Monocytoid B cell lymphoma: clinical and prognostic features of 21 patients

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Abstract

Twenty one patients between 34 and 83 years of age with monocytoid B cell lymphoma (MBCL) of the lymph node were studied. The histological picture characteristically showed broad strands of medium sized cells with irregularly shaped nuclei and a fairly broad rim of slightly basophilic cytoplasm. One case developed into a centroblastic polymorphic lymphoma. Bone marrow infiltration was documented in three cases and leukaemic conversion in one case of MBCL. Seven patients had enlarged spleens. Eight patients were in stage I, five in stage II/II_E, two in stage III, and six in stage IV at the time of diagnosis. Of 18 patients subsequently followed up, eight were in complete remission, two in partial remission, and three were undergoing treatment at completion of the study; five patients had died. Relapse occurred in nine patients and was a common feature of MBCL. The prognosis of MBCL was comparable with that of other low grade malignant lymphomas. Fourteen patients presented with primary nodal lymphoma. In seven patients with nodal MBCL, however, a concomitant low grade B cell lymphoma of the mucosa-associated lymphoid tissue (MALT) was also found in the stomach (n = 4), nasopharynx (n = 1), salivary glands (n = 1) and thyroid gland (n = 1). Two of these cases developed into high grade lymphoma. These extra-nodal manifestations were found simultaneously with MBCL in five patients. In another two patients, however, these symptoms occurred in a later phase of the disease.

It is emphasised that adequate staging procedures must be carried out in any case of nodal MBCL to exclude underlying low grade B cell lymphoma of the MALT.

Immature sinus histiocytes,¹ also termed monocytoid cells,² were first described by Lennert in 1959 as a characteristic feature of Pinner's lymphadenitis¹ long before these cells were identified immunohistologically by four independent study groups (1984/85) as B lymphocytes that show positive reactivity with monoclonal B cell antibodies.³⁻⁶ These cells, for which the term monocytoid B cells has been accepted, have also been found in other

reactive lymph node lesions, including, increasingly, lymphadenopathy associated with AIDS^{7,8} and occasionally Hodgkin's disease.⁹ Despite thorough investigations of the lineage links between monocytoid B cells and other cell subsets, the exact position of monocytoid B cells in the B cell system is still unknown.^{3-6 10-16}

The first malignant lymphoma composed of monotypic monocytoid B cells was described by McGinn *et al* in 1985.¹⁷ To date 56 cases of monocytoid B cell lymphoma (MBCL) have been documented.¹⁷⁻²⁶ MBCL has been compared with other low grade lymphomas from a morphological, immunological, and clinical point of view.^{9 17-20 22 25 27 28} Though compatible with hairy cell leukaemia (HCL) in many aspects,^{21 27} MBCL has been established as a novel B cell neoplasm with a well defined morphological pattern and a distinct phenotype. Due to its extreme rarity few clinical data are available.^{23 25 28}

The objective of the present study was to evaluate diagnostic, clinical, and especially prognostic features of patients with monocytoid B cell lymphoma.

Methods

Twenty one cases of nodal MBCL were drawn from the files of the Lymph Node Registry in Kiel (table 1). In seven cases an additional lymphoma was documented in the stomach (n = 4), nasopharynx (n = 1), salivary glands (n = 1), or thyroid gland (n = 1) (table 2). The histological sections were re-examined. They had been fixed in 5-10% formaldehyde, embedded in paraffin wax, and routinely stained with Giemsa, haematoxylin and eosin, periodic acid Schiff and Gomori's silver impregnation. Additionally, the sections were dewaxed, rehydrated, digested in trypsin and immunostained using the peroxidase-antiperoxidase method.²⁹ Follow up of 18 patients provided prognostic data (table 3). Three of the patients could not be evaluated in terms of survival because the diagnosis was too recent. Clinical information was acquired from questionnaires and clinical reports provided by clinicians and general practitioners. Actuarial survival was calculated by the life table method of Kaplan and Meier.³⁰

Results

Low power magnification of slides of MBCL showed broad strands and sheets of tumour

