CASE REPORT

Lipomatosis of the Trigeminal Nerve Causing Trigeminal Neuralgia: Case Report and Literature Review

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ABSTRACT

Cerebellopontine angle lipomas are rare and attempts at surgical excision are associated with significant morbidity. Lipomatosis of nerve, the fatty infiltration of nerves, is a distinct entity. We present a case of intractible trigeminal neuralgia caused by lipomatosis of the trigeminal nerve. Clinical case: A 25-year-old male presented with severe right-sided trigeminal neuralgia. Imaging showed a lesion involving the trigeminal nerve with signal characteristics of fat. At surgery the lesion was found to be a fatty infiltration of the nerve itself. Surgery was therefore limited to arachnoid adhesiolysis. The patient remains symptom-free and neurologically intact to date. Correctly identifying these lesions as lipomatosis of nerve rather than lipoma of the cerebellopontine angle make it clear that even partial surgical excision will inevitably result in neurological deficit and should not be attempted. However, in the case of intractable trigeminal neuralgia we demonstrate that surgery can still play a role.

KEYWORDS: Lipomatosis, trigeminal nerve, neuralgia, cerebellopontine angle, lipoma

Lipomatosis of nerve is a rare condition in which the nerve is infiltrated by mature adipocytes and fibrous tissue. It is classified under mesenchymal tumors (ICD-0 code 8850/0; WHO Classification of Tumors of the Central Nervous System) but comprehensive literature searching is confounded by multiple synonyms including hamartomatous lipomatosis, fibrolipomatous hamartoma of nerve, and neural fibrolipoma. One of the principal changes in the 2002 WHO Classification of Soft Tissue Tumors was the renaming of fibrolipomatous hamartoma of nerve (1994 WHO Classification) as lipomatosis of nerve.[1,2] Essential to all descriptions is an infiltration of the epineurium by adipose and fibrous tissue in contrast to lipomas which are less likely to infiltrate nerves, although they can cause extrinsic compression.[1]

Lipomatosis of nerve most commonly affects peripheral nerves of the distal forearm and can present with compression symptoms. The lesions are benign but surgery for example, carpal tunnel decompression may be necessary for symptom relief. Lipomatosis of these peripheral nerves may be associated with metaplastic bone growth and is associated with macrodactyly in approximately one third of patients.[1] There is only one

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report of lipomatosis affecting a cranial nerve (CN)[3] and no previous reports have been found describing lipomatosis of the trigeminal nerve. There are several reports of cerebellopontine angle (CPA) lipomas.[4]

We present a case of intractable trigeminal neuralgia (TN) secondary to lipomatosis at this previously unreported site. Surgical lysis of arachnoid adhesions provided full symptomatic relief with no neurological deficit postoperatively. This case illustrates that surgery is a viable option in the treatment of symptomatic trigeminal nerve lipomatosis. Implications of the careful classification of this lesion are discussed.

CLINICAL CASE

Clinical Features

A 25-year-old male presented with a 1-year history of paroxysmal, lancinating right-sided facial pain, which had worsened in frequency and intensity over the previous month. The pain was exacerbated by light touch and talking and was confined to the territory of the second division of the trigeminal nerve (V2). The patient had no past medical history of note and no significant family history. There was no neurological deficit on examination.

Radiological Features

Magnetic resonance imaging (MRI) revealed a lesion expanding the right trigeminal nerve with the signal characteristics of fat. The lesion was hyperintense on T1- (Fig. 1), hypointense on T2-weighted images, and did not enhance after administration of gadolinium (Fig. 2). The lesion demonstrated characteristic signal "drop-out" on fat suppression sequences (Fig. 3) and chemical shift artifact on T2 images, confirming the fatty nature of the lesion (Fig. 4).

