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Non-Hodgkin's Lymphoma of the Head and Neck:
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Forty-five patients with non-Hodgkin's lymphoma (NHL) of the extracranial head and neck who had undergone CT as part of their evaluation were reviewed to assess the impact of CT on clinical management. The sites of tumor deposition were subdivided by location: I, nodal; II, extranodal, lymphatic (Waldeyer's ring); and III, extranodal, extralymphatic (orbit, sinonasal, deep facial spaces, mandible, salivary gland, skin, and larynx). The CT appearance of NHL in each of the three locations was analyzed for characteristic CT signatures. Nodal NHL was suspected when CT showed multiple, large, homogeneous lymph nodes, often in unusual nodal chains of the head and neck. Extranodal, lymphatic NHL of Waldeyer's ring was indistinguishable from squamous cell carcinoma of this area unless synchronous tumor deposit in an extranodal, extralymphatic location was also present. When NHL was in nodes and/or Waldeyer's ring, CT-derived information was of limited clinical value since treatment was unfocused (chemotherapy and/or large-field radiotherapy). The CT appearances of extranodal, extralymphatic NHL was generally not distinguishable from other malignancies of these areas. However, CT-derived information regarding deep-tissue tumor size and extent was critical to planning the radiotherapy ports.

Non-Hodgkin's lymphoma (NHL) is the second most common neoplasm found in the head and neck region behind squamous cell carcinoma [1, 2]. As CT has gained acceptance as the staging technique of choice for head and neck squamous cell carcinoma, NHL has undergone CT evaluation with increasing frequency [3–6]. However, the impact of CT evaluation on clinical management of NHL in this region has not been evaluated.

NHL in the extracranial head and neck can be either the only manifestation of lymphoma—that is, primary head and neck NHL—or part of disseminated NHL. When localized to the head and neck region, NHL is treated with radiotherapy [7]. When the tumor site is within the structures of the face, such as the orbit, sinus, or deep facial spaces, precise deep-tissue anatomic information is necessary to plan the radiation ports [8–10]. When disseminated NHL is present, chemotherapy becomes the primary treatment method, with focused radiotherapy reserved for patients with specific problem sites of involvement. If the diagnosis of NHL is already known, CT would be expected to contribute significant information to those patients in whom focused radiotherapy is being used as a primary or adjunctive treatment method.

We reviewed the impact of CT on clinical management of 45 cases of head and neck NHL. Each case was categorized into one of three major NHL sites of disease presentation in the head and neck: I, nodal; II, extranodal, lymphatic (Waldeyer's ring); and III, extranodal, extralymphatic (orbit, sinonasal, deep facial spaces, mandible, salivary gland, skin, and larynx). The purpose of this report was to assess the impact of CT on clinical management of NHL in the extracranial head and neck and to familiarize the practicing radiologist with the more characteristic CT appearances of this disease.

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Materials and Methods

We reviewed the clinical and radiographic records of 45 patients with both the final pathologic diagnosis of NHL and a CT scan of the extracranial head and neck. Clinical staging in each case was completed according to the Ann Arbor system of staging Hodgkin's lymphoma [11]: stage I, involvement of a single lymph-node region (I) or a single extralymphatic organ or site (I_E); stage II, involvement of two or more lymph-node regions on the same side of the diaphragm (II) or localized involvement of an extralymphatic organ or site (II_E); stage III, involvement of lymph-node regions on both sides of the diaphragm (III) or localized involvement of an extralymphatic organ or site (III_E) or spleen (IIIs) or both ($IIIs_E$); and stage IV, diffuse or disseminated involvement of one or more extralymphatic organ with or without associated lymph-node involvement. Radiographic staging routinely includes chest radiography, abdominal CT, and neck CT. Exploratory laparotomy, bipedal lymphangiography, chest CT, and upper gastrointestinal series were not used routinely.

Each case was analyzed for site of involvement by NHL in the head and neck area and placed into one or more of three major categories: (1) nodal; (2) extranodal, lymphatic; and (3) extranodal, extralymphatic. The CT appearance of NHL in each of these three sites was reviewed for characteristics that would independently suggest the correct pathologic diagnosis. The clinical uses of the data acquired during CT examination of the head and neck were evaluated to assess the impact of CT on clinical management.

