Lymph Node Imprint Cytology in the Diagnosis of Lymphadenopathy

by

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SUMMARY A cytological study of lymph nodes excised from 11 patients is reported. These patients had final diagnoses of Hodgkin's disease (3), non-Hodgkin's (lymphocytic) lymphoma (3), Tuberculous lymphadenitis (3), Infectious mononucleosis (1) and Squamous carcinoma deposit (1). Imprint cytology of lymph nodes was found to be an easy, rapid method which enabled identification of abnormal cells in lymph nodes with greater accuracy than histological examination. It is, therefore, a valuable adjunct to the histological diagnosis of lymphadenopathy.

INTRODUCTION

The final diagnosis in cases where lymph node enlargement is a feature, is usually made by histological examination of the excised node. The basis of this histological diagnosis is (*a*) the detection of aberrations in the architecture of the node, and (*b*) the identification of abnormal cells.

Loss of architecture of the lymph node cannot be made out by a study of imprints or smears, and the importance of this feature in the evaluation of lymph node disease makes histological examination indispensable for accurate diagnosis.

It is well known, however, that cytological examination is superior to histology when it comes to the identification of cellular abnormalities. This is clearly seen in the case of the bone marrow, where smears of aspirated marrow give better results than histological examination of biopsy material. The present study tests the hypothesis that cytological examination of lymph node imprints, by improving the quality of identification of cellular abnormalities, will be a valuable aid to histological diagnosis.

MATERIAL AND METHODS

The material consisted of lymph nodes removed from 11 patients. The nodes were obtained prior to fixation, soon after surgical excision. The node was cut, the surface dried thoroughly, and imprints made. The technique of making imprints is simple, and excellent results were obtained by lightly touching the dry cut surface of the node on a glass slide. This produces no mechanical trauma to the cells, and gives a result which is superior to smear and crush techniques.

The imprints were fixed in absolute alcohol, and stained with Leishman's stain and haematoxylin and eosin. Leishman-stained films were satisfactory, and have the advantage of affording comparison with the familiar bone marrow smears.

The cytological examination of the imprints was made before the histological examination. This examination of the imprints attempted (1) to identify the cellular components of the node and count their numbers and (2) to detect any abnormal cells that were present. The results were correlated with the histological section prepared from the same node.

RESULTS

No normal lymph nodes were examined in this study. Cytological studies of normal lymph nodes have shown that most of the cells seen belong to the lymphocyte series (Morrison, Samwick, Rubinstein, Stich and Loewe, 1952). Both mature and immature lymphocytes are found, and these belong to two distinct populations, corresponding to the small and large lymphocytes of the peripheral blood. A variety of other cells are present in small numbers in a normal node (Lucas, 1955). Reticulum cells are very infrequent, and constitute less than 1% of the differential count of a normal node (Lucas, 1955). Mitotic figures are not infrequent. The background cell pattern of the pathological nodes in the present series (Fig. 1) was the same as that described in normal nodes.

Differential counts of the cells were found to have little value, and the cytological examination was concentrated in a search for abnormal cells.

The 11 patients had final diagnoses of Hodgkin's Disease (3), tuberculous lymphadenitis (3), lymphocytic lymphoma (3), infectious mononucleosis (1) and a deposit of squamous carcinoma (1). The features observed in the imprints in these cases were as follows:

Hodgkin's Disease :

In all three cases, there was a marked increase in the number of reticulum cells. In one case, there were a large number of Sternberg-Reed cells. These included typical binucleate forms with mirror-image nuclei (Fig. 2). The nuclei were characterised by the presence of one or sometimes two very large, inclusion-like nucleoli. These were rounded or indented, and stained blue with Leishman stain. Many variants of this typical Sternberg-Reed cell were also seen. There were very large cells with multiple nuclei ; and mononuclear cells with bilobed or round nuclei containing the characteristic nucleolus (Fig. 3).

In the other two cases, there was an increased number of reticulum cells, some of which had a prominent nucleolus. However, no typical Sternberg-Reed cells were seen, and a cytological diagnosis was not made. Other cells, such as plasma cells, eosinophil and neutrophil polymorphonuclear leucocytes were also seen in all three cases of Hodgkin's disease.

Histological sections of these nodes showed the complete loss of architecture, pleomorphism and the presence of Sternberg-Reed cells characteristic of Hodgkin's disease. The features of the Sternberg-Reed cells are seen much more clearly in cytological studies of imprints than in the histological sections (Fig. 4).

