Virchows Archiv (1994) 424:321–326

ORIGINAL ARTICLE

L. Plank · M.-L. Hansmann · R. Fischer

Monocytoid B-cells occurring in Hodgkin's disease

Received: 15 September 1993 / Accepted: 20 December 1993

Abstract In contrast with various forms of lymphadenitis, the presence of reactive monocytoid B-cells (MBCs) has only rarely been reported in Hodgkin's disease (HD). In order to analyse their occurrence in HD, we reviewed 120 cases before or after treatment. MBCs were identified morphologically and immunohistochemically in 8 cases (nodular paragranuloma, $n=2$; nodular sclerosis, $n=2$; and interfollicular mixed cellularity HD, $n=4$). Acute toxoplasmic, cytomegalovirus, or Epstein-Barr virus (EBV) infections were excluded by serological tests and immunohistochemistry. MBCs were negative by immunostaining for EBV encoded latent membrane protein, while Sternberg-Reed and Hodgkin's cells expressed positivity in 50% of cases. MBCs were only identified in cases with partial or incomplete lymph node infiltration by HD together with an activated B-zone of residual non-infiltrated tissue. The relation of MBCs and HD infiltrates followed three distinct patterns: large HD infiltrates without any connection to MBC foci; small areas containing various numbers of Sternberg-Reed and Hodgkin's cells at the border between MBC foci and surrounding lymphoid tissue; and HD infiltrates within at least some MBC clusters. The data obtained suggest that MBCs occurring in HD represent a transient phenomenon associated with a B-zone activation irrespective of treatment and that they are usually not histogenetically related to HD.

Key words Hodgkin's disease · Monocytoid B-cells Monocytoid B-cell reaction · B-zone activation

Introduction

Reactive monocytoid B-cells (MBCs) represent a distinct B-cell population which occurs most frequently in different forms of lymphadenitis (Lennert 1961; Stansfeld 1961; Sheibani et al. 1984; Stein et al. 1984). Whereas clusters of MBCs may occasionally form a monocytoid B-cell reaction (MBCR) in non-Hodgkin's lymphomas (Nathwani 1992), there are only few reports on MBCR associated with Hodgkin's disease (HD).

The first observation of two cases of MBCR in lymph nodes with partial involvement by HD was reported by Lennert (1958, 1961) and in studying the differential diagnostic criteria of toxoplasmic lymphadenitis, Miettinen and Fransilla (1982) described an additional case. Recently, Mohrmann et al. (1991) were the first to report three cases of HD occurring in MBC clusters. A comparison of two consecutive biopsies allowed Miettinen and Fransilla (1982) to assume that MBCR in such cases might represent a transient phenomenon, disappearing during the progress of the disease. However, Mohrmann et al. (1991) emphasized that they were not able find a definitive histogenetic relationship between MBCs and HD.

Such cases need to be distinguished from Epstein-Barr virus (EBV), cytomegalovirus (CMV), and toxoplasmic lymphadenitis showing MBCR and/or Sternberg-Reed-like cells (Lennert 1961; Sheibani et al. 1984; Fellbaum et al. 1988; Rushin et al. 1992). Moreover, EBV may also be related to the development of HD (Pallesen et al. 1991; Purtillo et al. 1992; Stein et al. 1992).

The association of MBCs with HD has not been investigated systematically as all published data are based on case reports. We undertook this study to analyse a large series of cases with HD both before and after treatment.

Materials and methods

One hundred and twenty consecutive cases of HD were retrieved from the files. The formalin-fixed and paraffin-embedded specimens of diagnostic, staging or restaging procedures consisted of lymph node biopsies in every case together with additional extranodal tissue biopsies (liver, spleen, lungs, skin, bone marrow) in 12

L. Plank (✉) · M. L. Hansmann · R. Fischer
Department of Pathology, University of Cologne,
Joseph Stelzmannstrasse 9, D-50924 Cologne, Germany

Table 1 Primary antibodies used in the study (*EBV* Epstein-Barr virus, *Ig* immunoglobulin)

