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Metastases to the parotid gland - A review of the clinicopathological evolution, molecular mechanisms and management

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ABSTRACT

Metastases to the parotid gland are the commonest cause of parotid malignancies in many regions of the world including Australia. The most common etiology of these metastases is head and neck cutaneous squamous cell carcinoma (HNcSCC) followed by melanoma of the head and neck. This article focuses on the management of the aforementioned pathologies including Merkel cell carcinoma (MCC).

Contents

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1. Introduction

In many regions of the world including Australia, metastasis to the intra and periparotid lymph nodes is the most common cause of parotid malignancy. Head and neck cutaneous squamous cell carcinoma (HNcSCC) and melanoma are the principal pathologies followed by metastases from other primary cutaneous malignancies such as Merkel cell carcinoma (MCC), and pleomorphic sarcoma. Rarely malignancies from sites other than the head and neck such as breast, prostate, kidney, and ovaries can also metastasise to the parotid lymph nodes via the thoracic duct and Batson's paraspinal venous plexus [1]. This review will focus on the management of the more common metastatic parotid cancers: HNcSCC, melanoma and MCC.

The complex structural makeup of the parotid including associated lymphatic tissue makes it susceptible to a variety of different malignancies including metastases from skin cancer. The superficial lobe on average contains 8–9 lymph nodes while the deep lobe contains 1–3 nodes [2,3]. Lymph nodes are also present superficial to the parotid fascia in the preauricular region, postauricular region and immediately inferior in the external jugular region. Parotid nodes are the primary sites of drainage from the scalp, forehead, cheek and auricle en-route to the upper deep cervical nodes making them a portal for metastases from cutaneous primaries.

2. Metastatic cutaneous squamous cell carcinoma of the parotid gland

The true incidence of cutaneous squamous cell carcinoma (cSCC) in Australia is not known, as cancer registries do not record this information due to the epidemic of cSCC in the Australian population. Approximately 90% of cSCC occur in the sun exposed head and neck region [4,5]. There has been a rise in incidence which is attributed to ozone depletion, increase in life expectancy, and recently the increasing number and life expectancy of immunosuppressed transplant recipients and also patients developing a hematological malignancy such as chronic lymphocytic leukemia [6,7].

Solar radiation is the single most important eitiologic factor on a population level. Ultraviolet (UV) B (wavelength 290–320 nm), and to a lesser extent UVA (320–400 nm) induce DNA damage in the epidermal cells, particularly in Fitzpatrick skin types I and II. Solid organ and stem cell transplant recipients are at increased risk of developing cSCC. The risk is proportional to the type, duration and degree of immunosuppression in solid organ and stem cell transplant recipients [8]. Other risk factors include male gender, increasing age, and chemical exposure [5,6].

Metastases to the intraparotid and/or cervical lymph nodes occurs in less than 5% of all HNcSCC and in approximately 14% of patients with high-risk cSCC based on a large Australian study [9]. Table 1 highlights the risk factors for developing nodal metastases but it overestimates the metastatic likelihood as it is mainly based on small retrospective studies.

Table 1
Probability of developing nodal metastases based on individual clinicopathological risk factors [6,7,49].

Risk Factor	Metastatic likelihood
Local recurrence	25-62%
Perineural invasion	40-47%
Invasion into subcutaneous fat (Depth $\geq$ 5 mm[a])	16-45%
Lymphovascular invasion	40%
SCC in pre-existing scar	38%
Poorly differentiated	12-32%
Size > 2 cm	21-30%
Immunosuppression	13-20%
Location ear or lip	10-30%

[a] AJCC 8th edition have increased the depth of upstage to $\geq$6 mm.

2.1. Presentation and diagnosis

Patients generally present with a lump in the preauricular region/upper neck with either a preceding history of actinic lesions that have either been treated topically or excised. 20–30% of patients developing metastatic nodal parotid metastases do not have an obvious index lesion [5,10]. Fig. 1 outlines the algorithm for the workup of a lump in the parotid. The standard method of diagnosis is an ultrasound guided fine needle aspiration (FNA) and contrast enhanced computer tomography (CT) scan of the head, neck, chest and upper abdomen in the case of nodal parotid metastases from cSCC (Fig. 1). Magnetic resonance imaging (MRI) is useful in patients with suspected clinical perineural invasion (Fig. 1). Distant metastases at presentation are very uncommon making positron emission scan (PET) a low yield investigation.

The prognosis of a patient depends on the nodal size, number of nodes, and presence of extra-nodal extension (ENE). The 5-year disease specific survival ranges from 97% in patients with small isolated metastases and declining to 42% in patients with multiple large metastases [4,5,11].

Staging of metastatic HNcSCC to the parotid and its ramifications on prognostication is still controversial. The American Joint Committee of Cancer (AJCC) staging manual is widely used, however it has shortcomings. The 8th edition of the AJCC staging manual has ascribed T3 status to include the presence of perineural invasion in the primary HNcSCC and N3 status to all nodal metastases with ENE. Unfortunately, due to frequency of ENE, this will render most patients with nodal metastases (many of whom have highly curable disease) as stage IV. Due to inappropriate grouping of TNM categories, the AJCC TNM system continues to have limited value as a prognostic tool in HNcSCC. Furthermore, the AJCC staging system does not take into account certain clinicopathologic parameters that may influence prognosis in HNcSCC (Table 2) [12,13].

Alternative staging systems for patients with nodal metastases include the P/N system [14]. This system classifies metastatic HNcSSC according to the location, number and size of parotid (P) and cervical (N) metastases. Forest et al. simplified the P/N system by incorporating the parotid and cervical nodes as one to create the