제224회 대한 결핵 및 호흡기학회 심포지엄
증례 보고

2013년 2월 18일
서울대학교병원 전임의 최선미

Case : Female / 54

- **Chief complaint**
  - Newly developed abnormal findings of chest x ray (6MA)

- **Past medical history**
  - Pancreatic cyst on F/U
  - Hyperlipidemia on medication
  - History of intake omega-3/squalene

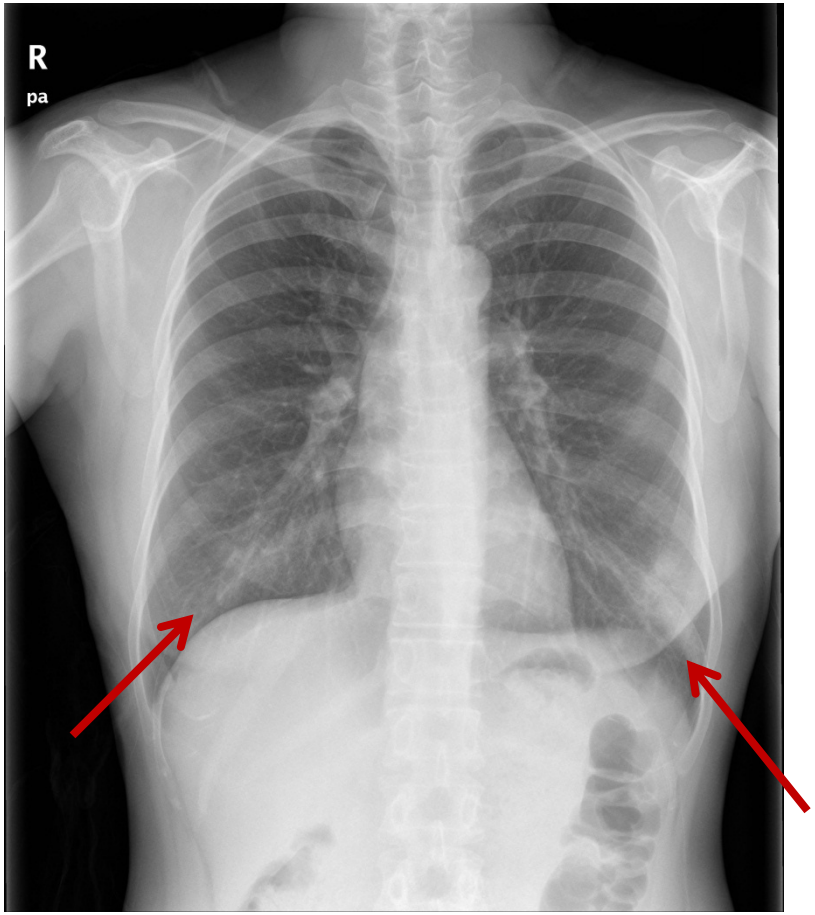
- **Social history**
  - Never smoker

Case : Female / 54

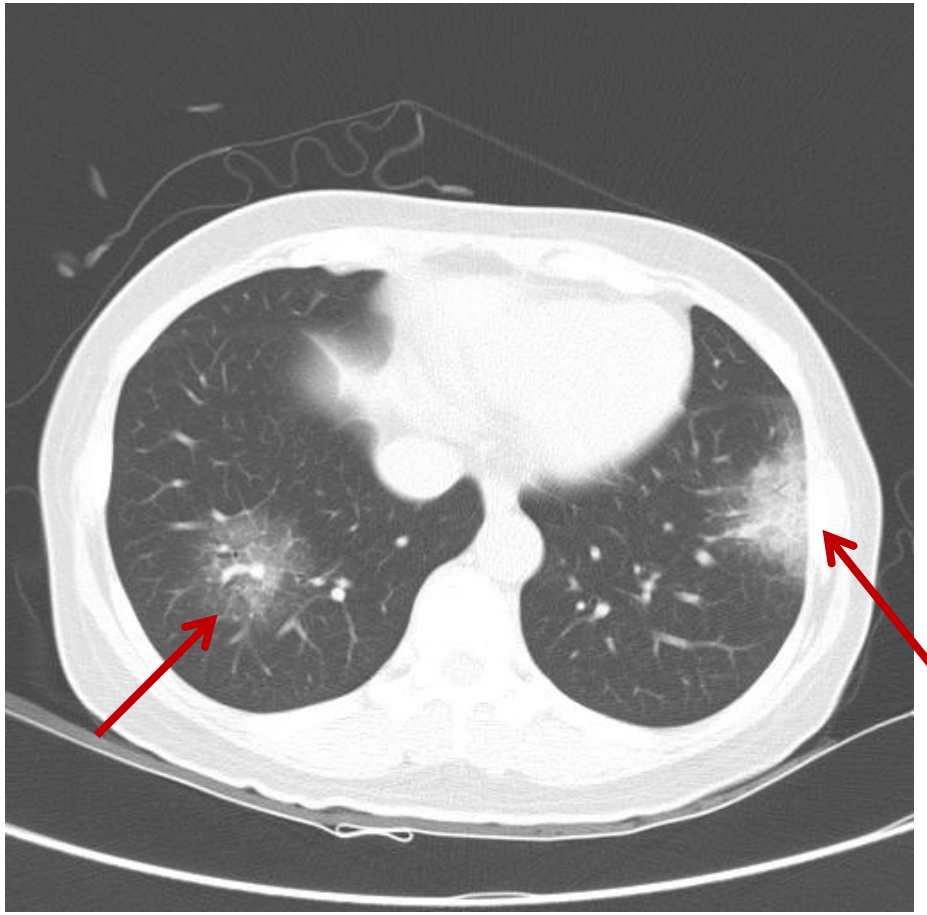
- **Review of systems**
  - fever(-) chilling(-) fatigue(+) Bwt loss(-)
  - cough(-) sputum(+) dyspnea(-)
  - Otherwise normal