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Table 1 Clinical data on MBCL (*n* = 21)

Case No	Age (years)/sex	Presenting symptoms	Prediagnostic history (months)	Stage	Extra-nodal disease
1	68F	Cervical and supraclavicular lymphadenopathy	4	II ₂ E ₁ A	
2	72M	Cervical lymphadenopathy	2	IA	
3	55F	Cervical lymphadenopathy	2	IA	
4	74M	Inguinal lymphadenopathy	—	IA	
5	80F	Cervical lymphadenopathy	6	IA	Spleen*
6	80M	Submandibular lymphadenopathy	6	IA	
7	56M	Cervical lymphadenopathy	12	III ₁ B(CS)	
8	64M	Generalised lymphadenopathy	24	III ₁ A(CS)	
9	53F	Gastric ulcer	12	II ₁ E ₁ B	
10	45M	Gastric ulcer	18	II ₁ E ₁ A	
11	57M	Generalised lymphadenopathy	†	IVB	Spleen,* liver*
12	59F	Gastric ulcer	48	IVA	Bone marrow, liver
13	34M	Generalised lymphadenopathy initial flu	2	IVB	Bone marrow
14	77F	Progressive goiter	48	II ₁ E ₁ A	
15	83F	Generalised lymphadenopathy	3	IVA (CS)	
16	42M	Generalised lymphadenopathy	1	IVB	Bone marrow
17	76M	Inguinal lymphadenopathy	1	IB	
18	69F	Swelling of buttock	1	IA	
19	46M	Supraclavicular lymphadenopathy	8	IVA	Liver
		Generalised lymphadenopathy			
		Initial flu			
20	54F	Cervical/submandibular lymphadenopathy	6	II ₁ B	
21	40F	Cervical lymphadenopathy	—	IA	

*Disease verified at necropsy or at a later stage of disease.

†Not evaluable.

Table 2 Patients in whom extranodal lymphoma was found simultaneously (*n* = 5) with nodal MBCL or in a later phase of disease* (*n* = 2)

Extranodal lymphoma	Case No	<i>n</i>
Stomach	Cases 5, 9, 10, 12	3 (+ 1*)
Nasopharynx	1	1
Salivary gland	13	1*
Thyroid	14	1
Total		7

cells, focally confined to enlarged sinuses (in situ lymphoma²³), but most often affecting the adjoining pulp. The capsule was always infiltrated and the nodal architecture was effaced to varying degrees (fig 1). The presence of reactive looking germinal centres was a feature in 11 cases. In some cases the growth pattern was noticeably perifollicular: in two mesenteric lymph nodes the tumour had spread within the marginal zone of some germinal centres adjacent to the subcapsular sinus (figs 2a and b). Silver impregnation showed an

increase in high endothelial venules in the tumour infiltrates. Under high power magnification the cytological appearance of the tumour cells varied considerably. In general, the cells were medium sized and showed slightly or extremely irregular, roundish to reniform or indented nuclei, with one to three inconspicuous nucleoli and a fairly broad rim of slightly basophilic cytoplasm (fig 3). In a paragastric lymph node from one case the tumour had developed into a centroblastic polymorphic lymphoma at the time of diagnosis.

The monocytic B cells exhibited monoclonal surface immunoglobulins in 14 cases and cytoplasmic immunoglobulins, predominantly IgM/κ (*n* = 7) in eight cases. Three of these cases exhibited plasmacytic differentiation with plasma cells of the same clone. In two other cases, however, monoclonality was evident only in plasma cells (table 4). Varying numbers of immunoblasts (from the same clone) were found intermingled with the monocytoid B cells. Infiltration of the pulp by plasmacytoid and plasma cells was occasionally a dominant feature of the tumour.

When they were localised in the stomach or nasopharynx (fig 4), the extra-nodal manifestations that were combined with nodal MBCL in seven patients showed the characteristic features of a low grade B cell lymphoma of the mucosa-associated lymphoid tissue (MALT) including lymphoepithelial lesions (*n* = 4) and reactive intratumoural germinal centres (*n* = 4). One case, however, had developed into a centroblastic polymorphic lymphoma in the stomach and one into an unclassified high grade lymphoma in the salivary glands.

