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ORIGINAL ARTICLES

- Multichannel cochlear nucleus stimulation H. K. El-Kashlan 169
- Standardized format for depicting hearing preservation results in the management of acoustic neuroma J. M. Rappaport et al 176
- Role of motor unit number estimate electromyography in experimental canine laryngeal reinnervation K. L. Peterson et al 180
- Thermal myringotomy for eustachian tube dysfunction in hyperbaric oxygen therapy S. E. Potocki and D. S. Hoffman 185
- Impact of resistant pneumococcus on rates of acute mastoiditis P. J. Antonelli et al 190
- Clinical and histologic evaluation of an indwelling, inflatable, long-term laryngeal stent in the canine model A. G. C. Milo et al 195
- Benefits of routine maxillectomy and orbital reconstruction with the rectus abdominis free flap J. D. Browne and A. J. C. Burke 203
- Facial nerve function after partial superficial parotidectomy R. L. Witt 210
- Training the physician-scholar in otolaryngology-head and neck surgery J. B. Naddi, Jr, in collaboration with the Resident Education Committee of the Society of University Otolaryngologists 214
- For additional articles, see Table of Contents, p. 7A.

CASE REPORTS

285

INTERNATIONAL ARTICLES

INTERNATIONAL ORIGINAL ARTICLES

- Assessment of nasal mucosa blood supply by quantitative endoscopic imaging of the back-scattered light E. P. Prokopakis et al 307
- Does choice of hearing selection criterion and reporting criteria affect the hearing preservation rate in vestibular schwannoma surgery? M. J. da Cruz et al 313
- Relationship of human papillomavirus to ploidy in squamous cell carcinomas of the head and neck J. P. Rodrigo et al 318
- Sinonasal lymphoma G. Fajardo-Dolci et al 323

INTERNATIONAL CASE REPORTS

327

CLINICAL PHOTOGRAPHS

- Endoscopy during neurotomy of the nervus intermedius for trigeminal neuralgia N. Alcaraz et al 334
- T-cell non-Hodgkin's lymphoma of the larynx and hypopharynx M. W. Pak et al 335



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Does choice of hearing selection criterion and reporting criteria affect the hearing preservation rate in vestibular schwannoma surgery? 313
 Melville J. da Cruz, FRACS, BSc, David A. Moffat, FRCS, MSc, David M. Baguley, MSc, MBA, Graham J. Beynon, MSc, and David G. Hardy, FRCS, *Cambridge, United Kingdom*

Relationship of human papillomavirus to ploidy in squamous cell carcinomas of the head and neck 318
 Juan Pablo Rodrigo, MD, Ignacio Alvarez, MD, José Antonio Martínez, MD, Pedro Sánchez Lazo, PhD, Sofía Ramos, PhD, and Carlos Suárez, MD, *León and Oviedo, Spain*

Sinonasal lymphoma 323
 German Fajardo-Dolci, MD, Rogelio Chavolla Magaña, MD, Enrique Lamadrid Bautista, MD, and Daniel Huerta, MD, *Mexico City, Mexico*

INTERNATIONAL CASE REPORTS

Temporal bone chondroblastoma 327
 Noritake Watanabe, MD, Kazuhide Yoshida, MD, Hideo Shigemí, MD, Yuichi Kurono, MD, and Goro Mogi, MD, *Oita, Japan*

Benign fibrous histiocytoma of the floor of the mouth 330
 Ki Hwan Hong, MD, Young Ki Kim, MD, and Jong Kwon Park, MD, *Chonju, Chonbuk, South Korea*

CLINICAL PHOTOGRAPHS

Endoscopy during neurotomy of the nervus intermedius for geniculate neuralgia 334
 Nelson Alcaraz, MD, Wesley A. King, MD, and Phillip A. Wackym, MD, FACS, *New York, New York*

