Trigeminal Amyloidoma: Case Report and Review of the Literature

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ABSTRACT

The authors present a case of amyloid infiltration involving the trigeminal nerve that mimicked a malignant cavernous sinus tumor with perineural tumor infiltration. A 64-year-old man presented with trigeminal nerve numbness. Imaging revealed a plaque-like enhancing lesion along the right lateral cavernous sinus extending anteriorly into Meckel's cave and involving the proximal V2 and V3 branches of the trigeminal nerve. The patient underwent an extradural frontotemporal craniotomy with middle fossa exposure of the cavernous sinus to diagnose and treat the presumed malignant cavernous sinus tumor. A reddish mass involving the lateral dural wall of the cavernous sinus was resected. The gasserian ganglion, V2, and V3, the latter of which was biopsied, were enlarged. Permanent histopathological studies showed microscopic eosinophilic, amorphous material, which stained positive for Congo red, and an absence of neoplastic cells. The final diagnosis was amyloidoma. Thus, amyloidomas can involve the trigeminal nerve or ganglia and should be considered in the differential diagnosis of a cavernous sinus lesion mimicking a tumor. Patients may have symptomatic improvement of trigeminal neuropathy with resection of the amyloidoma outside the nerve capsule that is compressing the nerve, while resection of the lesion from within the capsule may result in permanent trigeminal nerve dysfunction.

KEYWORDS: Gasserian ganglion, trigeminal, amyloidoma

Amyloidomas of the nervous system are extremely uncommon and are invariably of the amyloid light-chain lambda type.¹ Typically, cerebral amyloidomas occur as single or multiple supra-

tentorial masses located in the white matter of the brain parenchyma.¹ Only rarely has amyloid disease been described to involve other nervous tissue, and only 12 cases of amyloid involving the gasserian

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ganglion or trigeminal nerve have been reported.²⁻¹¹ These patients may present with a pattern of trigeminal amyloidosis, starting with trigeminal anesthesia, hypalgesia, or dysesthesia associated with progressive facial anesthesia and, possibly, weakness or atrophy of the muscles of mastication.¹² When imaging reveals a mass in Meckel's cave, a mass around the gasserian ganglion or trigeminal branches, or a cavernous sinus lesion, it is important to consider amyloidoma, a benign process, in the differential diagnosis to select the appropriate management and surgical strategy. We report a patient with progressive trigeminal nerve sensory loss from an amyloidoma of the trigeminal nerve; this patient had a dural-based mass and an enlarged trigeminal nerve that mimicked a malignant cavernous sinus tumor with perineural tumor infiltration.

CASE REPORT

A 64-year-old man had a 9-month history of progressive numbness and tingling on the right side of his face without associated pain. He had decreased sensation in the distribution of V2 and V3 of the trigeminal nerve. Magnetic resonance imaging (MRI) showed a plaque-like enhancing lesion along the right cavernous sinus extending anteriorly into Meckel's cave. The mass involved the proximal V2 and V3, extending to the foramina rotundum and ovale, respectively, and to the vidian nerve. These nerves also appeared enlarged (Fig. 1). The preoperative diagnosis of this lesion was malignant cavernous sinus tumor associated with perineural tumor infiltration or, less likely, meningioma or schwannoma.

Figure 1 (A-C) Axial T1-weighted magnetic resonance images through the central skull base after contrast administration. (A) Enhancing tissue representing amyloidoma is evident in the lower Meckel's cave region on the right (arrow). (B) Perineural enhancement extends into the foramen rotundum (arrow) and (C) foramen ovale (arrow). Coronal STIR and postcontrast T1-weighted magnetic resonance images. (D) Amyloid deposition appears as a filling defect in the lateral aspect of Meckel's cave on STIR image (arrow). (E) Corresponding enhancement is demonstrated (arrow).

Figure 2 Photomicrograph. (A) Specimen shows deposits of eosinophilic, amorphous material. No significant inflammatory cells or neoplastic cells are present. (Hematoxylin and eosin staining, original magnification, $\times 100$). (B) Typical pattern of apple-green birefringence is present in specimen stained with Congo red and viewed with polarized light, $\times 40$.

The results of a chest x-ray, complete blood count, and serum chemistry test were normal. Given the patient's progressive trigeminal symptoms, he was offered surgery for the purpose of diagnosis and possible resection. He underwent a right fronto-temporal craniotomy with middle fossa exposure of the cavernous sinus through an extradural exposure. A reddish mass involving the lateral dural wall of the cavernous sinus was noted. The bone around the foramen rotundum and foramen ovale was drilled to afford decompression of the enlarged V2 and V3 branches. After the lateral wall of the cavernous sinus was removed, the trigeminal nerve was inspected. The gasserian ganglion and the V2 and V3 were enlarged and appeared infiltrated, although the fascicular pattern of the nerve was maintained. A biopsy of a fascicle of the V3 at the entrance of the nerve branch through the foramen ovale was obtained.

Permanent histopathological studies showed microscopic eosinophilic, amorphous material, which stained positive for Congo red (Fig. 2) and thioflavine S. Immunohistochemistry studies showed staining for lambda light chains. No neoplastic cells were identified, but reactive meningo-epithelial cells were present. The samples from the dural mass and the fascicle of V3 were identified to contain extensive amyloid deposition consistent with amyloidoma.