Of a total of 21 patients, aged 34 to 83 years, 11 were male and 10 female. The age distribution curve showed peaks in the 6th and 8th decades (fig 5).

Table 3 Follow up data on MBCL (*n* = 18)

Case No	Follow up (months)	Primary treatment	Response (months) relapse +/−
1	54 ■	Neck dissection	CR 4+
2	68	EFR (45 Gy)	CR 66−
3	66	IFR	CR 55+
4	35 ■	Lymph node excision	CR 23+
5	13 ■	Lymph node excision	CR 3+
6	61	IFR (36 Gy)	CR 60−
7	49	4 × COP, 3 × ABVD	CR 36+
8	48	9 × CHOP	CR 23+
		Abdominal radiotherapy (30 Gy)	
9	36	Gastrectomy	CR 22+
10	21	Gastrectomy, abdominal radiotherapy	CR 16−
11	3 ■	Leukeran/Decortin	PR
12	15 ■	Gastrectomy, 6 × CHOP	CR 1+
13	13	6 × COP	CR 10+
14	20	Strumectomy, EFR (45 Gy)	CR 18−
15	10	10 × KNOSPE	PR
16	9	Leukeran/Decortin	PR
17	6	Local excision	CR 6−
18	83	4 × KNOSPE	CR 78−

ABVD—Adriamycin, bleomycin, vinblastin, Decarbazine.

CHOP—Cyclophosphamide, 14-Hydroxydaunomycin, Oncovin, prednisone.

COP—Cyclophosphamide, oncovin, prednisone.

COP-BLAM—Cyclophosphamide, vincristine, prednisone, bleomycin, adriamycin, procarbazine.

CR/PR—Complete/partial remission due to primary treatment.

IFR/EFR—Involved/extended field radiation.

KNOSPE—Chlorambucil, prednisone.

■—Died during follow up.

HISTORY BEFORE DIAGNOSIS AND INITIAL SYMPTOMS

In 17 patients the initial symptoms were peripheral lymphadenopathy, localised at one site (*n* = 9), two sites (*n* = 2), or generalised

Figure 1 Lymph node infiltrated by MBCL spreading in broad inter- and perfollicular strands. The tumour cells react weakly with monoclonal surface μ heavy chain

Figure 2 (A) Paragastric lymph node infiltrated by MBCL. A noticeably broadened marginal zone is clearly distinguishable from an inner mantle zone and a reactive germinal centre (Giemsa). (B) High power magnification of fig 2a (Giemsa).

($n = 6$), lasting for between one month to two years. In one case a previous biopsy specimen of submandibular soft tissue had shown an undefinable lymphoid infiltration, and in another a previous submandibular swelling had shown spontaneous regression. Additional symptoms were flu-like episodes in two cases and swelling of the ipsilateral buttock in one case of inguinal lymphadenopathy. Three other patients with paragastric MBCL associated with gastric lymphoma had a history of persistent ulcers for one to four years. Finally, in one patient a history of progressing goitre over a period of four years and an earlier occurrence of Hashimoto's disease preceded an asymptomatic lymphoma in the thyroid combined with MBCL in a regional lymph node, both unexpectedly discovered in the thyroidectomy specimen.

Seven patients with MBCL initially had B symptoms. Fever was reported in three patients, night sweating in four, itching in one, and alcohol intolerance in two as well as weight loss in one patient with an additional gastric lymphoma.

ASSOCIATED DISEASES AND PREVIOUS AILMENTS

Nine patients also had minor or major cardiovascular disease. One patient presented with atopic trias and porphyria cutanea tarda due to liver cirrhosis and carcinoma, another with ethylic liver disease, and one with chronic persistent hepatitis. One patient had had benign colon polyps, three had tuberculosis, one had mononucleosis, and one had parotitis epidemica.

