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Perineural tumor extension along the trigeminal nerve: magnetic resonance imaging findings

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Abstract

Objective: To evaluate the magnetic resonance imaging (MRI) findings of 15 patients with perineural tumor extension along the trigeminal nerve in correlation with clinical data. **Methods:** The clinical records and MRI studies of 15 patients with perineural tumor extension along the trigeminal nerve were retrospectively reviewed. Imaging studies included plain and contrast-enhanced thin section T1-weighted spin echo (T1-WSE) MRI with and without fat-suppression. The studies were compared to determine which sequence provided greatest tumor conspicuity and best depiction of tumor extent. The conspicuity of these tumors was assessed on the available sequences by two observers by consensus. **Results:** The contrast-enhanced T1-weighted spin echo fat-suppressed images (T1-WSECEFS) demonstrated greatest tumor conspicuity and best depiction of tumor extent in the extracranial head and neck and skull base region. The conventional T1-weighted spin echo pre- and postcontrast images were, however, diagnostic of perineural tumor extension in 11 patients due to the presence of considerable tumor bulk and extension well above the skull base. In the other four patients the perineural tumor was poorly visualized on the conventional T1-WSE images and well visualized on the fat-suppressed images. The mandibular division of the trigeminal nerve (V3) was most commonly involved ($n = 10$), followed by the maxillary (V2; $n = 5$) and ophthalmic (V1; $n = 2$) division. Two patients had both mandibular as well as maxillary nerve involvement. The finding of perineural tumor extension had significant impact on patient management: based on the MR imaging study, the primary tumor was considered inoperable ($n = 13$), the extent of surgery was expanded ($n = 2$) and radiation therapy (RT) ports were extended ($n = 12$). **Conclusion:** Complete trigeminal nerve imaging is recommended when evaluating (suspected) head and neck malignancies with a high risk for perineural extension. In these cases thin section axial and coronal precontrast T1-WSE MR images and postcontrast T1-WSE MR images with fat-suppression should be obtained. In the rare event that artifacts degrade the quality of the fat-suppressed images, contrast-enhanced T1-WSE sequences without fat-suppression can additionally be used. © 1997 Elsevier Science Ireland Ltd.

Keywords: Head and neck; Magnetic resonance imaging; Nerves; Neoplasms; Trigeminal

1. Introduction

Malignancy arising in the extracranial head and neck region can spread by perineural tumor extension

to areas apparently removed from the primary tumor [1–5].

Carcinomas with prominent neurotropism (tendency to spread perineurally), spread along nerves by two main routes: along tissue planes of the neural sheaths (peri-, epi-, and endoneurium) or, less often, within lymphatics of the epineurium and perineural sheaths

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([6], Fig. 1). For imaging purposes these methods of spread are grouped together and are called perineural tumor extension. The trigeminal nerve serves as a common pathway for perineural extension of head and neck tumors. The pertinent anatomy of the trigeminal nerve is depicted in Fig. 2.

Patients with malignant disease involving the skin of the forehead or the orbit should be carefully examined for perineural spread involving the ophthalmic nerve (V1). Those with tumor involving the cheek or the sinonasal area should be examined for involvement of the maxillary nerve (V2). Involvement of the mandibular nerve (V3) is most frequently encountered in patients with masticator space tumors and also with tumors of the nasopharyngeal mucosal space and parotid space [5]. The third division of the trigeminal nerve has numerous sensory and motor branches supplying deep and superficial facial structures and is a common route for perineural extension. The close relationship of the auriculotemporal division of the mandibular nerve to the parotid gland permits perineural spread by tumors such as adenoid cystic carcinomas of the parotid gland [7]. These tumors also commonly involve the mastoid segment of the facial nerve (VII). Additionally, the rich anastomoses that occur between the fifth and seventh cranial nerves (CNs) within the face may allow for direct involvement of both nerves [2,4].