- **Physical examination**
  - G/A> not so ill looking, alert, oriented
  - HEENT> not anemic, anicteric
    PI(-) PTH(-/-)
    LNE(-/-) V/E(-/-) T/E(-/-) carotid bruit(-/-)
  - Chest> symmetric expansion without retraction
    RHB without murmur
    CBS without rale, wheezing

Initial chest images

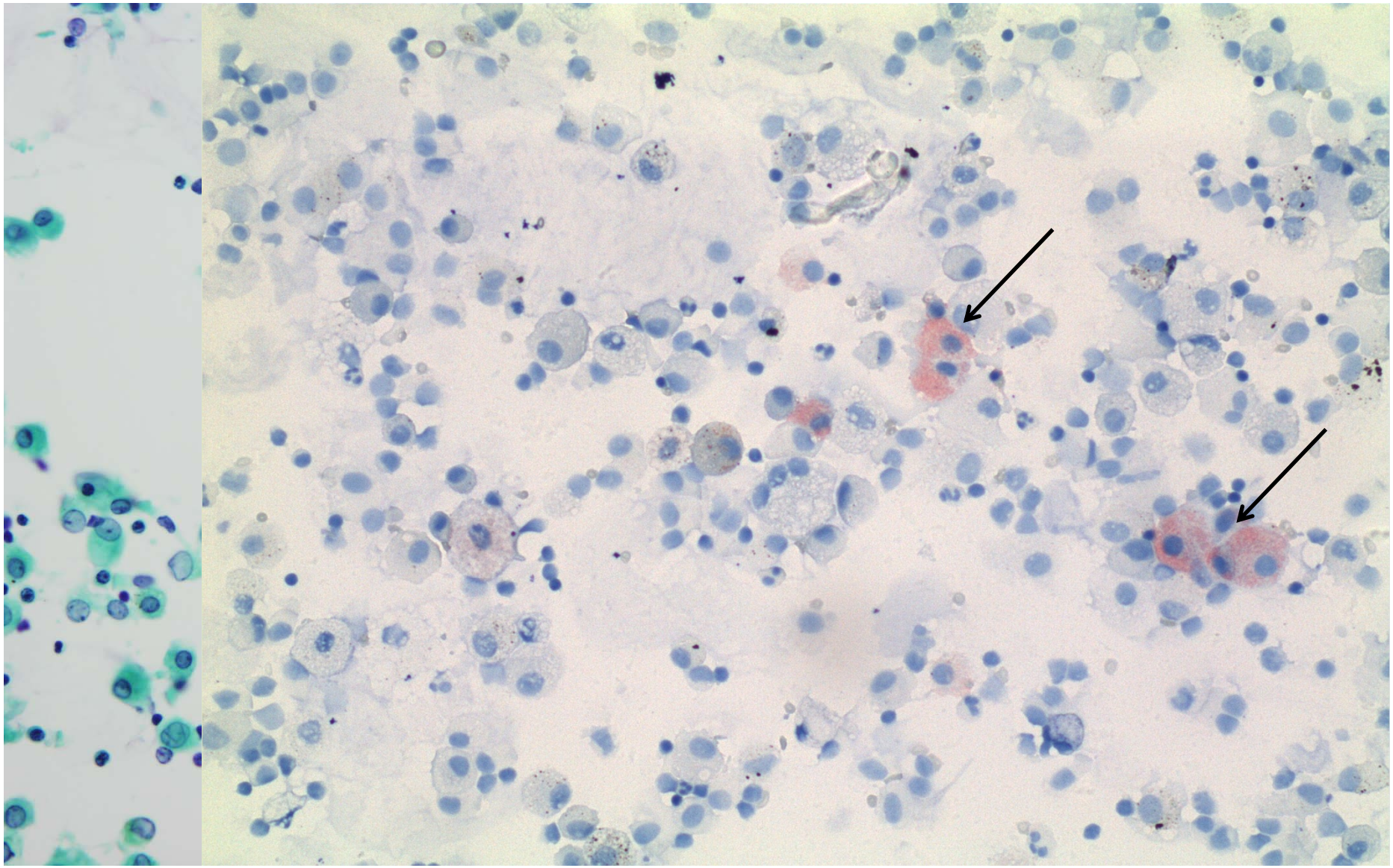


2012.07.23

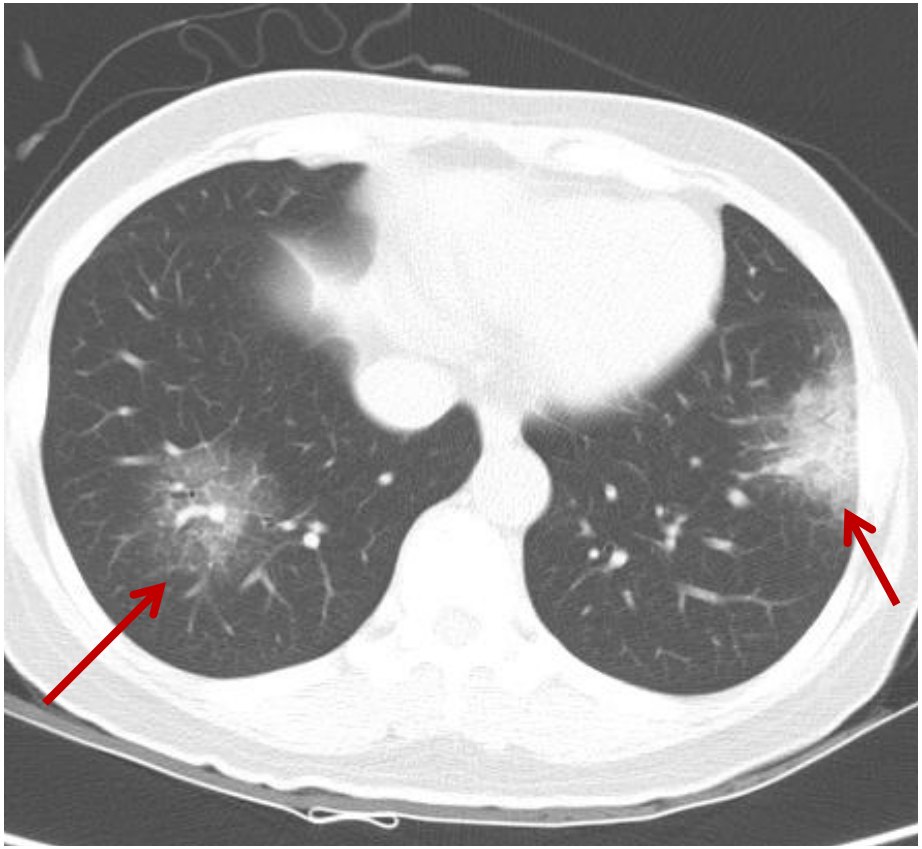


2012.07.27

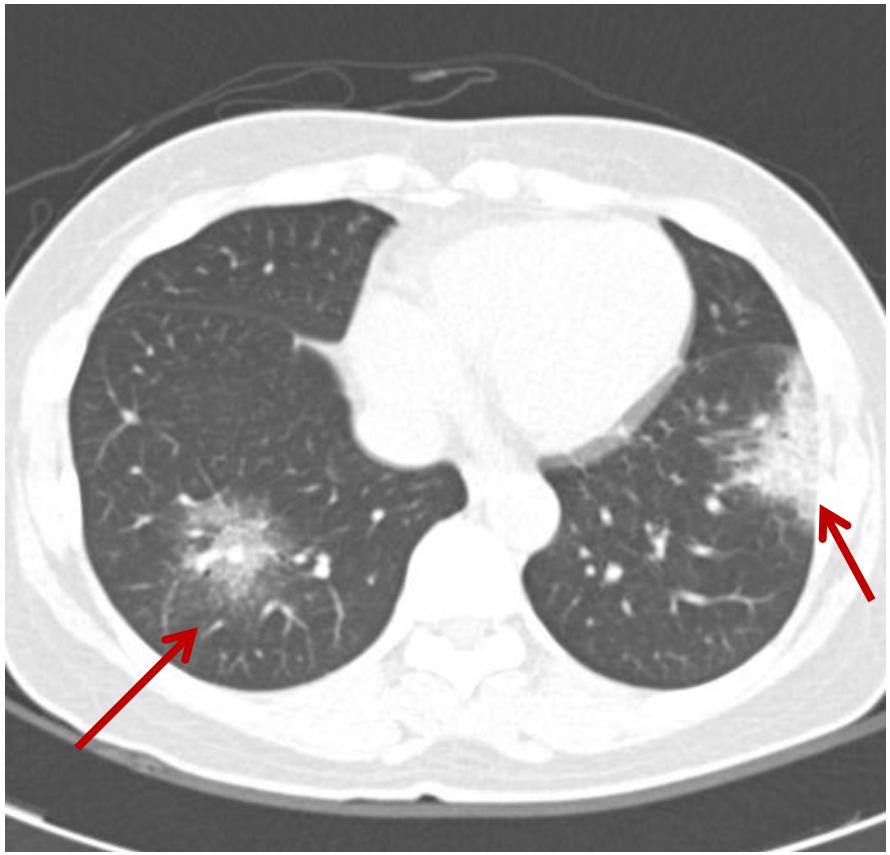
Admission and FOB (2012.8.9)



