THE DIAGNOSTIC VALUE OF LYMPH NODE ASPIRATION BIOPSY

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Excision of a lymph node often requires general anaesthesia and admission to hospital which may entail considerable delay in diagnosis and treatment—a delay which is prolonged by the fixation, cutting and staining of sections. Aspiration biopsy is done under local analgesia so that admission to hospital is unnecessary and much time and expense saved. Against these advantages must be placed the difficulty of interpretation caused by the paucity of material obtained which may not be fully representative of the node, and by the inability to assess the architecture of the node and the occasional failure to obtain tissue. These drawbacks are diminished by the ease with which further aspirations can be carried out and by the general distribution of abnormalities of cytology by the time a node is large enough to puncture. A more serious danger is dissemination of disease. Manipulation and aspiration of animal tumours has led to dissemination in some investigations (Tizzer, 1913; Young *et al.*, 1950) but not in others (McLean and Sugiura, 1937). The method has been strongly condemned on this ground (*British Medical Journal*, 1951; Craver, 1940) and on the ground of difficulty of assessment (Robb-Smith, 1947; Symmers, 1951). The danger of spreading disease is difficult to assess but there is no account of fungation or local spread in the literature. The only complications recorded are six cases of haemorrhage which were easily controlled (Estrada, 1936; Cathie, 1938; Christiansen, 1942; Hermitte and Ellis, 1948), one of infection (Strunge, 1944) and one of pneumothorax (Stanel, 1939). The method has been little used in this country and this paper is an attempt to assess its value in diagnosis.

Material and Methods

One hundred consecutive patients with lymphadenopathy have been examined by aspiration biopsy. The final diagnosis was confirmed histologically in the majority of cases.

Aspiration is carried out under local analgesia with a 20 cc. syringe through 18 gauge needles.

The needles are fitted with stylets so that skin, blood and tissue fluid do not enter them. The capsule is pierced only once and no attempt is made to massage the node or to break up its substance with the needle. The few drops of tissue obtained are pushed on to grease-free slides, smeared by pressure with another slide and stained by the May-Grunwald-Giemsa technique. A search is made for abnormal cells under the 1/6 inch objective of the microscope and the oil immersion lens used to confirm detail.

The diagnosis of many of these cases was known before aspiration was carried out. In order to test the value of the method and to rule out clinical bias, one smear from each aspiration was numbered and arranged at random by an assistant. Each smear was examined for an arbitrary period of 15 minutes as the time which a practising pathologist might be able to give. At the end of the time a diagnosis or an alternative diagnosis was made or the smear was put aside with no diagnosis.

Results

The table shows that a diagnosis was made in 57 cases; 49 of these are correct. If 'inflammation' and 'neoplasm' are accepted as diagnoses, the only error is that a diagnosis of reticulosarcoma was made in a patient with monocytic leucosis. In the other seven cases the diagnosis of the type of inflammation or neoplasm was uncertain or wrong.

There were no complications of puncture but from nine patients no tissue was aspirated. Seven of these had Hodgkin's disease and one each tuberculous and non-specific lymphadenitis. Three nodes were small and hard and were not penetrated, four were so dense that nothing could be aspirated; the other two patients had Hodgkin's disease with large masses of small nodes none of which could be fixed and from which there was no yield even after a second attempt. Morrison *et al.* (1952) failed to obtain tissue from 12 of 101 nodes. There is general agreement that the method fails most often in Hodgkin's disease.

Final Diagnosis	No. of Cases	Diagnosis Made	Doubt	No Diagnosis	Failure
Inflammation:					
1. Non-specific	4	1	2	—	1
2. Glandular fever	2	1	1	—	—
3. Herpes zoster	1	1	—	—	—
4. Syphilis	3	2	—	1	—
5. Tuberculosis	7	1	1	4	1
6. Erythrodermia	3	2	1	—	—
Reticulosis:					
1. Hodgkin's disease	26	8	5	6	7
2. Lymphoid follicular	1	—	1	—	—
3. Reticulum cell medullary	1	—	1	—	—
4. Uncertain type	1	1	—	—	—
5. Boeck's sarcoid	1	—	1	—	—
6. Lymphatic leucosis	20	14	3	3	—
7. Monocytic leucosis	1	1	—	—	—
8. Myeloid leucosis	1	1	—	—	—
Neoplasm:					
1. Lympho- and reticulosarcoma	15	11	3	1	—
2. Secondary carcinoma	10	10	—	—	—
3. Secondary melanoma	2	2	—	—	—
4. Salivary tumour	1	1	—	—	—
	100	57	19	15	0

Necrotic tissue was aspirated from five cases and a diagnosis could be made in only one of these.

Analysis on the basis of the final diagnoses shows:

Inflammation. The criterion for the diagnosis is excess of primitive cells at the expense of lymphocytes. Monocytosis suggests glandular fever, plasmocytosis syphilis, histiocytosis erythrodermia. Monocytosis with Langhans' cells suggests tuberculosis. The diagnosis was confirmed histologically in all cases except those of glandular fever, syphilis and herpes zoster; these were confirmed by other investigations.

Of the 18 cases in this group a diagnosis of inflammation of correct type was made in only six—two cases each of syphilis and erythrodermia, one each of tuberculosis and glandular fever. Two others were correctly diagnosed inflammatory but were thought to be glandular fever, the final diagnoses being non-specific inflammation and herpes zoster. Of the remaining 10 cases, in five there was doubt between inflammation and other disorders and in five no diagnosis was made.

Reticulosis (Plates 1-3). The criteria for the diagnosis of Hodgkin's disease are the presence of pre-Sternberg cells, some of which must be greater than 30 microns in diameter, or Sternberg cells, together with an excess of monocytes, plasma cells or polymorphs. For the diagnosis of lymphatic leucosis, 99 per cent. of the cells must be lymphocytes, some of which must contain nucleoli in nuclei of adult type. The diagnosis was confirmed histologically in all the reticuloses except one and by blood and marrow examination in the leucoses.