Antibody	Predominant reactivity/cluster	Source
Anti-kappa	Kappa light chain of Ig	Dako (Hamburg, Germany)
Anti-lambda	Lambda light chain of Ig	Dako
Anti-IgM	Mü heavy chain of Ig	Dako
L26	CD20 associated	Dako
UCHL1	CD45RO	Dako
Ber-H2	CD30	Dako
CMV	Anti-cytomegalovirus	Dako
Dako-EBV, CS1–4	Latent membrane protein of EBV	Dako
Leu-M1	CD15	Becton Dickinson (Heidelberg, Germany)
MT1	CD43	Biotest (Dreieich, Germany)
Ki-B5	B-cells[a]	Prof. M.R. Parwaresch (Kiel, Germany)
Ki-M1P	Monocytes/macrophages[b]	Prof. M.R. Parwaresch

[a] Hansmann et al. (1991)
[b] Radzun et al. (1991)

cases. Haematoxylin and eosin, periodic acid-Schiff, and Giemsa-stained sections were examined for the presence of MBCR and its relations to HD infiltrates as well as to residual lymph node structures. According to our previous study (Plank et al. 1993), we distinguished between MBCs of a common type and MBCR showing large cell transformation.

The histopathological classification of HD was based on pretreatment lymph node biopsies and followed generally accepted criteria (Lukes et al. 1966; Lennert and Mohri 1974). Data on the clinical stage of the disease and serological findings (titres of anti-toxoplasmic, anti-EBV, and anti-CMV antibodies) were obtained from the referring pathologists and/or clinicians.

The cases showing MBCR were analysed immunohistochemically by a panel of antibodies (Table 1) using a modified streptavidin-biotin-complex method (Hsu et al. 1981) as reported previously (Plank et al. 1993).

Results

We were able to identify distinct foci of MBCs in 8 out of 120 cases of HD (6.7%, Table 2). The unifying feature of all the cases with MBCR was incomplete nodal infiltration by HD (Table 3). Both the partially infiltrated and residual non-infiltrated lymphoid tissue showed secondary lymphoid follicles with active germinal centres (7 cases; Fig. 1) or large accumulations of B-lymphocytes with atrophic germinal centres (1 case). MBCR was multifocal in all but 1 case (case 2), which showed only two small MBC clusters. MBC clusters were usually confined to inter- and perifollicular areas of the activated follicular structures (Figs. 1, 2). Some were found to be intrasinusoidal. In 2 cases (5 and 8), the proliferation of MBCs expanded the marginal sinus as well. In all the cases investigated, MBCs of the common type predominated. However, in 2 cases their large cell transformation was apparent.

Evaluating the relation to MBCR, HD infiltrates displayed three different topographic patterns. In each case, the largest areas of HD infiltration occurred outside the MBCR foci. The second pattern showed irregularly large HD foci showing Sternberg-Reed and Hodgkin's cells at the outer borders of MBCR and surrounding lymphoid tissue (cases 3–8; Fig. 2). Finally,

Table 2 Summary of the reviewed cases of Hodgkin's disease (*LP* lymphocyte predominance, *NS* nodular sclerosis, *MC* mixed cellularity, *LD* lymphocyte depletion, MBCs monocytoid B-cells)

Histopathological type	LP	NS	MC	LD	Total
Number of cases (*n*):	25	48	41	6	120
Cases with MBCs (*n*):	2	2	4	–	8

Table 3 Histological patterns of Hodgkin's disease with associated monocytoid B-cell reaction (*HD* Hodgkin's disease, *NP* nodular paragranuloma, *NS* nodular sclerosis, *MC* mixed cellularity, *MBCs* monocytoid B-cells, *MBCR* monocytoid B-cell reaction, *CT* common type, *Tranf.* transformation of MBCs to large cell type)

Case number	Type of HD	Type of MBCs	HD infiltrates		Follicular hyperplasia
			in MBCR	out of MBCR	
1	NP	CT	+	+	+
2	NP	CT	–	+	+
3	NS	CT	+	+	+
4	NS	Transf.	+	+	+
5	MC	Transf.	+	+	–
6	MC	CT	+	+	+
7	MC	CT	+	+	+
8	MC	CT	+	+	+