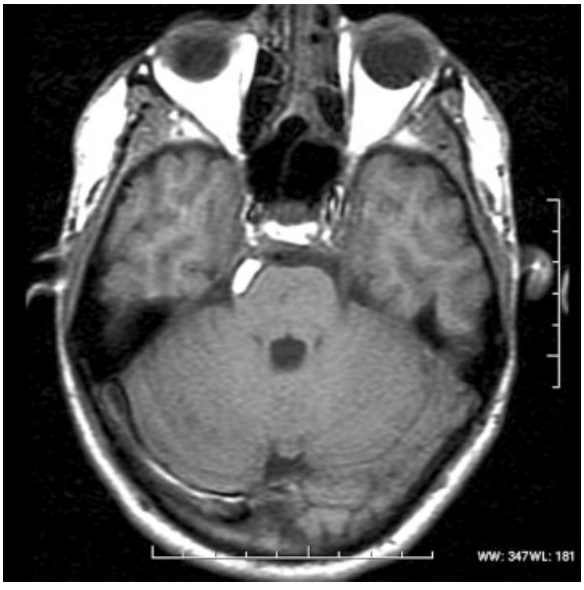

Figure 1 Axial T1 MRI without gadolinium showing a hyperintense focal lesion in the right lateral pontine cistern.

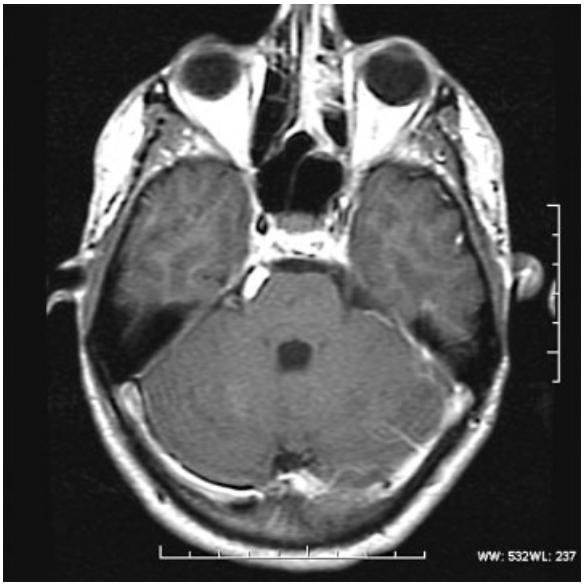

Figure 2 Axial T1 postgadolinium. No change or enhancement after contrast.

Clinical Course

The initial management plan was pharmacological symptom-control and imaging follow-up. The patient was started on carbamazepine (CBZ) orally 200 mg twice daily, which was increased to 1400 mg/d to achieve symptom control. Attempts to wean the medication after

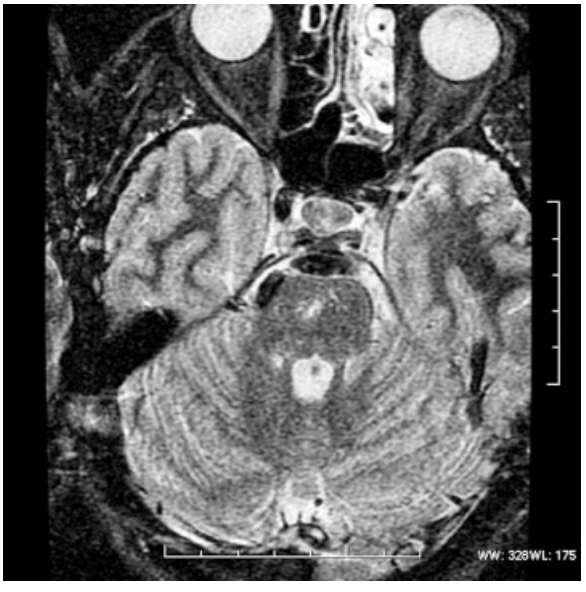

Figure 3 Axial short tau inversion recovery MRI showing the fatty component of the lesion.

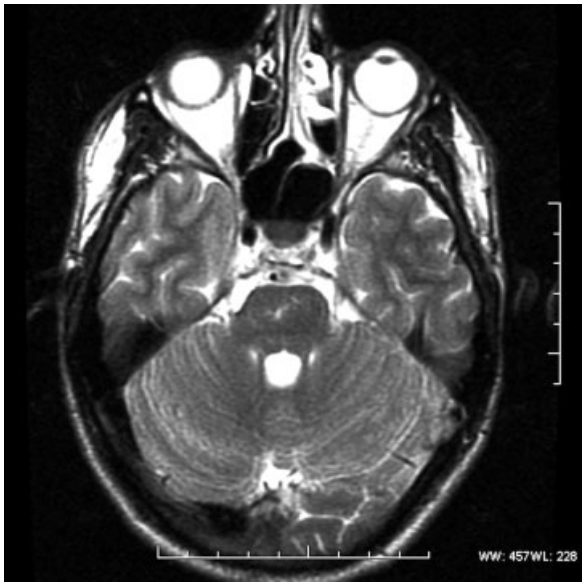

Figure 4 Axial Fast spin echo T2 MRI. Note the hypointense band surrounding the medial portion of the lesion to the right of the pons attributed to the chemical shift artifact characteristic of fatty lesions.