Detection of perineural spread is important as it can significantly alter the prognosis and the form of treatment. Its presence may be associated with a poor prognosis and a high incidence of recurrences and metastases, may change the extent of surgery, deem the tumor unresectable and affects the way radiation therapy (RT) will be delivered to the majority of patients [8]. Perineural tumor extension is most commonly seen with head and neck squamous cell carcinoma (SCC) and adenoid cystic carcinoma [1,5]. Additional tumor types that have been reported to spread perineurally include: malignant melanoma, lymphoma, mucoepidermoid carcinoma, adenocarcinoma and sarcomas [5]. Signs and symptoms of perineural tumor extension are often nonspecific or attributed to the primary lesion [3]. In early or moderately advanced cases symptoms may even be absent [2]. A high index of suspicion for perineural extension along the trigeminal nerve should therefore be present when evaluating the abovementioned tumors with magnetic resonance imaging (MRI). The purpose of this study was to review the clinical aspects and MRI findings in 15 patients with perineural tumor extension along the trigeminal nerve and to present an optimal MRI protocol for evaluating tumors with a high risk for perineural extension.

2. Materials and methods

We retrospectively analyzed the medical records and the MRI studies of 15 patients with perineural tumor extension along the trigeminal nerve as identified by MRI during the period from August 1992 through May 1995. Axial proton density and T2-weighted (T2W) spin echo images and axial, and coronal thin section (3 mm) precontrast T1-weighted spin echo (T1-WSE) images were obtained. After intravenous administration of gadopentetate dimeglumine (0.1 mmol/kg) axial and coronal thin section (3 mm) conventional T1-WSE images were obtained in 13 patients and a T1-weighted fat-suppression sequence in the axial and/or coronal projection in seven patients. For fat-suppression we used a technique called FATSAT which reduces the intensity of fat by radiofrequency presaturation. These studies were compared to determine which sequence provided greatest tumor conspicuity and best depiction of tumor extent. The conspicuity of these tumors was assessed on the available sequences by two observers by consensus. Qualitative tumor-to-background contrast was graded as follows: 0, not visualized; 1, poorly visualized; 2, fairly well visualized; 3, well visualized. Medical records were retrospectively reviewed for pertinent clinical information with special attention to type and duration of symptoms, histopathologic findings and clinical implications of the MR demonstration of perineural tumor spread.

Fig. 1. Schematic drawing of cross-cut nerve. Neurotropic carcinomas spread along nerves by two main routes: along tissue planes of the neural sheaths (peri-, epi- and endoneurium) or, less often within lymphatics of the epineurium and perineural sheaths. (Reprinted with permission from [6]).

A

B

Fig. 2. Pathways for perineural tumor extension along the trigeminal and facial nerves. (a) Patients with malignant disease of the orbit or the skin of the forehead should be examined for perineural spread involving the ophthalmic nerve (V1). Those with tumor involving the cheek or sinonasal area should be examined for involvement of the maxillary nerve (V2). (b) The third division of the trigeminal nerve has numerous branches supplying deep and superficial facial structures. Note the close relationship between the auriculotemporal division of the mandibular nerve (V3) and the facial nerve (VII) to the parotid gland, permitting perineural spread by tumors such as adenoid cystic carcinoma of the parotid gland. Note the multiple anastomoses between the trigeminal and facial nerves in (a) and (b) (motor branch of V3 not shown; V, trigeminal nerve; V1, ophthalmic nerve; V2, maxillary nerve; V3, mandibular nerve; VII, facial nerve; IX, glossopharyngeal nerve; SOF, superior orbital fissure; FR, foramen rotundum; FO, foramen ovale; GSPN, greater superior petrosal nerve; sup., superior; inf., inferior; alv., alveolar).