CT scans were obtained using multiple scanner units, with the more recent studies done on a Somatom II scanner (Siemens, Iselin, NJ), by using axial scans with 4-mm sections and 10-sec scanning times. The patient remained supine, breathing quietly with chin elevated. Coronal CT sections were obtained when the lesion was found to involve the nasopharynx and/or the base of the skull. All patients received IV contrast material via the most current IV contrast administration method, which involves an initial 50-ml bolus of 60% iothalamate meglumine (Conray 60%, Mallinckrodt), with subsequent rapid drip infusion of 300 ml of 30% iothalamate meglumine. Dose adjustments were made for younger patients.

Results

Of the 45 patients, each had a confirmed final pathologic diagnosis of NHL and all underwent a CT examination of the head and neck region. Thirteen patients had nodal NHL; four had extranodal, lymphatic; and 16 had extranodal, extralymphatic NHL alone. In 12 patients two or more of these sites were involved simultaneously. Twenty patients (44%) had primary head and neck NHL at presentation. The other 25 (56%) had systemic NHL that in part involved the extracranial head and neck.

Nodal NHL

Twenty-four patients presented with NHL involving the lymph-node chains of the head and neck region; 13 as an isolated finding, two in association with extranodal, lymphatic tumor; seven with associated extranodal, extralymphatic tumor; and two with both associated extranodal, lymphatic and extranodal, extralymphatic tumor deposits (Table 1).

TABLE 1: Nodal Non-Hodgkin's Lymphoma: Summary of Cases

Case No.	Age	Gender	Nodal Stations				Bilateral	Maximum Size (cm)	Uses of CT	Primary vs Systemic	Clinical Stage
			DCC	PT	RP	SM					
Nodal sites only:											
1	80	M	+	+	−	+	+	3	None	P	II
2	60	M	+	−	−	−	+	2	None	S	III
3	50	F	+	−	−	−	−	3	None	S	III
4	59	F	+	+	−	−	+	5	None	S	III
5	66	M	+	+	−	−	−	10	XRT	P	II
6	65	M	+	+	−	−	+	3	None	P	II
7	74	M	+	+	−	−	+	8	Dx abscess	P	II
8	65	M	+	+	−	−	+	10	None	S	III
9	35	F	+	−	−	−	+	5	None	S	II
10	30	M	+	−	−	−	−	4	None	P	II
11	59	M	+	−	−	−	−	4	Dx recurrence/XRT	S	IV
12	53	M	+	+	−	−	+	10	None	S	IV
13	50	F	+	+	+	−	+	5[a]	None	P	II
Associated extranodal, lymphatic (Waldeyer's ring) involvement:											
14	51	M	+	−	−	+	+	3	None	P	II
15	68	M	+	+	−	−	−	10	None	S	III
Associated extranodal, extralymphatic involvement:											
16	70	M	+	+	−	−	−	3	Dx recurrence	S	IV
17	44	M	−	−	−	+	−	3	XRT	P	II
18	73	F	+	−	−	−	−	2	Dx recurrence	S	IV
19	27	F	+	−	−	+	+	2	XRT	P	II
20	43	M	+	+	−	+	−	3	Dx recurrence/XRT	S	IV
21	70	F	+	−	−	−	+	3	XRT	S	III
22	40	M	+	−	−	+	+	6	None	S	IV
Associated extranodal, lymphatic *and* extranodal, extralymphatic involvement:											
23	90	M	+	+	−	−	−	10	XRT	P	II
24	57	F	+	−	+	−	−	3	XRT	S	IV

Note.—DCC = deep cervical chain adenopathy; PT = posterior triangle adenopathy; RP = retropharyngeal adenopathy; SM = submandibular adenopathy; P = primary head and neck non-Hodgkin's lymphoma at presentation; S = systemic non-Hodgkin's lymphoma; XRT = CT used to plan radiation therapy; Dx = diagnosed.

[a] This one patient had necrosis within the involved lymph nodes.

