Childhood non-Hodgkin lymphomas in the United Kingdom: findings from the UK Children's Cancer Study Group

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Abstract

Aim—To review the presenting clinical features and the histology of cases of non-Hodgkin lymphoma (NHL) entered into the United Kingdom Children's Cancer Study Group NHL Trial.

Methods—Sections of biopsy specimens from all cases entered into the trial were stained with Giemsa and haematoxylin and eosin. All cases were stained immunohistochemically for CD45, CD3, CD45RO, CD20, and CD30. Sections were stained with either naphthol AS-D chloroacetate esterase or KP1 (CD68) to identify granulocytic tumours. In a minority of cases, additional immunohistochemical stains were performed when necessary to establish the diagnosis. The sections were reviewed by three pathologists.

Results—Of 308 cases analysed, 293 were categorised as NHL. There was only one case of low grade lymphoma in the series. Over 80% of the cases fell into the categories Burkitt lymphoma (42.2%), lymphoblastic lymphoma (27.2%) and anaplastic large cell lymphoma (15.1%). Cases of Burkitt lymphoma presented most often with abdominal tumours mainly of the ileocaecal region. Tumours of the oropharynx and nasopharynx were also common in this group. Of the 84 lymphoblastic lymphomas, 56 were of the T-cell phenotype, 12 of the B-cell phenotype and 16 of indeterminate lineage. Most of the T-lymphoblastic lymphomas showed mediastinal or pleural involvement. Infiltration of the skin and soft tissues was seen in 25% of lymphoblastic lymphoma of B or indeterminate phenotype. Forty six children were diagnosed as having anaplastic large cell lymphoma, the majority being of T or indeterminate lineage. Most patients presented with lymphadenopathy but involvement of the bones, soft tissues or skin was seen in seven patients and of the mediastinum and lungs in five.

Conclusion—Childhood non-Hodgkin lymphomas are almost all high grade and frequently extranodal. They fall mainly into the categories Burkitt lymphoma, lymphoblastic lymphoma and anaplastic large cell lymphoma. The separation of these subcategories can be made on the basis of morphology and immunohistochemical features. The anatomical distribution of these different categories of non-Hodgkin lymphoma is distinctive.

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Keywords: childhood non-Hodgkin lymphoma; Burkitt lymphoma; lymphoblastic lymphoma; anaplastic large cell lymphoma.

Non-Hodgkin lymphomas represent 4–6% of all malignant neoplastic disease of childhood.[1] About 85% of children in the United Kingdom with non-Hodgkin lymphomas are enrolled in the NHL trials organised by the United Kingdom Children's Cancer Study Group (UKCCSG), amounting to approximately 80 new cases each year. The original diagnostic biopsy specimens from these children were examined by a separate review panel and, in this report, the panel's findings are presented for nearly 300 cases. Paediatric non-Hodgkin lymphomas differ from the adult disease, in that they are almost all high grade, have a diffuse growth pattern and commonly involve extranodal sites. The majority of our cases fell into one of three diagnostic groups: Burkitt lymphoma, lymphoblastic lymphoma and anaplastic large cell lymphoma. Treatment regimes for these three categories differ,[1] and as they are rapidly progressive tumours, optimum management requires both prompt and accurate histological diagnosis.

Methods

Ten unstained paraffin wax sections and a copy of the pathology report were requested for all patients entered into the UKCCSG NHL trials. In exceptional cases, a tissue block was submitted and occasionally the panel chairman obtained additional sections. Many of the biopsy specimens had already been referred to a paediatric pathologist at the treatment centre for review and the results of the investigations done at the referral laboratory were usually available. All sections were stained with haematoxylin and eosin and with Giemsa stain. Immunohistochemistry, using either the APAAP or the immunoperoxidase method, was performed routinely with CD45, the lineage markers CD3 and CD20, and with CD45RO (UCHL1) and CD30. In the early part of the study, one section was routinely stained for naphthol AS-D chloroacetate esterase to identify granulocytic tumours. This was later replaced by immunohistochemical staining for CD68 (KP1). Sections in individual cases were also stained with antibodies directed against

Table 1   UKCCSG NHL trials: overall summary of panel diagnoses and sex distribution of the cases