Table 1
Clinical and MRI findings in 15 patients with perineural tumor extension

Patient	Sex	Age	Primary tumor histology	Primary tumor location	L R	Symptoms and signs	Duration (months) ^a	Perineural tumor extension cranial nerves involved (MRI)	Clinical implication
1	Male	67	ACC	Parotid gland	L	Burning pain tongue, jaw and retromandibular fossa (V3) CN VII palsy	54	V3 → GG	Inoperable; RT port extended
2	Male	36	ACC	Parotid gland	R	Pain jaw and retromandibular fossa (V3) CN VII palsy	36	VII (mastoid segment) V3 → GG	Inoperable; RT port extended
3	Male	59	ACC	Parotid gland	R	Numbness (V3)	5	VII (mastoid segment → geniculate ganglion) V3 → GG	Inoperable; RT port extended
4	Female	55	ACC	Parotid gland	R	Trismus (V3) Pain jaw, ear and retromandibular fossa (V3) CN V (motor and sensory) VI and VII palsy	1	V3 → REFZ	Inoperable; RT port extended
5	Male	50	ACC	Maxillary sinus	R	Pain (V1-V3)	9	VII (mastoid segment) V2, V3 → GG	Inoperable; RT port extended
6	Female	35	ACC	Maxillary sinus	R	Paresthesias (V2) Pain (V2)	0.5	V2, V3 → GG	Inoperable; RT port extended
7	Male	66	ACC	Lacrimal gland	R	Numbness and pain (V1-V3) Decreased hearing	3	V1 → REFZ	Inoperable; RT port extended

Table 1 (continued)

8	Male	34	SCC	Nasopharynx	R	Pain (V1 V3)	9	V3 → GG	Inoperable; RT port extended
9	Male	64	SCC	Nasopharynx	L	Serous otitis media Numbness (V1 + V3)	1	V3 → GG	Inoperable; RT port extended
10	Male	58	SCC	Masticator space	L	Trismus (V3) Numbness and pain (V1 V3)	4	V3 → GG	Inoperable; RT port extended
11	Male	81	SCC	Parotid duct and facial node	R	Corneal reflex L < R CN III and IV palsy	4	V2 → PPF → FR	Inoperable
12	Female	48	SCC	Gingivobuccal sulcus	L	Pain (V2) Paresthesias (V2)	3	V2 → PPF → FR	Inoperable; RT port extended
13	Female	77	Malignant melanoma	Cheek	L	Pigmented lesion on left cheek	4	V2 → PPF	Surgery expanded but irresectability confirmed at operation; RT port extended
14	Female	51	Non-Hodgkin lymphoma	Orbit	R	Numbness and pain (V2) CN III palsy	5	V1 → GG	Inoperable; RT port extended
15	Male	78	Mucoepidermoid carcinoma	car-Parotid gland	R	Impairment of lacrimation Pain (V1, V2) Numbness (V3)	40	VII (vidian nerve) V3 → GG	Inoperable

FR, foramen rotundum; REZ, root entry zone of V; III, oculomotor nerve; IV, trochlear nerve.

^a Time between onset of symptoms and signs and final diagnosis with MRI.

3. Results

The clinical and MRI findings in our 15 patients are summarized in Tables 1 and 2. Of the 15 patients with perineural tumor extension ten were men and five were women. Their ages ranged from 34 to 81 years with a mean age of 57 years. Primary tumors (all confirmed by biopsy) included: adenoid cystic carcinoma of the parotid gland ($n = 4$), maxillary sinus ($n = 2$) and lacrimal gland ($n = 1$), mucoepidermoid carcinoma of the parotid gland ($n = 1$), squamous cell carcinoma of the nasopharynx ($n = 2$), masticator space ($n = 1$), parotid duct ($n = 1$) and gingivobuccal sulcus ($n = 1$), malignant melanoma of the cheek ($n = 1$), and orbital non-Hodgkin lymphoma ($n = 1$). Clinical findings at the time of the MR imaging study included facial pain ($n = 11$), numbness ($n = 7$), paresthesias ($n = 2$) and trismus ($n = 2$). In 4 patients additional facial nerve (VII) palsy was encountered. The interval between onset of symptoms and final diagnosis and MRI varied between 2 weeks and 54 months (mean 12 months). Biopsy of the primary tumor demonstrated perineural invasion in all cases. In two cases surgical specimens of the distal perineural tumor were available allowing direct comparison with the imaging study (cases 13 and 14). In these two cases the imaging study accurately predicted the extent of tumor. In the other 13 cases we assumed that the margins of abnormal signal defined the pathologic extent. In all 15 patients enlargement and/or pathologic enhancement of one or two of the peripheral trigeminal nerve branches was demonstrated. In 12 instances enlargement and pathologic enhancement of the gasserian ganglion (GG) was demonstrated. The cisternal portion of the trigeminal nerve demonstrated pathologic thickening and enhancement in two cases.