T-cell non-Hodgkin's lymphoma of the larynx and hypopharynx 335
 Martin Wai Pak, FRCS(Edin), John Kong Sang Woo, FRCS(Edin), and Charles Andrew van Hasselt, MMed(Otol), *Shatin, Hong Kong*

READER SERVICES

News and Announcements 184, 189, 202, 209, 223, 251, 268, 273, 282, 317, 322

Change of Address 326

Instructions for Authors 19A

Information for Readers 34A

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Sinonasal lymphoma

GERMAN FAJARDO-DOLCI, MD, ROGELIO CHAVOLLA MAGAÑA, MD, ENRIQUE LAMADRID BAUTISTA, MD, and DANIEL HUERTA, MD, Mexico City, Mexico

The clinical course of 49 patients with the diagnosis of non-Hodgkin's lymphoma were studied in the Department of Otolaryngology of the Hospital General de Mexico between December 1986 and March 1997. The most frequent clinical symptoms in these patients were: nasal obstruction, rhinorrhea, fever, weight loss, cervical lymph adenopathy, rhinopharyngeal tumor, ulceration on the palate and periorbital cellulitis. In 73% of the patients in this series the primary presentation was nasal. Sixty-six percent of the patients were classified as intermediate grade lymphoma according to the New Working Formulation, and 33% were in a I B state according to the Ann Arbor predominant immunotype was B cell in 63% of the cases. An extensive review of the literature is also presented. (Otolaryngol Head Neck Surg 1999;121:323-6.)

Lymphomas are a group of malignant neoplasms of lymphoreticular origin that are divided into 2 groups: (1) Hodgkin's disease and (2) non-Hodgkin's lymphomas (NHLs). Hodgkin's disease develops in lymph nodes and then disseminates to neighboring organs by contiguity, whereas NHL may be present in lymph nodes, but also in other areas in 25% to 40% of cases, which can make the determination of the primary site impossible.¹

Differences such as cells of origin, age distribution, clinical manifestations, grade at the time of diagnosis, complications, and responsiveness to treatment also exist. These entities do not constitute a unique clinical pathology but are part of a wide spectrum ranging from Burkitt's lymphoma in African children to diffuse and nodular lymphoma in adults.

When NHL is suspected, the differential diagnosis must include several pathologic entities such as

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Wegener's disease and other causes of adenopathies such as mononucleosis, sarcoidosis, tuberculosis, and other malignant diseases of the nose and paranasal sinuses.²

The NHLs are a group of pathologic entities originating from malignant lymphatic cells at different stages of maturation.³ NHL has been given many names in the literature, such as monoclonal B cell neoplasia, lethal granuloma, polymorphic reticulosis, and pseudolymphoma among others. According to a recent publication by Cleary and Batsakis,⁴ the correct name is exclusively *sinonasal lymphoma*, replacing all of the other names previously applied to this disease. A standardization of the nomenclature should help increase understanding of this disease entity.

It is estimated that NHLs make up almost 1.5% of the total neoplasms detected each year.⁵ The complexity of NHL reflects the complexity of the immune system. The incidence of NHL has increased by 150% since 1950 and continues to increase at a rate of 3% to 4% a year.⁶

The tonsils are the most common site of presentation in the United States and Europe, followed by Waldeyer's ring, rhinopharynx, maxillary sinus, and larynx. In some Asian countries and in Mexico the most common primary location is the nose.^{7,8}

The complications of NHL, following the natural history of the disease, may be caused by the gradual and progressive growth of lymph nodes, damage to various organs, and hematologic and immune abnormalities. Some other complications also may be the result of different treatment approaches. The enlargement of the lymph nodes produces compression of neighboring organs. Arteries, veins, the airway, the esophagus, and the gastrointestinal and urinary tracts may be affected. It may be found to extend to the central nervous system—affecting the cranial nerves, brain, and spina medulla—and may even produce meningitis.⁹

A few areas of pathology have awakened much controversy and confusion about its classification as NHL. The diagnosis can be established only by biopsy. Aspiration of the affected lymph nodes may suggest the diagnosis but does not always supply enough information for classification.

