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BIOPSY OF THE NASOPHARYNX AS A STAGING PROCEDURE IN HODGKIN'S DISEASE

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The remarkable progress achieved during the last decade in the treatment of Hodgkin's disease is the result of a more precise mapping of the extension of the disease and better therapeutic means. By use of lymphography and staging laparotomy silent involvement of abdominal tissues have frequently been revealed during the primary staging of patients.

Most patients with Hodgkin's disease have cervical lymphadenopathy at presentation. These nodes drain also the nasopharynx. However, reports on early involvement of the nasopharynx in Hodgkin's disease are scarce.

The present report gives the results of epipharyngoscopy in 76 previously untreated patients with Hodgkin's disease.

Material and Methods. During the years 1969 to 1975, totally 180 patients with Hodgkin's disease were seen at this hospital. The patients were staged according to the Ann Arbor system (ROSENBERG 1966) using standard staging procedures including lymphography and laparotomy with splenectomy. In 76 patients a detailed ENT-examination was performed, which included inspection of the nasal cavity and the

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Table 1

Microscopic type of lymph node biopsy in 45 patients

Microscopic type	Biopsy of the nasopharynx		
	Positive	Suggestive	Negative
Lymphocyte predominance	0	3	6
Mixed cellularity	3	0	17
Lymphocyte depletion	0	0	2
Nodular sclerosing type	1	0	13

laryngeal and pharyngeal spaces by a senior member of the ENT-staff. In 45 of these patients a biopsy was made from the nasopharyngeal region. In the remaining 104 patients no detailed ENT-examination was performed; the main reason being either advanced stage of disease or the fact that the patients had been staged and treated at other hospitals.

On the lying patient, the nasal cavities and the pharynx were anaesthetized with local anaesthesia, the head was tilted backwards and the epipharyngeal region inspected by a mirror. The biopsy forceps were introduced either through the nasal cavity or the pharynx, and the biopsy was made either from areas considered to be abnormal or from seemingly normal mucosa.

Microscopic classification of the initial lymph node biopsies was made according to LUKES et coll. (1966) and LUKES & BUTLER (1966). All epipharyngeal specimens were compared with the microscopic appearances of the initial lymph node biopsy. The presence of Reed-Sternberg cells or Hodgkin cells was considered necessary for a diagnosis of nasopharyngeal involvement. In some patients a conclusive microscopic diagnosis of nasopharyngeal involvement could not be achieved but the appearance was clearly abnormal with large mononuclear cells of histiocytic type and disarranged lymphatic tissue. These changes were considered a suggestive, but not a definite proof of involvement.

The analysis of the series was restricted to the 45 patients with biopsy of the nasopharynx; 34 were males and 11 females, the age ranged between 16 and 80 years with a mean of 41.

Results

At microscopy, typical abnormalities in the nasopharyngeal specimen indicating Hodgkin's disease were found in 4 patients and in a further 3 patients the findings were abnormal and suggestive of this disease. In 38 patients the microscopy was normal. Thus, in 7 of 45 (16%) patients abnormalities were revealed that either necessitated therapy or repeat examination.

Table 2

Stage before epipharyngoscopy in 45 patients

Stage before epipharyngoscopy	Biopsy	
	Positive or suggestive	Negative
1	2	14
2	3	8
3	1	11
4	1	5
No symptoms	5	26
Symptoms of systemic disease	2	12

Table 3

Signs of ENT involvement in 45 patients

Findings at epipharyngoscopy	Biopsy	
	Positive or suggestive	Negative
Normal	2	27
Swollen or adenoid-like	3	9
Granulated	1	2
Tumour	1	0
Total	7	38

The microscopic type of the lymph nodes on different groups of patients appears in Table 1. Of the 4 patients with a positive nasopharyngeal biopsy, 3 displayed mixed cellularity and one was of the nodular sclerosing type, whereas in all 3 patients with a non-conclusive, but possibly pathologic nasopharyngeal specimen, a lymphocyte predominance was observed in the initial lymph node biopsy. The 38 patients with a negative nasopharyngeal biopsy are distributed among the different microscopic types usually found at this hospital.

The stage before epipharyngoscopy for patients with positive or suggestive nasopharyngeal biopsy and for those with a negative biopsy appears in Table 2. The patients with a positive or suggestive biopsy were usually in an early stage, whereas this was not evident for patients with a negative biopsy. The two groups did not differ as regards the presence or absence of symptoms of a systemic disease.

Only one of the 7 patients with positive or suggestive biopsy had local symptoms, presenting as an otosalpingitis. The remaining 6 had no local symptoms, as was the case with the 38 patients with a negative biopsy. Local ENT signs are given in Table 3.

Table 4

Sites other than nasopharynx involved at presentation in 45 patients

Sites	Biopsy	
	Positive or suggestive	Negative
Other ENT-sites	1*	1**
Cervical lymph nodes		
Cranially only	2	5
Caudally only	0	11
Cranially and caudally	3	13
No cervical lymph nodes	2	9
Outside the head and neck region	4	29

* Tonsil

** Tonsil and parotid gland

Of the 4 patients with a positive biopsy, two had a normal, one a swollen or adenoid-like, and one a granular appearance of the nasopharynx at epipharyngoscopy. Of the 3 patients with abnormalities suggestive of Hodgkin's disease, two had an adenoid-like appearance and one a tumour.

The sites involved at presentation appear in Table 4 and for each of the 7 patients with abnormal biopsy in Table 5. In patient number 3 only the axilla was involved in addition to the nasopharynx. In this case the nasopharynx appeared macroscopically normal.