Sternberg-Reed and Hodgkin's cells were found inside the MBC clusters (cases 1, 3–8, Fig. 3), almost always in association with the second pattern. Rarely, Sternberg-Reed cells occurred within MBCR in otherwise intact non-infiltrated parts of the lymph node, as in the marginal sinus of case 8. The number of Sternberg-Reed and Hodgkin's cells within individual MBC foci varied from single cells to many, and differed from case to case. The same was true for associated plasma cells and leucocytes. Necrobiotic changes of HD infiltrates within MBC clusters were not observed.

All these patterns occurred irrespective of the individual HD histological type, but the extent of the sec-

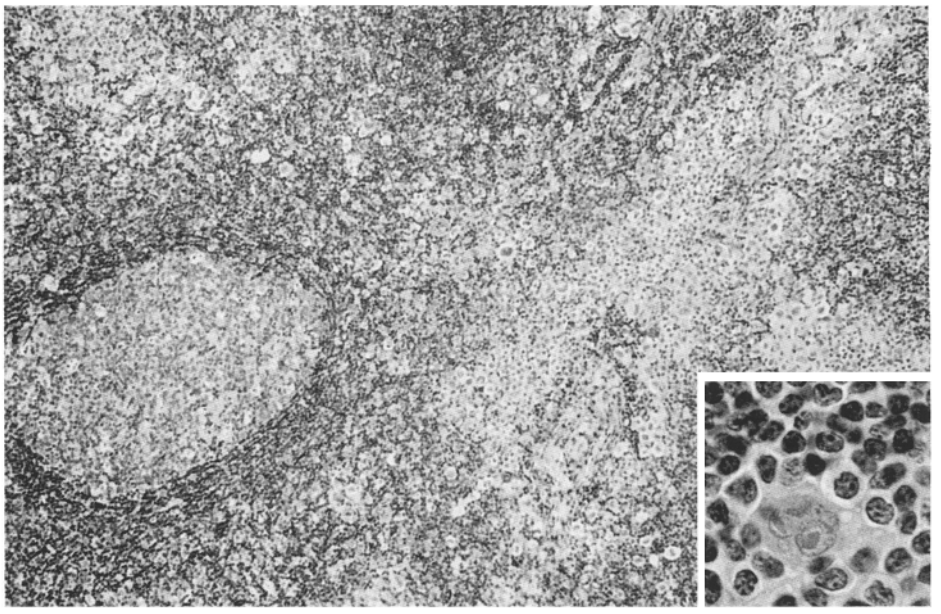

Fig. 1 Interfollicular spread of mixed cellularity Hodgkin's disease close to a reactive lymphoid follicle and to foci of extensive monocytoid B-cell reaction. Interfollicular infiltrate contains diagnostic Sternberg-Reed cells (*inset*). Haematoxylin and eosin (H & E), ×150; *inset* ×630