episodes of symptom control were initially successful but the respite was only ever temporary and a gradual stepwise increase of CBZ was required reaching a maximum of 2000 mg/d 18 months after presentation. Due to side effects at this dose the CBZ was reduced to 1800 mg/d and gabapentin was added-in and titrated up to 900 mg/d, initially with good effect. However, the pain returned and the CBZ was increased again to 2000 mg/d and gabapentin to 2600 mg/d. The gabapentin was changed to pregabalin 300 mg/d due to side effects and amitriptyline was added at 12.5 mg/d. Almost 2 years after presentation (February 2008) the patient was admitted with a severe trigeminal crisis. He was loaded with phenytoin (18 mg/kg) but even this gave only partial relief of symptoms and he was referred for consideration of surgery in March 2008.

Surgery

A right-sided suboccipital craniectomy was performed with the patient in a park-bench position. The dura mater was opened, cerebrospinal fluid was released from the cerebellopontine cistern and the flocculus was retracted medially. Cranial nerves V to XI were identified. The inferomedial portion of the trigeminal nerve was noted to be enlarged and to contain a yellowish, soft, fatty material. Arachnoid adhesions were freed along the length of the enlarged trigeminal nerve from Meckel's cave to the trigeminal root entry zone, sufficient only to leave the nerve free from compression. Resection was not attempted as damage to the trigeminal nerve would have been inevitable. The surgical site was washed with warm saline and the craniectomy closed with autologous bone graft and fibrin glue.

Outcome

The patient awoke from surgery pain free and with no neurological deficit. Postoperative recovery was uneventful. The neuropathic pain medication was gradually weaned from the first postoperative day.

At the latest follow-up (6 months postsurgery) the patient remained completely pain free with no neurological deficit. He was not taking any analgesia.

DISCUSSION

We present a case of trigeminal nerve lipomatosis presenting with intractable TN treated effectively and safely with arachnoid adhesiolysis. We propose that distinguishing between a lipoma of the CPA and lipomatosis of the CN of the CP angle has clinical significance.

Intracranial lipomas are rare with a prevalence at autopsy ranging from 0.08 to 0.3%[5] in general autopsies and rising to 0.2–0.5%[5] in neuropathological studies. These prevalence data are supported by computed tomography[6] and MRI[7] studies. The majority (81%) of intracranial lipomas are supratentorial, 82% are in the midline, 47% near the corpus callosum and only 12% in the CPA.[8] Supratentorial lipomas are frequently associated with other congenital malformations but in themselves are usually asymptomatic. It is recognized, however, that CP angle lipomas are usually isolated abnormalities[9] and are often symptomatic, presenting with slowly progressive CN deficits.[10] There are ~100 case reports in the literature[9] of lipomas of the CPA, comprising an estimated 0.14% of all CPA tumors[9] and 0.05% of operated ones.[11]

The majority of cases reported as CPA lipomas in the literature present with progressive sensorineural hearing loss.[4,9] Only 12 cases have been reported to present with TN[5,12–22] (see Table 1).

CPA lipomas are often found to be intimately related to blood vessels and CN and adipocytes have been shown to infiltrate and separate nerve fibers in several cases.[4,5,12–19] This intimate relationship prevents excision of the lesion without incurring significant CN deficits.

In the current case there was no extrinsic lipomatous mass but rather a fatty expansion of the trigeminal nerve itself. This is consistent with "lipomatosis of nerve" which is an infiltration of the epineurium by adipose and fibrous tissue resulting in a fusiform enlargement of the nerve with concentric perineural fibrosis.[1]

Lipomatosis of nerve is rare and has not been previously reported as affecting the trigeminal nerve. However, Kato and colleagues[16] report a patient with TN who underwent surgery to excise a CP angle lipoma

Table 1 Case Reports of Trigeminal Neuralgia Caused by Cerebellopontine Angle Lipomas

