Datia Langhans cells as tuberculous lymphadenitis diagnose parameter based on chemical reaction

W Purbaningsih1,2,*, T Respati2, D Setiabudi3, H Sastramihardja1,4 and I Parwati1,5
1 Postgraduate Program, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia
2 Faculty of Medicine Universitas Islam Bandung, Bandung, Indonesia
3 Department of Pediatric, Universitas Padjadjaran, Bandung, Indonesia
4 Department of Clinical Pharmacology, Universitas Padjadjaran, Bandung, Indonesia
5 Department of Clinical Pathology and Laboratory Medicine, Universitas Padjadjaran, Bandung, Indonesia

*wida@unisba.ac.id

Abstract. The incidence of tuberculosis in Indonesia increases every year, resulted in increased cases of tuberculous lymphadenitis. The histopathological picture is often similar to other types of lymphadenitis. This study was an in-depth exploration of the anatomical pathology of Langhans datia cells and necrosis in tuberculous lymphadenitis. This research used secondary data from medical record of the lymph node paraffin blocks in the Anatomical Pathology Department of Sadikin Hasan General Hospital Bandung from January to December 2017. There are 322 medical records of tuberculosis lymphadenitis patients, consisting of 179 types of tuberculous lymphadenitis, 144 types of non-lymphadenitis specific, and nine types of granulomatous lymphadenitis. In all kinds of lymphadenitis, necrosis shows a general picture, whereas datia Langhans are more dominant in the tuberculous and granulomatous lymphadenitis type. The description of necrosing in lymphadenitis is tuberculous type 176(98.3%), non-specific type 120(83.3%), and granulomatous type 7(77.8%), while datia Langhans cells are more common in 132(73.7%) tuberculosis lymphadenitis, and granulomatous lymphadenitis 7(77.8%), compared with non-specific lymphadenitis 42(29.2%). This study concludes that there is necrosis in almost every type of lymphadenitis, whereas datia Langhans cells are lower in the tuberculous and granulomatous lymphadenitis.

1. Introduction
Tuberculous lymphadenitis is the most common form of extra-pulmonary tuberculosis, according to the World Health Organization reports comprised of around 20% of all tuberculosis events although incidents varied by region. The diagnosis of lymphadenitis usually made by fine-needle aspiration of an affected lymph node. Although Acid Fast Bacterium smears are positive in only approximately 20% of cases, granulomatous inflammation may be evident. Overall, fine-needle aspiration has a sensitivity of 77% and specificity of 93% for TB infection. First-line treatment of tuberculous lymphadenitis consists of antituberculosis drugs, but surgical excision performed when medical therapy has failed or if the diagnosis is unclear. Incision and drainage should not be done to prevent permanent sinuses and prolonged drainage [1].
Pulmonary infection is present in a minority of cases. Considerations in the differential diagnosis include lymphoma, metastatic cancer, fungal disease, cat-scratch disease, sarcoidosis, toxoplasmosis, reactive adenitis, and bacterial adenitis [2]. The diagnosis of lymphadenitis is still a challenge because sometimes the histopathological picture of each type of lymphadenitis is similar. Datia Langhans cells are one of the multinucleated cells that are typical of tuberculous lymphadenitis. It showed the distribution of the nucleus in one of the cell poles and arranged like a horseshoe. Immunohistochemical studies using surface antigens of monocyte-macrophage lineage cells and adhesion molecules indicated that both types of multinucleated giant cells. They are formed from monocytes rather than tissue macrophages and are phenotypically the same cells with different distributions of nuclei [3]. Santa Cruz and Strayer have stressed the variety of histological changes seen in cutaneous tuberculosis. In many forms, particularly in early lesions, there is a mixture of inflammatory cells within the dermis that includes histiocytes and multinucleate cells without wellformed epithelioid granulomas. The changes seen in the overlying epidermis are varied. In some forms, inflammatory changes extend into the subcutis. Areas of necrosis caseation may or may not be present within granulomas. The number of acid-fast organisms varies in different lesions. In lesions with caseation, organism bodies most frequently found in the centers of necrotic foci. Generally, where there are well-formed granulomas without caseation necrosis, organisms are absent or difficult to find. Neutrophils may be a component of the inflammatory infiltrate, and abscesses form in some clinical subtypes [4].

2. Method
This research is quantitative in type using a crosssectional study design, using secondary data from medical records of lymph node paraffin blocks of lymphadenitis patients. The 322 medical records of paraffin block from lymphadenitis patients analyzed in this study included patients diagnosed between January and December 2017 as having lymphadenitis with lymph node enlargement. One hundred and seventy-nine patients had tuberculous lymphadenitis, 144 non-specific lymphadenites and 9 granulomatous lymphadenites. The lymphadenitis-type histologically diagnosed by a pathologist in Anatomical Pathology Departemen Dr. Hasan Sadikin General Hospital. The patients came to this department were referred from other departments or hospitals to confirm the diagnosis of lymphadenitis. All data collected is then presented in the form of distribution and frequency.

This study approved by the Faculty of medicine Padjadjaran University medical ethics committee with letter no 1050/UN6.C10/PN/2017.