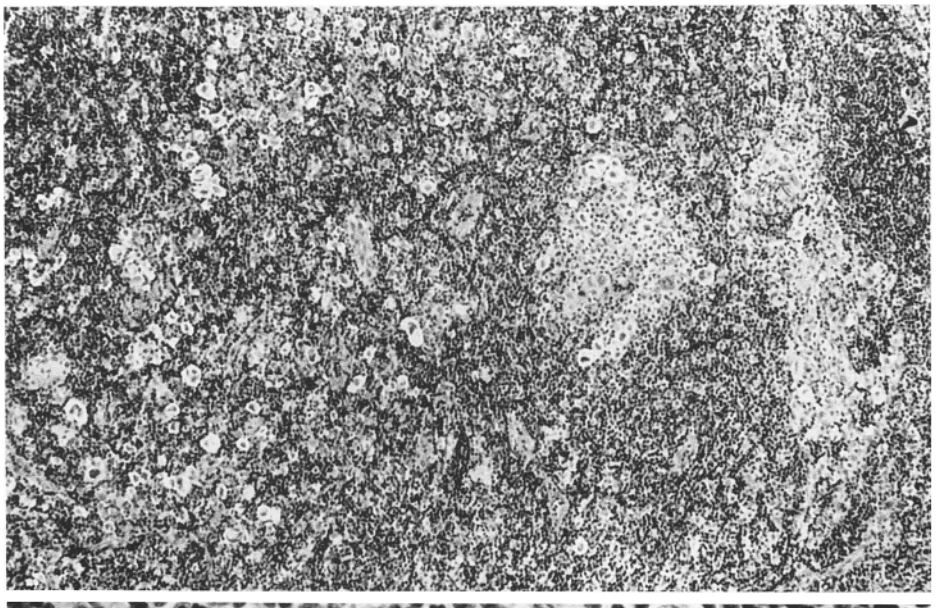

Fig. 2 Interfollicular area with numerous Hodgkin and Sternberg-Reed cells; some of them occur adjacent to and within monocytoid B-cells clusters. H & E, ×230

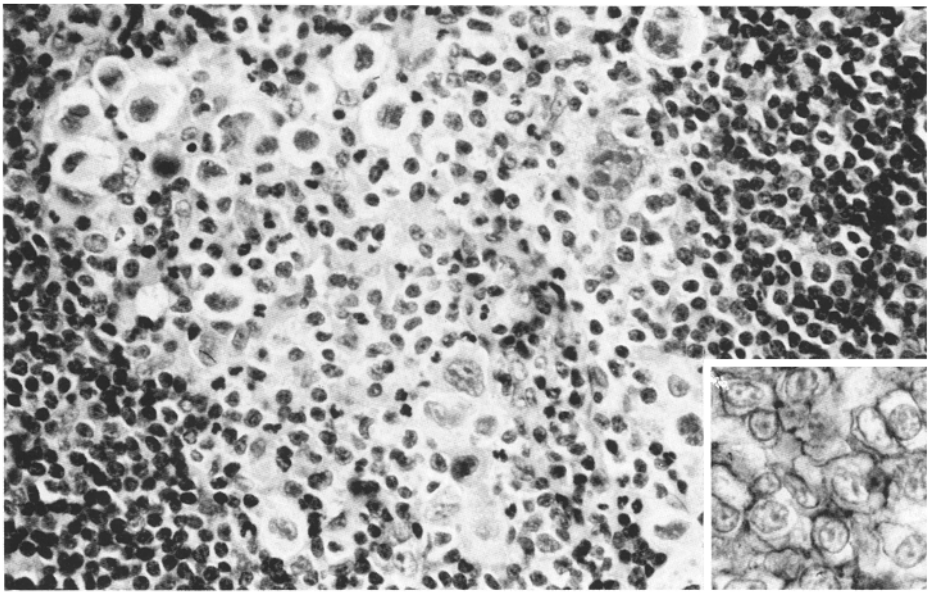

Fig. 3 Cluster of monocytoid B-cells contains intermingled Hodgkin and Sternberg-Reed cells. H & E, ×400. *Inset* Monocytoid B-cells showing membrane staining for the antibody L26. Streptavidin-biotin technique, ×630

Table 4 Clinical data of patients with Hodgkin's disease (*NP* nodular paragranuloma, *NS* nodular sclerosis, *MC* mixed cellularity, *M* male, *F* female)

Case number	Age (years)	Sex	Lymph node localisation	Type	Stage	Biopsy	
						prior to therapy	after therapy[a]
1	31	M	Axillary	NP	I a	+	
2	72	F	Cervical	NP	II a	+	
3	23	F	Axillary	NS	II B		+
4	22	F	Cervical	NS	II B		+
5	64	M	Cervical	MC	III B	+	
6	24	F	Axillary	MC	III B	+	
7	25	M	Inguinal	MC	not known		+
8	79	F	Nuchal	MC	not known	+	

[a] Hodgkin's disease previously treated by radio- and chemotherapy, diagnosis established or 36, 29, and 35 months respectively