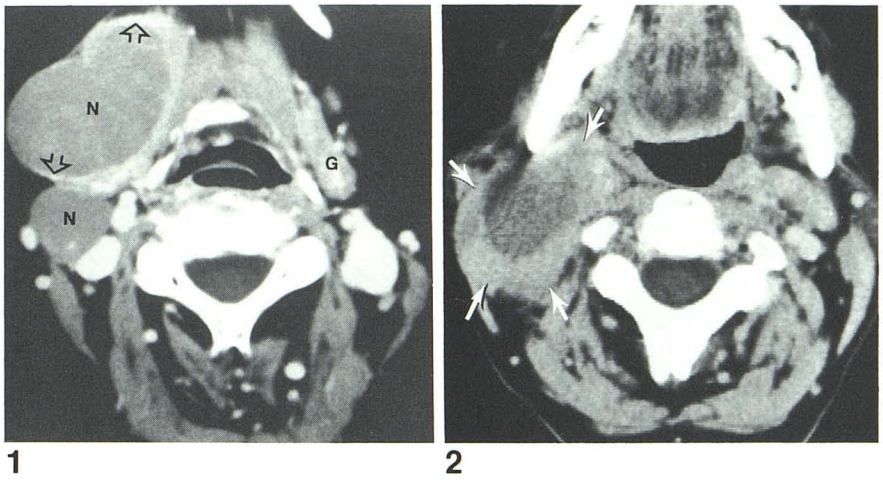

Fig. 1.—Case 22: nodal non-Hodgkin's lymphoma. Enhanced axial CT at level of hyoid bone shows two nonnecrotic nodes (N) containing non-Hodgkin's lymphoma. Anterior submandibular lymph node measures 4 cm and at first glance has appearance of central lucency. Nodal capsular enhancement (*arrows*) creates this impression with central density approximating density of surrounding normal neck muscles. G = submandibular glands.

Fig. 2.—Case 13: necrotic non-Hodgkin's lymphoma lymph node. Postcontrast axial CT scan through low oropharynx shows large, necrotic-appearing mass (*arrows*) in region of high deep cervical chain on right, which at surgery was found to be a necrotic nodal deposit of non-Hodgkin's lymphoma. This patient had been treated with steroids for 1 month before surgery. Central nodal necrosis is presumed to represent response of lymph-node deposit to steroid treatment.

CT manifestations of nodal NHL included lymph-node size of 1–10 cm, with 12 (50%) of 24 patients displaying at least one lymph node of 4 cm in maximum diameter (Fig. 1). Thirteen patients had bilateral neck lymphadenopathy. All but one patient had nodal involvement in the deep cervical chain; 12 were involved in the posterior triangle spinal accessory nodes; two, the retropharyngeal nodal chain; and six, the submandibular lymph nodes. Only one patient demonstrated evidence of necrosis within the involved lymph nodes (central low-density regions on CT) (Fig. 2). Two patients had nodal deposits that initially were thought to be necrotic but were found to have central attenuation values similar to muscle density but appeared to be necrotic because of nodal-rim (capsule) enhancement (Fig. 1).

In 12 of the 15 patients with isolated nodal NHL or nodal NHL plus extranodal, lymphatic tumor (cases 1–4, 6–8, 10, 12–15), no clinically useful data were derived from CT evaluation. In eight of the nine cases with extranodal, extralymphatic sites associated with nodal NHL (cases 16–24), CT contributed to the clinical assessment and/or treatment, either by diagnosing recurrence or by assisting radiation therapy with radiation port planning.

TABLE 2: Extranodal Lymphatic Sites (Waldeyer's Ring) in Non-Hodgkin's Lymphoma: Summary of Cases

Case No.	Age	Gender	Site(s)	Value of CT	Primary or Systemic	Clinical Stage
Associated nodal sites:						
14	51	M	LT, FT	None	P	II
15	68	M	FT	None	S	III
Associated nodal sites *and* extranodal, extralymphatic involvement:						
23	90	M	FT, A	XRT	P	II
24	57	F	A	XRT	S	IV
Extranodal, lymphatic sites only:						
25	55	F	FT	None	S	IV[a]
26	82	M	FT	None	S	IV[a]
27	77	F	FT	XRT	P	I
28	35	M	A	None	S	IV
29	70	M	FT, A	XRT	P	II

Note.—LT = lingual tonsil; FT = faucial tonsil; A = adenoids; P = primary non-Hodgkin's lymphoma at presentation; S = systemic non-Hodgkin's lymphoma; XRT = CT was used in planning radiation therapy.