Reference	Age (y)	M/F	Symptoms	Duration	L/R	Management	Findings	Complete/Incomplete Resection	Postoperatively
Budka et al[5]	26	F	L TN, Vertigo R TN, R hearing loss	2	R	Surgery	Pea sized lipoma Lipomatous infiltration of acoustic nerve	Incomplete	TN relief No additional deficit
Graves and Schemm[12]	26	M	TN, dizziness, tinnitus Mild hearing loss	5	L	Surgery	CNVII, VIII, IX, X involved. CN V compressed. Adherent to brainstem. Rhizotomy	Incomplete. Nerves embedded & vascular	TN relief Complete hearing loss
Rosenbloom et al[13]	28	M	TN V2 Hypoaesthesia V1V2 Nausea dizziness Headaches L ptosis	1 y	L	Surgery	Yellow VII VIII IX incorporated V1,V2 adjacent	Incomplete Adherent to CN, vessels, brainstem	Headache & facial pain alleviated but new hearing loss & persistent dizziness
Delgado Mije et al[14]	35	F	TN V3	NR	R	Surgery	Yellow. Adherent to brainstem, enveloping V	Incomplete CN involved	TN relief
Aihara et al [15]	47	F	TN VII dysfunction	1 y	R	Surgery	CNVII, VIII encompassed. Attached to CNV	Incomplete	NR
Kato et al[16]	13	F	TN V3	6 m	R	Surgery	Yellow Encasing VII, VIII, AICA. V infiltrated Rhizotomy	Incomplete	TN relief. V2 V3 deficits. Transient tinnitus, hearing loss, nystagmus (3 mo)
Behar et al[17]	23	M	TN V3 L ptosis	6 m	R	CBZ Surgery	CN VII, VIII, IX, X course through mass	Incomplete (CN)	Hearing loss
Celik et al[18]	32	M	TN	8	L	Surgery	Yellow Encasing VII, VIII Displacing V	Incomplete Trauma to VII &VIII	TN relief Facial n. palsy, hearing loss
Raieli et al[20]	8	M	TN V3 Facial spasm	2 y	R	CBZ Imaging	NR	NR	NR
Alafaci et al[19]	16	F	TN V2 V3 Vertigo Hearing loss	2 y	R	Surgery	Yellow Incorporating VII VIII AICA displaced causing compression Histo: nerve fibers traversing adipose tissue	Incomplete CN involved	TN relief Hearing loss same Temporary facial n. palsy
Schlierter et al[21]	24	M	TN	NR	L	Medical	NR	NR	NR
Marton et al[22]	46	M	Hearing loss (12 y) TN (10 y) severe for year	1 y	L	Surgery	Between V and VII/VIII complex	Incomplete Arachnoid debridement only	TN relief Hearing deficit same

Note the intimate relationship between cranial nerves (CN) and the lipoma. Postoperative CN deficits are common and surgical approaches favor incomplete resection. AICA, anterior inferior cerebellar artery; CBZ, carbamazepine; NR, not reported; TN, trigeminal neuralgia.

enveloping CN VII and VIII and was found, at operation, to have a swollen trigeminal nerve with subpial fatty infiltration of the trigeminal rootlets for which they performed a rhizotomy. Similarly, in one of the earliest reviews of CPA lipomas Budka[5] clearly described fatty infiltration of CN VIII and IV, confirmed histologically.

Etiology and Pathogenesis

Lipomata and lipomatosis are both benign tumors of mesenchymal origin (WHO Classification ICD 8850/0). One proposed mechanism of pathogensis for CPA lipomas relates to the embryological origin of adipocytes.[23] Adipocytes are mesenchymal cells derived from mesoderm or ectomesenchyme, which is in turn derived from the neural crest. The meninx primitiva, which subsequently forms the pia and arachnoid mater, is derived from the same cell population. It has been proposed that CPA lipomas are formed from remnants of meninx primitiva trapped at the pontomedullary sulcus at the time of neural tube folding.[23] The adipocytes are then thought to extend in the subarachnoid space along the Virchow-Robin spaces adjacent to the pia. Adipocytes are indeed found in direct connection with the leptomeninges.[5] This theory has been used to explain the intimate relationship of CPA lipomas to CN and blood vessels, which also track through these spaces. However, it does not explain the lipomatous infiltration of these nerves. The etiology of lipomatosis of nerve is unknown.[1] It is possible that these trapped adipocytes surround and infiltrate the CN, though an alternative mechanism may involve the proliferation and expansion of the adipocytes found normally within nerves.[24]