Historically there exist 2 staging systems: Rappaport's and Lukes-Collins'. They use different criteria and terminology. In 1982 the New Working Formulation clas-

Table 1. New Working Formulation classification

Low-grade tumors
Small lymphatic
Follicular small cleaved
Follicular mixed small and large cell
Intermediate grade tumors
Follicular large cell
Diffuse large cell
Diffuse small cleaved cell
Diffuse mixed small and large cell
High-grade tumors
Large-cell immunoblastic
Lymphoblastic
Diffuse small noncleaved

Table 2. Ann Arbor staging system

Stages
1. Involvement of a single lymph node region or a single extralymphatic organ or site
2. Involvement of 2 or more lymph node regions on the same side of the diaphragm or localized involvement of an extralymphatic organ or site and 1 or more lymph node regions on the same side of the diaphragm
3. Involvement of lymph node regions on both sides of the diaphragm
4. Diffuse or disseminated involvement of 1 or more extralymphatic organs or tissues with or without lymph node enlargement
Symptoms
A. Absence of symptoms
B. Unexplained fever, night sweats, or weight loss

sification was created, and it divides NHL into 3 categories: low, intermediate, and high malignancy (Table 1).^{2,10} The Ann Arbor classification is used to determine the clinical stage and prognosis factor (Table 2).⁶ Today we have a new classification proposed by the international lymphoma study group that is very complete and complicated, and it involves immunohistochemical criteria, cells of origin, and histopathologic aspects.¹¹ Ninety percent of the cases of NHL are classified as high or intermediate grade of malignancy. B cells were found to predominate.

Some reports suggest a relationship between NHL and Epstein-Barr virus. In more recent years a clear relationship has been established between AIDS and T-cell lymphomas.¹² Identification of surface antigens characterizing lymphocytes, known as immunophenotyping, and techniques of cytogenetic and molecular genetic analysis are superseding the morphologic classifications of NHL. Many of these arise because of the chromosomal abnormalities, particularly translocations, occurring while specific immunoglobulins and T-cell receptors are being assembled. When the enhancer and

promoter regions of these antigen receptor genes are brought together with oncogenes by translocation, the normally tightly regulated are inappropriately expressed. The cell is transformed and, instead of dying, undergoes clonal expansion, which results in malignant disease. The treatment of NHL has changed in recent years. It is now based on the biologic behavior according to its classification and includes chemotherapy and radiotherapy.

The objective of this study was to determine the principal clinical presentation of NHL and the histopathological types.

METHODS AND MATERIAL

Nasal lymphoma is defined as the presence of obvious nasal lesions or nasal symptoms on presentation that are proved histologically to be lymphoma. This retrospective study includes 49 patients of both sexes in whom NHL has been diagnosed, who were in the Department of Otolaryngology of the Hospital General de Mexico from December 1986 to November 1997. The diagnosis in all cases was made by biopsy, electron microscopy, and immunohistochemistry. Other studies included a paranasal sinus CT scan, abdominal ultrasound, chest radiograph, full blood count, blood chemistry, lactic dehydrogenase, alkaline phosphate, and bone marrow aspiration.

In the last 16 patients we searched for Epstein-Barr virus and HIV. All cases were staged according to the Ann Arbor system, and the pathologic material was reviewed and classified according to the New Working Formulation. After the diagnosis was established, the patients were referred to the Department of Hematology for treatment.

RESULTS

We studied 49 patients with the diagnosis of NHL. Patients ranged in age from 13 to 67 years (median 33.6 years). Twenty-three patients were male, and 26 were female. Progression of the disease from onset of symptoms until presentation to the Department of Otolaryngology ranged from 3 to 24 months (median 10.5 months).