[a] The gastrointestinal tract was positive on barium-enema study.

Extranodal, Lymphatic NHL/Waldeyer's-Ring NHL

Nine patients had NHL involving the lymphatic tissue of Waldeyer's ring (nasopharyngeal adenoids and oropharyngeal faucial and lingual tonsils) (Table 2). Four patients had isolated extranodal, lymphatic NHL; two had simultaneous nodal NHL; one had associated extranodal, extralymphatic NHL; and two had both associated extranodal, lymphatic and extranodal, extralymphatic NHL deposits.

The CT appearance of extranodal, lymphatic NHL was indistinguishable from the CT picture of squamous cell carcinoma in Waldeyer's ring (Fig. 3). When extranodal, lymphatic NHL was associated with nonnecrotic, large nodes in atypical drainage sites, the diagnosis of NHL was suggested; however, the diagnosis of squamous cell carcinoma could not be excluded completely because large squamous nodes, although frequently necrotic, are not always necrotic (Fig. 4). When a second tumor focus was seen in an extranodal, extralymphatic site, the diagnosis of NHL was suggested more strongly, (Fig. 5), as synchronous sites of nonmucosal squamous cell carcinoma are exceedingly rare.

The impact of CT on patient management was again found to be significant only in patients with associated extranodal, extralymphatic tumor. In only one patient with extranodal, lymphatic NHL without associated extranodal, extralymphatic tumor (case 27) did CT provide useful information to the referring clinician.

Extranodal, Extralymphatic NHL

Twenty-five cases of extranodal, extralymphatic NHL were identified, 16 as an isolated area of involvement, seven with concurrent nodal NHL, and two with both extranodal, lymphatic and nodal NHL associated (Table 3). Nine patients had sinonasal (Fig. 5), eight orbital (Fig. 6), 11 deep facial space (Fig. 7), two mandibular, three parotid (Fig. 8), four dermal (Fig. 9), and one endolaryngeal NHL. In eight patients more

Fig. 3.—Case 25: extranodal, lymphatic non-Hodgkin's lymphoma of faucial tonsil. Enhanced axial CT scan at level of mandibular body shows tissue-density mass (L) in left faucial tonsil region. CT appearance of this Waldeyer's-ring lymphoma deposit is identical to CT appearance of squamous cell carcinoma of same region.

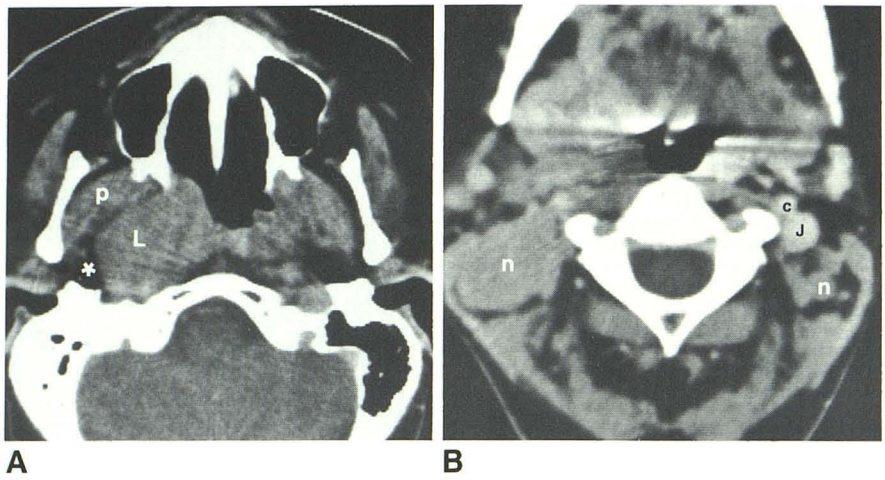

Fig. 4.—Case 15: extranodal, lymphatic, non-Hodgkin's lymphoma of nasopharyngeal adenoids.
A, Enhanced axial CT scan through nasopharynx shows large tissue-density mass (L) obscuring normal mucosal landmarks of nasopharynx and extending posterolaterally into parapharyngeal space (*asterisk*). p = lateral pterygoid muscle.
B, Associated nodal disease. Lower axial CT section shows nonnecrotic lymph nodes (n) in both posterior triangle regions. c = internal carotid artery; j = internal jugular vein. Large, nonnecrotic nodes suggest diagnosis of non-Hodgkin's lymphoma, but squamous cell carcinoma of nasopharynx with nodal metastases is indistinguishable on basis of CT findings alone.

than one extranodal, extralymphatic site was found on the same CT evaluation (Fig. 5).