F/U chest CT after 4 months

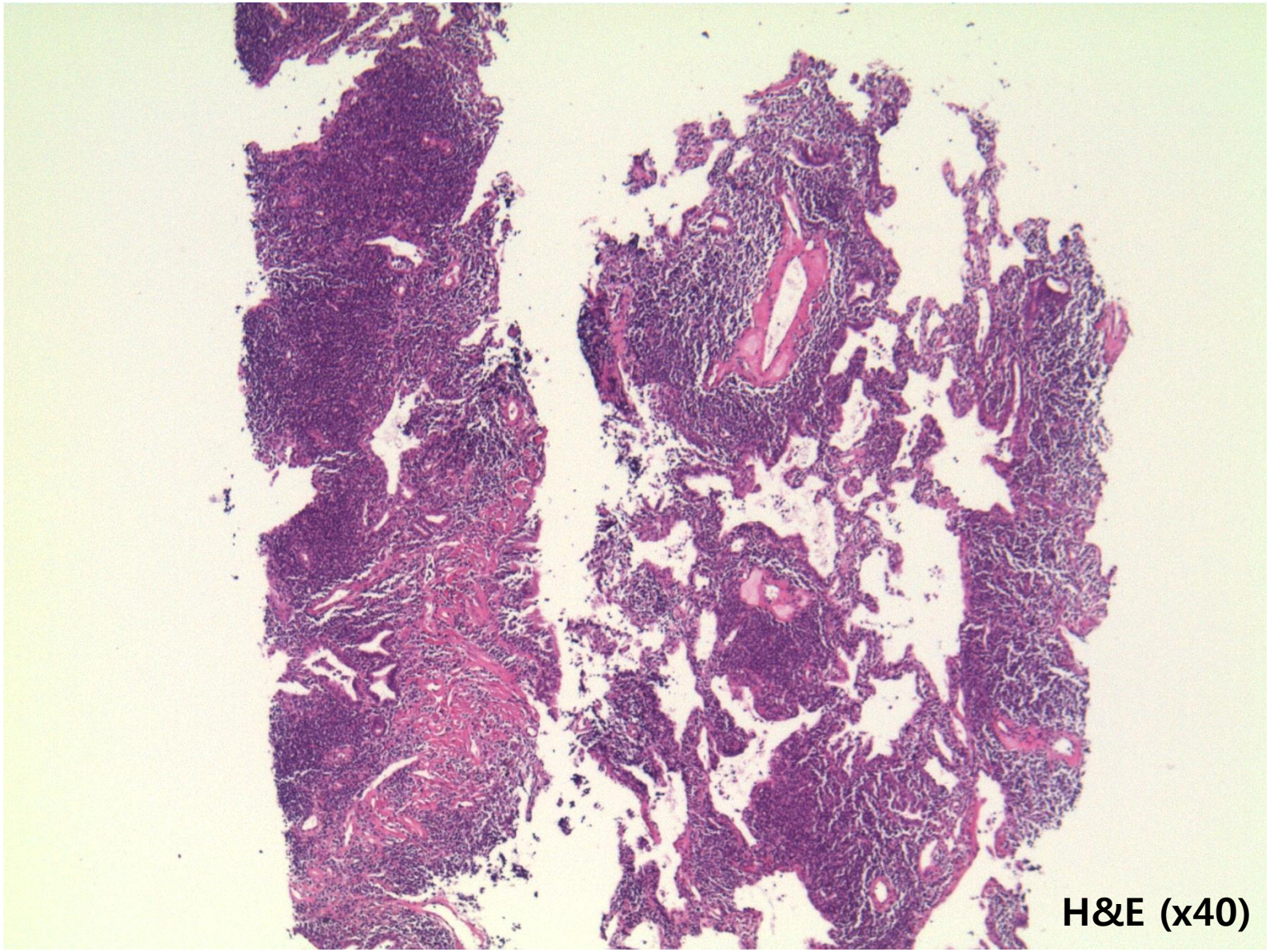


2012.07.27

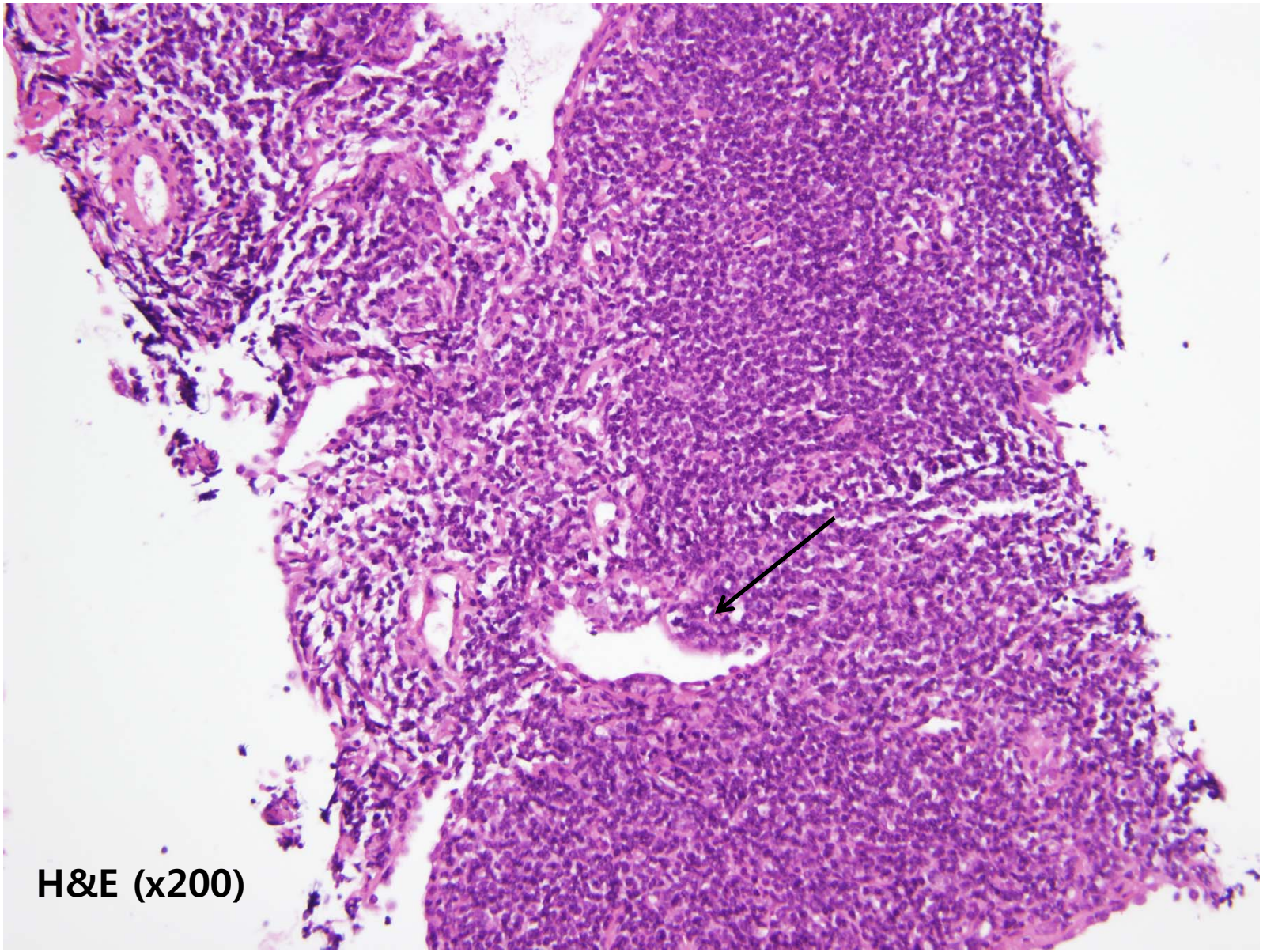


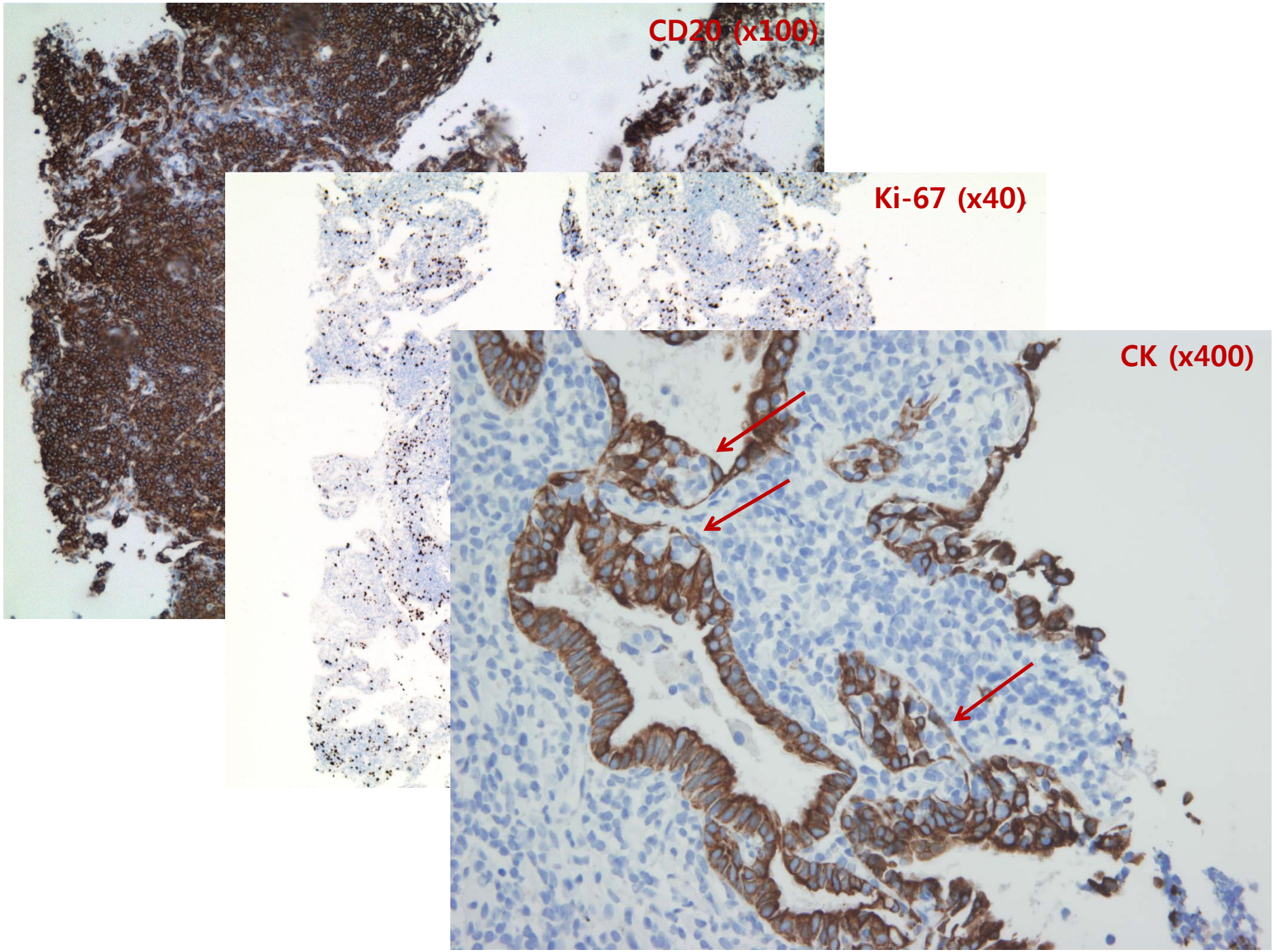
2012.11.29

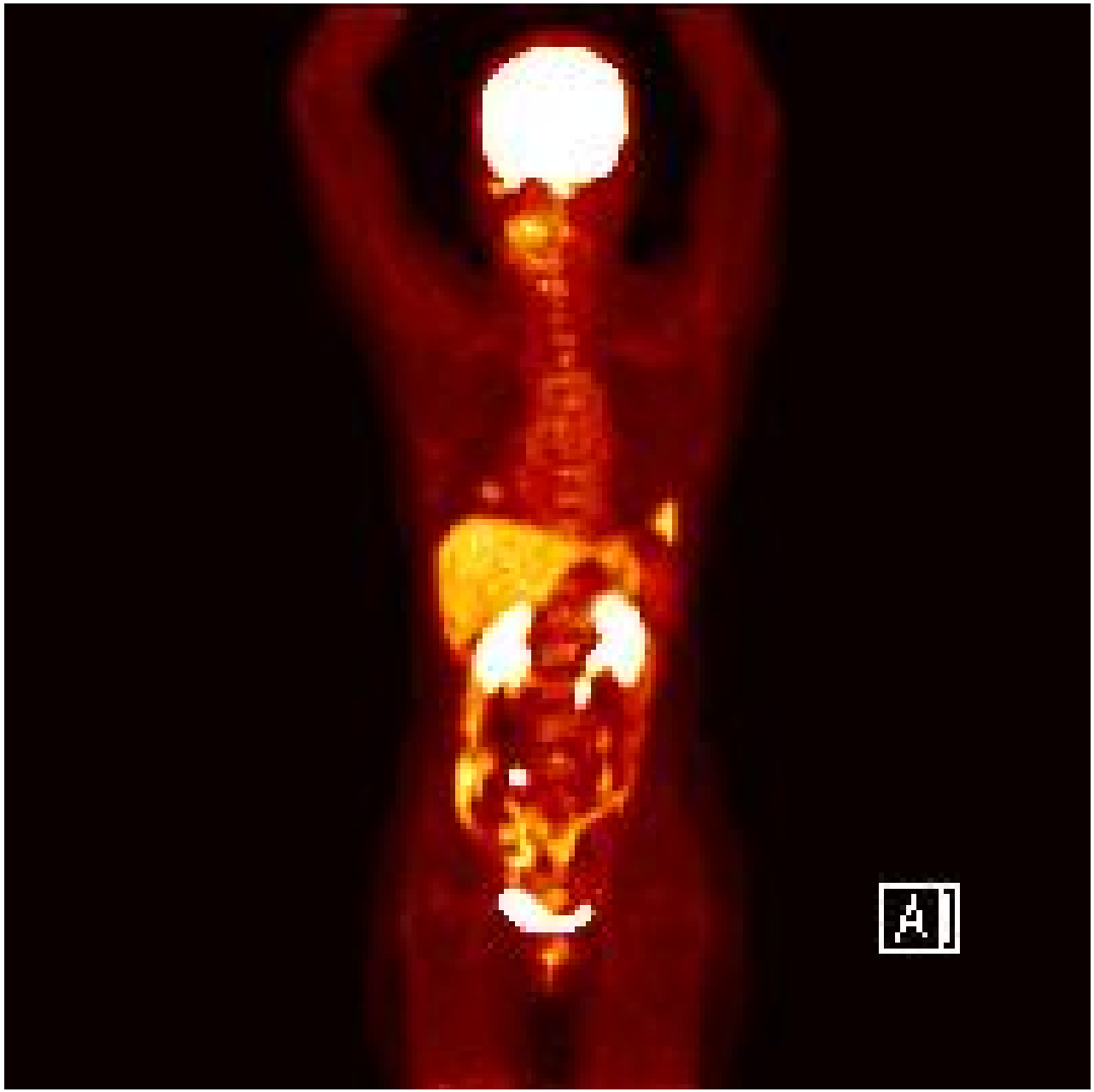
Admission for PCNB



Histology




CD20 (x100)
Ki-67 (x40)
CK (x400)


A

Assessment & Plan

- **Assessment**

  #1. Lipoid pneumonia

  #2. **BALToma, BLL, stage 1E**

- **Plan**

  #1. Chemotherapy (R-CVP)

Review

BALT lymphoma

Primary Lung Lymphoma

- **Non Hodgkin Lymphomas (NHL)**
  - Majority of PLL with MALTomas being 60-80%
  - Prognosis: MALT lymphoma > DLBL
- **Hodgkin lymphoma**
  - Reported in a small number of cases (1.5-2.4%)

- A rare entity
  - 0.4% of all lymphomas
  - 3.6% of NHL
  - < 1% of primary malignant lung tumors

- Heterogenous group of patients with some common characteristics

Characteristics

- Difficult to be diagnosed d/t a non specific clinical and radiological presentation
- Male to female ratio : variable (1/1 ~1/2)
- Average age of disease presentation : 53±12 years
- 83% of the patients have been reported to be above 40 years of age
- Indolent natural course (with a tendency to relapse) similar to that observed with MZL in other sites