Diagnosis	Number (%)	Male	Female
Burkitt lymphoma	130 (42.2)	110	20
Lymphoblastic	84 (27.2)	57	27
T 56; indeterminate 16; B 12			
Large cell anaplastic	46 (15.0)	29	17
Indeterminate 22; T16; ?T6; B2			
Centroblastic/Centroblastic centrocytic	10 (3.3)	6	4
Other B-lineage lymphomas	14 (4.5)	9	5
B-high grade (NOS) 12ᵃ; primary mediastinal large B-cell lymphoma 1; T-cell-rich B-cell lymphoma 1			
Other T-lineage lymphomas	4 (1.3)	2	2
Peripheral T3; T-high-grade (NOS) 1ᵇ			
Histiocytic	1 (0.3)	–	1
Non-Hodgkin lymphoma (NOS)ᶜ	4 (1.3)	2	2
Reactive/no evidence of lymphoma/inadequate material	11 (3.6)	6	5
No diagnosis made	4 (1.3)	3	1
Total	308 (100)	224	84

ᵃTen of the 12 cases incompletely classified because of poor quality material.
ᵇIncompletely classified because of poor quality material.
ᶜTwo of the four cases incompletely classified because of poor quality material.

epithelial membrane antigen (EMA), S-100 and, in a few instances, with antibodies
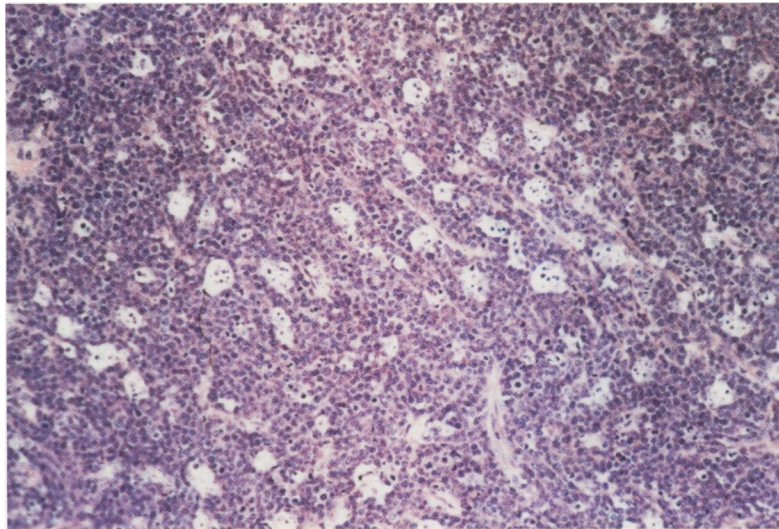

Figure 1   Low power view of Burkitt lymphoma showing sheets of monomorphic lymphoid cells interspersed with large, clear macrophages containing apoptotic debris, giving the characteristic starry sky pattern (original magnification ×80).
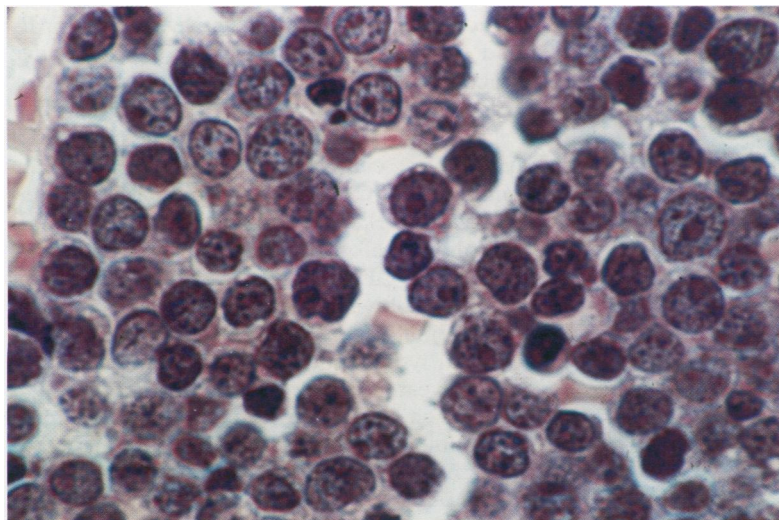

Figure 2   Burkitt lymphoma showing monomorphic blast cells with granular nuclear chromatin and one or more, usually inconspicuous, nucleoli. The cytoplasm of these cells is well-defined, amphophylic and contains small, lipid vacuoles (original magnification ×800).

directed against muramidase, bcl-2 and the Ki-67 antigen.

