NEOPLASMS, MALIGNANT


Retinoids play an essential role in cell differentiation and proliferation. The use of one of its active metabolites, atRA, has been limited clinically because the oral administration causes "acute retinoid resistance." The plasma level cannot be maintained because of the activation of cytochrome P-450 in the liver. To circumvent this difficulty, the authors have developed a different delivery system. Microspheres have been designed to slowly release the atRA and maintain a constant concentration in the plasma. These PDLLA/PLE microspheres loaded with atRA are injected subcutaneously. In one experiment, mice were injected with either atRA-loaded (n = 7) or atRA-unloaded (n = 7) microspheres. These animals were used to measure plasma concentration over time. This study showed that atRA was undetectable in the unloaded-microspheres mice and was maintained in the 1.2 to 3.7 x 10^-5 in the loaded microspheres group. In a parallel experiment, a human squamous cell carcinoma (SCC) cell line was implanted in 38 nude mice; 20 were then injected with atRA-unloaded (control) and 18 with the atRA-loaded microspheres. Tumor growth was compared between the groups. The main tumor volume was reduced in the atRA-treated animals by 51.3% (p < .01) at 14 days, and by 49.2% (p < .05) at 28 days. These authors have elegantly shown that this technique delivers an almost constant plasma concentration of atRA, which has resulted in a significant volume reduction of human SCC in a xenograft model.

Pierre Lavertu, MD


Chondrosarcomas of the larynx are rarely encountered by head and neck oncologists. They are considered relatively low-grade and have a relatively benign clinical course. The authors of this study reviewed their personal experience with eight patients who had chondrosarcomas of the cricoid. All eight patients underwent hemicricoidectomy in a manner previously described by these authors. Four patients had recurrences; two patients required total laryngectomies and two required endoscopic carbon dioxide laser excisions. Six patients were alive without recurrence at the time of the publication, one patient was alive with recurrence, and one patient was dead of unrelated causes. Six patients were decannulated following tracheotomy. The authors present a succinct technical approach with excellent results for treatment of this relatively rare disease. Excellent postoperative functional speech, airway preservation, and swallowing were obtained.

Mark K. Wax, MD

NEOPLASMS, BENIGN


Preoperative intravenous injection of technetium 99m-sestamibi and intraoperative use of a hand-held gamma probe is a technique used by some surgeons to facilitate localization of hyperfunctioning parathyroid tissue. This approach, which is referred to as radioguided parathyroidectomy, has been shown to be technically feasible in patients with hyperparathyroidism due to parathyroid adenomas. The authors of this study describe their experience with the use of radioguided parathyroidectomy in 102 patients.
who underwent neck exploration for treatment of primary \( (n = 77) \) and secondary/tertiary \( (n = 25) \) hyperparathyroidism. Twenty-five patients had had a previous neck exploration.

The authors report that in 59 cases a single adenoma was removed. Although the number of patients with multiglandular disease was not stated in the paper, it can be deduced that 18 of the patients with primary hyperparathyroidism had multiglandular disease. Of the possible 72 parathyroid glands in the patients with multiglandular disease, 29 glands were removed and were referred to as “double/triple adenomas.” The authors do not comment as to whether any of the other 43 parathyroid glands in the patients with multiglandular disease were identified. In the hyperplasia group, 92 were accounted for. It is not clear how many of these parathyroid glands were from patients with primary hyperparathyroidism and how many had secondary/tertiary hyperparathyroidism. It is not clear how many parathyroid glands in the double/triple adenoma and the hyperplasia groups were not found.

The authors defined surgical cure as a serum calcium level <10.5 at 6 months after surgery. They state that 96% of their patients were cured of hyperparathyroidism.

The authors report that all of the 180 enlarged parathyroid glands that they removed had “higher in vivo counts than background.” The authors report that, of the 180 enlarged, hyperfunctioning parathyroid glands that they removed, 58 of the 59 adenomas, all 29 of the double/triple adenomas, and all 92 of the hyperplastic parathyroid glands had ex vivo radionuclide counts of >20% of background. The authors note that although most studies report that single adenomas almost always have ex vivo counts of greater than 20%, theirs is the first to describe ex vivo counts of greater than 20% in hyperplastic glands. They note that several other series show lower ex vivo counts for hyperplastic glands.

The authors reported that in their hands radioguided surgery facilitated intraoperative localization of both adenomatous and hyperplastic parathyroid glands, including 22 ectopic glands. The incidence of ectopic glands in this series is unusually high (as best as I can tell, only three of the patients with ectopic glands had previous unsuccessful surgery). The authors also report that they relied on ex vivo counts of greater than 20% of background for confirmation of parathyroid tissue obviating the need for intraoperative frozen section. They conclude that in patients with hyperparathyroidism, radioguided surgery is a sensitive adjunct for the intraoperative localization of both adenomatous and hyperplastic parathyroid glands.