Tuberculous Lymphadenitis :

Imprints of the three tuberculous nodes showed (*a*) an increased number of histiocytes, which were easily distinguishable from the reticulum cells of Hodgkin's disease by the absence of the prominent nucleolus, (*b*) the caseous debris, which stained purple, and had a peculiar fibrillar appearance, and (*c*) giant cells. These giant cells were infrequent, and were seen as masses of cytoplasm about 100—150 microns in diameter, containing a large number of uniform nuclei (Fig. 5). Imprints stained for acid-fast bacilli gave negative results in all three cases. The histological sections showed typical caseous tuberculous lymphadenitis.

A portion of the node was pulverised and smears were made from this material. These smears were stained for acid-fast bacilli, and this gave a positive result in two cases. This technique is the most satisfactory method of demonstrating acid-fast bacilli in tuberculous lymph nodes. This same pulverised material can also be used to culture the tubercule bacillus.

Lymphocytic Lymphoma :

Imprint examination was not helpful in the diagnosis of lymphocytic lymphoma. It was not possible, even on reviewing the slides after histological diagnosis, to distinguish neoplastic cells of the lymphocyte series from the immature lymphocytes that are normally found in the nodes.

Infectious Mononucleosis :

One lymph node from a patient with infectious mono-nucleosis was examined. This clearly illustrated the superiority of imprint cytology over histology in the identification of cellular abnormalities. In the histological preparation, no abnormal cells could be made out, and a diagnosis of non-specific chronic lymphadenitis was made. In the imprints, a large number of abnormal monocytoid lymphocytes were seen, suggesting a diagnosis of infectious mononucleosis. These cells were 15—20 microns in diameter, had a clear blue cytoplasm, and a round or indented nucleus which contained coarse strands of chromatin (Fig. 6). In this case, therefore, the imprints definitely improved the quality of histological diagnosis.

Squamous Carcinoma Deposit :

This was characterised by replacement of the normal cellular pattern by large cells, 20—25 microns in diameter. The nuclear-cytoplasmic ratio was increased, and the cells tended to clump together (Fig. 7). These features, especially the size of the cells, which was much larger than any normal cell in a lymph node, enabled their identification as malignant epithelial cells. Histological examination of the node showed complete replacement of the nodal tissue by deposits of a squamous carcinoma.

CONCLUSIONS

Lymph node imprint cytology has been used in the present study as an adjunct to histological examination. The imprints were made immediately after the nodes were excised, fixed in absolute alcohol, and stained with Leishman stain. The total time for the procedure is about 15 minutes, and the entire examination can be made in the operating theatre.

Cytological studies suffer from a number of limitations, the most serious of which are (1) that it assays a very small amount of tissue. As such, early, focal lesions of the lymph node may be missed ; (2) more importantly, it gives no information about the architecture of the node, a vital consideration in diagnosis. Because of this, cytology alone will not give a satisfactory diagnosis of lymphadenopathy. Attempts to use cytological examination of smears made from material aspirated from lymph nodes (Lucas, 1955), have not gained acceptance.

However, a study of lymph node imprints has two important advantages over histological examination. These are (1) the speed with which a result can be obtained. Imprints can be used in conjunction with frozen sections when a rapid diagnosis of an enlarged node is required during surgery e.g., in breast or gastro-intestinal carcinoma. (2) More importantly, cytology enables identification of cellular characteristics with a great deal more accuracy than histological examination. This is clearly shown by the case of infectious mononucleosis in the present study. As such, imprint cytology will improve the quality of histological diagnosis of lymphadenopathy, where this depends to any extent on the identification of abnormal cells.

It is therefore concluded that, while imprint cytology will not replace histology, it is a valuable adjunct to the histological diagnosis of lymphadenopathy. The author is of the opinion that imprints should be made routinely in cases where a lymph node is excised for diagnostic purposes.

REFERENCES

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EXPLANATION OF PLATES

Fig. 1. Imprint of lymph node to show the background cellular pattern corresponding to that of a normal node. Leishman stain. X 1050.

Fig. 2. Hodgkin's disease showing binucleate Sternberg-Reed cell (arrow). Leishman Stain. X 1050.

Fig. 3. Hodgkin's disease—showing two binucleate cells (arrows) and an abnormal mononuclear reticulum cell with a large nucleolus (arrow—M). Leishman stain. X 1050.