Conspicuity grades for detecting the primary tumor are summarized in Table 2(a). The primary tumor was fairly well ($n = 9$) or well ($n = 1$) visualized on the conventional T1-WSE precontrast images (Fig. 3). In two cases the tumor was poorly and in two cases the tumor was not visualized on the precontrast T1-WSE images. In another case the primary tumor was previously excised. Contrast administration without fat-suppression did not increase the conspicuity grade for detection of the primary tumor. In 6 cases the primary tumor was less well visualized on the contrast-enhanced T1-WSE (T1-WSECE) images, compared with the precontrast T1-WSE images due to obscuration of enhancing lesions in or adjacent to the fat of the extracranial head and neck region. The T1-WSE contrast-enhanced fat-suppressed (T1-WSECEFS) images were superior ($n = 3$) or equal ($n = 1$) to the pre- and postcontrast T1-WSE images in detecting the primary tumor. In one case (case 2) the primary tumor was only visible on the fat-suppressed images (Fig. 4).

Conspicuity grades for detecting perineural tumor extension are summarized in Table 2(b). Although highest perineural tumor to background contrast was obtained with the T1-WSECEFS images (two of seven fairly well, and five of seven well visualized), the perineural tumor was also fairly well visualized on the conventional T1-WSECE images in three of seven cases in which fat-suppressed images were obtained, due to the presence of significant tumor bulk extending well above the skull base. In four cases tumor conspicuity was increased with two grades with fat-suppression. In eight cases no fat-suppressed images were obtained, in these cases the perineural tumor was fairly well visualized on the conventional pre- and postcontrast T1-WSE images. T1-WSECE images were inferior ($n = 4$), equal ($n = 3$) or superior ($n = 5$) compared with the precontrast T1-WSE images in detecting perineural tumor extension. In the cases where T1-WSECE images were superior to the precontrast T1-WSE images there was a significant amount of tumor bulk extending above the skull base. The T2-weighted (T2W) and proton density weighted (PDW) images contributed little to the detection of both the primary tumor as well as perineural extension. The mandibular division of the trigeminal nerve was most commonly involved ($n = 10$), followed by the maxillary ($n = 5$) and ophthalmic division ($n = 2$). Two patients had both mandibular as well as maxillary nerve involvement. Atrophy of the masticator muscles was found in seven of ten patients with mandibular nerve involvement. In four patients associated perineural tumor extension along the facial nerve (VII) was present: in three cases of parotid adenoid cystic carcinoma tumor extended along the mastoid segment of the facial nerve (VII; $n = 2$) and to the facial geniculate ganglion ($n = 1$); in the case of orbital non-Hodgkin lymphoma additional perineural extension along the vidian nerve from tumor in the pterygo-palatine fossa was demonstrated. The finding of perineural tumor extension had significant impact on patient management: the extent of surgery was expanded ($n = 2$), the tumor was considered inoperable ($n = 13$) and RT ports were extended ($n = 12$).

4. Discussion

4.1. Symptoms and signs

In early or moderately advanced cases of perineural tumor spread, symptoms may be mild or even absent due to the fact that nerves fibres themselves are usually intact, presumably owing to the distensibility of both the perineural and endoneurial spaces. They undergo pressure degeneration only in the later stages of the disease or in confined spaces (e.g. skull base foramina or extracranial nerve canals) [2].