LABORATORY FINDINGS

An increased erythrocyte sedimentation rate (ESR) in six patients and anaemia in four were the most common, albeit unspecific, laboratory findings. Immunoelectrophoresis was performed on 12 patients showing a case of monoclonal IgG/ κ gammopathy (case 19). Leukaemic conversion of MBCL was documented in case 16 who had a leucocytosis of $14 \times 10^9/l$ with 80% medium sized lymphoid cells. In a mononuclear cell fraction from filtered, anticoagulated venous blood, medium sized cells with reniform or indented nuclei and abundant slightly basophilic cytoplasm were phenotypically identical with the tumour cells in the lymph node (fig 6).

STAGING

The initial stage of disease, according to the Ann Arbor classification, as modified by Musshoff, was determined by pathological or clinical staging methods, or a combination. Malignant pathology in lymph nodes and extranodal tissue was therefore histologically confirmed in 18 patients, but in cases 7, 8, and 15 it was presumed on the basis of findings from ultrasound scans, computed tomography, x-ray picture and palpation (clinical stage).

Eight (38%) patients were in stage I. Cervical lymph nodes were affected in four of them, inguinal in two, submandibular in one, and supraclavicular lymph nodes in one. In

Figure 3 MBCL in the lymph node showing medium sized cells with irregularly shaped, indented nuclei and a broad rim of slightly basophilic cytoplasm (Giemsa).

Table 4 Immunophenotypes of tumour cells in MBCL showing plasmacytic differentiation in five cases (n = 21)

Case No	Immunophenotype	Monocytoid B cells		Plasma cells cIg
		sIg	cIg	
1	IgM/ κ	+	+	+
2	IgM/ κ	+	+	—
3	IgM/ λ	+	+	—
4	IgM/ κ	+	—	—
5	IgG/ κ	—	—	++
6	IgM/ κ	+	(+)	—
7	IgM/ κ	+	+	—
8	IgM/ κ	+	+	—
9	—/ κ	+	+	—
10	—/ κ	+	—	—
11	IgM/ λ	(+)	—	—
12	IgM/ λ	+	—	—
13	?*	—	—	—
14	?*	—	—	—
15	IgM/ λ	+	+	+
16	IgM/ κ	—	—	+
17	?*	—	—	—
18	?*	—	—	—
19	IgG/ κ	+	—	+
20	—/ λ	(+)	—	—
21	?*	—	—	—

* Immunophenotypes not available.

Figure 4 Lymphoepithelial lesion in a low grade B cell lymphoma of the MALT in the nasopharynx (Giemsa).

Figure 5 Age and sex distribution of monocytoid B cell lymphoma (n = 21).

case 5, however, who had cervical MBCL, a post mortem examination 13 months after diagnosis showed lymphoma in the stomach.

Five (24%) patients were in stage II/II_E. In one of them submandibular and cervical lymph nodes were affected. In four others with coincidental lymphomas in the stomach (n = 2), nasopharynx (n = 1), and thyroid (n = 1) MBCL affected the corresponding regional lymph nodes.

Two patients in clinical stage III_S (10%) had generalised or localised lymphadenopathy together with enlarged livers and spleens.

Six (28%) patients were in stage IV. They had hepatosplenomegaly (n = 4), splenomegaly (n = 1), or hepatomegaly (n = 1) combined with generalised (n = 5) or localised (n = 1) lymphadenopathy. Pathological staging was performed in four patients with positive biopsy specimens of bone marrow (n = 2), liver (n = 1), or both (n = 1). In another patient spleen and liver disease were first confirmed during post mortem examination. In one case MBCL was combined with a lymphoma in the stomach and in one with a lymphoma in the salivary glands.

Treatment protocols for each case varied widely, irrespective of the stage of disease.

Diagnostic lymph node excision (n = 2) or complete removal of affected nodal and extranodal tissue (n = 3) was the only treatment given to three patients in stage I and two patients in stage II_E.