Thus, histologic type, stage of disease, presence or absence of symptoms and signs of involvement of the nasopharynx, or general presentation of disease, did not select patients with abnormal from those with normal biopsy of the nasopharynx.

Discussion

Contrary to observations in other malignant lymphomas, the involvement of Waldeyer's lymphoid ring including nasopharynx seems to be rare in Hodgkin's disease as judged from the previous literature. ENNUYER et coll. (1961) gave synopses of 7 patients in the literature from the years 1927 to 1958 with nasopharyngeal involvement, but reported no case of their own. KAPLAN (1972) stated that there is a remarkably low frequency of involvement of the tonsil and the lymphatic structures of Waldeyer's ring in this disease and, that, when it occurs, it is usually associated with involvement of the upper cervical and sometimes the preauricular lymph nodes. TODD & MICHAELS (1974) reported on 16 patients with Hodgkin's disease involving the lymphoid ring of Waldeyer; 8 had involvement of the nasopharynx, 7 of the tonsil, and one of the posterior pharyngeal wall. At the time of diagnosis, 2 of the 8 with nasopharyngeal involvement had this site affected as sole manifestation, whereas

Table 5

Sites involved at presentation in 7 patients with pathologic biopsy from the nasopharynx

Sites	Patient number						
	1	2	3	4	5	6	7
	Biopsy positive				Biopsy suggestive		
Other ENT-sites					+*		
Cervical lymph nodes							
Cranially only		+					+
Caudally only							
Cranially and caudally	+			+	+		
No cervical lymph nodes			+			+	
Outside the head and neck region	+		+**		+	+	

* Tonsil
** Axilla only

the remaining 6 had more widespread disease. In 7 of the 8 mixed cellularity was found and in one lymphocyte predominance.

In the present prospective series the frequency of abnormal microscopic findings in the nasopharynx at the primary staging is high (16%) compared with previous reports. Some of the examiners did not always perform a biopsy in patients with a normal appearance at epipharyngoscopy. If the present series is taken to include all 76 patients with a detailed ENT-examination, the frequency of proven microscopic abnormalities in the nasopharynx will still be high (7/76, 9%). No simple explanation of the discrepancy between the present findings and those previously reported seems to exist. One explanation may be that the nasopharyngeal involvements in the present series represent early involvement. Previous reports (GHOSSEIN & NAJJAR 1967), are usually considering symptom-giving involvement. There seems to be no other series where biopsy of the nasopharynx has been performed as part of the primary staging procedures in Hodgkin's disease. Apparently the institution of chemotherapy for relapsing disease may conceal any involvement of the nasopharynx. Such relapsing disease may be due to re-seeding from an undiagnosed involvement of the nasopharynx, and this was actually seen in one of the patients in the present series, where a nasopharyngeal involvement was not established initially but only at review of the original nasopharyngeal biopsy.

Neither the microscopic appearance of the lymph node biopsy, stage of disease, presence or absence of symptoms and signs of ENT-involvement, nor the general presentation of the disease did indicate nasopharyngeal involvement. It is obvious that merely an inspection of the nasopharynx in order to detect early involvement is not sufficient. The ENT-examination should be performed by an experienced ex-

aminer, who must obtain adequate biopsy specimens. The biopsy should be directed not only towards possibly pathologic areas but also include seemingly normal mucosa. In general, it is difficult to evaluate small fragmented pieces of tissue from the nasopharynx microscopically. This is especially true if the microscopic type of disease is lymphocyte predominance, where diagnostic cells might be scarce.

In conclusion, a generous biopsy of the nasopharynx is recommended to be included in the pretherapeutic staging of patients with Hodgkin's disease.

SUMMARY

Biopsy of the nasopharynx was performed in 45 patients with Hodgkin's disease as part of the pretherapeutic staging. Seven of the 45 (16%) had microscopic abnormalities in the nasopharynx compatible with Hodgkin's disease. Such abnormalities occurred even in the absence of local ENT-symptoms or signs, and they could not be predicted from the microscopic type of lymph node biopsy, stage of disease or general presentation. A generous biopsy of the nasopharynx is recommended to be included in the staging procedures in Hodgkin's disease.

ZUSAMMENFASSUNG

Biopsien des Nasopharynx wurden bei 45 Patienten mit Hodgkin'scher Erkrankung als Teil der prätherapeutischen Stadieneinteilung vorgenommen. Sieben der 45 Patienten (16%) hatten mikroskopische Veränderungen im Nasopharynx, die mit einer Hodgkin'scher Erkrankung vereinbar waren. Derartige Veränderungen traten auch in Abwesenheit lokaler ENT-Symptome oder Zeichen auf und liessen sich nicht vom mikroskopischen Typus der Lymphknotenbiopsie, dem Stadium der Erkrankung oder dem Allgemeinbild vorhersagen. Es wird empfohlen, bei den Verfahren zur Stadieneinteilung der Hodgkin'schen Erkrankung eine grosszügige Biopsie des Nasopharynx mit einzubeziehen.

RÉSUMÉ

Une biopsie du nasopharynx a été faite chez 45 malades atteints de maladie de Hodgkin comme élément de la détermination préthérapeutique du stade. Dans sept cas sur 45 (16%) il y avait des anomalies microscopiques du nasopharynx compatibles avec le diagnostic de maladie de Hodgkin. Des anomalies semblables existaient même en l'absence de signes fonctionnels ou physiques oto-rhino-laryngologiques locaux; elles n'avaient pas pu être prévues d'après le type microscopique de la biopsie des ganglions lymphatiques, ni d'après le stade de la maladie ou l'état général. Les auteurs recommandent d'inclure dans les techniques de détermination du stade de la maladie de Hodgkin une biopsie généreuse du nasopharynx.

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