Table 2
Conspicuity grades for tumors

Patient No.	T2W	PDW	T1-WSE		T1-WSECE		T1-WSECEFS	
	Axial	Axial	Axial	Coronal	Axial	Coronal	Axial	Coronal
(a) Conspicuity grades for the primary tumor in 15 patients with perineural tumor extension								
1	1	1	2	—	0	0	3	—
2	0	0	0	—	0	0	3	1
3	—	—	2	2	1	1	—	—
4	1	1	2	2	2	2	—	—
5	—	—	—	1	0	1	—	—
6	1	—	2	2	1	2	—	—
7 ^a	—	—	—	—	—	—	—	—
8	—	—	1	1	1	1	—	2
9	0	0	1	2	0	0	—	—
10	1	1	NA	2	NA	2	—	—
11	NA	NA	NA	NA	—	—	2	NA
12	1	—	2	—	2	2	—	—
13	—	—	2	1	1	—	—	NA
14	1	1	2	2	1	0	0	2
15	2	2	3	3	—	—	—	—
(b) Conspicuity grades for perineural tumor extension along the trigeminal nerve in 15 patients								
1	0	0	1	—	1	2	3	—
2	0	0	1	—	0	2	3	3
3	—	—	1	2	0	1	—	—
4	1	1	2	2	2	2	—	—
5	—	—	1	1	1	2	—	—
6	0	—	1	—	1	2	—	—
7	1	1	2	2	2	2	3	3
8	—	—	0	1	1	1	—	3
9	0	0	1	2	1	1	—	—
10	1	1	1	2	2	3	—	—
11	0	0	1	1	—	—	1	3
12	1	—	2	—	1	2	—	—
13	—	—	1	1	0	—	—	3
14	1	1	1	1	1	1	0	3
15	1	1	1	2	—	—	—	—

0, not visualized; 1, poorly visualized; 2, fairly well visualized; 3, well visualized.

—, not performed; NA, not appropriate, because imaging sections did not contain primary tumor site.

^a Primary tumor previously excised.

When present, symptoms are often nonspecific or attributed to the primary lesion [3]. Occasionally, the perineural spread, rather than the primary lesion, causes the presenting signs and symptoms. In such cases, including seven of our 15 cases, the primary lesion may go undetected and progress for months or years before diagnosis. Facial pain is the least specific symptom, but the character of this pain may be an important clue to the presence of perineural spread. Burning, shooting or stinging pains are highly suggestive of perineural invasion. Numbness in the distribution of the trigeminal nerve or one of its branches is almost pathognomonic of nerve involvement [1]. When the ophthalmic nerve (V1) is affected, the corneal reflex may be diminished or absent. Involvement of the motor branches of the mandibular nerve (V3) may result in denervation atrophy of the masticator muscles including the medial and lateral ptery-

goid, the masseter, the temporalis, the mylohyoid and the anterior belly of digastric muscles [9]. Decreased hearing due to serous otitis media caused by dysfunction of the tensor veli palatini muscle (innervated by V3) may be present [9].

4.2. Pathology and clinical features

Perineural tumor extension is most commonly seen with head and neck SCC and adenoid cystic carcinoma (ACC) [1,5]. Although SCC is the most common head and neck cancer, the strongest association with perineural tumor extension is with ACC [7]. Additional tumor types that have been reported to spread perineurally include: malignant melanoma, lymphoma, mucoepidermoid carcinoma and sarcomas [1,2,5,6].

Fig. 3. Perineural tumor extension of adenoid cystic carcinoma of the left parotid gland in a 67-year-old man with left mandibular nerve pain and facial nerve palsy (case 1). (a) Axial T1-weighted MR image shows a hypointense mass in superficial and deep lobe of left parotid gland (arrow). (b) and (c) Axial T1-weighted MR images before (b) and after (c) contrast administration demonstrate poor visualization of thickened left mandibular nerve (arrow). (d) Axial contrast-enhanced T1-weighted MR image with fat-suppression clearly shows enhancement of thickened left mandibular nerve just below the foramen ovale (black arrow). Note also enhancement of left facial nerve (white arrow). (e) Coronal contrast-enhanced T1-weighted MR image shows enhancing thickened left mandibular nerve (arrows) extending through expanded foramen ovale into Meckel's cave area. Note denervation atrophy of left masticator muscles and normal mandibular nerve on opposite side.

