Management of Skull Base Tumor–Associated Facial Pain

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KEYWORDS

• Trigeminal neuralgia • Cancer pain • Surgical treatment • Medical treatment • Radiation therapy

KEY POINTS

- Intracranial tumors and head and neck tumors can be frequently associated with facial pain through a variety of mechanisms.
- Effective medical treatment of cancer-associated facial pain is achieved through treatment of the underlying tumor as well as treatment of associated symptoms.
- Radiosurgery treatment can be both a source and a cure for facial pain associated with cancer.
- Surgery is often the most effective treatment of cancer-associated pain and includes both tumor resection as well as destructive procedures.

INTRODUCTION

Tumor-associated facial pain is a complex diagnosis that does not lend itself to easy classification. Modern classifications are moving away from terms such as *typical* and *atypical* facial pain in favor of those that convey a deeper understanding of the underlying etiology.[1] Attempting to categorize the facial pain that accompanies tumors is complicated, however, by the myriad ways in which tumors can cause this pain. These causes include perineural tumor invasion, mucosal irritation, infection/inflammation, soft tissue invasion, and necrosis.[2,3] Further complicating the picture are the side effects of standard cancer treatments, specifically chemotherapy, radiation, and surgery, which can either alleviate facial pain or cause/worsen it. To better characterize this complex and unique type of facial pain, the authors divide the tumors that cause facial pain into 3 types based on the anatomy and describe the symptoms associated with these categories. The authors then discuss the effectiveness and drawbacks of various treatment modalities, including medication/chemotherapy, radiosurgery, and surgery.

CATEGORIES OF SKULL BASE TUMORS ASSOCIATED WITH FACIAL PAIN

One of the simplest methods of classifying the variety of tumors associated with facial pain is by anatomic location along the trigeminal system. Using this paradigm, the most common lesions are posterior cranial fossa tumors (trigeminal root), middle cranial fossa tumors (gasserian ganglion and trigeminal divisions), and head and neck tumors (trigeminal divisions and distal branches). Additionally, distal tumors can result in trigeminal neuralgia; these will also be briefly discussed later.

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Each of these categories can present with facial or trigeminal pain through a variety of mechanisms, and the incidence at each anatomic location can be estimated from large published case series (Table 1).

Posterior and Middle Cranial Fossa Tumors

Classically, intracranial tumors are associated with a "brain tumor headache," which has been defined by the International Headache Society as progressive, worse in the morning, and aggravated by Valsalvalike maneuvers.[4] Intracranial mass lesions often compress and obstruct cerebral spinal fluid pathways, leading to the aforementioned symptoms of elevated intracranial pressure. However, although the correlation between brain tumors and headaches is well established, with incidences ranging upwards of 70%[5] for both metastatic and primary tumors, this classic "brain tumor headache" has been shown in recent studies to happen infrequently.[6]

Instead, skull base tumors can present with a variety of pain syndromes, including facial pain that is often diagnosed as trigeminal neuralgia. The constellation of symptoms seen in this cohort can not only be that of typical trigeminal neuralgia (ie, sharp lancinating pain with clear triggers) but also associated with a neuropathy (ie, decreased sensation in any one of the trigeminal divisions or masseter dysfunction). This has been well described in the literature in various case reports, particularly for tumors of the cerebellopontine angle.[7,8] Larger studies have also been done to confirm this, but have shown variable rates of incidence. For example, in a retrospective series from the Mayfield clinic, only 0.8% of 2000 patients with facial pain were found to have an intracranial tumor,[9] with peripherally located tumors causing atypical facial pain associated with a sensory loss and middle/posterior fossa tumors causing trigeminal neuralgia symptoms. On the other hand, in a 15-year retrospective review of more than 5000 patients evaluated for facial pain at the Mayo Clinic, more than 2900 patients were diagnosed with trigeminal neuralgia and nearly 6% were found to have causal intracranial masses, most commonly in the posterior fossa.[10] Examples of tumors in the posterior and middle cranial fossa that can present with trigeminal neuralgia are shown in Table 2.

With tumors of the posterior fossa (ie, petroclival meningiomas, vestibular schwannomas) and middle fossa (ie, trigeminal schwannoma) (Fig. 1), direct mechanical compression of the trigeminal root is thought to be the primary pain generator. A similar mechanism can also be seen with middle fossa tumors (see Fig. 1). Of note, with prolongation of time without treatment, this prolonged mechanical compression is thought to result in breakdown in Schwann cells and axonal degeneration. On the other hand, histologic studies of cavernous meningiomas have demonstrated tumor invasion of the perineural layer of involved cranial nerves. This phenomenon can be independent of histologic grade and likely represents another mechanism of tumor: associated trigeminal neuralgia beyond the standard mechanical compression seen with benign tumors of the middle and posterior cranial fossa.

More recent studies have also shown an association between brain tumors and trigeminal autonomic cephalalgias (TACs). These TACs are recently described entities by the International Headache Society that resemble trigeminal neuralgia but encompass a unilateral facial pain syndrome with an associated ipsilateral autonomic dysfunction. Although most often associated with pituitary tumors,[11–13] TACs have also been reported in other tumors that invade the cavernous sinus.[14–16]

Table 1
Tumors associated with facial pain: symptoms and incidences

	Symptoms	Incidence
Intracranial tumors	Headache, TN, TAC	70%
Head and neck tumors	Orofacial pain, TN	80%
Distal tumors	Neuropathies	Rare

Abbreviations: TAC, trigeminal autonomic cephalalgia; TN, trigeminal neuralgia.

Head and Neck Tumors

Head and neck malignancies can also present with facial pain. The rich network of distal trigeminal nerve branches along the skin and within the subcranial structures (ie, nasal cavity, paranasal sinuses, pterygopalatine fossa, infratemporal fossa) exposes them to the risk of perineural invasion (PNI) with neurotrophic cancers (Table 3). PNI represents a mode of cancer spread whereby tumor cells invade the perineural space and spread along those nerves to distant locations. Clinical PNI refers to a clinical deficit on presentation as a result of tumor spread involved in a large named nerve (ie, infraorbital nerve, buccal nerve). Regardless, the presence of clinical or radiographic PNI must be accounted for during any oncologic treatment. For nonmelanoma cutaneous malignancies, the rates of PNI can vary; but up to 14% of