On average 2.3 biopsy specimens were necessary to establish the diagnosis for each patient. The most frequent primary clinical presentation of the NHL was nasal obstruction in 73% of cases, followed by anterior rhinorrhea and nasal discharge and hyperthermia in 68% (Fig 1). Presenting symptoms included weight loss, rhinopharyngeal tumor, halitosis, nasal pain, mass in Waldeyer's ring, rhinolalia, dysphagia-odynophagia, lymph adenopathy, perforation of the septum, ulceration of the palate, hepatosplenomegaly, and orbital involvement manifested as ocular pain, exophthalmos, edema, and periorbital cellulitis. Two of the patients had

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bone marrow involvement. Three cases presented initially as acute ethmoiditis with cellulitis and periorbital edema, and 1 case required surgical drainage of the involved sinuses.

The laboratory findings were normocytic normochromic anemia in 73% of the cases, followed by elevation of the lactic dehydrogenase and alkaline phosphate levels in 26%. The most frequent findings on CT scan were tumor in the nose, pharynx, palate, and paranasal sinuses (most frequently the left maxillary sinus), with bone erosion and in 3 cases orbital involvement. Six patients were found to have hepatosplenomegaly. Four patients were also diagnosed with AIDS.

According to the New Working Formulation, histology revealed 66% of the cases had intermediate-grade malignancy, 26.6% had high-grade malignancy, and 6.6% had low-grade malignancy. In the Ann Arbor classification 33% were found to be IB stage, 13% IIA, 26% IIIB, and 26.6% IVB. The most frequent immunophenotype was NHL of B cells (66%); 14% had no B or T cells, 8% had T cells, and 12% could not be staged.

Treatment included chemotherapy (cyclophosphamide, Adriamycin, Oncovin, vincristine, bleomycin, and prednisone) in 73%, chemotherapy-radiotherapy in 19%, and radiotherapy alone in 8%, depending on the stage. Twenty-eight percent of the patients have died, 60% are still living, and 12% have been lost to follow-up.

DISCUSSION

The occurrence of NHL in otolaryngology is unusual, and it is often difficult to establish whether the NHL is localized in the head and neck or whether there is systemic involvement.^{7,13} In our study only 12.2% of the patients had hepatosplenomegaly, so in 87.7% the initial presentation was in the head and neck. The age of presentation in our study (33.6 years) was younger than that in other studies (the fifth decade).^{1,14}

The nasal region is an uncommon site for extranodal lymphoma. Although the nasal cavity and surrounding paranasal sinuses are anatomically adjacent to Waldeyer's ring, nasal lymphomas appear to be pathologically and clinically different. We can establish that in our country the most frequent clinical presentation is nasal obstruction followed by anterior rhinorrhea and nasal discharge. Several reports indicate that the most frequent presentation is dysphagia-odynophagia (68%).¹⁻³ We found this symptom in only 26%. Liang⁸ in China also found that the nose is affected primarily.

In this study 53% of the patients had halitosis and nasal pain, with a low percentage of septal perforation, clinical findings that we could not find in the literature.