Fig. 3 (continued).

4.2.1. Adenoid cystic carcinoma

Adenoid cystic carcinoma is a relatively rare tumor that constitutes 5–15% of all salivary gland tumors [10,11]. It is usually found in the minor salivary glands where it constitutes 25–31% of malignant neoplasms and is the most common malignant tumor [12,13].

ACC constitutes 15% of tumors of the submandibular gland, but only 2–6% of tumors of the parotid gland [11,14]. Clinical features at presentation (nasal obstruction, swelling and facial pain) are nonspecific and more than 50% of patients have had symptoms for 1–5 years before presentation [11]. Facial nerve (VII) palsy and pain or paresthesias in the distribution of the trigeminal nerve, particularly V3, signals the onset of perineural spread [1]. Two patients of our study with adenoid cystic carcinoma of the parotid gland (cases 1 and 2) presented with facial nerve (VII) palsy and pain in the distribution of the mandibular nerve (V3) several years (3 and 4.5 years, respectively) before the final diagnostic MR examination that revealed an unexpected primary tumor in the parotid gland with perineural extension (Figs. 3 and 4).

Perineural infiltration was noted on MR images in nine of 27 patients with ACC in a previous study [15]. Additionally, 11 of 80 cases of perineural tumor extension reported by Ballantyne [1] and 11 of 52 cases reported by Parker [5] were of adenoid cystic origin. In our study seven of 15 patients had ACC. Despite

the relatively benign histologic appearance and slow growth of ACC, the natural history of this carcinoma is characterized by a slow relentlessly malignant course. Repeat recurrences and distant metastases occur over many years finally killing the patient. Repeat surgical excision and RT are the treatment of choice [15].

Nerve invasion of ACC has been reported to worsen the prognosis [16].

In a study of 63 patients with ACC, perineural invasion appeared to have a profound impact on survival, i.e. 94% 5-year survival in patients without perineural invasion ($n=26$) in contrast to 37% 5-year survival in patients with perineural invasion ($n=37$); ($P<0.001$). In the patients with perineural invasion a significant higher incidence of distant metastases and locoregional recurrences was found [16].

Massive perineural tumor extension from a large primary tumor may be an indication for less, rather than more radical surgery since complete resection may be beyond the scope of surgical treatment. Based on the MRI findings RT ports should be expanded. Apart from the primary site the field of irradiation should also comprise the involved nerve trunks and even the skull base in order to stop perineural spread [16]. In our study, MRI demonstrated perineural extension above the skull base in all patients with ACC, which deemed the tumor inoperable; RT ports were extended appropriately.

Fig. 4. Perineural tumor extension of adenoid cystic carcinoma along the trigeminal and facial nerves in a 36-year-old man: value of fat-suppression (case 2). (a) Axial T1-weighted MR image shows inhomogeneous signal intensity within the right parotid gland. No definite tumor mass is visible. (b) Axial contrast-enhanced T1-weighted MR image at the same level as (a) does not definitely reveal a mass in the right parotid gland. (c) Axial contrast-enhanced T1-weighted MR image with fat-suppression reveals enhancing mass in deep and superficial lobe of right parotid gland (arrow). Note increased conspicuity as compared with (b). (d) Axial contrast-enhanced T1-weighted MR image with fat-suppression clearly shows pathologic enhancement and thickening of right V3 in the prestyloid compartment of lateral parapharyngeal space (black arrow) and of right facial nerve (white arrow). (e) Coronal contrast-enhanced T1-weighted MR image at the level of foramen ovale shows possible enhancement of right V3 and gasserian ganglion (arrow). Note denervation atrophy of right masticator muscles (arrowhead). (f) Coronal contrast-enhanced T1-weighted MR image with fat-suppression more clearly shows the pathologic enhancement and thickening of right V3 and gasserian ganglion due to perineural tumor extension (arrow). Note also enhancement of primary tumor in right parotid gland (arrowhead). (g) Surgical biopsy of the primary tumor shows adenoid cystic carcinoma (arrow) infiltrating the perineural sheath of a peripheral nerve branch. (Nerve fascicle indicated with arrowhead).