Three patients in stage I were treated with radiotherapy alone; two patients in stage II_E had radiotherapy postoperatively, and one patient in stage III_S was treated with a combination of radiotherapy and chemotherapy. Different forms of radiotherapy were applied: involved field radiation (IFR) (n = 2), extended field radiation (ERF) (n = 2), or abdominal radiation (n = 2) with a dose ranging from 30 to 45 Gy.

Chemotherapy alone was used to treat one patient in stage I, one patient in stage III_S, and four patients in stage IV. It was given as a supplement to gastrectomy in one patient in stage IV_E. The cytotoxic drugs were given most often as cycles of COP (cyclophosphamide,

Figure 6 Mononuclear cell fraction from filtered, anticoagulated venous blood in a case of leukaemic MBCL. Medium sized cells show reniform or indented nuclei and a broad rim of slightly basophilic cytoplasm (May-Grünwald-Giemsa).

Oncovin, prednisone); CHOP (cyclophosphamide, 14-hydroxydaunomycin, Oncovin, prednisone) ABVD (adriamycin, bleomycin, vinblastine, decarbazine), and according to the KNOPSE scheme (chlorambucil, prednisone) and two patients received continuous Leukeran and Decortin.

RESULTS OF TREATMENT

Seven of the patients in stage I were followed up. They were all brought into complete remission, and four of them stayed free of relapse (maximum of 78 months). Case 2 with cervical lymphoma went into remission after EFR (45 Gy) and case 6 with submandibular lymphoma after IFR (36 Gy). In case 18, with a supraclavicular manifestation, remission was achieved after four cycles of KNOSPE and in case 17, with inguinal lymphoma, after lymph node excision and complete removal of an undetermined infiltration in the ipsilateral buttock. Case 3, with cervical MBCL treated with IFR, had a relapse in an axillary lymph node after 55 months in remission. The lymph node was removed. No further evidence of lymphoma was found. Case 4, with inguinal MBCL, was not treated after diagnostic lymph node excision due to a myocardial infarction. Nodal and cerebral relapse occurred after 23 months and was treated with central nervous system radiation (50 Gy) and chemotherapy (COP), but the patient died 35 months after diagnosis. After one year case 5, who had recurrent cervical MBCL, deteriorated rapidly with severe anaemia, diarrhoea, and ascites. She died soon after, following severe bleeding from a formerly ulcerated gastric lymphoma with peritoneal spreading and splenic disease.

The four patients in stage II_E were followed up. They all went into complete remission and two of them remained free of relapse. Case 10, who had shown malignant disease in the stomach and paragastric lymph nodes, went into remission after gastrectomy and abdominal radiation, and case 14 with manifest lymphoma in the thyroid and a regional lymph

node, after strumectomy and EFR (45 Gy). Case 1, who had cervical and supraclavicular lymphadenopathy associated with nasopharyngeal lymphoma, experienced a local relapse four months after removal of the tumour and neck dissection. In spite of repeated surgery and radiotherapy the patient died 54 months after diagnosis in an unknown condition. Case 9, with gastric and paragastric disease, underwent gastrectomy. Local and para-aortal relapse after 22 months was treated with chemotherapy (COP) and abdominal radiation, and no further lymphoma was found.

The two patients in clinical stage III_S were both brought into complete remission and both were followed up. Case 8 was treated with chemotherapy (CHOP) and abdominal radiation (30 Gy). After 23 months of complete remission a relapse occurred in the supradiaphragmatic lymph nodes accompanied by pleural effusion. Further chemotherapy (COP-BLAM) resulted in only partial remission. Case 7, treated with chemotherapy (COP and ABV), had a relapse in cervical and axillary lymph nodes after 36 months of complete remission and was undergoing renewed chemotherapy (ABVD) at the completion of this study.