Table 5 Immunohistochemical and serological data of cytomegalovirus (*CMV*), Epstein-Barr virus (*EBV*) and toxoplasmic infections (*ND* not done, *NK* not known)

Case number	Immunohistochemistry		Serological findings of an acute infection		
	anti-CMV	LMP	toxoplasmic	CMV	EBV
1	–	–	–	–	–
2	–	+	–	–	–
3	–	+	ND	–	ND
4	–	–	–	–	–
5	–	–	ND	ND	ND
6	–	+	–	–	–
7	–	–	NK	NK	NK
8	–	+	NK	NK	NK

ond and third pattern was greater in mixed cellularity and nodular sclerosis (NS) than in nodular paragranuloma (NP). In NP cases, MBCR consisted of an isolated cluster (case 2) or two small clusters (case 1) at the border with residual lymphoid tissue. One small MBC cluster was found within HD infiltrate (case 1) – it was localized on the outer edge of one of NP nodules and contained Sternberg-Reed cells of L & H type. In both NS cases multiple lymph nodes were examined; one of them showed interfollicular infiltrates of an early cellular NS phase and others advanced NS infiltration. Foci of MBCs with intermingled HD cells were extensive in the early NS phase (cases 3 and 4), but inapparent (case 4) or missing (case 3) in the more advanced NS infiltrates.

The clinical data of the patients studied are summarized in Table 4. Four of the cases investigated (cases 1, 2, 5, and 6) represented diagnostic biopsies prior to therapy. An additional 3 patients (cases 3, 4, and 7) had a biopsy for a HD relapse following chemo- and radiotherapy-induced remission, with occasional areas of focal fibrosis and lymphocytic depletion (case 7). For 2 of these cases (3 and 7) a retrospective review of the previous biopsies was possible – it showed complete lymph node infiltration by HD without the presence of MBCR.

All 8 cases represented nodal HD associated with MBCR. In 3 of them, additional extranodal tissue was also examined (subcutaneous infiltrate, liver and bone marrow biopsies) and was found not to contain MBCs.

Serological data of anti-toxoplasmic, anti-EBV and anti-CMV antibody tests are summarized in Table 5. In case 3 anti-herpes simplex virus (HSV) antibodies were also examined. The serological tests did not indicate acute infection in any of the examined cases; in cases 4 and 6 anti-EBV and in case 1 both anti-EBV and anti-toxoplasmic anti-IgG antibodies wee increased, while those of anti-IgM type were within normal limits.

The MBCs in all the cases investigated showed a positivity for L26 (Fig. 3) and Ki-B5, rarely fine granular cytoplasmic positivity for Ki-M1p (case 5) and a constant negativity for all other antibodies applied (CD43, UCHL1, CD30, IgM, and light chains of Ig). The Sternberg-Reed and Hodgkin's cells showed positivity for CD15 and CD30; in case 1 alone they were CD15 positive and CD30 negative. With the exception of the L & H cells of cases 1 and 2 (CD20+, Ki-B5+), the neoplastic cells were negative for L26, Ki-B5, MT1, UCHL1, Ki-M1p and CMV. The intermingled plasmacytes expressed both light chains of Ig. The positivity of follicular structures for L26 and Ki-B5, of interfollicular lymphocytes for MT-1 and UCHL1, and of histiocytes and epitheloid cells for Ki-M1p antibody served as internal controls.

Staining for CMV was negative in all of the cases. Hodgkin and Sternberg-Reed cells showed cytoplasmic and membrane labelling for LMP in 50% of the cases (cases 2, 3, 6, and 8; Table 5). In cases 3 and 6 also a few interfollicular small lymphocytes were LMP-positive. However, the MBCs of all cases did not react with this antibody.