The sections were then circulated among the three members of the review panel who categorised them independently using the Kiel classification. The panel came together, on a few occasions, to review those cases in which there was disagreement and to reach a consensus opinion.

Results

Of 308 cases analysed by the panel, 293 were categorised as non-Hodgkin lymphoma (table 1). In 11 cases, the sections were considered to be inadequate for diagnosis or to show no evidence of lymphoma. No diagnosis was made in four cases. There was only one case of low grade lymphoma in the series. This was a follicle centre cell lymphoma, centroblastic/centrocytic follicular, presenting as lymphadenopathy in a 14 year old boy. Two cases of centroblastic lymphoma, follicular and diffuse, and seven cases categorised as centroblastic, diffuse would fall into the intermediate grade of the Working Formulation. Twelve biopsy specimens designated B-cell, high grade NOS, because the quality of the histological preparations did not permit a more exact diagnosis, were probably Burkitt lymphomas. Almost 90% of the cases, therefore, fell within the categories of Burkitt lymphoma, lymphoblastic lymphoma and anaplastic large cell lymphoma.

BURKITT LYMPHOMAS

Burkitt lymphomas showed a monomorphic proliferation of blast cells with rounded nuclei and granular nuclear chromatin. The cells contained one to four nucleoli which were identifiable but rarely prominent. Tumours always showed a high mitotic index and large numbers of apoptotic cells and nuclear fragments. The latter were often engulfed by macrophages that gave the tumour a characteristic starry sky appearance (fig 1). Burkitt lymphoma cells had a well-defined, but narrow, rim of deeply basophilic cytoplasm, best seen in Giemsa stained sections and usually best visualised at the edge of the section (fig 2). Small vacuoles corresponding to lipid droplets were seen within this rim of cytoplasm in many cases (fig 2). The tumour cells were positive for CD45 and CD20 and negative for T-lineage markers and CD30.

LYMPHOBLASTIC LYMPHOMAS

Lymphoblastic lymphomas also showed a monomorphic proliferation of blast cells with round, oval or convoluted nuclear outlines. The nuclear chromatin was fine and dispersed with two to four small nucleoli. Tumours showed a high mitotic index with frequent apoptotic cells. A starry sky pattern with vacuolated macrophages was occasionally seen but was rarely as prominent as in Burkitt lymphoma (fig 3). The cytoplasm of these cells was inconspicuous and showed weak to moderate basophilia in the Giemsa stain in contrast to Burkitt lymphoma cells (fig 4). Most lymphoblastic lymphomas were positive for CD45 but 13 examples did not stain; nine
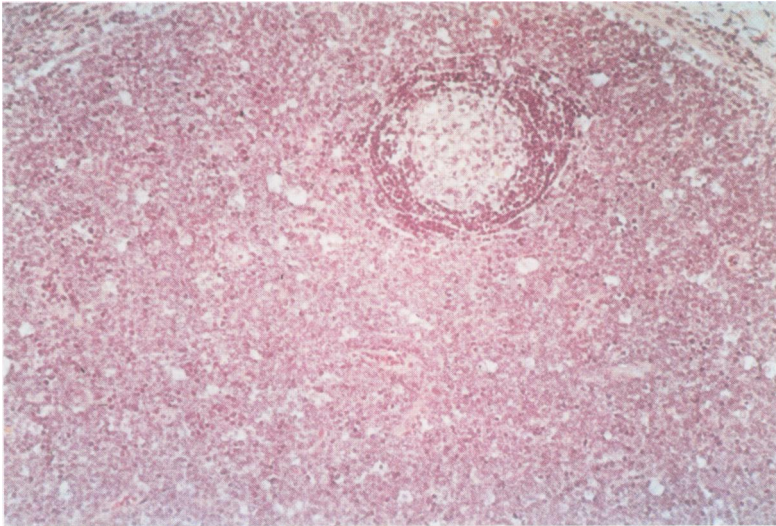
Figure 3 Lymphoblastic lymphoma showing a diffuse infiltrate of blast cells replacing most of the lymph node structure, apart from one residual germinal centre. There are scattered clear histiocytes, giving a starry sky pattern less noticeable than that seen in Burkitt lymphoma (original magnification ×80).
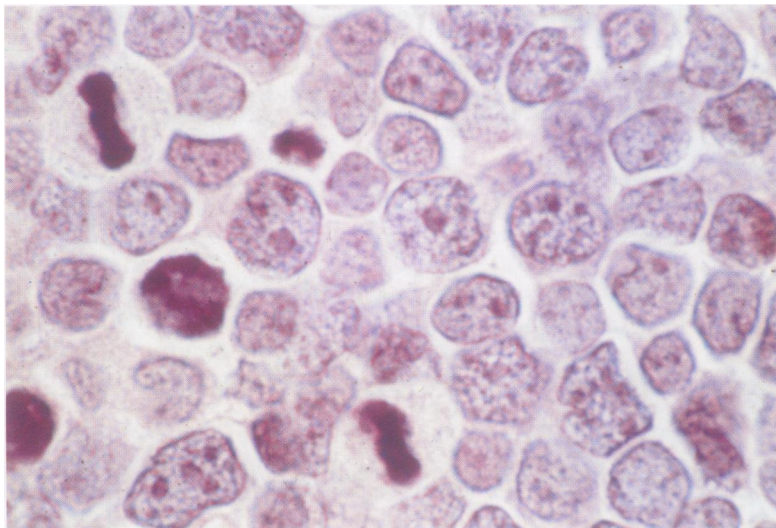