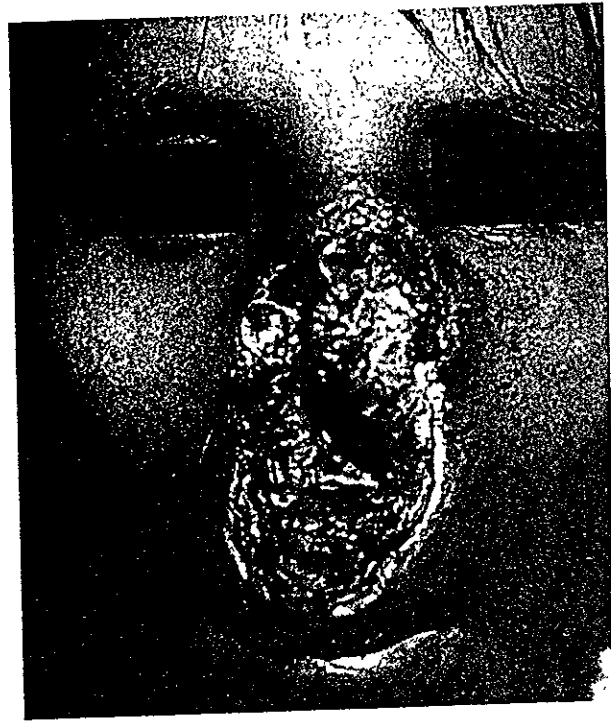


Fig 1. Patient with sinonasal lymphoma.

A very important sign is the presence of tumor, ulcerations, or perforation of the palate, clinical findings that are rarely seen in our specialty even with other head and neck malignancies. In our work we did not find involvement of the central nervous system, which has been reported by others.¹⁵

The average of development of this pathology is almost a year (10.6 months) before the diagnosis is suspected, despite presentation to other physicians. According to the classifications our results are in agreement with those of other studies.¹⁶

CONCLUSIONS

The primary clinical presentation is in the nose, and involvement of the palate and nose is frequent. The initial symptoms are nonspecific and are more frequently found in benign nasal diseases. The histopathologic diagnosis may be difficult.

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DISCUSSION

The occurrence of NHL in otolaryngology is unusual, and it is often difficult to establish whether the NHL is localized in the head and neck or whether there is systemic involvement.^{7,13} In our study only 12.2% of the patients had hepatosplenomegaly, so in 87.7% the initial presentation was in the head and neck. The age of presentation in our study (33.6 years) was younger than that in other studies (the fifth decade).^{1,14}

The nasal region is an uncommon site for extranodal lymphoma. Although the nasal cavity and surrounding paranasal sinuses are anatomically adjacent to Waldeyer's ring, nasal lymphomas appear to be pathologically and clinically different. We can establish that in our country the most frequent clinical presentation is nasal obstruction followed by anterior rhinorrhea and nasal discharge. Several reports indicate that the most frequent presentation is dysphagia-odynophagia (68%).¹⁻³ We found this symptom in only 26%. Liang⁸ in China also found that the nose is affected primarily.

In this study 53% of the patients had halitosis and nasal pain, with a low percentage of septal perforation. clinical findings that we could not find in the literature.

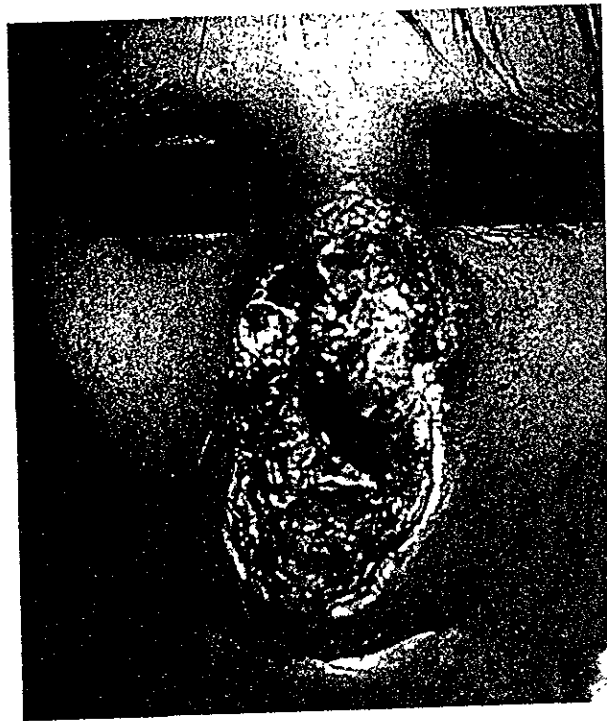


Fig 1. Patient with sinonasal lymphoma.