William I. Kuhel, MD

VOICE AND SWALLOWING


The purpose of this research was to assess the voice characteristics and speech of patients who had undergone total laryngectomy and compare them with those of patients who had undergone organ-preservation laser surgical partial laryngectomy. Two voice assessment procedures and a speech intelligibility test were conducted on 29 patients with advanced-stage laryngeal cancer; 18 had total laryngectomy surgery and used tracheoesophageal speech with the Gronningen voice prosthesis, and 11 had partial transoral laser organ preservation surgery.

Speech intelligibility of the 29 patients was assessed with a standardized telephone test used previously by Hilgers and others. Voice characteristics were assessed by the computerized Kay multidimensional voice profile (MDVP) and by the Gottingen hoarseness diagram, a computerized voice-analysis system developed for severely dysphonic voices.

With regard to the speech intelligibility tests, the results indicated that the 11 subjects who had undergone partial laser resection with organ preservation had significantly higher speech intelligibility scores than the patients who had undergone a total laryngectomy. The voice characteristics of both groups were too irregular to obtain reliable acoustic measures using the Kay multidimensional voice profile. The Gottingen hoarseness diagram was able to reliably identify the voice characteristics of both groups. There were significantly more regular voice characteristics seen in the transoral laser surgery group than in the total laryngectomy with voice prosthesis group. The results of the voice analysis using the Gottingen hoarseness diagram were significantly related to the speech intelligibility scores obtained from the telephone speech intelligibility test in both groups of subjects. The results of this study suggest that the Gottingen voice diagram is suitable for analysis of severely irregular voices. In addition, the results suggest that laser organ-preservation surgery for advanced-stage laryngeal cancer results in higher speech intelligibility than that seen in patients who have undergone total laryngectomy and use prosthetic-aided speech.

Thomas Murry, PhD

MEDICAL ONCOLOGY


This intergroup study evaluated the benefit of adding chemotherapy to radiation in patients with unresect-
able squamous cell cancers of the head and neck. Patients were assigned to one of three arms: standard radiation, identical radiation with concurrent cisplatin on days 1, 22, and 43, and a split course of radiation and three cycles of concurrent infusional fluorouracil and cisplatin with radiation. Only 295 patients were entered on this trial, although the accrual goal was 362; for that reason, the study was closed prematurely. Nevertheless, it appeared that there was an advantage to the addition of concurrent high dose single-agent cisplatin to conventional fractionated radiotherapy. Three-year projected overall survival rates improved from 23% to 37% with this approach. The third arm of split course radiation with multiagent chemotherapy did not appear to offer any clear advantage. Toxicity was greater in both combined-modality arms compared with the radiation therapy alone approach.

This study appears to confirm the widely held opinion that high-dose cisplatin given concurrently with standard radiotherapy is beneficial despite the increased toxicity associated with such treatment.

Martin W. Oster, MD

RADIOLOGIC SCIENCES


Tumor attack by macrophages and cytotoxic T lymphocytes is mediated by the interaction of leukocyte function-associated antigen (LFA)-1 on lymphocytes with intercellular adhesion molecule (ICAM)-1 on the tumor surface. The authors postulated that reduced expression of ICAM-1 on tumor by cells could result in less infiltration of the tumor by cytotoxic T lymphocytes and macrophages and thus a lower likelihood of tumor destruction by the immune system.

An immunohistochemical study of ICAM-1, T/natural-killer (NK) cells, and macrophages was performed on the paraffin sections from 42 patients with adenoid cystic carcinoma of the head and neck.

ICAM-1 expression was not associated with age, sex, T classification, N classification, overall stage, histologic pattern, or locoregional recurrence. Low ICAM-1 expression was associated with less tumor infiltration by cytotoxic T lymphocytes, NK cells, and macrophages, a higher incidence of distant metastases, and a lower disease-free survival.

The authors concluded that reduced ICAM-1 expression might promote immune evasion and metastases, thus resulting in a poor outcome.

William M. Mendenhall, MD

MISCELLANEOUS


Oropharyngeal candidiasis is commonly found in patients receiving radiotherapy for head and neck tumors. When pathologic, it can lead to marked symptomatology and be quite debilitating for patients. Although most isolated candida species are *albicans*, non-albicans species are becoming more and more prevalent.

The authors of this study reviewed 37 patients who were receiving external beam radiotherapy for a variety of head and neck cancers. The authors used a variety of techniques, particularly a new culture medium to identify multiple candida species. Ten patients (27%) developed oropharyngeal candidiasis based on symptomatology. Twenty-six (70%) displayed the Candida carrier state. There was no difference in the mean dose of external beam radiotherapy at the time of positive culture.

Six patients received concomitant chemotherapy with their external beam radiation, and four (66%) of these developed oropharyngeal candidiasis.

Three patients (8%) were infected with non–albicans candida. All infections resolved with fluconazole. In the non-albicans group, a higher dose was required.

Oropharyngeal candidiasis can increase the morbidity associated with radiation-induced mucositis. The authors of the study demonstrate a high incidence of the presence of candida, even in those patients who are asymptomatic. The relevance of non-albicans species has yet to be determined.

Mark K. Wax, MD