3. Result and discussion
The diagnosis of tuberculosis lymphadenitis is essential to be made to distinguish from other types of lymphadenitis, for the benefit of patient therapy. The differential diagnosis of isolated peripheral tuberculous lymphadenitis includes adenitis due to other mycobacteria, bacterial adenitis, fungal disease, toxoplasmosis, sarcoidosis, cat-scratch disease, cystic hygroma, nonspecific hyperplasia, and primary or metastatic neoplasms. Identification of caseating granulomatous inflammation with Langhans and foreign body giant cells supports a diagnosis of tuberculous lymphadenitis, but histopathological features in certain conditions are often similar [5]. Diagnosis of lymphadenitis required microbiological and histopathology examination. Ziehl Neelsen staining is often negative at the beginning of the inflammatory process, in these conditions granuloma often has no necrosis. The acid-fast staining often found in areas of necrosing, granulomas without necrosis are usually not found smeared. The golden standard for microbiological examination of tuberculous lymphadenitis is culture from tissue specimens, but a culture takes a long time [6]. The accuracy of histopathologic diagnosis is very important because it can be performed in a shorter time.

Histopathological picture of tuberculous lymphadenitis based on the presence of epithelioid cells, cells from Langhans, and necrosis. The three characteristics often found in other types of lymphadenitis. In this research show, more than fifty percent of all kinds of lymphadenitis provide a picture of necrosis (table 1). Necrosis, in this case, cannot be a specific feature for tuberculous lymphadenitis, although the
pathogenesis of Mycobacterium tuberculosis tends to provide a picture of decay in the granuloma, because it is challenging to eradicate [7].

Datia Langhans cells often used as parameters for diagnosis for tuberculous lymphadenitis, but these cells can also found in lymphadenitis due to fungi, viruses, protozoa and other bacteria [8]. Datia Langhans are one of the multinucleated cell types (fig. 1 and 2). Multinucleated giant cells classified as Datia Langhans-type or foreign-body-type cells based on their nucleus array. Datia Langhans cells characterized by the accurate arrangement of their nuclei (fig. 1, 2 and 3), while foreign-body cells have randomly arranged nuclei. Datia Langhans cells are considered to be characteristic of sarcoidosis and tuberculosis, while foreign-body cells have been reported to be predominant in foreign-body granulomas [3]. In this research, Datia Langhans cells found in all three types of lymphadenitis, especially on the tuberculous and granulomatous in addition to tuberculosis (table 2).

Table 1. Distribution of necrosis.

| Lymphadenitis Type | Necrosis (+) | Necrosis (-) | Total |
|--------------------|--------------|--------------|-------|
| Tuberculosis       | 176(98,8)    | 3(1,2)       | 179   |
| Non-spesific       | 120(83,3)    | 24(16,7)     | 144   |
| Granulomatous      | 7(77,8)      | 2(22,2)      | 9     |

Table 2. Distribution of Datia Langhans cells.

| Lymphadenitis Type | Datia Langhans Cells (+) | Datia Langhans Cells (-) |
|--------------------|--------------------------|--------------------------|
| Tuberculosis       | 132(73,3)                | 47(26,3)                 | 179   |
| Non-spesific       | 42(29,2)                 | 102(70,8)                | 144   |
| Granulomatous      | 7(77,8)                  | 2(22,2)                  | 9     |

Necrosis and Datia Langhans cells stained by Hematoxylin-Eosin, in Figure 1 below shows necrosis, Figure 3 shows granulomas with necrosis, while Figure 4 shows granulomatous without necrosis.

**Figure 1.** Granuloma of tuberculous lymphadenitis containing Datia Langhans cells (arrow) and necrosis area (arrow head), at 100x magnification.

**Figure 2.** Datia Langhans cells , at 1000x magnification.
4. Conclusion
Necrosis is present in all types of lymphadenitis, but datia Langhans cells are more common in the type of tuberculosis and granulomatous.

Acknowledgments
This research could be carried out with full support from the Education and Research Department and the Department of Pathology Anatomy Dr. Hasan Sadikin. Research funding supports comes from the Doctoral grant from Ministry of Research Technology and Higher education, contract number: 156/B.04/Rek/III/2018.

References
[1] World Health Organization 2016 Global Tuberculosis Report (Switzerland)
[2] Sokolove P E, Derlet R W 2010 Tuberculosis Emergency Medicine. 7th edition 1809-20
[3] Okamoto H, Mizuno K, Horio T 2003 Langhans-type and Foreign-body-type Multinucleated Giant Cells in Cutaneous Lesions of Sarcoidosis 171–4
[4] Sarcoïdal I, Miscellaneous X 2018 The granulomatous reaction pattern
[5] Handa U, Mundi I, Mohan S 2012 Nodal tuberculosis revisited: A review Journal of Infection in Developing Countries 6 6–12
[6] Kumar S N, Prasad T S, Narayan P A and Muruganandhan J 2013 Granuloma with langhans giant cells: An overview J Oral Maxillofac Pathol 17(3) 420–3
[7] Murphy K, Weaver C 2016 Janeway’s Immunobiology: Ninth edition (Washington) 855
[8] Kumar S N, Prasad T S, Narayan P A, Muruganandhan J 2013 Granuloma with Langhans giant cells: An overview 17(3) 420–3