EUROPEAN HEMATOLOGY ASSOCIATION

EHA-MSH Hematology Tutorial

Clinical Case –Session 2: Histopathology and Diagnosis

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Disclosure

- The presenter has no conflicts of interest to disclose as related to companies or products mentioned in this presentation

Learning objectives

Following participation in this activity, attendees will be able to:

- Recognize the importance of repeating proper biopsy and pursuing diagnosis
- Recognize the value of differential diagnosis of persistent lymphadenopathy

Clinical history

- A 38-year-old woman presented with swelling of multiple cervical lymph nodes
  - Duration of swelling: four years
  - Swelling subsided and recurred over the years
  - Swelling more frequent in recent months
  - Patient reported left-side otalgia
    - Sought medical attention
    - Resolved with a course of antibiotics
  - Weight loss (unable to quantify, but on diet modification) and night sweats
  - Underlying type 2 diabetes treated with an oral hypoglycemic agent

Clinical history

- On examination:
  - Multiple left-cervical lymphadenopathies
    - Largest measured 3 × 3 cm
    - Systemic examinations were normal
- Initial blood results
  - Hemoglobin: 89 g/L
  - White blood cells: 11.37 × 10^9/L
  - Platelets: 421 × 10^9/L
  - ESR: 20 mm/hour (1–20)

Clinical history

- Fine needle aspiration cytology was performed → reactive lymphadenitis
- QuantiFERON test for TB → negative

- No diagnosis established; some delay before subsequent management
- CT of the neck and thorax
  - Multiple bilateral cervical and mediastinal lymphadenopathies

- Excisional biopsy of left-cervical lymph node done – with some hiccups

Clinical history

HPE

- Near-total effacement of nodal architecture with formation of nodules separated by fibrotic bands
- Scattered Reed–Sternberg cells showing bi- to trinuclear lobes with prominent nucleoli and abundant cytoplasm
- Occasional lacunar cells with pale retracted cytoplasm
  - Positive for CD30, CD15, and MUM-1
  - Negative for ALK-1
  - Variable positivity for CD20
- Mitosis is occasionally seen
- Mature lymphocytes (highlighted by CD3) and occasional eosinophils are seen in the background

Diagnosis → nodular sclerosing Hodgkin lymphoma

Clinical history

- Staging with PET/CT and bone-marrow examination → stage III
- Started on chemotherapy
  - ABVD protocol
- Interim imaging assessment → partial response
- EOT-PET/CT → residual cervical lymphadenopathy
  - 20–10 mm
  - Deauville score of 4
- Decided to go for radiotherapy
  - 30 Gy in 15#
- Repeated PET/CT scan→ no evidence of FDG-avid nodal or extranodal disease

Clinical history

- Patient underwent peripheral-blood stem-cell collection
- Patient remained well, then defaulted follow-up
- Referred back for recurrent left-neck swelling (painless) 5 years later
- Examination → matted left infra-auricular swelling measuring 2 × 3 cm
  - Further swelling measuring 5–6 cm (fluctuating)
- Incision and drainage, followed by biopsy via cup forceps

Clinical history

HPE

- Scant fragments of inflamed fibrogranulation tissue admixed with blood, displaying scattered atypical lymphocytes in a background of lymphocytes, neutrophils, and occasional plasma cells
- Rare Reed–Sternberg-like cells exhibiting multilobated nuclei and ample cytoplasm are seen
- No obvious increase in mitotic activity or tumor necrosis
- No fungal element is observed

IHC

- The rare Reed–Sternberg-like cells are positive for CD30, CD15, and PAX5
- Background lymphocytes are positive for CD3 and CD20

Clinical history

- Treated with brentuximab + gemcitabine
- Initially showed good response, but still has residual disease at the end of cycle 6
- Switched to ICE regime due to financial constraints

Discussion

- Classical Hodgkin lymphoma
- Microscopic:
  - Total or partial effacement of nodal architecture
  - Diagnostic cells
    - Reed–Sternberg cells
    - Large size with bilobed or multilobed nucleus, prominent eosinophilic nucleoli (may be rare!)
  - Lacunar cells
    - Characteristic of nodular sclerosis subtype
    - Pale retracted cytoplasm creating lacunae-like spaces
  - Mixed inflammatory background
    - Lymphocytes, neutrophils, eosinophils, plasma cells, necrosis

Discussion

- In Malaysia, one of the important differential diagnoses for lymphadenopathy is TB (TB lymphadenitis)
- Due to the overlapping clinical symptoms, it may be difficult to distinguish between Hodgkin lymphoma and tuberculosis
  - Fever, loss of weight and appetite
  - Lymphadenopathy
- According to a local study (single center):
  - 47% of patients that had lymph-node biopsy were diagnosed with malignancy
  - 29% were diagnosed with lymphadenitis (including TB)

Darnal HK, et al. The profile of lymphadenopathy in adults and children. Med J Malaysia. 2005; 60: 590-598.

Discussion

- Diagnosis of tuberculosis
  - Can be challenging to confirm
    - Smear-negative (culture positive) pulmonary tuberculosis
  - Some cases would be treated empirically as pulmonary tuberculosis
- Repeated investigations (especially biopsy) are required to establish correct diagnosis

- Other differential diagnosis:
  - Anaplastic large cell lymphoma
    - $CD15^-$, $PAX5^-$; positive for T-cell antigens
  - Primary mediastinal B-cell lymphoma
    - Weak expression of CD30, $CD15^-$, pan B-cell antigens
  - Mediastinal gray zone lymphoma
    - Discordance between morphology and immunophenotype?
    - Hodgkin?
    - Primary mediastinal B-cell lymphoma?

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