of Waldenström's disease.

  : possible transformation into a **diffuse large B-cell ML** (immunoblastic type with plasmacytoid differentiation) with nests and sheets of blasts replacing parts of the follicles.

- **Immunohistochemistry**

  Positive: CD20, CD79a, IgD (often), DBA44 (sometimes), bcl-2, Cig monotypic (mostly mu-kappa), Ki67 (less than 5%)

  Negative: CD5 (mostly), CD10, CD23, Cyclin D1

- **Differential diagnosis**:

  all small B-cell ML

  follicular hyperplasia: be careful in children and young adults, MZ may be prominent in reactive follicles! Value of the weight of the spleen +++

6. Lymphoplasmacytic MZ

- Does this ML exist? Possible **simplified MZ lymphoma**. Pattern, morphology and immunohistochemistry: more or less similar to MZ lymphoma.
- **Differential diagnosis**

  Lymphoploasmacytoid variant of B-CLL

  Splenic MZ lymphoma

7. Hairy cell leukaemia

- ***Diffuse macroscopic pattern***
- Diffuse infiltration of the red pulp (cords, sinuses). Atrophy of the white pulp. Distension of sinuses (pseudo-angiomatous, in fact "peliosis"). Medium-sized cells, round ovoid or kidney-shaped nucleus, small nucleolus, abundant pale cytoplasm regularly distributed around the nucleus. No "hairy" appearance.
- **Immunohistochemistry**

  Positive: CD20, CD79a, DBA44, Cyclin D1 (50 to 75% of cases), tartrat-resistant acid phosphatase, sometimes CD68

  Negative: CD5, CD10

- **Differential diagnosis**

  Diffuse variant of B-CLL or mantle cell ML

  Hepato-splenic lymphoma

  Some peripheral NK/T-cell ML

  Acute leukaemia either lymphoblastic or myeloid

  Chronic myeloproliferative diseases

8. Plasmacytoma

- Primary splenic involvement exceptional. Plasmacytic myeloma should always be excluded+++
- **Macroscopy**: either diffuse, multimicronodular or with polycyclic mass
- Sheets of mature plasma cells with a variable number of proplasmacytes and blasts Destruction of the white pulp, infiltration of the red pulp
- **Immunohistochemistry**

CD20 and CD79a may be positive or negative

CD38 and CD138 positive as EMA

Cig: restriction of light chain, IgA or IgG most frequent heavy chain

- **Differential diagnosis**

Lymphoplasmacytoid variant of B-CLL (IgM)

MZ lymphoma (IgM)

Lymphoplasmacytic lymphoma (IgM)

Dissemination of multiple myeloma +++ (bone pain, radiology) or of primary plasmacytoma of other sites (digestive tract)

Viral diseases (MNI, HIV)

Castleman disease (even in the absence of typical localization in a patient with solitary or multicentric nodal involvement)

9. Burkitt's lymphoma

- Multimacronodular pattern
- Areas of medum-sized cells (scanty basophilic cytoplasm, round nucleus, dispersed chromatin with a spotted pattern, multiple medium-sized nucleoli) with sometimes a few number of centroblasts, small immunoblasts, defining **Burkitt's variant**. Numerous macrophages with apoptotic cells.
- **Immunohistochemistry**

Positive: CD20, CD79a, CD10, bcl-6, Ki67 (100%), sometimes monotypic Cig defining a plasmacytic subtype
LMP-1 and EBER-1 positive (variable proportion of cases)

Negative: CD5, CD23

- **Differential diagnosis**

Lymphoblastic leukaemia/lymphoma of B or T-cell precursor

Blastic transformation of mantle cell ML

Rarely monomorphic centroblastic lymphoma with high mitotic rate and high apoptosis

10. Diffuse large B-cell ML

- large polycyclic masses or multimacronodular
- sheets of centroblasts, immunoblasts, plasmablasts. WHO propoes to recognizes six types: **centroblastic** (monomorphic, multilobated, polymorphic)
  immunoblastic with or without plasmablastic differentiation
  T-cell/histiocyte rich (multimacronodular)
- **Immunohistochemistry**
  Positive: CD20 and CD79a
  CD38 and CD138 in cases of plasmacytoid differentiation
  EMA, CD30 (sometimes)
  Cig with light chain restriction
  Sometimes CD5, CD10, bcl-2, bcl-6
- **Differential diagnosis**
  Acute myeloid leukaemia
  Malignant mastocytosis
  Histiocytic sarcoma
  Metastasis +++ of carcinoma or melanoma
  Some non-hematopoietic sarcomas

11. Peripheral NK/T-cell

Leukaemic/ disseminated

- **NK/T-cell leukaemia with large granular lymphocytes**
  "small" splenomegaly
  apparent normal architecture of the white and red pulp
  infiltration of the cords by medium-sized cells
  Immunohistochemistry
  common variant: CD3(-), TCR alpha-beta(+) with either CD4 and CD8(-), CD4(+) and CD8(-) or CD4 and CD8(+) or CD4(-) and CD8(+), CD57(-), TiA-1(+)
  Other: CD3(+), TCR gamma-delta(+)
  CD3(-), TCR alpha-beta(-), CD56(+)
- Other: **aggressive NK/T leukaemia**
  diffuse infiltrations (red pulp), medium-sized cells
  : **adult lymphoma/leukaemia HTLV-1 associated,**

diffuse infiltration (red pulp), small, medium, large cells (irregular nuclei, "flower" cells)

Nodal

- **AILD type and anaplastic large cell ML**

  Multimacronodular pattern

  Areas of neoplastic cells near the follicles, destroying them with typical pattern of of the corresponding type of ML

- **NK/T, unspecified,**

  mostly diffuse, with predominant infiltraton of the red pulp (medium and/or large cells)

Extra-nodal

- **nasal type** : rarely
- **intestinal T-cell**: rarely
- **MF/Sézary syndrom** (at the end of the evolution)
- **Panniculitic-like** (no information)

  Either small foci near follicles or diffuse infiltration of the red pulp.

- **Hepatosplenic lymphoma**

  . Homogeneous pattern

  . Atrophy of white pulp, more or less severe

  . Infiltration of the sinuses and the cords by medium-sized lymphoid cells (round/oval nucleus, slightly irregular, dispersed chromatin, unconspicuous nucleoli, pale cytoplasm) sometimes with hemophagocytic histiocytes.

  . **Immunohistochemistry**

  Positive: CD3, CD2, CD7+/-, sometimes CD8, CD56, TiA-1

  Mostly γδ-T-cell receptor (βF1-, TCRγ-1+)

  A few cases αβ-Tcell receptor (βF1+, TCRδ−1−)

  Negative: CD5, sometimes CD7, mostly CD4 and CD8, granzyme B, perforin

- **Differential diagnosis**

T-cell leukaemia with large granular l ymphocytes
Aggressive NK lymphoma/leukaemia
Peripheral NK/T-cell lymphoma unspeficied

REFERENCES

1. Jaffe ES, Harris NL, Stein H, Vardiman JW editors, Pathology and Genetics of Tumours of Haematopoietic and lymphoid tissues. Lyon: IARC Press, 2001

2. Feller A, Diebold J: Histopathology of nodal and extranodal non-Hodgkin's Lymphomas. Springer Verlag. 2003 (in press 2004)

3. Diebold J, Le Tourneau A, Audouin J, Molina T. Spleen. Rate. Atlas of Pathology. CDROM-1-Springer Verlag, 1998