BALT lymphoma

- Distinct subgroup of low-grade malignant B-cell extranodal non-Hodgkin's lymphoma (NHL)
- Pulmonary marginal zone B cell lymphoma (MZL)
  - MALT lymphoma of the lung
  - Arises from bronchial-associated lymphoid tissue (BALT)
- Most common subtype of pulmonary NHL (up to 90%)
- Considered to be the consequence of long-term exposure to a variety of antigenic stimuli— smoking, inflammatory disorders, or autoimmune diseases (Sjogren's disease and rheumatoid arthritis, etc)

Radiologic appearance

- Non specific patchy opacities or mass-like consolidation was the case in the majority of the patients (up to 68%)
- Multiple nodules : 40-50% of the cases
- Single lesions are present in 55% of the cases
- Bilateral disease varies : 21~44%
- PET : may provide additional valuable information in the initial assessment or monitoring of patients

Staging

- Ann Arbor Pulmonary Lymphoma Staging System
  - I : Involvement of one lymph node group only
  - IE : Involvement of lung parenchyma only (can be bilateral)
  - II : Involvement of two or more lymph node groups above the diaphragm
  - IIE : Involvement of lung parenchyma and lymph nodes above the diaphragm
  - III : Involvement of lymph node groups on both sides of the diaphragm
  - IIIE : Involvement of lung parenchyma and lymph nodes below the diaphragm
  - IV : Diffuse involvement of one or more extralymphatic organs or tissues

Histologic diagnosis

- PCNBx
- Bronchoscopy (TBLB and BAL)
- VATS or open lung biopsy

- Characteristic histological and immunophenotypical features of extranodal marginal zone lymphoma of MALT type
  - a small lymphocytic infiltrate – occasionally containing cells resembling germinal centre centrocytes, cells with monocytoid appearance or plasmacytoid differentiation, and scattered transformed blasts
  - abnormal population of B-lymphocytes (positive for CD20 and negative for CD10, CD5, CD23 and cyclin D1 expression)
  - B-cell monoclonality - by molecular studies for immunoglobulin gene rearrangements

Treatment

- The optimal management with regard to surgery, chemotherapy, radiation, radioimmunotherapy (^{131}I-tositumomab (Bexxar) or ^{90}Y-ibritumomab tiuxetan (Zevalin) therapy alone or in combination, as well as abstention from therapy, has yet to be clearly determined

  - Localized disease (limited to one side of the lung)
    - ✓ may be a marker of favorable response to local radiation or operation
    - ✓ radiation and surgical excision of lung should be carefully considered due to surgical complications, reductions in organ function, and a favorable clinical course of MZL itself
  - Advanced or disseminated disease (involving bilateral lung or extra-pulmonary sites)
    - ✓ could be controlled via chemotherapy

Treatments and outcomes in case series

n	Treatment	Response	Outcome
61	Surgery (21), surgery + chemotherapy (16), surgery + radiation (3), surgery + chemotherapy + radiation (2), chemotherapy* (16), observation (3)	Not reported	94% 5-year OS
19	Chemotherapy† (14), surgery (2), surgery + chemotherapy (2), chemotherapy + radiation (1)	79% CR, 21% PR	Not reported
35	Surgery, surgery + chemotherapy,‡ surgery + radiation therapy	Not reported	68% 5-year OS
41	Observation (5), surgery (17), chemotherapy§ (12), surgery + chemotherapy (3), surgery + radiation (1), prednisone (2)	Not reported	70% 5-year OS, 85% 5-year DSS
15	Various, not specified	Not reported	100% 5-year OS, 75% 5-year PFS
12	Chemotherapy¶ (8), surgery (2), surgery + chemotherapy (2)	100% CR	100% 6-year OS, 50% relapse-free survival
22	Observation (2), chemotherapy** ± rituximab (12), surgery (6), radiotherapy (2)	41% CR, 45% PR	53 months median PFS
14	Observation (1), surgery (6), surgery + chemotherapy†† (8), surgery + radiotherapy (1), surgery + chemotherapy + radiotherapy (2)	Not reported	6 years median time to disease recurrence or death

Prognosis

- Favorable prognosis
  - 5-year survival rates > 85%
  - median survival > 10YR in the largest reported series

- Possible but rare transformation to high-grade lymphoma

- Relapses are common and typically occur with longer periods of follow-up
  - cf) MALT lymphomas of different primary sites

  - CR after initial treatment → 37% relapsed at a median follow-up time of 47 months

- No significant differences between patients presenting with localised and advanced disease

Summary

- A rare disease entity with generally indolent clinical features and favourable outcome
- No standard approach
- Treatment must be individualised, considering patients' age, clinical presentation,and comorbidities
  - surgery, radiotherapy, chemotherapy, immunotherapy, radioimmunotherapy, and expectant observation
- Despite median survival in excess of 10 years, relapses are common and warrant life-long follow-up