Fig. 4. Hodgkin's disease—histological section showing a Sternberg-Reed cell with a prominent nucleolus (arrow). H & E. X 525

Fig. 5. Tuberculous lymphadenitis—showing a Langhan's giant cell. Leishman stain. X 525.

Fig. 6. Infectious mononucleosis—showing abnormal monocytoid lymphocytes (arrows). Leishman stain. X 1050.

Fig. 7. Squamous carcinoma deposit—showing malignant epithelial cells. These cells are larger than cells of the lymphocyte series (compare Fig. 1), and show disproportionately large nuclei containing nucleoli. Leishman stain. X 1050

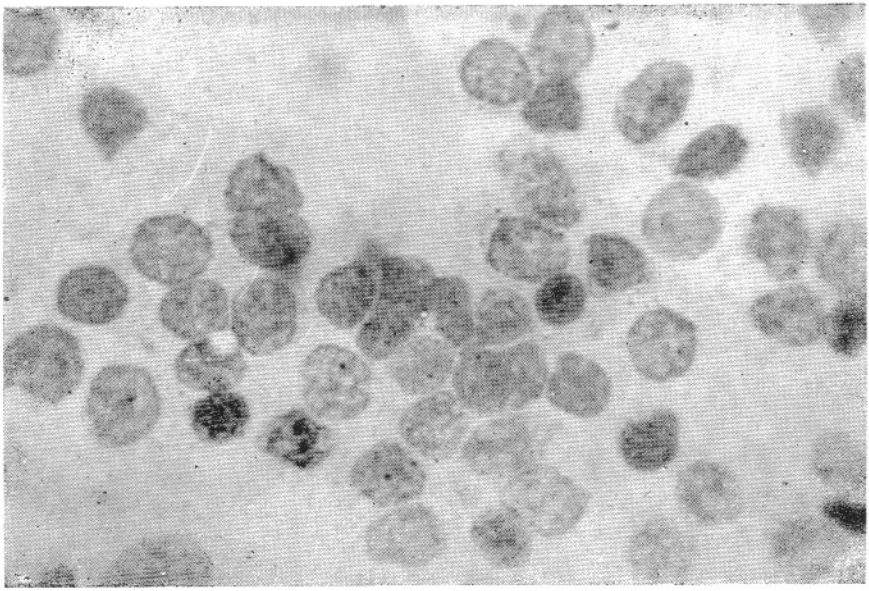

