



Combined approaches to the skull base for intracranial extension of tumors via perineural spread can improve patient outcomes



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ABSTRACT

Many neoplasms of the head and neck extend centripetally, gaining access to the central nervous system via nerves through the skull base foramina. Often patients with perineural spread have been excluded from aggressive interventions given the overall poor prognosis and technical difficulty when addressing the perineural components. However, in carefully selected patients combined surgical approaches can provide the greatest potential for disease control as well as neural decompression for symptom relief. We performed a retrospective chart review of 20 consecutive patients who underwent skull base approaches for resection of tumors with intracranial extension via perineural spread from 2011 to 2014. Patients were evaluated for symptom change, surgical approaches, histopathology, adjuvant therapy, outcome, and prognosis. The most common presenting symptoms were pain or cranial nerve palsies. 55% of patients underwent endoscopic endonasal approaches, 50% transcranial approaches, and 15% underwent transfacial approaches. Overall 85% of patients reported symptom improvement in the post-operative period while 40% were completely asymptomatic following surgical resection. Ultimately, we observed a 45% mortality rate with an average survival of 8 months after diagnosis. In carefully selected patients, an aggressive multidisciplinary approach using a combination of surgical avenues to the skull base for the treatment of intracranial tumor via perineural extension can improve patient quality of life.

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Abbreviations: AJCC, American Joint Commission on Cancer; CN III, cranial nerve III, oculomotor nerve; CN V2, cranial nerve V, maxillary division of the trigeminal nerve; CN VI, cranial nerve VI, abducens nerve; CSF, cerebrospinal fluid; ENT, ear nose and throat; Gy, gray; IV, intravenous; MRI, magnetic resonance imaging; OR, operating room.

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1. Introduction

Perineural tumor spread is the presence of tumor cells in the epineurium, perineurium, and/or endoneurium of a nerve, or involving at least one-third of the circumference around a nerve [1]. Spread typically occurs centripetally towards the skull base and central nervous system and occurs in less than 5% of head and neck carcinoma [2,3]. The most common malignancies with perineural spread include adenocystic carcinoma, in which up to 50% of cases have some degree of perineural involvement, mucosal squamous cell carcinomas, including nasopharyngeal carcinoma, and cutaneous neoplasms, such as melanoma and squamous cell carcinoma, the latter of which has an overall 3–14% incidence of intracranial perineural extension [2–4].

Typically, 60–70% of patients with perineural tumor invasion are asymptomatic, and diagnosed primarily with magnetic resonance imaging (MRI) which has a sensitivity of 95–100% [3–5]. Those that do have symptoms can present with pain, paresthesias, numbness, or muscle weakness, such as with mastication or facial expression [6]. Those patients who present with clinical manifestations of perineural spread, especially cranial nerve involvement, have a decidedly worse prognosis than those who have incidentally or radiographically discovered disease [3,5,7–12]. Ultimately cases of malignancies that have extended through the cranial base via perineural tumor spread are best managed by multidisciplinary teams of head and neck surgeons, skull base otolaryngologists and neurosurgeons, neuroradiologists, and radiation and medical oncologists [3]. The goal of the current review was to better elucidate if aggressive multi-disciplinary surgical approaches confer a benefit in symptomatology for patients with skull base tumor extension from perineural spread. Additionally, we sought to identify any patient or treatment factors that corresponded to a reduction in overall mortality.

2. Methods

2.1. Chart review

We performed a retrospective chart review of the patients admitted to our institution from 2011 to 2014 who underwent endoscopic, transcranial, and/or transfacial skull base approaches for resection of tumors with intracranial extension via perineural spread. Their medical records were reviewed for basic demographic information, clinical presentation, exam and imaging findings, surgical procedures, adjuvant therapy, and outcome. Due to the retrospective design of this case series, our institutional review board deemed that written patient consent was not required.

2.2. Clinical decision-making

We performed 24 surgical procedures in 20 patients. All decision-making regarding surgical approaches was performed at the discretion of the senior authors and other operating surgeons. Multidisciplinary neuro-oncology and ENT tumor boards, as well as interdisciplinary skull base meetings were the primary sources of clinical decision-making. In brief, an endoscopic endonasal approach was chosen if there was substantial medial tumor burden without significant carotid or lateral involvement. Transfacial approaches were reserved for anterior tumor extension,

with tumors that were already erosive or visible, and those with distal neural involvement. Finally, transcranial techniques were reserved for those lesions with significant intracranial involvement, especially if intradural or intraparenchymal extension was suspected. A combination of approaches was used whenever patients fit in more than one of the aforementioned categories. The use of adjuvant therapies including chemotherapy and radiation treatment was based on the decision of our multidisciplinary tumor boards, in conjunction with the patients and their treating physicians.

2.3. Statistics

Chi-square statistical analysis were undertaken to determine if distributions of the different categorical variables listed in Table 1 differed from one another against the primary outcome variable of mortality. More specifically, Fisher's exact tests were conducted using SPSS Version 21 software to establish the presence of any significant associations between the variables. SPSS was also used to create a Kaplan-Meier survival curve to better evaluate overall mortality by the end of the study period.

2.4. Literature review

A MedLine search was conducted to analyze the available literature for current practices of surgical resection in cases with radiographically and/or clinically diagnosed perineural spread, especially as it related to surgical indications and outcomes. The goal of the review was to gauge our practices against published results. Search terms included "perineural tumor spread," "perineural invasion," "skull base invasion," "head and neck carcinoma," and variations of the above. The manuscripts were reviewed and often led to other relevant studies and reviews. Special attention was given to studies that focused on operability, prognosis, and symptom relief.

3. Results

3.1. Chart review

We reviewed 20 consecutive patients that presented with perineural tumor spread through the skull base who underwent surgical resection, all of whom were classified as American Joint Commission on Cancer (AJCC) Class T4b by definition [13]. A summary of patient findings can be found in Table 1 with specific parameters further elaborated in Table 2. The average age was 59 years, with one occurrence of nasopharyngeal carcinoma in a 4-year-old patient. Three-fourths of the patients were male. Most patients presented with pain (headache or facial pain) or cranial nerve palsies, including diplopia, with only one patient who was asymptomatic and diagnosed radiographically. Some presented with facial deformity such as visible masses or proptosis.

After reviewing radiographic findings, prior histologic diagnoses from cutaneous biopsies, neo-adjuvant therapies, and affecting symptoms, a total of 24 surgical operations were performed in the 20 patients with a multidisciplinary team of neurosurgeons, rhinology and anterior skull base surgeons, neurootologists, and head and neck surgeons. Eleven patients had endoscopic approaches to the sinuses, facial contents, and skull base, while half under-

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