Of 45 cases in this group a correct diagnosis was made in 24—Hodgkin's disease, eight; lymphatic leucosis, 14; myeloid leucosis, one; a diagnosis from smears of 'reticulosis of uncertain type' is accepted as correct in one patient who has had progressive lymphadenopathy for three years with constitutional deterioration, although reports of non-specific changes only were made on two surgical biopsies. A case of monocytic leucosis was diagnosed reticulosarcoma. Of the remaining 20 cases, one histologically atypical case of Hodgkin's disease was diagnosed 'reticulosis of uncertain type,' in ten there was doubt between reticulosis and inflammation and in nine no diagnosis was made.

Neoplasm (Plates 4 and 5). The criterion for the diagnosis is that 80 per cent. of the cells must be of the same type but show differences in their structure and contain large, dark nuclei some of which must contain nucleoli. The presence of cells adherent to one another suggests carcinoma, very large nucleoli suggest reticulosarcoma. Otherwise distinction depends upon the detailed morphology of the cells. The diagnosis was confirmed histologically in every case except two.

Of 28 cases in this group a diagnosis of neoplasm of correct type was made in 19—lympho- and reticulosarcoma, ten; secondary carcinoma, six; melanoma, two; salivary tumour, one. Five other cases were correctly diagnosed malignant but the type of malignancy was wrong. Of the four cases remaining there was doubt between lymphosarcoma and lymphatic leucosis in two and between reticulosarcoma and an unusually cellular case of Hodgkin's disease in one; necrotic tissue was

PLATE 1.

PLATE 2.

PLATE 3.

PLATE 4.

PLATE 5.

aspirated from the fourth case. A wedge biopsy from one correctly diagnosed carcinoma shows non-specific changes only, but the diagnosis of carcinoma was confirmed at autopsy.

Discussion

The literature contains little critical assessment of lymph node aspiration biopsy. The impression given is that the value of the method has been greatly exaggerated, although the few figures available of cases in which the diagnosis was confirmed are less extravagant in their claims. Khanolkar and Sharpune (1944) examined 505 nodes and diagnosed 47 inflammatory lesions and 336 neoplasms but there is little information on the means of confirmation. Other figures show a diagnosis in 21 of 25 nodes (Forkner, 1927), 18 of 32 nodes (Cathie, 1938) and 2/3 of 157 nodes (Blinkenberg, 1938). It is probable that more diagnoses would have been made in this series, especially in Hodgkin's disease, if more time had been spent in examination of smears, and particularly if more than one smear had been examined and more than one node punctured.

A search for abnormal cells is the most important step in diagnosis. If 80 per cent. of cells are abnormal and are of the same type the diagnosis lies between neoplasm and leucosis. The only exception is the rare case of tuberculosis in which as many as 80 per cent. epithelioid cells are present (Leitner, 1940); Langhans' cells are usually seen in such cases. Distinction of the type of neoplasm is often impossible but may be of little importance. Strunge (1944) made the diagnosis in 30 of 35 secondary carcinomata and Morrison *et al.* (1952) in all of seven carcinomata and 80 per cent. of 12 sarcomata. The method may be valuable in diagnosis of aleukaemic leucosis, as in two cases in this series. The presence of small numbers of abnormal cells suggests Hodgkin's disease, tuberculosis or sarcoid; the latter two cannot be distinguished unless tubercle bacilli are seen. The literature contains very variable reports of the percentage of cases of Hodgkin's disease which can be diagnosed by aspiration biopsy from 31 of 32 cases (Stuyt, 1947) to 7 of 32 cases (Tempka and Kubiczek, 1948). In tuberculosis figures vary from 13 of 16 cases (Hermansky, 1949) to 3 of 29 cases (Strunge, 1944). Equally variable figures are given for other types of inflammation. This investigation suggests that a confident diagnosis of inflammation can rarely be made from smears. Analysis of the doubtful diagnoses shows them to be of no value to the clinician so if a diagnosis cannot be made a node should be excised for histology.

It is well to stress that necrotic tissue may be aspirated from malignant nodes. Of five necrotic

aspirates in this series, three are tuberculous, one a reticulosarcoma and one a carcinoma; recognizable malignant cells were seen in the latter.

The accuracy of the method should be assessed on the number of errors rather than on the number of diagnoses made. The method can then be used as a means of screening patients with lymphadenopathy particularly if neoplasm is suspected. If a diagnosis can be made the patient has been saved a much more time-consuming, expensive and unpleasant operation, often necessitating admission to hospital. If it fails or if there is doubt, only the pathologist's time has been lost and a node can be excised. The smear and section methods can then be considered as complimentary to one another. Alternatively, especially perhaps in Hodgkin's disease in which it may be possible to make a diagnosis from smears at an early stage of the disease, imprints can be made from excised nodes, examination of which may assist diagnosis if histology is uncertain.

Summary

The results are described of aspiration biopsy of 100 consecutive patients with lymphadenopathy. One smear from each patient was examined for 15 minutes without clinical or pathological information. A diagnosis was made in 57 cases; 49 of these are correct and a further seven were correctly diagnosed inflammation, reticulosis or neoplasm, but the exact type of lesion was wrong. A diagnosis of reticulosarcoma was made in the last patient who had monocytic leucosis. No tissue was aspirated from nine patients and in the remainder there was doubt of the diagnosis or none could be made. The value of the method is discussed and the conclusion reached that if the criteria for diagnosis are strict, accurate diagnoses can be made and the method can be used to screen patients with lymphadenopathy, excision of a node being necessary in case of doubt.

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