Discussion

The association of MBCs with HD disease has been documented in six cases. They include two cases described by Lennert (1958, 1961), one by Miettinen and Fransilla (1982) and three recent cases reported by Mohrmann et al. (1991). The additional eight cases found in the present study, representing 6.7% of a systematically reviewed large series of HD, indicate that this finding is not as rare as previously expected. However, the occurrence of MBCR in HD seems to be limited to nodal HD, as extranodal HD infiltrates did not contain any MBCs even in cases showing MBCR in nodal localizations. All the previous data have reported an association of MBC clusters with HD in its pretreatment phase. Three cases in this study (cases 3, 4 and 7) prove that MBCR may occur during histological relapse after previous radio- and chemotherapy.

In contrast with other B-cell populations, the function of MBCs remains enigmatic (Cousar 1992). However, the association of MBC proliferation with nodal HD involvement raises the question of their mutual relationship. It has been considered that MBCR might represent an "initial lymph node change specific for HD" (Lennert 1958), although neither Lennert (1958, 1961) nor Miettinen and Fransilla (1982) have described the eventual occurrence of HD infiltrates within MBCR. Mohrmann et al. (1991) were the first to describe a subtle involvement of lymph nodes by HD occurring in MBCs clusters. While definitive histogenetic conclusions on the relationships between MBCs and HD could not be drawn, Mohrmann and co-workers have hypothesized that HD originating in the interfollicular area (Lukes 1971) might arise within MBC clusters. This hypothesis was based on the occurrence of HD exclusively within (2 cases) or primarily within MBC clusters (1 case).

The unifying common feature of HD cases with associated MBC clusters in our study as well as in all previously reported six cases is the incomplete or partial nodal HD infiltration. Simultaneously, all the cases considered also showed foci of MBCR associated with follicular hyperplasia in non-infiltrated or partially infiltrated lymphoid tissue. Clusters of MBCs of intact non-infiltrated nodal parts of our cases contained Sternberg-Reed cells only exceptionally, while HD infiltrates in MBC clusters were regularly associated with Sternberg-Reed and Hodgkin's cells in the outer borders of MBC foci and in the surrounding lymphoid tissue. Mohrmann et al. (1991) have also found Sternberg-Reed cells adjacent to MBC foci. In our cases, HD infiltrates near MBC clusters or intermingled with MBCs always represented a minor part of the whole HD infiltration.

Previously reported cases (Lennert 1958, 1961; Miettinen and Fransilla 1982; Mohrmann et al. 1991) and 6 of the cases of this study consist of HD originating in the interfollicular area (Lukes 1971). However, we have also observed the previously undescribed occurrence of MBCR in NP, which is thought to originate in the follicular region (Hansmann et al. 1986; Timens et al. 1986; Pinkus and Said 1988). Our results indicate that MBCs in such cases are not related to HD or its histopathological type, but are associated with B-zonal activation of the non- or partially infiltrated parts of the lymph node. These patterns occur in pretherapeutic as well as relapse stages of HD. Whether B-zone activation with associated MBCR in these cases represents an antitumour reaction of the host, or whether it is associated with other antigenic or post-therapeutic immunological stimuli, remains to be determined.

Although MBCR is often associated with toxoplasmic and EBV-induced lymphadenitis (Lennert 1961; Stansfeld 1961; Sheibani et al. 1984; Stein et al. 1984), the direct relationship of MBCR to certain aethiological agents has not been demonstrated. By in situ hybridization for EBV-encoded RNAs, EBV was not demonstrated in neoplastic or in reactive MBCs (Niedobitek et al. 1992; Chang et al. 1993). MBCR in reactive lymphadenopathies (Stansfeld 1961; Sohn et al. 1985; Plank et al. 1993) and probably in HD reflects a transient pattern associated with follicular hyperplasia which dissappears with the involution of the activated B-zones. Moreover, HD infiltrates advancing within the B-zones might lead to the secondary occurrence of HD cells infiltrating the MBC clusters. In one of the cases previously reported, the strands of MBCs were associated with partial HD involvement, but absent in a second sequential biopsy showing fully developed HD (Miettine and Fransilla 1982). Also in our study, the examination of multiple lymph nodes in cases of NS showed more extensive MBC clusters with HD infiltrates in the early NS phases than in the nodes with more advanced NS. It seems to be obvious that MBC clusters may become obliterated, disrupted, and hence difficult to identify during the histological progression of HD (Mohrmann et al. 1991).

