INTRODUCTION
Langerhans’ cell histiocytosis (LCH) is a proliferative histiocytic disorder of unknown cause originating from dendritic cells, with an estimated incidence of one to two cases per million population. The disease mostly occurs in individuals aged 21 to 69 years, with a mean age of 32 years. It belongs to a group of disorders with common primary event of accumulation and infiltration of monocytes, macrophages, and dendritic cells into the affected tissues. Its clinical presentation varies greatly, with symptoms ranging from mild to severe. The pathogenesis of LCH is not well understood and an optimal therapeutic strategy has yet to be established. LCH is a rare disease with multiple clinical features; only histologic examination and immunohistochemical assays can lead to a final diagnosis.

CASE
On 26 July 2010, a 29-year-old Indonesian woman was referred to our clinic with a 10-month history of neck enlargement. Neck lymphadenopathy was noted, with erythematous plaques and hyperpigmented macules on the skin over the node. (Fig. 1). She didn’t complain anything concerning her bones. Other physical examination was normal. She had previously visited her primary physician on February 2004 because of itching all over her body; an anti-pruritic drug was prescribed, and the symptom was reduced after four months. The itch recur after three years, without any pruritic lesion. During pregnancy one year later, the itch became worse. It lasts until present; she had some pigmented macules as a result of scratching in her lower extremity (Fig. 2). Physical examination revealed normothermia, normal blood pressure and pulse.
Chest X-Ray performed on 26 June 2010 showed more enlarged mediastinal area (Fig. 4) compared with examination on 24 August 2009 (Fig. 3).

Laboratory findings showed slight normocytic normochromic anemia - Hb 10.8 g/dL, Hct 34.66%, leukocytes 7,900/mm³, eosinophilia (7.9%), slight monocytes (11.5%), relative lymphopenia (12.5%), neutrophils (67.7%), and thrombocytes 383,000/mm³.

**PATHOLOGICAL EXAMINATION**

She was consulted to our clinic. Aspiration biopsy was performed and diagnosed as tuberculous process. She took anti-tuberculous drug but there was no improvement. Reevaluation of the slides was done and it showed just eosinophiles (fig. 5).

Because of swelling persistence, the patient was sent to our clinic on 26 August 2009. Aspiration biopsy was done. There were a lot of medium sized dendritic cells and epitheloid like cells.

Dendritic cells had moderate pleomorphism of nuclei, elongated, angulated, polygonal cytoplasm (fig. 6-8); epitheloid like cells showed variation of nuclear shapes: oval, plump, rectangular with ragged margin. (fig. 9-10). Eosinophiles scattered between lymphoid cells.
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Figure 15 Photomicrography of histologic specimen showed medium-sized Langerhans cells with vesicular nuclei and nuclear grooves

Figure 16 Immunohistochemical expression of S-100 protein

Figure 17 Immunohistochemical expression of CD1a protein

(fig. 11). Immunocytochemical examination (i.e. positivity for S-100 protein) established LCH diagnosis (fig. 12).

An incisional biopsy specimen measured 2x1x0.5 cm, grey, and elastic consistency. Paraffin section showed area with large number of eosinophils, histiocytic-like cells, collection of lymphocytes, and some plasma cells (fig. 13-15). Immunohistochemical examination revealed expression of S-100 and CD1a proteins (fig. 16-17).

She received etoposide, ondansetron, prednisolone. The itch was diminished after one serie of chemotherapy, and complete response of the neck lesion was observed at the 4-month follow up (six series).

DISCUSSION

Scarcity of eosinophils in aspirate specimens is not in accordance with characteristic histopathology. It might be caused by eosinophils concentration in certain spot, i.e. between histiocytic-like cells cluster rather than diffusely infiltrated the tissue.

LCH can be discussed:

1. Based on clinicopathologic presentation, it can be divided to three entities:

   1.1 Multifocal multisystem Langerhans cell histiocytosis (Letterer-Siwe disease) occurs most frequently before 2 years of age but occasionally affects adults. A dominant clinical feature is the development of cutaneous lesions resembling a seborrheic eruption, caused by infiltration of Langerhans cells over the front and back of the trunk and on the scalp. Most of those affected have concurrent hepatosplenomegaly, lymphadenopathy, pulmonary lesions, and eventually destructive osteolytic bone lesions. Extensive infiltration of the marrow often leads to anemia, thrombocytopenia, and predisposition to recurrent infections such as otitis media and mastoiditis. The course of untreated disease is rapidly fatal. With intensive chemotherapy, 50% of patients survive 5 years.

