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CT Evidence of Mucosal Thickening in the Maxillary Antra in Patients with Nasopharyngeal Carcinoma

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CT scans of the maxillary antra in a group of 51 patients with nasopharyngeal carcinoma were compared with those of a control group of 50 patients. Inflammatory thickening of the antral mucosa was demonstrated in 39 of 42 patients with grade WHO (World Health Organization) 2 and 3 nasopharyngeal carcinoma. Biopsy of the antral mucosa in eight of these patients established inflammation and excluded the presence of nasopharyngeal carcinoma in the antrum. In a group of nine patients with WHO 1 tumors, the antral mucosa was normal. Thickening of the antral mucosa was observed in six patients of the control group. The inflammatory thickening of the antral mucosa in the patients with WHO 2 and 3 tumors was obviously more frequent than in the control group. This combination was not found in patients with WHO 1 tumors. The phenomenon cannot be explained by direct extension of nasopharyngeal carcinoma or obstruction of the maxillary osteum. The cause of the mucosal thickening may be immunologic, but remains unclear at this stage.

The high frequency of inflammatory thickening of the antral mucosa observed in patients with WHO 2 and 3 tumors should encourage further investigation of causative factors in nasopharyngeal carcinoma.

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The division of nasopharyngeal carcinomas (NPC) into two distinct diseases was first proposed by Scanlon et al. [1], who classified the tumors as (1) keratinizing squamous cell carcinomas and combined grade 4 undifferentiated carcinomas (which are lymphoepitheliomas, anaplastic carcinomas, and transitional cell carcinomas in the old terminology). These would currently be classified as WHO (World Health Organization) 1 tumors and combined WHO 2 and 3 tumors, respectively. Even with the use of electron microscopy, this classification cannot be definitive in WHO 2 and 3 tumors. The WHO 1 carcinomas demonstrate distinct intercellular bridges and abundant keratin production. This tumor is similar microscopically to other squamous carcinomas of the upper aerodigestive tract. About 25% of the tumors fall into this category. The WHO 2 and 3 tumors have a greater pleomorphism than the keratinizing type. There may be any of several microscopic patterns, including spindle cell, transitional cell, lymphoepithelioma, clear cell, anaplastic, or a combination of these. The positive Epstein-Barr virus serologic findings in patients with WHO 2 and 3 tumors are similar to those in infectious mononucleosis and differ from the seronegative examinations in patients with WHO 1 tumors. With WHO 2 and 3 tumors, onset is at an earlier age, disease-free periods after treatment are longer, and early and advanced neck metastases are more common [1–4]. At presentation, these tumors are often small, submucosal, and difficult to detect, and may be clinically occult. They appear to be more radiation-sensitive than the WHO 1 carcinomas. Such clinical and serologic evidence supports the concept that NPC can be considered as two distinct diseases; namely, squamous cell carcinomas (WHO 1) and a combined group of nonkeratinizing and undifferentiated carcinomas (WHO 2 and 3). In addition to these differences, we have found the combination of

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NPC and thickened antral mucosa to be much more frequent in WHO 2 and 3 tumors. This mucosal thickening is inflammatory and does not reflect direct extension of NPC. We report on these findings and their clinical significance.

Materials and Methods

The study included 101 patients who were divided into three groups. A control group (group 1) consisted of 50 patients aged 10 to 70 years, in whom CT scans of the head were obtained because of symptomatology related to the orbits, sella turcica, or posterior fossa. None of those subjects had a history of headache or evidence of NPC. Group 2 included nine patients aged 59 to 78 years, with histologically proved keratinizing squamous cell carcinoma (WHO 1 tumor) of the nasopharynx. Group 3 included 42 patients aged 9 to 62 years, with combined WHO 2 and 3 tumors of the nasopharynx, proved by biopsy (Table 1).

TABLE 1: Distribution of 101 Patients Included in the Study

GROUP 1 (Controls)		GROUP 2 (WHO 1 Tumors)		GROUP 3 (WHO 2 and 3 Tumors)	
No. of Patients	Age (years)	No. of Patients	Age (years)	No. of Patients	Age (years)
50	10–70	9	59–78	42	9–62

The local extent of the tumors in patients of groups 2 and 3 was staged as T1 and T2 [5, 6]. Patients with T3 and T4 lesions were not included in this study.

CT was performed in all patients on an Elscint 2400 CT scanner. Consecutive, 5-mm-thick axial slices were taken from the alveolar process of the maxilla to the suprasellar cistern. The patients of groups 2 and 3 also had coronal CT scans with 5-mm-thick slices and 5-mm increments. The CT scans were obtained before any treatment was initiated and were read independently by two experienced radiologists.

Eight patients of group 3, who had thickened antral mucosa, underwent biopsy of the involved antrum.