Fig. 4 (continued).

4.2.2. Squamous cell carcinoma

In a series of 807 patients with metastasis from superficial SCC of the head and neck the incidence of perineural extension was reported as 2.5% [17].

Beyers showed a 2% incidence of perineural invasion in 1308 cases of SCC of the lower lip [18].

Additionally, 55 of 80 cases of perineural tumor extension reported by Ballantyne [1] and 24 of 52 cases reported by Parker [5] were of squamous cell origin.

In 520 patients with 967 SCCs of the skin of the face 14% of patients were noted to have perineural tumor extension [19]. In this study an increased incidence of distant metastases, cervical lymphadenopathy and significantly reduced survival curves were reported in patients with perineural spread compared with those without. Perineural invasion of SCC can necessitate wider surgical excision. In advanced perineural extension even aggressive surgical resection may fail to yield

tumor-free margins and may require postoperative RT [20].

In our study five of 15 patients had SCC. Based on the MRI study, these patients were considered inoperable due to perineural tumor extension above the skull base (Fig. 5), and RT ports were extended appropriately.

4.2.3. Other tumor types

Additional tumor types that have been reported to spread perineurally were also encountered in our series including malignant melanoma, lymphoma and mucoepidermoid carcinoma.

In our case of neurotropic malignant melanoma (NTM) MRI showed perineural tumor extension from the cheek along the infraorbital nerve (V2) into the pterygopalatine fossa (PPF) (Fig. 6). Because of the locally aggressive neurotropic potential and its high incidence of local recurrence following inadequate excision, wide surgical excision has been the recommended treatment [21]. If neural invasion has occurred, the possibility of cure may exist as long as the extension of the NTM is recognized and adequately resected prior to entry into the cranial vault [22]. Based on the imaging study, surgery was expanded in our patient in order to remove as much tumor bulk as possible but irresectability was confirmed due to tumor extension into the PPF (case 13, published previously: [23]).

One of our patients had orbital non-Hodgkin lymphoma that spread perineurally along the ophthalmic nerve (V1) toward the GG and also along the vidian nerve. Surgical biopsy of the tumor mass in Meckel's cave confirmed the MRI findings (case 14).

One patient had mucoepidermoid carcinoma of the parotid gland (case 15). The primary tumor was ill defined and demonstrated low to intermediate signal intensity on both the T1-weighted and T2-weighted images, indicating a high grade tumor [11], confirmed by surgical biopsy. Tumor extended along V3 into the GG, deeming the lesion unresectable.

4.3. Imaging

Imaging of perineural tumor extension is best accomplished by acquiring thin section (3 mm) precontrast T1-WSE MR images and contrast-enhanced T1-WSE MR images with fat-suppression in the axial and coronal planes [24–26]. Precontrast T1-WSE MR images are necessary to confirm that all hyperintense lesions detected with fat-suppression are in fact contrast-enhancing rather than substances which are intrinsically bright on T1-weighting such as proteinaceous fluid or hemorrhage [25]. Furthermore, in our study, precontrast T1-WSE MR images were superior or equal to the T1-WSECE images in detecting the primary tumor due to obscuration of enhancing lesions in or adjacent to the

fat of the extracranial head and neck region. Fat-suppressed contrast-enhanced T1-WSE MR images should be obtained to identify enhancing primary and perineu-

Fig. 5. Perineural extension of squamous cell carcinoma arising from the mucosa at the left upper gingivobuccal sulcus in a 48-year-old woman with left maxillary nerve paresthesias (case 12). (a) Axial contrast-enhanced T1-weighted MR image with fat suppression shows an enhancing mass in the left upper buccal space near the superior alveolar ridge (arrow). (b) Coronal contrast-enhanced T1-weighted MR image with fat suppression shows thickening and enhancement of the left maxillary nerve (V2) as it passes through the foramen rotundum (arrow). The tumor extended via the superior alveolar nerves and the infraorbital nerve to the maxillary nerve at the foramen rotundum (see also Fig. 2). (Courtesy of Johan A. Dol, MD).