In contrast to the better known occurrence of MBCR in a variety of reactive lymphadenopathies (Lennert 1961; Stansfeld 1961), the recognition of MBCR associated with nodal HD may cause diagnostic problems. In a reply to the report of Mohrmann et al. (1991), Rushin et al. (1992) have stressed the necessity to exclude CMV infection. The same is true for other infectious lymphadenopathies that may show Sternberg-Reed-like cells (Fellbaum et al. 1988). In this study, MBCs did not express positivity for LMP. MBCR occurred in both EBV latently infected and non-infected cases of HD, as defined by the expression of LMP (Pallesen et al. 1991; Stein et al. 1992). Serological tests did not demonstrate features of an acute toxoplasmic, CMV, or EBV infection in any of our cases. Staining for CMV in our cases, as well as in the cases of Mohrmann et al. (1991) was negative (Nathwani and Brynes 1992). Moreover, in contrast to the cases of Mohrmann et al. (1991), we did not observe necrosis of HD infiltrates within MBC clusters or any features of other infectious lymphadenopathies. However, our data indicate that, like the reactive lymphadenopathies, MBCs occurring

in HD may also show large cell transformation (Plank et al. 1993).

In the series of Mohrmann et al. (1991), the inconspicuous foci of HD were exclusively or to a major extent located within MBC clusters. This was not the case in our study and by careful evaluation the diagnosis of HD could not have been missed in our cases. However, we support the opinion of Mohrmann et al. (1991) that minor or partial involvement of HD should not be overlooked following the finding of MBCR associated with reactive features of non-infiltrated lymphoid tissue. The pathologist should be aware that clusters of MBCs may occur not only in the early stages of HD but also in the post-treatment relapse.

Acknowledgements This study was carried out while Dr. Plank (from the Department of Pathology, Komensky University Medical Faculty in Martin, Slovak Republic) was recipient of a fellowship from the Alexander von Humboldt Foundation (Germany) and guest in the Department of Pathology, University of Cologne. This work was supported by grants from the Deutsche Krebshilfe (M23/89/Fi1 and M16/88/Ha1). We are grateful to Mrs. U. Weihrauch, Mrs. C. Dumont, and Mrs. T. Lipinski for technical assistance.

References

Chang KL, Chen Y-Y, Weiss LM (1993) Lack of evidence of Epstein-Barr virus in hairy cell leukaemia and monocytoid B-cell lymphoma. Hum Pathol 24:58–61

Cousar JB (1992) Immunological features of parafollicular (monocytoid) B-cell lymphoma (abstract). Am J Surg Pathol 16:203–203

Fellbaum C, Hansmann ML, Parwaresch MR, Lennert K (1988) Monoclonal antibodies Ki-B3 and Leu-M1 discriminate giant cells of infectious mononucleosis and of Hodgkin's disease. Hum Pathol 19:1168–1173

Hansmann M-L, Wacker HH, Radzun HJ (1986) Paragranuloma is variant of Hodgkin's disease with predominance of B-cells. Virchows Arch [A] 409:171–181

Hansmann M-L, Wacker HH, Gralla J, Lumbeck H, Kossmahl M, Heidebrecht HJ, Radzun HJ, Parwaresch MR (1991) Ki-B5: a monoclonal antibody unrelated to CD45 recognizes normal and neoplastic human B cells in routine paraffin sections. Blood 77:809–817

Hsu S-M, Raine L, Fanger H (1981) A comparative study of the peroxidase-antiperoxidase method and an avidin-biotin complex method for studying polypeptide hormones with radioimmunoassay antibodies. Am J Clin Pathol 75:734–738

Lennert K (1958) Die Frühveränderungen der Lymphogranulomatose. Frankf Z Pathol 69:103–122

Lennert K (1961) Cytologie und Lymphadenitis. In: Uehlinger E (ed) Handbuch der speziellen pathologischen Anatomie und Histologie, vol 1, part 3. Lymphknoten Bandteil A Cytologie und Lymphadenitis. Springer, Berlin Heidelberg New York, pp 1–605