CT had a significant impact on patient management in this group. In nine cases, CT alone correctly diagnosed either the primary NHL or tumor recurrence as a consequence of the fact that the tumor occurred or recurred in an area inaccessible to clinical evaluation. In 23 of the 25 patients, CT was useful in designing radiation ports.

Discussion

NHL can involve virtually any site in the extracranial head and neck [2]. Because squamous cell carcinoma is statistically a much more common lesion in this area, NHL occasionally is mistaken for squamous cell carcinoma by the radiologist, surgeon, and pathologist. Only when there is a high degree of suspicion can the patient with NHL in the head and neck

Fig. 5.—Case 36: synchronous non-Hodgkin's lymphoma extranodal, extralymphatic sites.
A, Contrast-enhanced axial CT scan through maxillary sinuses reveals lymphoma deposits (T) in both sinuses invading nasopharyngeal masticator spaces through lateral sinus walls (*arrows*).
B, More cephalad scan. Multiple other extranodal, extralymphatic sites of non-Hodgkin's lymphoma are involved including (1) lacrimal glands, (2) lateral rectus muscles, (3) temporalis muscle, and (4) epidural space.

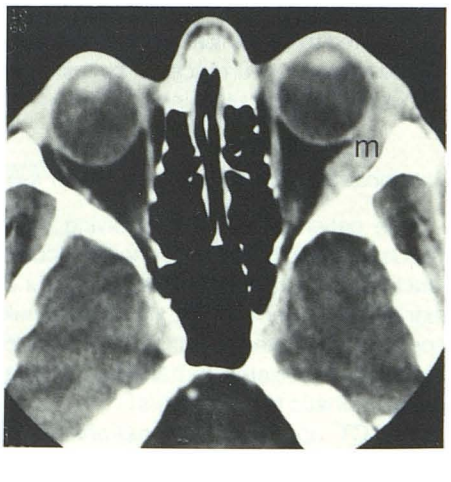

Fig. 6.—Case 42: orbital non-Hodgkin's lymphoma. Enhanced axial CT scan through orbit shows mass extending posteroinferiorly in extraconal space, molding to lateral bony wall of orbit (m). Opposite orbit is normal. More cephalad scans showed unilateral lacrimal gland enlargement. Non-Hodgkin's lymphoma is part of differential diagnosis including orbital pseudotumor, lacrimal gland primary malignancy, and orbital metastases.

TABLE 3: Extranodal, Extralymphatic Sites in Non-Hodgkin's Lymphoma: Summary of Cases

Case No.	Age	Gender	Sites	Value of CT	Primary or Secondary	Clinical Stage
Associated nodal sites:						
16	70	M	Orbit	Dx rec/XRT	S	IV
17	44	M	Sinus/nose, orbit, deep facial space, dermis	XRT	P	II
18	73	F	Dermis	Dx rec/XRT	S	IV
19	77	F	Sinus/nose	XRT	P	II
20	43	M	Parotid, dermis	Dx rec/XRT	S	IV
21	70	F	Larynx	XRT	S	III
22	40	M	Deep facial space	XRT	S	III
Associated nodal sites *and* extranodal, lymphatic involvement:						
23	90	M	Sinus/nose	XRT	P	II
24	57	F	Deep facial space	XRT	S	IV
Extranodal, extralymphatic involvement only:						
30	76	F	Sinus/nose, deep facial space, dermis	XRT/Dx rec	S	IV
31	73	M	Sinus/nose	Dx tumor	P	I
32	70	F	Mandible	XRT/Dx rec	S	IV
33	90	M	SInus/nose	XRT	P	I
34	79	F	Deep facial space	XRT	S	IV
35	64	M	Sinus/nose, orbit, deep facial space	XRT	S	IV
36	15	M	Sinus/nose, orbit, deep facial space	XRT	S	IV
37	32	M	Orbit, deep facial space	XRT	P	I
38	73	M	Deep facial space	Dx tumor/XRT	S	IV
39	55	M	Orbit	Dx rec	S	IV
40	68	F	Orbit	XRT	P	I
41	62	M	Parotid	XRT	P	I
42	63	M	Orbit	XRT	P	I
43	54	M	Deep facial space, mandible	XRT	P	II
44	71	F	Sinus/nose parotid	XRT	P	II
45	87	M	Deep facial space	Dx tumor/XRT	S	III

