REPORT ON THE EDUCATION AND RESEARCH OF LYMPHOMA IN CHINA

Wen-Qi Jiang, M.D.
Sun Yat-sen University Cancer Center,
Shenzhen University School of Medicine
Overview

- Education Activity of Chinese Society of Lymphoma, CACA
- Frequencies of Lymphoma Subtypes & NK/T Cell Lymphoma Research in China
Epidemiology of lymphoma in China

Incidence trend of malignant lymphoma from 1998 to 2008:
6.4/100,000 in 1998 and 10-11/100,000
The Mission of Committee of Malignant Lymphoma, Chinese Anti-cancer Association

Revision of the Chinese Lymphoma Guideline

National interpretation of the Chinese Lymphoma Guideline

Committee of Malignant Lymphoma, Chinese Anti-cancer Association

Tour of lymphoma experts

Chinese collaborative group of pathology in malignant lymphoma

Further education of the physicians

Education & Management of the patients
The interpretation of the Chinese Lymphoma Guideline was carried out in more than 25 cities in China from Sept 2011 to May 2012. Establishing 14 training centers of lymphoma pathology, training more than 100 pathologists of lymphoma each year.
Chinese collaborative group of pathology in malignant lymphoma

- Members of the Chinese collaborative group visit the departments of pathology in more than 80 hospitals with academic exchanges and guidance.
Education and Care of Patients with Lymphoma

Homeland-care for lymphoma patients 2011
Recovery Classroom

- Recovery Classroom:
  - Teaching the knowledge of lymphoma
  - Doctor-patient communication
  - Good platform for patients’ communication

- Recovery Classroom was held more than 70 times in 37 hospitals
Website of Homeland-care for lymphoma patients

Website is easy to use, ie:
• About me
Lymphoma Hotline

Transfer standardized treatment & Recovery Classroom, Free Clinic Notice, Web Caution
The Mission of Committee of Malignant Lymphoma, Chinese Anti-cancer Association

- Revision of the Chinese Lymphoma Guideline
- National interpretation of the Chinese Lymphoma Guideline
- Committee of Malignant Lymphoma, Chinese Anti-cancer Association
- Education & Management of the patients
- Further education of the physicians
- Chinese collaborative group of pathology in malignant lymphoma
- Tour of lymphoma experts
Overview

- Education Activity of Chinese Society of Lymphoma, CACA
- Frequencies of Lymphoma Subtypes & NK/T Cell Lymphoma Research in China
The Relative Frequencies of Lymphoma Subtypes in China: A Nationwide Study of 10002 Cases by the Chinese Lymphoma Study Group (CLSG)
Geographic distribution of the 24 institutes
The relative frequencies of NHL and HL subtypes

Total number of cases: 10,002
Li XQ, et al.
Ann Oncol 2011; 22(suppl 4): iv 141
The relative frequencies of HL and NHLs

- B-NHL: 66%
- T/NK-NHL: 21%
- HL: 9%
- UC: 4%

Total number of cases: 10,002
The relative frequencies of T/NK-NHL subtypes

Total number of cases: 2,138
Clinical features of NK/T cell lymphoma

- Ann Arbor staging I/II > 70%
- CHOP often resistance
- Media OS < 1 year for extra-nasal NK/T cell lymphoma
- EBV infection, EBER(+) 21-92%
NK/T cell lymphoma: different locations, different outcomes

N=304

N=117

EJH, 2012
# Chemotherapy alone in NK/T cell lymphoma

<table>
<thead>
<tr>
<th>Author</th>
<th>Pub. Time</th>
<th>n</th>
<th>Lesions</th>
<th>Stage</th>
<th>Chemotherapy Regimen</th>
<th>Effects (%)</th>
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Radiotherapy alone in NK/T cell lymphoma

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# CMT in NK/T cell lymphoma

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<td>Chin</td>
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<td>67</td>
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<td>Nasal</td>
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<td>108</td>
<td>Nasal</td>
<td>I-II</td>
<td>CT + RT: 81</td>
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<td>0.001</td>
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<td>CHOP: 27</td>
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<td>Huang MJ</td>
<td>2008</td>
<td>82</td>
<td>Nasal</td>
<td>I-II</td>
<td>RT + CT: 74</td>
<td>62</td>
<td>0.000</td>
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<td>CT alone: 8</td>
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<td>Au</td>
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<td>67</td>
<td>Upper AD tracts</td>
<td>I-II</td>
<td>RT + CT: 34</td>
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<td>CT alone: 23</td>
<td>30</td>
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</table>
Treatment failures after radiation therapy of NK/T cell lymphoma patients with stage I / II

N = 92, 1976-1994
5y-OS 40.1%
5y-DFS 37.8%

N=214 (RT 96, RT+CT 118), 1987-2009
5y-OS 72%, 5y-DFS 65%
5y-LRF 12%, 5y-SF 25.5%, 5y-OF 32.9%

High Systemic failure suggests new chemotherapy should be explored!
L-asparaginase-based salvage regimen for refractory and relapsed ENKTL

- Refractory and relapsed ENKTL, N=45, 1996-2008
- 39 pts received RT after CT
- ORR 82.2% (CR 55.6 %, PR 26.7%)
- 3 y-OS and 5 y-OS are both 66.9 %
- The major adverse effects of L-asparaginase were myelosuppression, liver dysfunction hyperglycemia, and allergic reaction

