Nodular Lymphocyte Predominant Hodgkin Lymphoma: A retrospective review of consecutive cases managed through a single MDT in the East of England between 1999 and 2015

Jessica C Griffin, Shalal Sadullah, Laszlo Igalii, Nimish K Shah, Kristian M Bowles and Jennie Z Wimperis

Department of Haematology, Norfolk and Norwich University Hospitals NHS Trust, Colney Lane, Norwich, Norfolk, NR4 7UY, United Kingdom.
Department of Haematology, James Paget University Hospital, Lowestoft Rd, Gorleston-on-Sea, Great Yarmouth, Norfolk NR31 6LA, United Kingdom.

Introduction
Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL) is a rare subtype of Hodgkin Lymphoma (HL), representing 5% of cases of HL. It has a distinct clinical course, which differs remarkably from classical HL (cHL).

There are no prospective randomised controlled trials assessing optimum treatment of this condition and consequently information is gained mainly from a modest number of retrospective reviews or single arm phase 2 trials. Some larger cHL studies have included NLPHL patients, however subset analyses have not been powered to give reliable outcome data for this subset.

Methods
We undertook a retrospective review of patients de novo NLPHL diagnosed and managed through the Joint Norfolk and Norwich University Hospitals NHS Foundation Trust (NNHU) and James Paget University Hospital Foundation Trust (JPH) Haematology MDT between 1999 and 2015. The catchment area for our MDT is 825,000.

Patients were identified through a computer search of histopathology records and of the Haematology departments' patient databases. Clinical data was extracted from local hospitals' patient electronic records.

Results
30 patients with NLPHL were identified by the computer search. 3 patients with NLPHL plus evidence of transformed disease at presentation, and 1 patient with an uncertain diagnosis on retrospective review, were excluded from analysis. Median follow up was 84 months (range: 4 months-17 years).

Fig. 1- Patient demographics. (a) The median age was 44 years (range 11-83 years). (b) 25 patients (86%) were male. (c) 21 patients (81%) had stage 1 or stage 2 disease.

STAGE ONE DISEASE (n = 13)
(a) Watchful waiting: (n = 5; 38%)
1. Disease progression in 1 patient (20%) at median follow up of 144 months:
   • PROGRESSION: after 48 months to stage 4 disease.
   • TREATMENT: Refractory to ABVD, salvaged with ESHAP® and autologous stem cell transplant to achieve complete metabolic remission.

2. RELAPSE 1, 26 months after PBST treated with x4 Rituximab to achieve complete response.

3. RELAPSE 2 after a further 36 months → treated with x4 Rituximab to good partial response. Remains stable after a further 12 months (168 months post diagnosis)

(b) Radiotherapy: (n = 7; 54%)
6 patients achieved complete response.
1 patient achieved good partial response, requiring no further treatment and remaining stable 24 months post radiotherapy.

Disease relapse in 1 patient (15%) at median follow up of 72 months:
• RELAPSE: 100 months after achieving complete response to radiotherapy. Stage 4 relapsed disease.
• TREATMENT: with ABVD x 6 and Rituximab. 3, achieving complete metabolic response. Remains in remission at 9 months follow up post ABVD/Rituximab.

(c) Combined modality therapy: (n = 1; 8%)
This patient had stage 1 disease with a mass superficial to the diaphragm. Due to significant disease bulk, patient was given ABVD x 6 prior to motivated radiotherapy to mediastinal disease.

Achieved complete response.
No relapsed disease at follow up of 108 months.

STAGE TWO DISEASE (n = 8)
(a) Watchful waiting: (n = 4; 50%)
Disease progression in 1 patient (23%) at median follow up of 54 months:
• PROGRESSION: after 11 months, remained stage 2 disease but increase in bulk.
• TREATMENT: with Rituximab x 4 to achieve a good partial response. No relapsed disease at follow up of post Rituximab.

(b) Radiotherapy: (n = 2; 25%)
Both patients achieved complete response. No relapsed disease follow up (12 and 108 months)

(c) Chemotherapy: (n = 2; 25%)
Patient One: Treated with 3 CHOEP as initial histological misdiagnosis as DLBCL (NLPHL diagnosis retrospective). Complete response to treatment. No relapsed disease at follow up of 120 months.

Patient Two: 11 year old male child managed by Paediatric Haematologists. Treated with OPEA x 2 to achieve complete response. No relapsed disease at follow up of 120 months.

Conclusions
We report outcomes for 26 consecutive patients with NLPHL treated through a single MDT within a 16 year period.

At a median follow up of 84 months (7 years) overall survival is 88% for all patients.

13/26 patients in our cohort (50%) had stage 1 NLPHL at presentation. For this group 7-year survival is 100%.

7/26 patients in this review (26.9%) have required no treatment to date, at a median follow up of 84 months.

Relapses amongst our cohort tended to occur late, with a median time to relapse of 26 months (range 7 to 192 months).

In our cohort we can draw no definite conclusions about therapy but report encouraging outcomes for patients diagnosed with this disease broadly in keeping with other published series.

Limitations:
Although the median follow up in this case series is long, the total number of patients is not sufficient to draw significant conclusions regarding therapy in NLPHL.

References

Fig. 2- Stage 1 disease : Management (a) Watchful waiting (b) Radiotherapy (c) Combined Modality Therapy

Fig. 3- Stage 2 disease: Management (a) Watchful waiting (b) Radiotherapy (c) Chemotherapy

Fig. 4- Stages 3-4 disease: Management. (a) Chemotherapy (b) Rituximab monotherapy

Fig. 5- Overall Survival. (a) Overall survival (all stages): (b) Overall survival adjusted for stage:

Survival

Overall survival

Overall survival adjusted for stage

Follow up in months

Survival

5 years

10 years


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