Note.—Dx rec = CT diagnosed recurrent tumor; XRT = CT was used in planning radiation therapy; Dx tumor = CT made the initial tumor diagnosis; P = primary head and neck lymphoma at presentation; S = systemic non-Hodgkin's lymphoma.

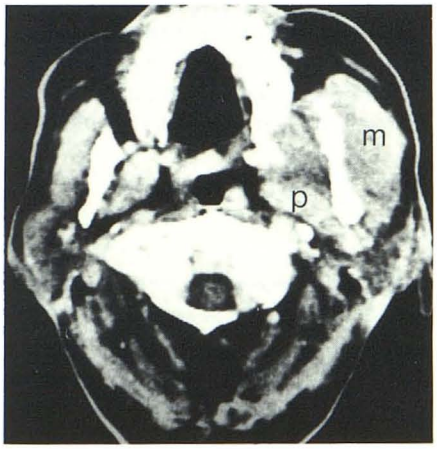

Fig. 7.—Case 43: extranodal, extralymphatic non-Hodgkin's lymphoma of nasopharyngeal masticator space. Enhanced axial CT scan through level of superior alveolar ridge shows mass in left masticator space with diffuse enlargement of masseter muscle (m) and medial pterygoid muscle (p). Minor salivary gland malignancy and deeply infiltrating squamous cell carcinoma from retromolar trigone could have similar CT appearance.

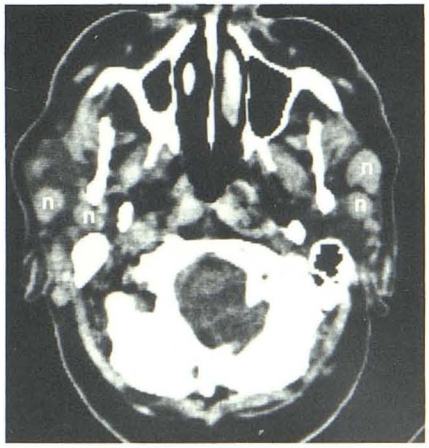

Fig. 8.—Case 20: intranodal parotid non-Hodgkin's lymphoma. Multiple tissue-density masses (n) are seen on enhanced axial CT scan through maxillary sinuses. Parotid involvement with non-Hodgkin's lymphoma is usually a manifestation of nodal lymphoma within substance of parotid gland. Parenchymal lymphoma is extremely rare.

Fig. 9.—Case 17: dermal non-Hodgkin's lymphoma. Appearance of enhancing mass in subcutaneous tissues of both temporal spaces (L) is suggestive of dermal non-Hodgkin's lymphoma. Preseptal ocular non-Hodgkin's lymphoma (o) is also present.

be correctly diagnosed, thus avoiding unnecessary radiologic and surgical procedures.

The clinical signs and CT manifestations of NHL in the extracranial head and neck are frequently diverse. The sites of NHL involvement in this area can be subdivided into three distinct categories: (1) nodal; (2) extranodal, lymphatic; and (3) extranodal, extralymphatic. Extranodal, lymphatic NHL refers to tumor found in Waldeyer's lymphatic ring. The extranodal, extralymphatic category includes all NHL not in nodes or Waldeyer's ring with the major areas of involvement including the orbit, sinus, nose, mandible, deep facial spaces, parotid gland, and dermis. Of the three major sites of involvement of NHL in the head and neck region, nodal NHL is the most common, followed by extranodal, extralymphatic and the extranodal, lymphatic sites [2].