Figure 4 Lymphoblastic lymphoma showing blast cells with fine nuclear chromatin and one or more nucleoli. Mitotic figures are frequent. The cytoplasm is ill-defined and pale staining (original magnification ×800).
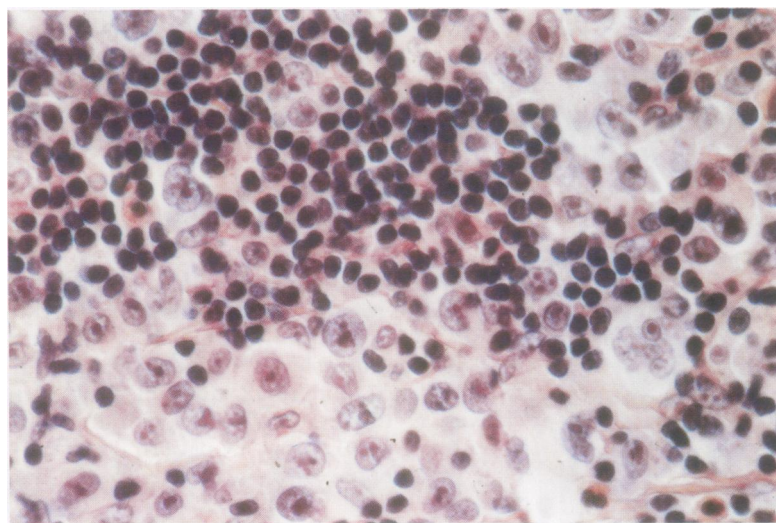

Figure 5 Anaplastic large cell lymphoma. In this tumour, the neoplastic cells have regular, oval nuclei, usually with a single nucleolus. The cytoplasm of these cell is abundant and eosinophilic (original magnification ×320).

of these were of T-lineage. T-lymphoblastic lymphomas were identified by the expression of

CD3, and B-lineage tumours by the expression of CD20. Tumours expressing neither CD3 nor CD20 were categorised as being of indeterminate lineage.

ANAPLASTIC LARGE CELL LYMPHOMA

Anaplastic large cell lymphomas were composed of large cells with pleomorphic, horse-shoe shaped (embryo-like) nuclei. In some instances, multiple nuclei occurred in a wreath-like pattern and sometimes gave rise to cells resembling Reed-Sternberg cells (although in no instance did the panel have difficulty in separating anaplastic large cell lymphoma from Hodgkin disease). Tumour cells with more monomorphic rounded nuclei also frequently occurred, either as the predominant population or mixed with the more pleomorphic variants (fig 5). Anaplastic large cell lymphoma cells had more abundant cytoplasm than other lymphomas, although the staining quality of this cytoplasm was variable. In biopsy specimens where the lymph node architecture was partially retained, the tumour cells characteristically grew within the sinuses. In a few cases, they showed a very notable perivascular distribution. In some examples, the tumour was accompanied by an intense infiltrate of inflammatory cells which, on occasions, masked the neoplastic cells. All cases diagnosed as anaplastic large cell lymphoma showed expression of CD30 (BERH2) on the tumour cell membrane and in the Golgi region (fig 6). It highlighted the tumour cells and frequently accentuated their cohesive nature. Expression of CD45 was variable, with no staining observed in 18 cases. Cases in which the tumour cells expressed CD3 were categorised as being of the T-cell phenotype. In two cases, the tumour cells expressed CD20 in the absence of T-lineage markers and were classified as being of the B-cell lineage. Cases not expressing CD3 or CD20 were categorised as being of indeterminate lineage. In 22 biopsy specimens, the tumour cells expressed EMA, although staining was sometimes weak, focal, and present in only a few of the neoplastic cells.