   1.2 Unifocal and multifocal unisystem Langerhans cell histiocytosis (eosinophilic granuloma) are characterized by expanding, erosive accumulations of Langerhans cells, usually within the medullary bone cavities. Histiocytes are variably admixed with eosinophils, lymphocytes, plasma cells, and neutrophils. The eosinophilic infiltrate is usually prominent but is sparse in a subset of cases. Virtually any bone in the skeletal system can be involved, most commonly the calvarium, ribs, and femur. Less commonly, unisystem lesions of identical histology arise in the skin, lungs, or stomach. Unifocal lesions usually affect the skeletal system in older children or adults. They can be asymptomatic, or can cause pain, tenderness, and, in some instances, pathologic fractures. This is an indolent disorder that can heal spontaneously or be cured by local excision or irradiation.

   1.3 Multifocal unisystem Langerhans cell histiocytosis usually affects young children, who present with multiple erosive bony masses that sometimes expand into adjacent soft tissue. In about 50% of patients, involvement of the posterior pituitary stalk leads to diabetes insipidus. The combination of calvarial bone defects, diabetes insipidus, and exophthalmos is referred to as the Hand-Schuller-Christian triad. Many patients experience spontaneous regression; others can be treated successfully with chemotherapy.

2. Based on involved organs, it can be divided into two categories:

   2.1 those with isolated skin, lymph node, or bone lesions

   2.2 those with disseminated form involving two or more organ systems, such as lungs, liver and spleen.

Clinicopathological grouping is difficult, as there is no bone (focal) lesion, eventhough two organs (system) are involved i.e. neck and mediastinal lymph nodes. It is reasonable if we use the second classification, so that it can be categorized to LCH with isolated (lymph node) lesion.

Possibility of tuberculosis and Kimura’s disease should be important consideration.

This case is misdiagnosed as tuberculosis because of epitheloid-like cells findings and the high prevalence of tuberculosis in Indonesia. Epitheloid cells of tuberculosis are slender...
than epitheloid-like cells of LCH being more plump in appearance. Mycobacterium tuberculosis antibody (eg. Ab905, Abcam) can be used immunohistochemically to confirm diagnosis of tuberculosis rather than of eosinophilic granuloma. Oriental ethnicity and the prominent eosinophilic component of the lesion validated Kimura’s disease as differential diagnosis in our case. Kimura’s disease is a distinctive inflammatory lesion occurring primarily in head and neck region in Far East people. Histologically, Kimura’s disease is characterized by lymphoid follicles, eosinophilic infiltration, vascular proliferation, and fibrosis. Stains for CD15, CD 30, S100 protein, and CD1a were negative.7 The presence of characteristic Langerhans’ cells with S100 and CD1a expression in our case, confirmed the diagnosis of LCH.2

Lymph node involvement in LCH may be seen as a reaction to bone or skin lesions. However, it may also be present as a solitary lesion or part of the more extensive type.3 Urticaria pigmentosa could be presented with a neck mass. The lesion composed of unusually large epitheloid mast cells, including a prominent subset with bi-lobed and multi-lobed nuclei. By immunohistochemistry, cells of mastocytoma expressed CD117 (C-Kit), mast cell tryptase, CD68, and CD25, and were negative for CD163, CD1a, and S-100.9 Although the pathogenesis of LCH is not well understood, the possibility of intermediate (type I) hypersensitvity should be considered. Antigens are captured by dendritic cells (DCs) residing in epithelia, and transport the antigens to lymph nodes. DCs become mature, and express MHC molecules and costimulators. Naïve T cells recognise MHC-associated peptide antigens displayed on DCs. The T cells are activated to proliferate and differentiated into cells of T_H2 subset. T_H2 cells produce cytokines i.e IL-4, IL-5, IL-13 which stimulate IgE production, activate mast cells and eosinophils. The mast cells release histamine mediator responsible for the itch.

Treatment depends on the extent of the disease. Steroids may help to slow or even stop the progression of LCH.6 Chemotherapeutic agents, such as vinblastine, methotrexate, cyclophosphamide, etoposide, and cladribine have been successful in patients with progressive disease unresponsive to corticosteroids and in those with multiorgan involvement.10 Nevertheless, no systematic series of treatments for adults have been published and the optimal strategy has yet to be defined.

CONCLUSION

An uncommon case of eosinophilic granuloma was reported, it is a variant of Langerhans’ cell histiocytosis involving neck and mediastinal lymph nodes, with an unusual symptom of itching, that was disappeared after one cycle of chemotherapy.

REFERENCES

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