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Management of the Neck in Salivary Gland Carcinoma

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Major salivary gland malignancies are rare tumors, representing between 1% and 3% of head and neck cancers and 0.3% of all cancers [1]. This incidence, in conjunction with the variety of histologic types and grades, makes a consensus on the treatment of salivary gland cancers particularly challenging. It is difficult for any single institution to accrue a significant number of patients prospectively in less than a decade. It is also difficult to predict prognosis because of the tendency of these tumors for delayed recurrence. Therefore, there is no single accepted approach to the management of the neck, particularly the N0 neck, in patients with major salivary gland malignancies.

Treatment of the primary tumor

The treatment of the primary in salivary gland tumors is well accepted and includes, when possible, resection of the primary tumor. As with any cancer resection, the goal is to resect all clinical disease with a curative attempt. This primary resection frequently includes the paraparotid and periparotid lymph nodes, which can provide an important prognostic tool. Postoperative radiation to the primary bed has been proven to be beneficial for tumors with aggressive histology, large size, or facial nerve involvement. Leverstein et al [2] found that among patients with tumors dissected off the facial nerve, postoperative radiation significantly decreased locoregional 5- and 10-year recurrence rates.

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Treatment of the neck

The treatment of the neck presents more of a challenge. Although the reported incidence of clinical cervical metastasis is only 16% for parotid gland and 8% for the other major salivary gland malignancies [3], nodal disease has a significant effect on prognosis. Most reports show poorer outcomes in patients with clinical cervical disease than in those without cervical disease. Battacharyya et al [4] demonstrated a 50% decrease in mean survival in patients with neck disease versus those without disease. Shah [5] and Kelley and Spiro [6] corroborate a similar significant decrease in 5-year survival in both parotid and submandibular gland malignancy. The current most widely accepted treatment of the neck in salivary gland malignancy is summarized in Fig. 1.

The N-positive neck

The approach to clinically positive nodal disease is well accepted and well standardized. Therapeutic neck dissection is the accepted treatment for patients with clinically obvious cervical nodal involvement. The extent of the neck dissection is determined by the grossly involved lymph nodes, and an attempt should be made to spare vital structures. The most common levels of the neck involved are levels II and III [3]. Because contralateral neck involvement is rare, only the ipsilateral neck is usually treated. Many studies have shown that there is improved locoregional control and increased survival with the addition of postoperative radiation. Armstrong et al [7] evaluated patients with salivary malignancy and surgical treatment of clinical neck disease and found a 5-year local control rate of 69% in those

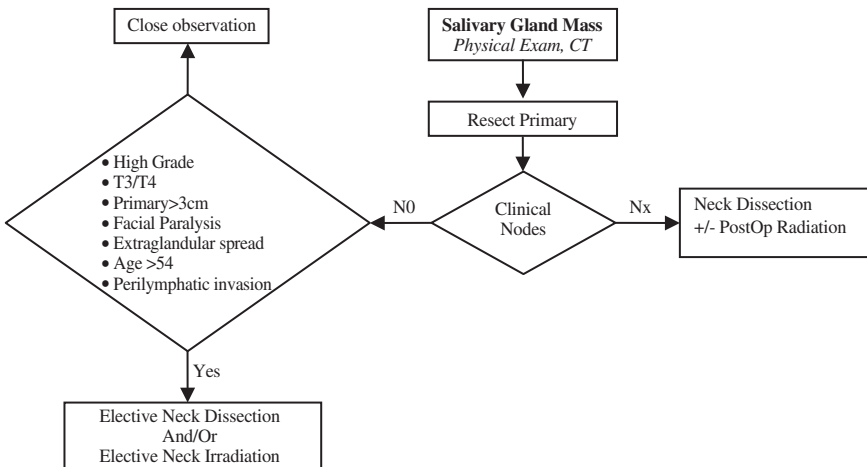


Fig. 1. Summary of treatment of neck in major salivary gland malignancy.

who received postsurgical radiation versus a 40% control rate in those treated with surgery alone. Similarly 5-year survival rates were higher in the group treated with surgery and radiation group (49%) than in the group treated with surgery alone (19%). Therefore, most institutions favor postoperative radiation therapy in patients with clinical neck disease in an attempt to treat any additional occult disease that may exist after dissection.