A single case was diagnosed as a histiocytic sarcoma on the basis of negative staining for B- and T-cell lineage markers with positive reactivity for CD68 and muramidase. This tumour occurred as a pelvic mass in a three year old girl. The case of follicle centre cell lymphoma, centroblastic/centrocytic and the nine cases of centroblastic lymphoma (follicular or diffuse) were diagnosed using standard morphological criteria; all of them expressed CD45 and CD20. A mediastinal tumour from a 15 year old girl was diagnosed as a primary mediastinal (thymic) large B-cell lymphoma. A cervical lymph node biopsy specimen from a seven year old boy was diagnosed as a T-cell-rich B-cell lymphoma, on the basis of its morphology and phenotype. Four biopsy specimens were categorised as peripheral T-cell lymphomas, as distinct from anaplastic large cell lymphoma. All of them were negative for CD30.

The main anatomical sites of disease for the three major groups of childhood non-Hodgkin
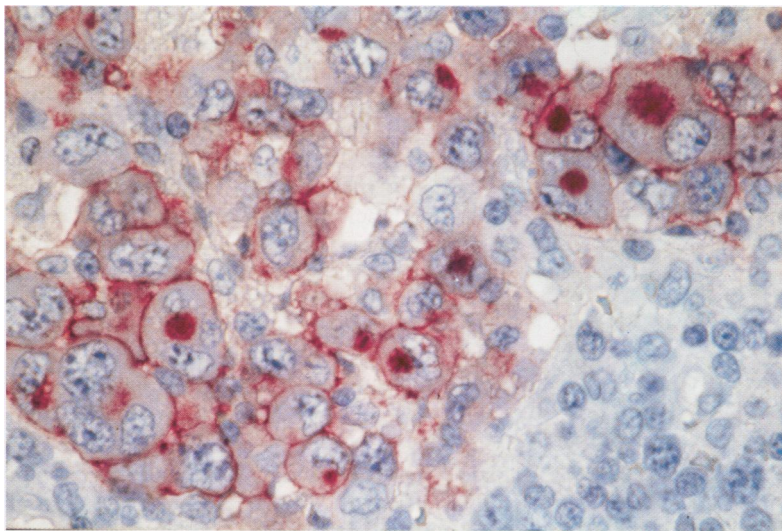
Figure 6 Anaplastic large cell lymphoma stained to show CD30. Note the strong membrane and Golgi staining. Many of the tumour cells in this neoplasm have irregular nuclei or appear multinucleated (APAAP; original magnification ×320).

Eighty four (27.2%) cases were diagnosed as lymphoblastic lymphoma. Of these, 56 were T-cell, 12 B-cell and 16 of indeterminate lineage. Thirty two (38% of the whole series) presented with peripheral lymphadenopathy. Infiltration of the skin and soft tissues was observed in 25% of patients with lymphoblastic lymphomas of B and indeterminate lineages. Twenty seven (32%) of the 56 T-lymphoblastic lymphomas showed involvement of the mediastinum or pleura, a localisation not seen in lymphoblastic lymphomas of B-cell or indeterminate subtypes.

Forty six (15%) cases were diagnosed as anaplastic large cell lymphoma. About 70% presented with peripheral lymphadenopathy, but several other sites were also involved. Seven patients presented with lymphoma in bones, soft tissue or skin, and five with disease in the mediastinum or lungs.

In the whole series, there were 224 males and 84 females, giving a male to female sex ratio of 2.7:1 (table 3). The male to female sex ratio of Burkitt lymphoma was 5.5:1, whereas for lymphoblastic lymphomas it was 2.1:1 and for anaplastic large cell lymphoma 1.5:1. Of the 293 cases, 288 fell within the age range of one to 15 years (table 3). There was only one patient under the age of one year and four over the age of 16, although the small number of patients in the latter category was due to the selection criteria for the trial. The patients seem to be roughly equally spread over the age range from one to 15 years, although Burkitt lymphoma is slightly more common in the middle, lymphoblastic lymphoma in the first, and anaplastic large cell lymphoma in the last quinquennium.

