Survey of the eventual diagnosis in 226 cases referred for a second histological opinion after an initial biopsy diagnosis of reticulum cell sarcoma

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SYNOPSIS In a series of 226 cases of lymphadenopathy in which an initial histological diagnosis of reticulum cell sarcoma was reviewed in a reference laboratory this interpretation was confirmed in 165 cases (73%). In the 61 other cases the diagnosis of reticulum cell sarcoma was considered to be mistaken. The conditions most frequently confused with reticulum cell sarcoma were Hodgkin's disease (particularly its ordinary form) and metastatic tumours.

The sources of the material reviewed in this account of errors in the histological diagnosis of reticulum cell sarcoma are noted in the complementary paper on the misdiagnosis of Hodgkin's disease (Symmers, 1968).

MATERIAL

The material comprises lymph node biopsy specimens from 226 patients in whom the diagnosis of reticulum cell sarcoma had been made histologically. This diagnosis was confirmed on review of the histological findings and by the course of the disease in 165 cases (73%); in the 61 other cases some condition other than reticulum cell sarcoma turned out to be present. The eventual diagnoses in these cases are shown in Table I.

COMMENT

With the exception of confusion with the anaplastic metastatic tumours, some of which are notoriously difficult to distinguish from poorly differentiated reticulum cell sarcomas, most of the errors tabulated here are explicable primarily as due to inexperience.

Comparison with the complementary series of cases relating to the diagnosis of Hodgkin's disease (Symmers, 1968) shows that the original biopsy diagnosis was wrong in a substantially smaller proportion of cases in which reticulum cell sarcoma

was diagnosed initially than when Hodgkin's disease was diagnosed: the figures are respectively 27% and 47%. This difference reflects the relative frequency with which the two diseases were confused with other malignant diseases and with inflammatory conditions. In 90% of the cases in which the lymph node biopsy was wrongly considered to show a reticulum cell sarcoma the correct diagnosis was another malignant disease; inflammatory conditions accounted for the remainder (only 10%). In contrast, the correct diagnosis was another malignant disease in only 21% of the cases in which the lymph node biopsy was wrongly interpreted as showing Hodgkin's disease, whereas in no less than 68% the correct diagnosis was an inflammatory condition. From this evidence it is clear that inflammatory conditions are very much likelier to be mistaken for Hodgkin's disease than for sarcoma, an observation that is in keeping with the closer histological resemblance of the lesions of Hodgkin's disease to inflammatory processes than to neoplastic ones.

RETICULUM CELL SARCOMA MISTAKEN FOR OTHER DISEASES As in the complementary study of Hodgkin's disease (Symmers, 1968), there were cases in the present study in which reticulum cell sarcoma was initially mistaken for other conditions, as well as the converse situation referred to above and summarized in Table I. The original diagnoses in 66 cases of eventually proven reticulum cell sarcoma are indicated in Table II: as in the converse situation, the confusion was with another malignant disease in a large majority of the cases (97%).

The number of cases of reticulum cell sarcoma mistaken for other conditions (64) was practically

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TABLE I

EVENTUAL DIAGNOSIS IN 226 CASES OF LYMPHADENOPATHY REFERRED WITH AN INITIAL HISTOLOGICAL DIAGNOSIS OF RETICULUM CELL SARCOMA (1947 TO 1966 INCLUSIVE)

Eventual Diagnosis	Number of Cases
<i>Group A: Reticulum cell sarcoma</i>	Total 165
<i>Group B: Other malignant diseases</i>	Total 55
Hodgkin's disease	Total 24
(a) Ordinary type	20
(b) Indolent type ('Hodgkin's paraganuloma')	4
Lymphosarcoma	8
Metastatic tumours	Total 23
(a) Squamous carcinoma (usually anaplastic)	10
(b) Melanoma	3
(c) Lymphoepithelioma	2
(d) Seminoma	2
(e) Malignant glioma (spreading from the brain through a craniotomy wound and hence to cervical lymph nodes in one case; arising in an ovarian teratoma in one case)	2
(f) Dysgerminoma (in cervical lymph nodes)	1
(g) Hepatoma (in axillary lymph nodes)	1
(h) 'Granular cell myoblastoma'	1
(i) Non-chromaffin paraganglioma	1
<i>Group C: Non-neoplastic conditions</i>	Total 6
Chronic (non-specific) lymphadenitis	3
Infectious mononucleosis	1
Dermatopathic lymphadenopathy	1
Drug-induced lymphadenopathy (due to phenytoin)	1

TABLE II

ORIGINAL HISTOLOGICAL DIAGNOSIS IN 66 INITIALLY MISDIAGNOSED CASES OF RETICULUM CELL SARCOMA

Original Diagnosis	Number of Cases
<i>Malignant diseases</i>	Total 64
Hodgkin's disease	Total 34
(a) Ordinary type	22
(b) Indolent type ('Hodgkin's paraganuloma')	12
Lymphosarcoma	12
Metastatic tumours	Total 18
(a) Anaplastic carcinoma	14
(b) Lymphoepithelioma	2
(c) Melanoma	1
(d) Choriocarcinoma	1
<i>Non-neoplastic conditions</i>	Total 2
Chronic (non-specific) lymphadenitis	1
Brucellosis	1

the same as the number of cases in which other conditions were mistaken for reticulum cell sarcoma (61). This is in contrast to the situation revealed by the complementary study of Hodgkin's disease (Symmers, 1968): Hodgkin's disease was mistaken for other conditions with less than one-third of the frequency of the converse error.

CONFUSION BETWEEN RETICULUM CELL SARCOMA AND NON-CANCEROUS CONDITIONS The tables in this paper and in the complementary paper on Hodgkin's disease (Symmers, 1968) indicate that there is substantially less risk of confusion between reticulum cell sarcoma and non-cancerous conditions than between Hodgkin's disease and non-cancerous conditions. Reticulum cell sarcoma was misdiagnosed as a non-cancerous condition in 3% of the cases in which the correct diagnosis was not made when the biopsy sections were first examined; in contrast, Hodgkin's disease was misdiagnosed as a non-cancerous condition in 49% of the cases in which the correct diagnosis was not made initially. Conversely, a non-cancerous disease accounted for 10% of the cases in which an incorrect diagnosis of reticulum cell sarcoma was made and for 71% of those in which an incorrect diagnosis of Hodgkin's disease was made.

FREQUENCY OF DIAGNOSTIC FAILURE

This paper is primarily concerned with a series of 226 cases in which the initial lymph node biopsy diagnosis was reticulum cell sarcoma: this diagnosis had been made either confidently or at least with a strong assumption of its accuracy. Eventually, the diagnosis of reticulum cell sarcoma proved to be wrong in 61 cases: in other words, in 27% of patients who were initially considered to show histological evidence of reticulum cell sarcoma some other condition was in fact responsible for the lymphadenopathy.

The series of 226 cases under discussion consisted exclusively of cases specifically referred for a second histological opinion (Symmers, 1968). The 165 confirmed cases of reticulum cell sarcoma that were in this series (Table I), together with 66 cases of reticulum cell sarcoma that had been referred with a mistaken biopsy diagnosis of some other disease (Table II), and 78 cases from the hospitals served by the reference laboratory, constitute a group of altogether 309 proven cases of reticulum cell sarcoma. Of these 309 cases, 243 were correctly diagnosed at the time of the initial biopsy examination: the remaining 66 were at first misdiagnosed histologically. In other words there was a failure of the initial biopsy diagnosis in 21% of cases of reticulum cell sarcoma.

REFERENCE

Symmers, W. St. C., Sr (1968). *J. clin. Path.* 21, 650.