Five of the patients in stage IV were followed up and two of them went into complete remission. Case 12, who showed a coincidental gastric lymphoma and transformation into a centroblastic polymorphic lymphoma at gastric and paragastric sites, underwent gastrectomy and primary chemotherapy (CHOP). A generalised relapse occurred after one month of complete remission and the patient died before renewed radiotherapy had been fully administered, 15 months after diagnosis. In case 13 chemotherapy (COP) resulted in complete remission for 10 months, when an additional unclassified high grade lymphoma was discovered in bilateral salivary glands, just at the completion of this study. Three patients only were brought into partial remission: case 15 after 10 cycles of KNOSPE and cases 11 and 16, who were treated with continuous Leukeran or Decortin chemotherapy. Case 16 was still undergoing treatment at the completion of our study, but case 11 had died three months after diagnosis.

PROGNOSIS

Eighteen patients with MBCL were followed up for three to 83 months (mean follow up period 34 months). With treatment 15 patients were brought into complete remission for periods ranging from one to 78 months (mean 28 months). Six patients, all in early stages, stayed free of relapse (maximum 78 months). Nine (50%) patients, however, relapsed after complete remissions lasting from one to 55 months (mean 20 months). Four were in an early stage and five in an advanced stage. In case 5 this was only discovered at necropsy. Only three patients managed to go into partial remission.

Five patients died within three to 54 months after diagnosis. Two of them were in an early stage and three in an advanced stage at diag-

Figure 7 Actuarial survival of 18 patients with monocytoid B cell lymphoma (MBCL) in comparison with the normal population.

nosis. Patients in an advanced stage died within a much shorter time than those in an early stage.

When this study had been completed eight patients were in complete remission, two in partial remission, and three were undergoing treatment.

Overall, the probability of survival for the whole group after 83 months was lower than that for a comparable normal population. The survival curve showed a constant downward slope with no plateau (fig 7), comparable with the progression seen in other low grade lymphomas.

Discussion

Twenty one patients with MBCL were studied and 18 of them evaluated for prognostic features. Special emphasis was placed on seven cases in which the nodal MBCL occurred in combination with a lymphoma in the stomach ($n = 4$), nasopharynx ($n = 1$), salivary glands ($n = 1$), or thyroid gland ($n = 1$).

Our morphological and immunological findings were compatible with those of previous studies^{9 17-25 27} and will be published in a separate paper. The observation that monoclonality was evident only in plasma cells in two cases with pronounced plasmacytic differentiation, while monocytoid B cells did not express any immunoglobulin at all, is worth mentioning for its diagnostic implications.

We found that MBCL, like other low grade lymphomas, mainly affects the elderly. High rates of complete remission, relapse, and long term survival are common features. Our patients presented in all stages and had splenomegaly in seven cases. In one case of MBCL the tumour transformed into a centroblastic polymorphic lymphoma. Unlike other low grade lymphomas, bone marrow disease ($n = 3$) and leukaemic conversion ($n = 1$) were uncommon features of MBCL.^{21 24 25 28 31} The clinical features of 21 patients with MBCL recently published by Sheibani *et al*²³ agreed with our results on age distribution, rare bone marrow disease, rare development into a high grade lymphoma, treatment and high rates of complete remission and long term survival. They were at variance with our results regarding the distribution of primary disease, predominance of early stages

of the disease, and low rates of splenomegaly and relapse. Clinically, four of Sheibani's patients with salivary gland disease had Sjögren's syndrome. One of our patients had an unclassified high grade lymphoma in bilateral salivary glands following a primary generalised MBCL, but no Sjögren's syndrome was documented. A history of Hashimoto's disease, an autoimmune disease which may also be considered a precursor to lymphoma,³² however, preceded a low grade B cell lymphoma in the thyroid diagnosed coincidentally with an MBCL in a regional lymph node.

According to the survival curve evaluated over a period of 83 months, the prognosis of MBCL was comparable with that of other low grade lymphomas. Additional extranodal components were found in three of the five patients who died and in five of the nine patients who relapsed. According to our results, however, patients in advanced stage MBCL had a worse prognosis and a higher risk of relapse than those in early stages. All three patients who died in spite of an early initial stage had a more complex history. Case 4, therefore, was not treated, because of myocardial infarction. Case 1 was lost to medical follow up and died in an unknown condition. Case 5 was not treated, because of an incorrectly diagnosed plasmacytoma in stage I; furthermore, this patient was most probably initially in a more advanced stage, according to the necropsy findings.