After an initial settling in period, the review panel achieved a concordance rate of over 90% on first review. This is, perhaps, not surprising, as 90% of the patients fell within three categories that differed, not only in their morphology

lymphomas are shown in table 2. One hundred and thirty (42.2%) cases were categorised as Burkitt lymphoma (table 1). Eighty eight of these 130 patients presented with abdominal tumours. These were often extensive and their exact location was not recorded. In 37 cases, the tumour was noted to involve the terminal ileum or ileocaecal region. Three tumours involved the stomach and four were localised to the ovaries. Seventeen patients presented with tumours in Waldeyer's ring. Nine of these involved the oropharynx or tonsil and eight the nasopharynx. Only 13 of the 130 patients presented with peripheral lymphadenopathy. Twelve cases designated high grade, B-cell lymphoma, NOS were probably poorly preserved Burkitt lymphomas with a similar anatomical distribution to the cases diagnosed as Burkitt lymphoma. With the addition of these cases, Burkitt lymphoma would constitute 46% of the whole series.

Table 2   UKCCSG NHL trials: principal anatomical sites of disease for the three major histological subtypes

Anatomical site	Burkitt lymphoma (n = 130)	Lymphoblastic			Anaplastic large cell (n = 46)
		T (n = 56)	Indeterminate (n = 16)	B (n = 12)	
Peripheral lymph nodes	13	21	5	6	32
Abdominal/pelvic mass[a]	40	–	1	–	–
Ileum, ileocaecal region	37	–	–	–	–
Mediastinum, pleura[b]	–	27	–	–	3
Oropharynx, tonsil	9	1	–	1	–
Skin, soft tissue	–	3	4	3	5
Bone	7	1	–	–	2
Nasopharynx, nasal cavity	8	1	–	–	–
Salivary glands	2	1	2	–	1
Brain[c]	1	1	2	–	–
Bone marrow	2	–	1	2	–
Liver	3	–	–	–	–
Testis	–	2	1	1	–
Ovary[d]	4	–	–	–	–
Stomach	3	–	–	–	–
Duodenum, pancreas	1	–	–	–	1
Lungs	–	–	–	–	2
Oral cavity[e]	–	–	–	–	–
Total	130	56 (+2)[f]	16	12 (+2)[g]	46

[a]Includes biopsy specimens of mesentery, mesenteric nodes, omentum, and an umbilical nodule.
[b]Includes biopsy specimens of mediastinal nodes, thymic region, and pericardium.
[c]Includes one mass in cerebellopontine angle.
[d]Only includes specified ovarian masses. Other examples are likely to be classified under abdominal/pelvic mass.
[e]Soft tissues, distinct from jaws.
[f]Two biopsy specimens from two different sites, submitted from two patients.
[g]Two biopsy specimens from two different sites, submitted from two patients.

Table 3   UKCCSG NHL trials: distribution of diagnoses by age

Diagnosis	Age (years)				
	<1	1–5	6–10	11–15	>16
Burkitt lymphoma (n = 130)	–	38	50	41	1
Lymphoblastic (n = 84)	1	34	25	24	–
Large cell anaplastic (n = 4)	–	9	13	23	1
Centroblastic Centroblastic/centrocytic (n = 10)	–	2	2	6	–
Other B-lineage (n = 14)	–	2	6	5	1
Peripheral T, Other T-lineage (n = 4)	–	2	1	–	1
Histocytic (n = 1)	–	1	–	–	–
Non-Hodgkin lymphoma (NOS) (n = 4)	–	1	1	2	–
Reactive/no evidence of lymphoma seen (n = 11)	–	3	4	4	–
No diagnosis made (n = 4)	–	2	1	1	–
Total	1	94	103	106	4

but also in their immunophenotype. There was also a high level of agreement between the panel diagnoses and those of the referring pathologists. Two referred diagnoses of non-Hodgkin lymphoma, single examples of T-non-Hodgkin lymphoma NOS and anaplastic large cell lymphoma, were eventually rejected by the panel as non-neoplastic. One referred diagnosis of anaplastic large cell lymphoma was re-classified as Hodgkin disease. No examples of non-lymphomatous, round cell tumours, mis-diagnosed as non-Hodgkin lymphoma, were encountered. The largest area of disagreement would seem to be amongst the Burkitt lymphomas, 35 of which were diagnosed by the referring pathologist as B-lymphoblastic lymphomas (see discussion). Many of the other discrepancies between the submitted and the panel diagnoses were minor and related to the immunophenotype assignment or were of a semantic nature.