The N0 neck

Treatment of the clinically negative neck has been more controversial. The treatment of the N0 neck in major salivary gland malignancies has included observation, elective neck dissection, and primary radiation. Currently, there are differing recommendations in the literature as the best treatment. The reason for treating at all is the hope of eradicating any micrometastatic, occult disease. Because elective neck dissection and radiation therapy seem to have equivalent outcomes, the choice is based on the features of the primary tumor or on patient or clinician preference. Thus, in general, treatment of the N0 neck is appropriate when the risk for occult metastasis is high.

Predictive factors

The reported incidence of occult lymph node metastasis varies from 12% to 48% [6]. A number of studies have looked at possible predictive factors for the presence of occult metastatic neck disease. The strongest predictors of occult disease have been histology, pathologic grade, stage, and size of the primary lesion [6]. Pain and involvement of the facial nerve have also been found to be predictors of occult metastasis [4,6]. Weaker associations have been shown with age greater than 54 years at diagnosis, extraglandular involvement, and lymphatic invasion [6].

Intuitively, the histology of the primary salivary gland malignancy should be an important factor in the risk of occult metastasis. In fact, during the past decades several studies have shown that certain tumor pathologies carry a powerful significant trend in the risk of occult nodal involvement, and others do not. The incidence is found to be higher in anaplastic, high-grade mucoepidermoid, squamous cell, adenocarcinoma, and salivary duct carcinoma than in low-grade mucoepidermoid and acinic cell carcinoma (Table 1) [1,3,4,8]. In general high-grade tumors are more frequently associated with occult metastasis than are low-grade tumors. One recent study differs slightly from the others. Stenert et al [8] reported higher-than-expected occult nodal disease in the accepted low-risk pathologies. The incidence was still significantly less than for the high-grade tumors but was greater than seen in other reports. The significance if this finding is unclear, because the reported survival in this study is the same as that of the rest of the literature.

Table 1
Risk of occult disease based on histology of primary tumor

High risk	Low risk
Squamous cell carcinoma	Adenoid cystic
Adenocarcinoma	Acinic cell
High-grade Mucoepidermoid	Low-grade mucoepidermoid
Undifferentiated malignant mixed salivary duct carcinoma	Sarcoma
Expleomorphic adenoma	

An increased risk of occult disease is also associated with advanced-stage disease. Armstrong et al [3] found that among patients with N0 necks, T4 lesions had a 24% risk of occult cervical disease, versus 16% for T3 lesions and 7% for T1/T2 lesions. They also showed an independent increased risk for primary tumors larger than 3 cm (20%) versus those smaller than 3 cm (4%).

Facial nerve paralysis has long been recognized as a prognostic factor in local recurrence, and recent studies have also shown an association with an increased risk of regional disease. Frankenthaler et al [9] showed that occult nodal metastases were more common in the presence of facial nerve paralysis (80%) than in the absence of facial nerve involvement (19%). Similarly, Califano et al [10] observed facial paralysis in 69% of patients with nodal metastasis but in only 21% of patients without nodal metastasis.

N0 treatment

The treatment of the N0 neck in major salivary gland malignancies has included observation, elective neck dissection, and primary radiation. Some of these recommendations have been based on the data obtained from the statistics and treatment of squamous cell carcinoma of the head and neck. Care must be exercised in using these data, because there is no proof in the literature that malignancy of the major salivary glands behaves or responds in a fashion similar to squamous cell carcinoma of mucosal origin. In fact, given the range of histologic types of salivary gland cancers, it is unlikely their treatment and response will be the same as mucosally derived squamous cell carcinoma.

Surgery

Historically, observation and possibly radiation of the neck have been the treatment for occult cervical metastasis. There have been reports recommending surgery, in particular recent reports from Europe. If elective neck dissection is to be performed, levels I through III need to be addressed. Armstrong et al [3] have shown that with clinically positive necks a thorough neck dissection is needed. They found metastasis from parotid primary tumors frequently involves level II and level II cervical nodes; however, up to 25% of lesions skipped to levels III and IV. Their findings are slightly

different in elective N0 neck dissections. With an N0 neck, they found if levels I through III were removed all occult disease was removed. No occult disease was found in levels IV or V. Bardwil [11] also recommended dissection of first-echelon nodes in all salivary gland malignancies. This limited dissection was believed to add minimal morbidity to the primary resection and to be adequate treatment.