A very important sign is the presence of tumor, ulcerations, or perforation of the palate, clinical findings that are rarely seen in our specialty even with other head and neck malignancies. In our work we did not find involvement of the central nervous system, which has been reported by others.¹⁵

The average of development of this pathology is almost a year (10.6 months) before the diagnosis is suspected, despite presentation to other physicians. According to the classifications our results are in agreement with those of other studies.¹⁶

CONCLUSIONS

The primary clinical presentation is in the nose, and involvement of the palate and nose is frequent. The initial symptoms are nonspecific and are more frequently found in benign nasal diseases. The histopathologic diagnosis may be difficult.

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The laboratory findings were normocytic normochromic anemia in 73% of the cases, followed by elevation of the lactic dehydrogenase and alkaline phosphate levels in 26%. The most frequent findings on CT scan were tumor in the nose, pharynx, palate, and paranasal sinuses (most frequently the left maxillary sinus), with bone erosion and in 3 cases orbital involvement. Six patients were found to have hepatosplenomegaly. Four patients were also diagnosed with AIDS.

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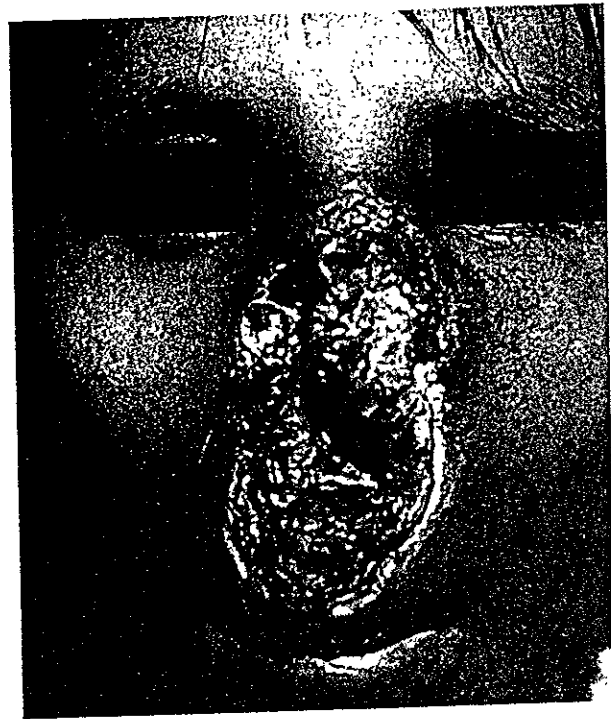


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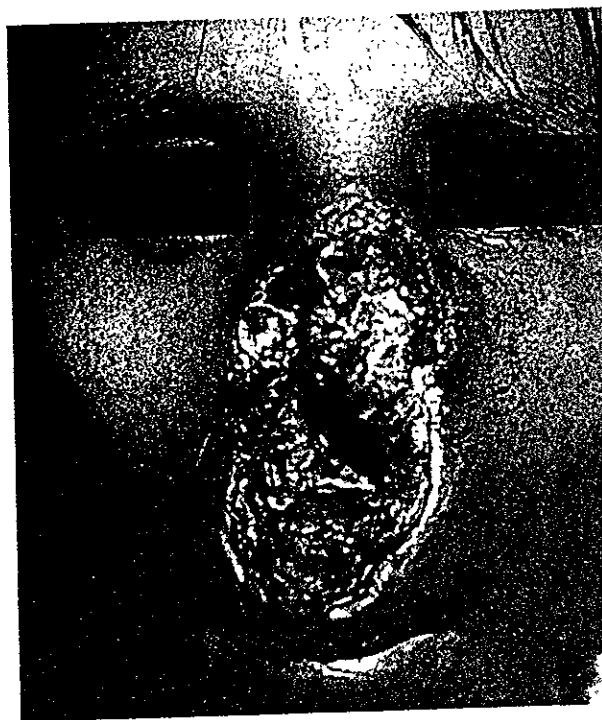


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