Discussion

This study gave us an unprecedented opportunity to examine and categorise a large series of unselected non-Hodgkin lymphomas in children. It does, however, have a number of limitations. The amount of clinical information available to us was usually small and it was sometimes necessary to obtain more details from the paediatricians. The anatomical sites of disease, listed in table 2, represent the major areas of involvement and also, in children with multifocal disease, the regions which were most accessible for biopsy. The diagnostic material submitted to the panel was usually restricted to 10 paraffin wax sections, with little opportunity to undertake detailed immunophenotypic analysis in difficult cases. When setting up our study in 1990, we selected L26 (CD20) as the best available B-lineage marker at that time.[2] L26 does, however, have limitations, especially for a study of childhood lymphomas, as it does not stain very early B cells. In contrast, CD79a is expressed on B cells at the time when immunoglobulin is first synthesised.[3] If we had used this antibody, throughout the study, we should probably have detected more B-lymphoblastic lymphomas which may not express CD20. This problem does not apply to Burkitt lymphoma which represents a later stage of B-cell development at which CD20 is always

expressed. Staining for terminal deoxynucleotidyl transferase, which has recently been reported in paraffin wax embedded tissue sections,[4] would also provide a marker for precursor B- or T-cell lymphomas (lymphoblastic lymphomas).

The only major area of disagreement between the panel diagnosis and that of the referring pathologists was of Burkitt lymphoma which was originally described as B-lymphoblastic lymphoma in 35 cases. This discordance, however, relates more to the use of terminology than to histological interpretation. Burkitt lymphoma was categorised as a B-lymphoblastic lymphoma in the first version of the Kiel classification,[5] an error that was subsequently rectified in the updated version of this classification.[6] In the FAB classification of lymphoblastic leukaemia, cases of Burkitt lymphoma with extensive bone marrow involvement and overspill into the peripheral blood are still referred to as acute lymphoblastic lymphoma (ALL-L3).[7] Lymphoblastic lymphomas arise from early or progenitor B and T cells, whereas Burkitt lymphoma cells show features of more mature B cells in their expression of lineage markers and surface immunoglobulin. The molecular genetics of Burkitt lymphoma and B-lymphoblastic lymphoma are different, as are their immunophenotype and morphology.[8] There is a need for classification systems to make a clear distinction between these separate diseases.

Burkitt lymphoma is the commonest subtype of childhood non-Hodgkin lymphoma in the UK. By definition, this is categorised as sporadic or non-endemic Burkitt lymphoma. Endemic and non-endemic Burkitt lymphoma are morphologically indistinguishable,[9] probably because both groups of tumours have translocations between the c-myc gene and one of the immunoglobulin genes, leading to c-myc deregulation.[10] Deregulated c-myc results in cells that continuously replicate but do not differentiate and, therefore, show little morphological variation. Despite their morphological identity, endemic and sporadic Burkitt lymphoma differ in their molecular genetics, in that the breakpoints in relation to the c-myc and immunoglobulin genes are usually different.[11-13] In addition, endemic Burkitt lymphoma is always associated with Epstein-Barr virus, whereas only one third of non-endemic cases carry the virus.[14] The two tumours also differ in their clinico-anatomical features. Endemic Burkitt lymphoma has a sex ratio of 2.1 males to one female,[15] whereas in this series the ratio was 5.5:1. Non-endemic Burkitt lymphoma presents most frequently with abdominal and pelvic tumours, often involving the ileocaecal region. The oropharynx and nasopharynx are the second most common tumour sites. This anatomical distribution would be uncommon in endemic Burkitt lymphoma in which abdominal tumours are usually retroperitoneal and tumours of Waldeyer's ring are rare.[16] Peripheral lymphadenopathy is almost never seen in endemic Burkitt lymphoma, whereas it was a presenting

feature in 10% of the cases of non-endemic Burkitt lymphoma in this series.