Lennert K, Mohri N (1974) Histologische Klassifizierung und Vorkommen des M. Hodgkin. Internist (Berl) 15:57–65

Lukes RJ (1971) Criteria for involvement of lymph node, bone marrow, spleen, and liver in Hodgkin's disease. Cancer Res 31:1755–1767

Lukes RJ, Butler JJ, Hicks EB (1966) Natural history of Hodgkin's disease as related to its pathologic picture. Cancer 19:317–344

Miettinen M, Fransilla K (1982) Malignant lymphomas simulating lymph node toxoplasmosis. Histopathology 6:129–140

Mohrmann RL, Nathwani BN, Brynes RK, Sheibani K (1991) Hodgkin's disease occurring in monocytoid B-cell clusters. Am J Clin Pathol 95:802–808

Nathwani BN (1992) Diagnostic significance of morphologic patterns in lymph node proliferation. In: Knowles DM (ed) Diagnostic hematopathology. Williams and Wilkins, Baltimore, pp 407–426

Nathwani BN, Brynes RK (1992) The author's reply. Am J Clin Pathol 97:159

Niedobitek G, Herbst H, Young LS, Brooks L, Masucci MG, Crocker J, Rickinson AB, Stein H (1992) Patterns of Epstein-Barr virus infection in non-neoplastic lymphoid tissue. Blood 79:2520–2526

Pallesen G, Hamilton-Dutoit SJ, Rowe M, Young LS (1991) Expression of Epstein-Barr virus latent gene products in tumour cells of Hodgkin's disease. Lancet 337:320–322

Pinkus GS, Said J (1988) Hodgkin's disease, lymphocytic predominance type, nodular – further evidence for a B-cell derivation. Am J Pathol 133:211–217

Plank L, Hansmann M-L, Fischer R (1993) The cytologic spectrum of monocytoid B-cell reaction: recognition of its large cell type. Histopathology 23:425–431

Purtillo DT, Strobach RS, Okano M, Davis JR (1992) Biology of disease. Epstein-Barr virus-associated lymphoproliferative disorders. Lab Invest 67:5–14

Radzun HJ, Hansmann ML, Heidebrecht HJ, Bödewadt-Radzun S, Lumbeck H, Hernandez C, Kuhn C, Parwaresch MR (1991) Detection of a monocyte/macrophage restricted antigen in routinely processed tissue sections by monoclonal antibody Ki-M1p. Lab Invest 65:306–315

Rushin JM, Cotelingam JD, Heaton RB (1992) Hodgkin's disease in monocytoid B-cell clusters and cytomegalovirus infection (letter to the Editor). Am J Clin Pathol 97:158–159

Sheibani K, Fritz R, Winberg C, Burke JS, Rappaport H (1984) "Monocytoid" cells in reactive follicular hyperplasia with and without histiocytic reactions: an immunohistochemical study of 21 cases including suspected cases of toxoplasmic lymphadenitis. Am J Clin Pathol 81:453–458

Sohn CC, Sheibani K, Winberg CD, Rappaport H (1985) Monocytoid B-lymphocytes: their relation to the patterns of acquired immunodeficiency syndrome (AIDS) and AIDS-related lymphadenopathy. Hum Pathol 16:979–985

Stansfeld AG (1961) The histological diagnosis of toxoplasmic lymphadenitis. J Clin Pathol 14:565–573

Stein H, Lennert K, Mason DY, Liangru S, Ziegler A (1984) Immature sinus histiocytosis. Their identification as a novel B-cell population. Am J Pathol 117:44–52

Stein H, Hummel M, Anagnostopoulos I, Korbjuhn P, Niedobitek G, Dallenbach F, Herbst H (1992) Epstein-Barr-Virus-assoziierte Lymphoproliferationen. Verh Dtsch Ges Pathol 76:79–95

Timens W, Visser L, Poppema S (1986) Nodular lymphocyte predominance type Hodgkin's disease is a germinal centre lymphoma. Lab Invest 54:457–461