Histopathological Features

Histopathological features of lipomatosis of nerve include infiltration of epineural and perineural compartments by adipocytes and fibrous tissue resulting in fusiform enlargement of the nerve with concentric perineural fibrosis. Immunostaining is positive for S100 but is otherwise not informative. The nerves may appear macroscopically enlarged. The adipose tissue may be found surrounding as well as infiltrating the nerve.[1]

Imaging

MRI of peripheral nerve lipomatosis shows thickened nerve fascicles (low intensity on T1-weighted sequences) surrounded by tissue with characteristics of fat (high signal on T1-weighted and low signal on T2-weighted sequences) with a coaxial-cable-like appearance on cross section and spaghetti-like appearance on longitudinal planes of the nerves.[25] The authors suggest these findings are pathognomomic.

Although these imaging characteristics are difficult to identify at the skull base several studies of CPA lipoma imaging describe nerve complexes within fatty tissue.[11,23,26,27] As with lipomas at other sites, lipomatous lesions at the CPA have been shown to be high signal on T1 with variable/low signal on T2 and signal drop-out with fat-suppression sequences.[18,23,28,29] In an MR study of 44 intracranial lipomas chemical shift artifact was appreciated in all those greater than 1 cm diameter (69%).[23] Chemical shift artifact can be used to confirm the presence of fat in a lesion and disappears with fat suppression. The differential diagnosis of CPA lesions with some of these features includes epidermoids, lipomatous meningiomas, and lipomatous degeneration of schwannomas but the diagnosis of lipoma or lipomatosis of nerve can usually be made confidently with imaging alone.

Management

Surgery for CPA lipomas has poor results with studies showing improvement without additional neurological deficits in only 18 to 19%[4] of patients and new neurological deficits in 68[4] to 72%.[9] In one review[4] all but two patients who underwent "complete resection" had postoperative neurological deficits. This can be explained by the intimate relationship of the lesion to blood vessels and CN within the cerebellopontine cistern.

As current imaging modalities allow for confident diagnosis of CPA lipomas[29] surgery is no longer indicated for diagnosis. There are no reports of malignant transformation of intracranial lipomas (although there are two reports of clinically insignificant growth[4,30]) so neither is surgery indicated to prevent neoplastic progression. This, combined with the high risk of postoperative neurological deficits has led most authors to advise conservative management (imaging surveillance and neurological examination) for asymptomatic cases.

However, management of symptomatic cases remains controversial. Of the 12 cases in the literature of TN associated with CPA lipomas (see Table 1) surgery was performed in 10 cases (2 medical management[20,21]) all using a suboccipital retromastoid approach. Surgical resection was limited in most cases due to the incorporation of CN within the mass.[12–15,17,19] Of those who underwent surgery all patients had complete relief of TN but at the expense of other CN deficits, notably hearing, in six cases (see Table 1).

Some authors advocate rhizotomy,[12,16] nerve decompression[22] or, as in the current case, arachnoid debridement[22] without lipoma resection to achieve symptom relief while avoiding additional neurological deficits. Alafaci et al[19] described the lipoma causing neurovascular compression via displacement of the anterior inferior cerebellar artery[19] and advise neurovascular decompression alone.

The presence of CN within the lipomatous mass is the reason that surgical resection of CPA lipomas is often incomplete[11] and is associated with a high incidence of additional CN deficits postoperatively.[9,10] In the case of an extrinsic mass with CN coursing through it (a classic CPA lipoma) partial excision can decompress the nerve and provide symptom relief. The surgical approach is different in true lipomatosis of nerve where the nerve is expanded by adipocytes—in such cases any attempt at surgical excision would inevitably lead to nerve damage and likely neurological deficit. However, as demonstrated in the current case, adhesiolysis can provide symptomatic relief.

CONCLUSION

We report a case of TN caused by trigeminal nerve lipomatosis. Our case provides evidence that arachnoid adhesiolysis can achieve effective, safe symptom relief.

We encourage the distinction to be made between lipomatosis of nerve (nerves filled with adipocytes) and CPA lipomas (nerves embedded in adipocytes). Once defined in this way it is clear that to attempt surgical excision of a lipomatous nerve would inevitably result in neurological deficits, whereas some true CPA lipomas may be amenable to cautious partial resection. We aim to illustrate that safe surgical treatment is possible and remains appropriate in patients with intractable symptoms. Patients should be warned of the high risk of postoperative CN deficits.

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