The clinical and anatomical differences between endemic and sporadic Burkitt lymphoma have been recorded previously.[17] If Burkitt lymphoma had not been defined on the basis of its microscopic features which, as stated above, are probably directly related to c-myc deregulation, the sporadic disease would not have been labelled as Burkitt lymphoma. The semantic confusion surrounding these tumours has been further complicated by the use of the terms "Burkitt-like" or "small non-cleaved cell non-Burkitt". When applied to childhood lymphomas, the distinction between Burkitt and non-Burkitt lymphomas seems to lack clinical importance and may be because of minor morphological variation or histological artefact.[18] Morphological, phenotypic and clinical differences have emerged when this distinction is applied to lymphomas at all ages, with Burkitt lymphomas predominating in children and Burkitt-like lymphomas in adults.[19][20] These Burkitt-like lymphomas do not show the rearrangements of the c-myc and immunoglobulin genes that characterise Burkitt lymphoma.[20] It is our opinion that the designation Burkitt-like, as a single diagnostic term, should be avoided and that, at the present time, such cases should be designated high grade B-cell lymphomas, Burkitt-like, as recommended in the REAL classification.[8] Staining sections with the proliferation marker MIB1 (Ki-67) is used by one of the authors (DHW) as an aid to the identification of Burkitt lymphoma. All Burkitt lymphomas show c-myc deregulation and, thus, have 100% labelling index of the tumour cells. This level of labelling is rarely seen in other lymphomas.

The majority of the lymphoblastic lymphomas were of the T-cell phenotype. Mediastinal tumours were common in this group and in 27 patients this was the site of biopsy, although, in 21 patients, enlarged cervical or supraclavicular lymph nodes provided a more accessible biopsy site. The use of an antibody directed against CD79a would probably have identified a B-cell lineage for some of the cases of indeterminate phenotype.[3] Involvement of the skin and soft tissues, which is said to be a characteristic of B- and pre-B-lymphoblastic lymphomas,[21-23] was seen in 25% of the B-cell and indeterminate group but in only 5% of the T-lymphoblastic lymphomas. Although bone marrow infiltration was observed in three cases of lymphoblastic lymphoma, this constituted less than 25% of the cells at which level the case would have been designated as lymphoblastic leukaemia and not entered into the non-Hodgkin lymphoma trial.

Primary anaplastic large cell lymphoma is the third commonest childhood non-Hodgkin lymphoma in this series. These patients were generally older than the children with Burkitt lymphoma and lymphoblastic lymphoma, and most presented with cervical lymphadenopathy. Skin, soft tissues and bone were the presenting sites in seven patients and the mediastinum in three. Pathologists will be aware of the diagnostic pitfalls associated with this neo-plasm. The abundant cytoplasm of the tumour cells, their cohesive growth pattern and tendency to infiltrate the sinuses of lymph nodes may lead to a diagnosis of metastatic tumour, particularly undifferentiated carcinoma or amelanotic melanoma. The frequent expression of EMA[24][25] by the tumour cells and, in rare instances, cytokeratins,[26][27] together with the failure of some cases to express CD45[27][28] or lineage markers, may compound this error. Some cases induce an intense histiocytic reaction that may obscure the tumour cells.[29][30] The entity anaplastic large cell lymphoma, Hodgkin-like,[8] may be impossible to differentiate from Hodgkin disease, but no such cases occurred in this series. The chromosomal translocation (2;5)(p23;q35) occurs in about 30–40% of cases of anaplastic large cell lymphoma and seems to be more common in childhood than adult cases.[31-34] The (2;5) translocation results in the fusion of the nucleophosmin gene on chromosome 5q35 to a novel tyrosine kinase encoding gene designated anaplastic lymphoma kinase on chromosome 2p23[35] and in the production of an abnormal fusion protein.[36] The deregulated tyrosine kinase activity of this fusion protein may be important in the pathogenesis of anaplastic large cell lymphoma. Antibodies to this fusion protein have been shown to stain both the nucleus and cytoplasm of tumour cells in about 30% of cases of anaplastic large cell lymphoma, mainly those occurring in childhood and having a good prognosis.[36] It seems, therefore, that most cases of anaplastic large cell lymphoma in adults have a different pathogenesis from those occurring in childhood. It is yet to be determined how homogeneous the childhood cases in our series are. Five cases showed t(2;5) by conventional cytogenetics.

Patients with congenital immunodeficiency syndromes are at increased risk of developing non-Hodgkin lymphomas. There were two children with ataxia telangiectasia in this series. One developed high grade non-Hodgkin lymphoma of indeterminate lineage, involving the brain and cervical lymph nodes, at the age of three years. The other patient developed an anaplastic large cell lymphoma of B-phenotype involving an axillary lymph node at the age of 10.

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