Ann Hematol, 2009
Long-term follow-up results of EPOCH regimen as first-line therapy of NK/T cell lymphoma

Huang H etc. Leuk Lymphoma, 2011
Long-term follow-up results of EPOCH regimen as first-line therapy of NK/T cell lymphoma

3 y-OS 75%
3 y-OS 60%

$P = 0.528$

Table III. Adverse effects of EPOCH chemotherapy.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>1/2 (%)</th>
<th>3/4 (%)</th>
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</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>44.1</td>
<td>31.4</td>
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<tr>
<td>Febrile neutropenia</td>
<td>0</td>
<td>15.7</td>
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<tr>
<td>Anemia</td>
<td>15.7</td>
<td>3.9</td>
</tr>
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<td>Thrombocytopenia</td>
<td>34.3</td>
<td>8.8</td>
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<tr>
<td>Nausea/vomiting</td>
<td>39.2</td>
<td>0.0</td>
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<tr>
<td>Diarrhea</td>
<td>0</td>
<td>2.0</td>
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<tr>
<td>Mucitis</td>
<td>3.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>31.4</td>
<td>4.9</td>
</tr>
<tr>
<td>Abnormal transaminase</td>
<td>7.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Cardiotoxicity</td>
<td>2.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Peripheral neuritis</td>
<td>2.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Figure 6. Survival curves of patients with stage I/II nasal ENKL according to first-line treatment modalities.

Huang H etc. Leuk Lymphoma, 2011
NK/T-cell Lymphoma

- Clinical pathological correlation is required to establish diagnosis.
- Optimal first-line therapy is controversial.
- For localized presentation in the nasopharynx:
  - Short course of CHOP or CHOP-like chemotherapy for up to 3 cycles followed by involved field RT
  - SMILE (steroid [dexamethasone/prednisolone], methotrexate, ifosfamide, L-asparaginase and etoposide) followed by involved field RT
  - Dose-adjusted EPOCH for up to 3 cycles followed by involved field RT (category 2B)
- Optimal treatment for advanced NK/T-cell lymphoma is not established. CHOP based chemotherapy is associated with poor outcomes. Consider other aggressive regimens such as:
  - L-asparaginase based regimen
  - SMILE (steroid [dexamethasone/prednisolone], methotrexate, ifosfamide, L-asparaginase and etoposide)
NK/T-CELL TREATMENT REGIMENS

References

SMILE (steroid [dexamethasone]prednisolone), methotrexate, ifosfamide, L-asparaginase and etoposide) followed by involved field RT


IMEP (ifosfamide, methotrexate, etoposide, prednisolone) - SMILES core regimen


Dose-adjusted EPOCH


L-asparaginase based regimen

Untreated IE/IIE NKTL, N=27
- ORR 96.3% (CR 74.1%, PR 22.2%), PD 0
- 3/4 toxicity: leukopenia (33.3%) and thrombocytopenia (29.6%). No treatment related death
- Medial follow-up 27.37 months, PD 25.9%, 4 cases of death
- 2-year OS and PFS are both 86%, 3-year OS and PFS are 78% and 75%, respectively

*Cai Q, Huang H. etc*  *Cancer, 2012*
Poor prognostic factors of NK/T cell lymphoma

- Age > 60
- B symptoms
- ECOG PS 2
- LDH ↑
- Local lymph nodes involvement
- LTI, bone or cutaneous involvement
- High Ki-67 expression
- EBV DNA copy numbers \( \geq 6.1 \times 10^7/\text{ml} \)
Prognostic factors research in China

- Beclin-1
- Absolute lymphocyte count (ALC)
- \( \beta_2 \)-MG
N = 65
In this series, more than 80% of patients were in low-risk IPI category, but some of them with poor prognosis
Low Beclin 1 expression showed a significant association with the advanced stage and intermediate to high IPI risk
Our model placed patients into different risk categories with superior predictive value than IPI

Autophagy, 2010
N = 128

Patients with low ALC ($<1.0 \times 10^9/l$) at diagnosis tended to have more adverse clinical features.

Using the IPI, PTI, or KPI for nasal NK/T-cell lymphoma, the majority of patients were in the low-risk category (with no or one adverse factor). ALC was helpful to differentiate the low-risk patients with different survival outcomes.
N = 82

Serum $\beta_2$-MG $\geq 2.5$ mg/L was significantly associated with poor OS and PFS.

For patients with early stage, serum $\beta_2$-MG at diagnosis could also help to distinguish those with favorable outcomes from those with poor outcomes.
Conclusion

- The most important task of Chinese Committee of Lymphoma: Promoting and improving the standardize of the diagnosis & treatment of lymphoma in different hospitals
- Very big differences in frequencies of lymphoma subtypes between China and western countries
- So far there is no standardize treatment method for NK/T cell lymphoma. Further investigation is required
- Welcome your collaborations!
Sino-US Center of Lymphoma and Leukemia (Tianjin, 2009)
Sun Yat-sen University Cancer Center, Guangzhou, 1500 beds by the end of 2012

Thank you for attention!