Results

Six patients (15%) of group 1 had uni- or bilateral thickening of the mucosa of the maxillary antra. The remaining 44

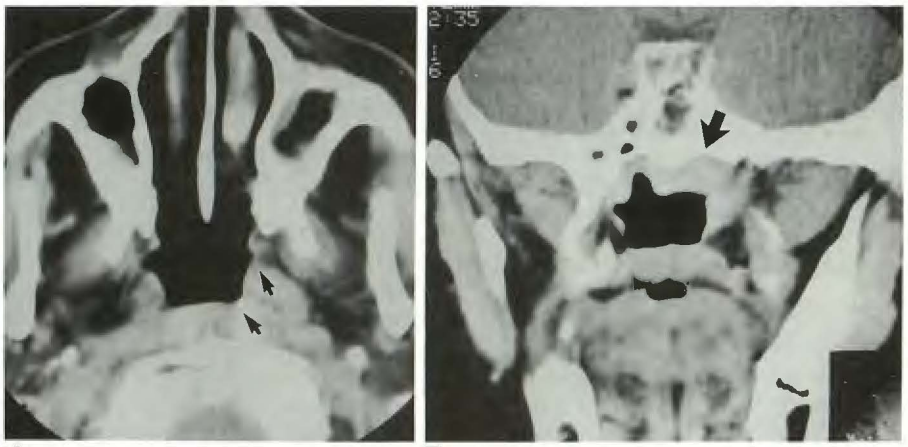

Fig. 1.—19-year-old woman with proved WHO 2–3 left nasopharyngeal carcinoma.

***A*, Axial CT shows effacement of fossa of Rosenmueller and entrance of eustachian tube on left side (*arrows*). Note mild thickening of antral mucosa.**

***B*, Coronal CT shows thickening of nasopharyngeal mucosa due to mass lesion on left side (*arrow*).**

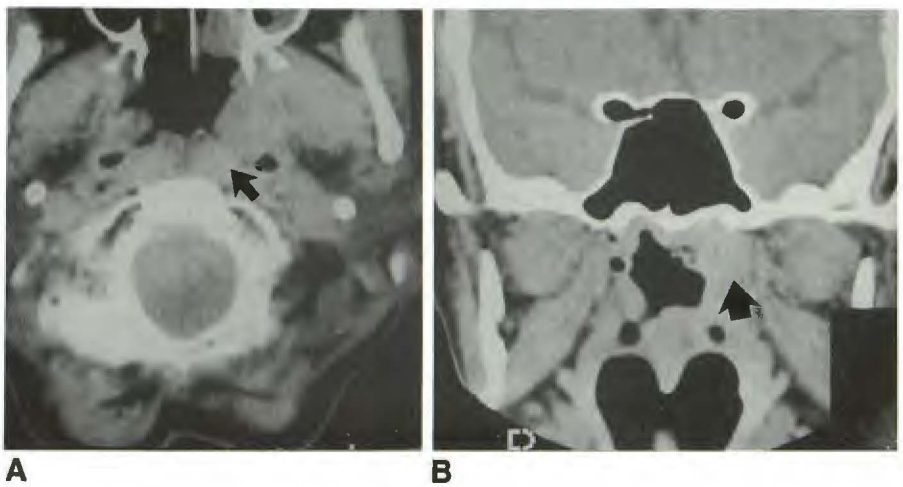

Fig. 2.—42-year-old man with WHO 2–3 left nasopharyngeal carcinoma.

***A*, Axial CT shows tumor mass of nasopharynx on left side (*arrow*). Note almost complete loss of aeration in left maxillary antrum.**

***B*, Coronal CT shows left nasopharyngeal carcinoma (*arrow*).**

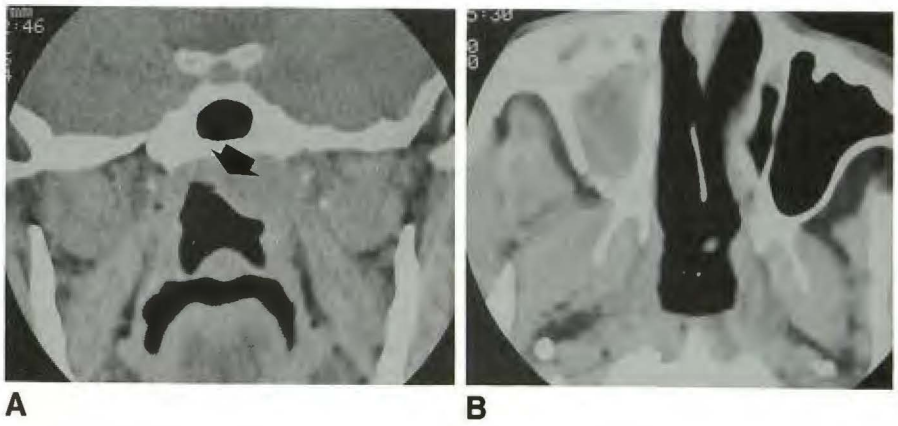

Fig. 3.—39-year-old man with WHO 2–3 bilateral nasopharyngeal carcinoma.
***A*, Coronal CT shows left nasopharyngeal mass extending beyond midline to the right (*arrow*).**
***B*, Axial CT shows thickening of right antral mucosa. Note that fossa of Rosenmueller and entrance to eustachian tube are not visible.**