When nodal NHL presents as an unbiopsied neck mass with no mucosal disease evident, CT is frequently requested to search for an unknown primary squamous cell carcinoma [12]. If CT shows multiple large, bilateral lymph nodes without necrosis, NHL should be suspected. An additional clue to the CT diagnosis of nodal NHL is found when some of the nodes are located in sites atypical of the usual drainage routes for squamous cell carcinoma such as the submental, submandibular, retropharyngeal, or posterior triangle nodal chains (Fig. 1). Only when the patient has been treated will nodal NHL manifest central necrosis on CT (Fig. 2). When central necrosis is present, nodal involvement by squamous cell carcinoma or other malignant metastatic disease should become the leading diagnosis.

Waldeyer's lymphatic ring is made of the nasopharyngeal adenoids and the oropharyngeal faucial and lingual tonsils. When NHL involves this extranodal, lymphatic site, it is usually indistinguishable on CT from squamous cell carcinoma (Fig. 3). Only when the tumor deposit was associated with extranodal, extralymphatic disease could the diagnosis of NHL be suggested from CT findings.

Waldeyer's-ring NHL has a known association with gastrointestinal tract NHL [13–15]. If the disease can be palpated or seen on CT—that is, if it is macroscopic in this extranodal, lymphatic site—it is usually part of systemic NHL [13]. Abdominal CT and chest radiography are used in staging this type of NHL with neck CT having limited clinical value. In patients with extranodal, lymphatic NHL and symptoms referable to the gastrointestinal tract, barium examination is indicated because of the known association of Waldeyer's-ring NHL and other gastrointestinal foci of disease.

Extranodal, extralymphatic NHL can be further subdivided into an infinite number of categories since NHL can occur in any location from the skull base to the clavicles [16]. We have chosen seven groups based on the major anatomic areas of involvement seen in our study population: (1) sinus/nose, (2) orbit, (3) deep facial spaces, (4) dermis, (5) parotid, (6) mandible, and (7) endolarynx. It is beyond the scope of this report to detail the CT manifestations of NHL in each of these areas, but salient observations regarding characteristic CT appearance will be delineated.

Extranodal, extralymphatic NHL usually mimics squamous cell carcinoma in its CT appearance. However, in our study eight of 25 cases (Table 3) had more than one synchronous extranodal, extralymphatic NHL site on CT examination (Fig. 5). These sites included the sinonasal area, orbit, deep facial spaces, dermis, mandible, and parotid. Since squamous cell carcinoma rarely presents synchronously with two separate primary tumors, this CT finding suggests the diagnosis of NHL.

Sinonasal NHL can be either expansile with permeative bony wall involvement, as suggested by Kondo et al. [17], or more infiltrating and destructive, as is commonly seen in squamous cell carcinoma [18] (Fig. 5A). Orbital NHL commonly involves the lacrimal gland and extraconal orbit and is bilateral in up to 40% of cases [19] (Figs. 5 and 6). The focal or infiltrating masses of NHL seen on CT in the deep facial spaces are indistinguishable from other malignancies in these areas (Fig. 7).

Parotid NHL is included under extranodal, extralymphatic NHL because primary parenchymal NHL of the parotid gland is extremely rare [2], and NHL involving intraparotid lymph nodes is the more common pathologic form of disease [2, 20] (Fig. 8). When NHL involves the subcutaneous tissues of the face and neck, a CT appearance results that is quite characteristic (Fig. 9). The enhancing sheets of dermal NHL seen on CT are highly suggestive of the diagnosis of NHL.

Reviewing the CT appearances in patients with NHL of the extracranial head and neck region reveals several important findings. First, nodal NHL is suggested when large, bilateral, nonnecrotic nodes are seen in atypical drainage areas. Extranodal, lymphatic deposits of NHL in Waldeyer's ring are indistinguishable from squamous cell carcinoma on CT. Extranodal, extralymphatic NHL when isolated cannot be differentiated from other head and neck malignancies, but when multifocal are highly suggestive of NHL.

The role of CT in patients with head and neck NHL is (1) quantitative assessment of known tumor, (2) identification of occult tumor sites, (3) assessment of treatment response, and (4) recurrent tumor diagnosis. Since Waldeyer's lymphatic ring can be seen and nodal disease felt, it is in the extranodal, extralymphatic group that CT plays its most important role. By providing an objective deep-tissue map of tumor, CT gives the radiation therapist the information necessary for radiation port planning [8–10].

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