In seven patients with nodal MBCL a low grade B cell lymphoma of the MALT was found—in four of them this was in the stomach, in one in the nasopharynx, in one in the salivary glands and in one in the thyroid gland, which possibly belongs to the MALT. In two cases the tumour had developed into a high grade lymphoma. This coincidence merits more thorough discussion. Except for one case, MBCL was diagnosed in the corresponding regional lymph nodes so the question arises whether MBCL represents the equivalent in the lymph node of a low grade B cell lymphoma of the MALT. Morphological and immunological evidence may support this presumption when we compare these two lymphomas.

MBCL was characterised by its typical growth pattern of broad strands, by reactive looking germinal centres, and increased venules within the tumour infiltrates. Cytologically, the medium sized monocytoid B cells mainly showed irregularly shaped nuclei and a fairly broad rim of slightly basophilic cytoplasm. They all expressed B cell antigens (positive reactions with L26, Ki-B3, and Ki-B5). In 14 cases monoclonal surface immunoglobulins were expressed, and five cases exhibited plasmacytic differentiation. One case of MBCL developed into a high grade lymphoma.

Low grade B cell lymphomas of the MALT, as described by Isaacson,¹⁴ show diffuse tumour invasion, lymphoid follicles, and lymphoepithelial lesions. Cytologically, the centrocyte-like tumour cells are small to intermediate in size, or of blastic appearance when the tumour has transformed into a high grade lymphoma.¹⁵ They exhibit monotypic immunoglobulin and other B cell antigens. Plasmacytic differentiation is reported in about 30% of all cases.

Similarities were most prominent in three cases of mesenteric MBCL associated with a low grade B cell lymphoma of the MALT in the stomach, one of which developed into a high grade lymphoma. Nodal components were not distinguishable from regional metastasis (fig 2a); additionally gastric components showed strands of monocytoid B cells that mimicked nodal MBCL to a varying degree. These strands of monocytoid B cells may have been described before, being interpreted as "clear cell" variants of centrocyte-like tumour cells.¹⁵ A striking resemblance between affected gastric lymph nodes and MBCL has been pointed out by us and other authors.¹⁵⁻³³ Slight or more noticeable differences in pattern and in the cytological appearance of the tumour cells in nodal and extra-nodal sites seen in other cases may well be due to different micro-environments. More evidence in favour of one and the same process may be provided by immunological data based on our material. Thus in three of seven cases it was evident that the immunophenotypes of monocytoid B cells and centrocyte-like tumour cells were identical.

According to our clinical results, the manifestation of lymphoma in the MALT may be preceded by a fairly long period of lymphadenopathy, both localised and generalised. Thus in five patients extranodal lymphoma was found simultaneously, but in two of them only in a later phase of the disease. Our diagnosis of MBCL, though, always referred to an affected lymph node. Therefore, cases in which we found only extra-nodal lymphoma manifestation, with prominent strands of monocytoid B cells mimicking MBCL but without lymph node infiltration, were excluded from this study. This is at variance with Sheibani's interpretation of eight cases of exclusively extra-nodal disease affecting the salivary glands (n = 3), the breast (n = 2), the perigastric space with spread to the liver (n = 1), the tonsil (n = 1), and the retroperitoneal space (n = 1). It is still a subject for discussion whether other tissues, such as the lung, lachrymal glands, tonsil, breast, and urinary genital tract may all belong to the MALT, but we think that the features reported in extra-nodal MBCL by Sheibani *et al*²³ are consistent with a low grade B cell lymphoma of the MALT.

We conclude that monocytoid B cell lymphoma of the lymph node is a very rare low grade lymphoma. It occurs fairly often in combination with a low grade B cell lymphoma of the MALT, most frequently localised in the stomach, indicating a close association between these two lymphomas.³⁴ We emphatically urge clinicians to rule out an underlying low grade B cell lymphoma of the MALT in any case of nodal MBCL.

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