Recently, European centers have recommended elective neck dissection in all patients with major salivary gland malignancies, including N0 necks. Zbaren et al [12] recommend elective neck dissection in all N0 necks, removing levels I through III. They also recommend postoperative radiation therapy in all patients staged T2 through T4. Their survival and recurrence rates are no different from those reported in the literature treated by radiation alone. Their main reason for recommending surgery is that frequently the correct histologic tumor type is not ascertained until after surgery.

Stennart et al [8] recommend elective neck dissection on all major salivary gland malignancies because they believe most salivary gland tumors have poor radiosensitivity and because a similar approach is used in other head and neck cancers. Despite their performing an elective neck dissection on every patient, however, their 5-year survival rate is no different from the literature recommending radiation therapy without a neck dissection.

Johns [13], who advocates treating the neck based on histology and stage of the primary tumor, suggests a more focused surgical treatment plan. He recommends no neck dissection for T1/T2 disease but neck dissection with or without postoperative radiotherapy for all T3/T4 primary tumors. Spiro et al [14] further refine this recommendation to include elective neck dissection for what they consider very high-risk histology (ie, anaplastic or squamous cell carcinoma). Kelly and Spiro [6] include in these indications all high-grade malignancies or any primary tumor larger than 4 cm.

Most authors who recommend surgery for the N0 neck do so to avoid radiation if possible. They prefer to leave radiation as an option in the future. In patients who are found to have occult positive adenopathy after an elective neck dissection, as with the clinically positive neck, surgical dissection and radiation may be used as complementary techniques. Jackson [15] suggests performing an upper neck dissection along with the primary resection. If sampled nodes are positive, the neck should be treated with radiation therapy. On the other hand, if sampled nodes are negative for occult disease, and no other indications for radiation exist, patients may be spared the cost and morbidity of radiation. Kormaz et al [16] recommend sampling of level I and II nodes with intraoperative frozen-section analysis for high-grade primary tumors. A full neck dissection is performed if frozen samples are positive for occult disease, and radiation therapy is added to control occult disease further in high-risk pathology. Armstrong et al [3] have also shown a benefit from the use of postoperative radiation in patients with clinically N0 necks and subsequent occult positive adenopathy.

Radiation

Historically, salivary gland malignancies have been thought to have poor radiosensitivity. This assumption was made because radiation therapy alone was not usually successful in controlling salivary gland malignancies. Newer radiotherapy techniques and options have changed this opinion. Several studies show a clear benefit to the use of radiation following surgery [3,7]. In fact several studies show similar outcomes between elective neck dissection and elective neck irradiation. Armstrong et al [3] noted that in a high-risk group with N0 necks, postoperative radiation had a low rate of recurrence with long-term outcome similar to elective neck dissection. Therefore in the patient with a N0 neck who will be treated with radiation for the primary tumor, it is sensible to treat the neck and avoid a neck dissection. Frequently, the characteristics of the primary tumor that place the neck at high risk are the same ones that increase the risk for local recurrence. Elective radiation of the neck is also supported by extensive evidence from the treatment of epidermoid head and neck cancer. Care must be taken, however, before applying these data to salivary histologies that look and behave differently from head and neck squamous cell carcinoma [14].

Summary

In conclusion, salivary malignancies are a rare group of tumors that are still relatively poorly understood. The management of the neck in major salivary gland malignancies, in particular the treatment of the N0 neck, is controversial. It is difficult for any single institution to accrue a significant number of patients. Multiple histopathologic subtypes and behavior patterns further confuse the management of neck disease.

The treatment of the clinically positive neck is fairly well accepted. Therapeutic neck dissection is the accepted treatment, usually with post-operative radiation.

Treatment of the N0 neck remains more controversial. The current approach favors basing the decision on the histology, stage of the primary tumor, facial nerve involvement, and pain. Those predictive factors are considered reasons for surgery or radiation. A growing number of reports recommend elective neck dissections for all major salivary gland malignancies, but this recommendation is far from universally accepted at this time. These studies not show an increased survival or control with elective neck dissection.

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