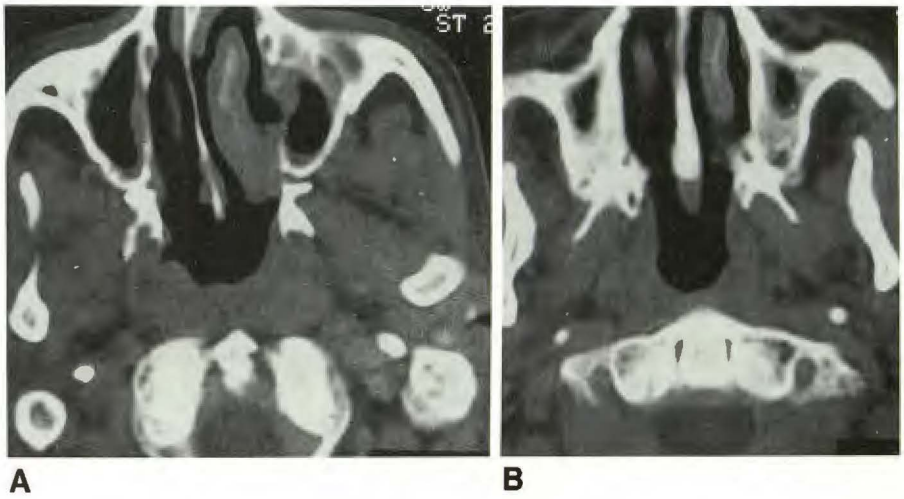

Fig. 4.—Bilateral nasopharyngeal carcinoma in 59-year-old man with WHO 2–3 tumor with bilateral thickening of antral mucosa.
***A*, Axial CT at level of foramen magnum–C1.**
***B*, Axial CT at level of C1–C2.**

TABLE 2: 39 Patients with Nasopharyngeal Carcinoma (NPC) WHO 2 and 3 Tumors with Thickening of Antral Mucosa

	Unilateral NPC	Bilateral NPC	Total
Unilateral thickening of antral mucosa	16	4	20
Bilateral thickening of antral mucosa	12	7	19
Total	28	11	39

patients of this group had normal CT scans. All nine patients of group 2 had normal antral mucosa. CT demonstrated thickening of the mucosa in one or both maxillary antra in 39 of the 42 patients in group 3. In eight of these patients biopsy of the thickened antral mucosa revealed inflammatory changes.

In 16 patients with unilateral NPC the mucosal thickening of the antrum was unilateral, ipsilateral to the NPC. The degree of thickening varied from mild to almost complete loss of antral aeration (Figs. 1 and 2). In the remaining 12 patients with unilateral NPC, bilateral antral mucosal thickening was demonstrated. Of the 11 patients with bilateral NPC, bilateral thickening of the antral mucosa was demonstrated in four patients, and unilateral thickening in seven patients (Figs. 3 and 4) (see Table 2).

Discussion

The frequency of thickening of the antral mucosa in group 3 patients with WHO 2 and 3 NPC was obviously higher than in control group patients. In 16 patients with WHO 2 and 3 tumors, the antral disease was ipsilateral to NPC. In the majority of the remaining patients of group 3, the findings were bilateral (Table 2). Biopsy of the antral mucosa in eight group 3 patients established inflammation but no tumoral involvement. The patients of group 2 with WHO 1 tumors had normal antral mucosa.

The proliferative changes of the antral mucosa in patients with WHO 2 and 3 tumors are possibly caused by an immunologic condition that is poorly understood. The difference in serologic findings in WHO 1 and WHO 2 and 3 tumors may reflect different immunologic resistance of the antral mucosa,

which is probably diminished in patients with WHO 2 and 3 tumors.

Lymphatic drainage of the maxillary antra is via the retropharyngeal nodes [7]. The possibility of obstruction of the antral lymphatics with drainage toward the nasopharynx is an unlikely explanation of our findings owing to the presence of a rich collateral net. The presence of mucosal thickening in the antrum contralateral to the tumor in some of the patients with WHO 2 and 3 tumors also does not support the possibility of lymphatic obstruction.

The percentage of WHO 2 and 3 tumors of all NPCs in our series is high and is consistent with the reports of some authors [8] and inconsistent with the reports of others [4]. Obviously, the total number of our patients is insufficient for broad statistical conclusions. However, when demonstrated, the antral disease may be an indirect risk indicator of NPC when no allergic condition exists. Since the early diagnosis of WHO 2 and 3 tumors is essential for good prognosis [4], such an early warning sign could be helpful.

We believe that our observation of the high frequency of inflammatory thickening of the antral mucosa in patients with WHO 2 and 3 tumors should encourage further investigation of causative factors in NPC.

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