Fig. 6. Perineural tumor extension of neurotropic malignant melanoma of the left cheek in a 77-year-old woman with left maxillary nerve numbness and pain (case 13). (a) Axial T1-weighted MR image shows retrograde perineural tumor extension along the enlarged left infraorbital nerve (white arrow) towards the upper pterygopalatine fossa (black arrow). (b) Coronal contrast enhanced T1-weighted MR image, obtained with fat suppression shows enhancement of the enlarged left infraorbital nerve (arrow). (c) Pathologic specimen of neurotropic malignant melanoma obtained during partial left maxillectomy shows massive tumor invasion (T) within the perineural sheath of the maxillary nerve. (Nerve fascicles indicated with arrows). (Reprinted with permission from [23]).

ral tumor in or adjacent to the fat of the extracranial head and neck region and/or fatty bone marrow of the skull base, especially in cases with a small amount of

perineural tumor bulk. With the use of fat-suppressed images, enhancing tumors, both primary tumors as well as perineural tumors, become more conspicuous and

lesional margins are better defined [25,26]. A disadvantage of fat-suppression imaging is an artifact that results in asymmetric fat-suppression [26]. This artifact occurs in regions of changing body contour, for example at the junction of the floor of the mouth and neck. Susceptibility artifacts at the interface of air and soft tissue (sinuses, airway) may also degrade image quality [25,26], which occurred in our study in only one patient on the axial T1-WSECEFS images (case 14). In four cases of perineural tumor extension in our series the perineural tumor was poorly visualized on the pre- and postcontrast T1-WSE MR images. In these cases fat-suppression imaging allowed clearly detection of perineural spread along the trigeminal nerve. In the other 11 cases the conventional pre- and postcontrast T1-WSE MR images were diagnostic of the perineural tumor extension due to the presence of considerable tumor bulk and extension well above the skull base. Although contrast enhanced non fat-suppressed T1-WSE MR images might be sufficient, we advocate their use only as an alternative when failure of fat-suppression interferes with interpretation of the study, because with fat-suppression lesion detectability and reader level of confidence was improved. MRI signs of perineural tumor involvement include: abnormal nerve thickening with enhancement after intravenous administration of contrast material; concentric expansion of the skull base foramina and extracranial nerve canals; replacement of the normal trigeminal cistern hypointensity on T1-weighted images or hyperintensity on T2-weighted images by an isointense mass or enhancement of a mass in the Meckel's cave/GG area; lateral bulging of the cavernous sinus dural membranes and denervation atrophy of the masticator muscles [7].

The normal perineural sheath surrounding the trigeminal nerve may enhance on fat-suppressed contrast-enhanced T1-WSE MR images, but not the nerve itself [25]. Enhancement of the GG on conventional contrast-enhanced T1-WSE MR images in asymptomatic patients is a normal finding [27], the combination of enlargement and enhancement is, however, pathologic. Enlargement and enhancement of a nerve are not always due to perineural tumor infiltration. The differential diagnosis includes other neoplastic diseases, such as primary neural tumor and inflammatory disorders such as inflammatory pseudotumor, viral neuritis, mucormycosis, sarcoidosis and histiocytosis [28–32].

5. Conclusion

The MRI demonstration of perineural tumor extension has significant impact on patient management. Complete trigeminal nerve imaging is therefore recommended when evaluating (suspected) head and neck malignancies with a high risk for perineural extension.

In these cases thin section axial and coronal precontrast T1 WSE MR images and contrast-enhanced T1 WSE MR images with fat-suppression should be obtained to detect both the primary as well as the perineural tumor. In the rare event that susceptibility artifacts degrade the quality of the fat-suppressed images, contrast-enhanced T1 WSE sequences without fat-suppression can additionally be used.

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