Fig. 1

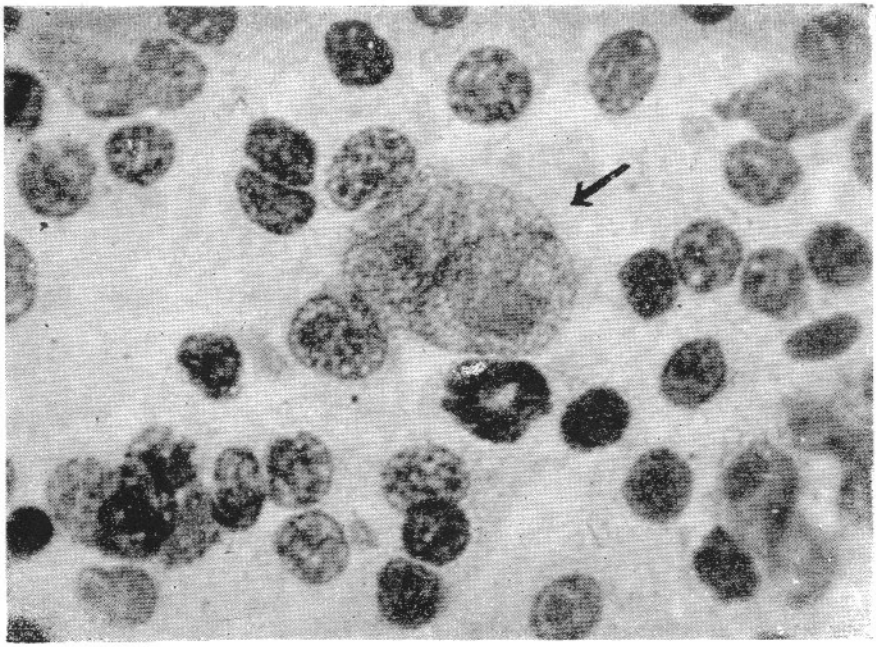

Fig. 2

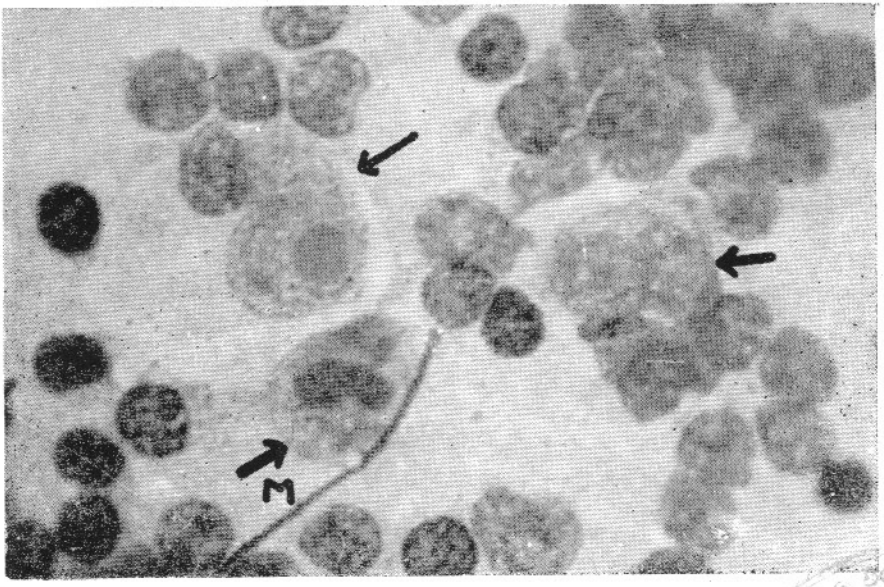

Fig. 3

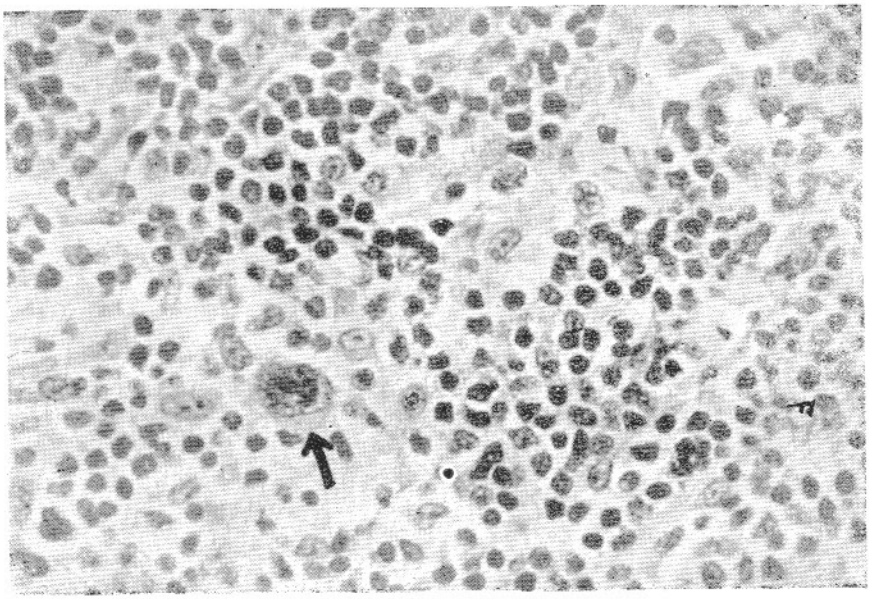

Fig. 4

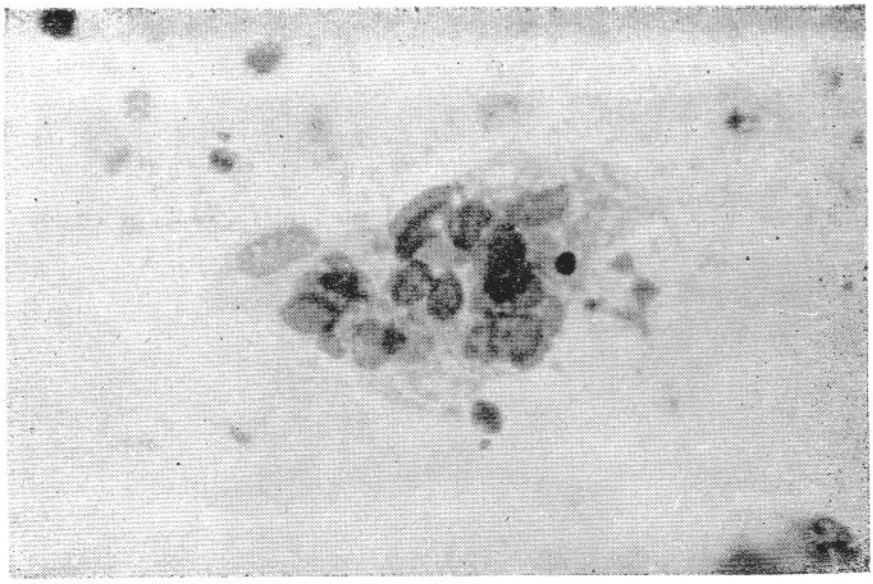

Fig. 5

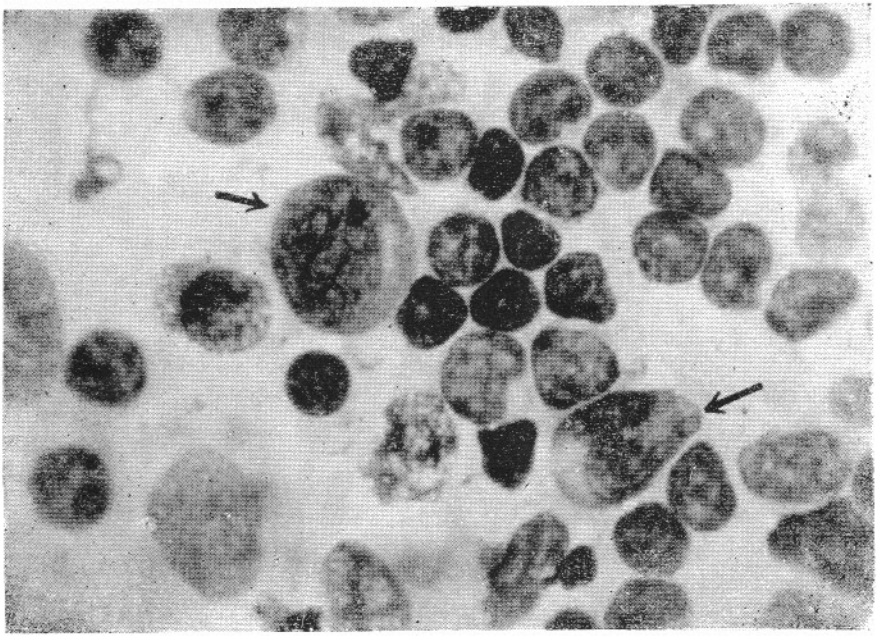

Fig. 6

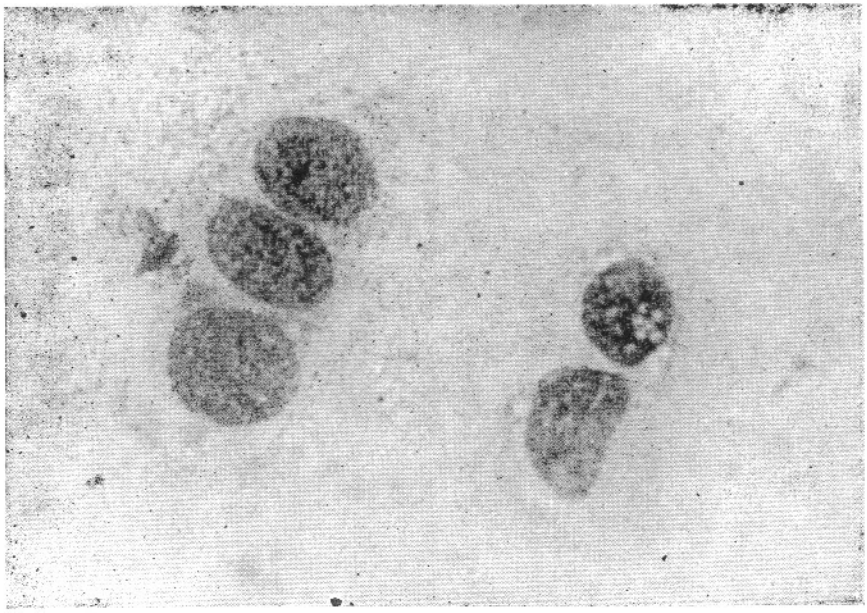

Fig. 7