The patient's postoperative course was uneventful. After decompression, sensation in his lower and middle face improved and the improvement has remained stable for more than 1 year of follow-up. Additional studies showed no evidence of systemic amyloidosis. MRI obtained at 1 year after treatment showed some diminished enhancement of the cavernous sinus.

DISCUSSION

Amyloid is an abnormal insoluble protein. Under certain pathological conditions, it can be deposited in the extracellular space and can involve almost every organ system.¹³ Although amyloid deposition within the brain can take many forms, including cerebral amyloid angiopathy or senile plaques of Alzheimer dementia, tumor-like deposition (amyloidoma) is extremely uncommon.¹³ Amyloidoma is defined as primary solitary amyloidosis where no plasma-cell dyscrasia or abnormal serum proteins are detectable.¹⁴ The source of amyloid protein that forms a tumor in the central nervous system is unclear. It is thought to derive from components that leak from vessels or to be synthesized at the site of deposition from coexistent plasma cells. However, the origins of intracerebral plasma cells

observed in some cerebral amyloidomas are not understood.^{13,15}

At presentation, the mean age of patients harboring cerebral amyloidomas is 47.8 years, and there is a slight female predominance.¹³ Amyloidomas are located in the brain parenchyma.¹ Patients have solitary or multiple supratentorial white matter masses that exert little or no mass effect on the surrounding anatomy; they extend medially to the lateral ventricle ependyma and have irregular margins.¹³ Computed tomography (CT) typically shows a mass that varies from hypodense to patchy increased density and contrast enhances. T1-weighted MRI of cerebral amyloidoma mostly shows hypointense lesions, but amyloidoma can also appear isointense or hyperintense. On T2-weighted MRI, mixed high and low signal intensity can be present, with lesions enhancing to a variable degree.¹³ The clinical course of intracerebral amyloidomas is benign, and these lesions can grow slowly. Occasionally, amyloidoma regrows after resection.^{13,15} However, the natural history of this rare lesion is not fully understood because of the low incidence of the disease.

Amyloidomas have affected other nervous tissue, including spinal roots,¹⁶ the brachial plexus,¹⁷ and peripheral nerves.¹⁸ Rarely, amyloid disease has caused trigeminal neuropathy from its involvement with the gasserian ganglion, and why there is a predisposition for these ganglia is unclear.²⁻¹¹ Overall, there have been 12 reports of patients with trigeminal amyloidomas, beginning with the first case described by Daly et al. in 1957⁴ (Table 1). These patients all presented with some form of trigeminal neuropathy, including trigeminal hypalgesia, dysesthesia, or face anesthesia, and rarely with V3 motor dysfunction manifesting as weakness or atrophy of the muscles of mastication. In most cases, the hypalgesia or dysesthesias preceded the onset of facial anesthesia. Over time the distribution of the numbness on the face increased. The duration of symptoms before treatment has ranged from 2 months to as long as 10 years.³ In two cases, patients had bilateral trigeminal nerve dysfunction from bilateral amyloidomas.^{6,8}

Although all patients presented with trigeminal neuropathy and many with continuous facial pain, the symptoms were distinct from trigeminal neuralgia, which is associated with episodes of intense, stabbing, electric shock-like pain and with specific triggers.

With advances in imaging, it has been possible to improve characterization of these lesions. With increased knowledge of amyloidomas, it may be possible to identify these lesions on imaging before surgery (Table 1). In only one study⁷ did the authors describe the density of the amyloidoma on CT, and they found that the tumor was isodense. In contrast to cerebral amyloidomas, these trigeminal variants often appeared isointense on T1-weighted MRI and hypointense or of mixed signal intensity (both hypointense and isointense) on T2-weighted MRI. The mixed signal intensities of amyloidomas on T2-weighted images have been attributed to the uneven deposition of amyloid protein.⁷ The low signal intensity on T2-weighted imaging related to increased amyloid deposition may suggest the diagnosis of amyloidoma, and this feature may differentiate amyloidoma from other lesions, including schwannomas.^{10,11} In fact, the most common preoperative diagnosis of the 12 reported patients with amyloidomas was schwannoma. Finally, a common characteristic on MRI was uniform enhancement localized to Meckel's cave with enhancement of the ganglion, nerve branches, or both.

Most authors have taken similar approaches to the management of trigeminal amyloidomas (Table 1). Typically, these tumors have been located exclusively within the nerve capsule and have infiltrated in and around the nerve fibers. Many of these patients underwent a craniotomy with incision of the nerve capsule and biopsy of the abnormal tissue without an attempt at further resection. In these cases, follow-up information and imaging were not provided. Thus it is unclear whether the biopsy affected the patients' symptoms or the natural history of the disease.

Several cases have involved resection of the lesion.^{2-5,7,10} Matsumoto and colleagues⁷ resected

Table 1 Clinical Review of 13 Reported Amyloidomas of the Gasserian Ganglion

Patient No.	Reference	Age	Sex	Symptom	Location per Symptoms or Imaging	CT	MRI	Tumor Location at Surgery	Treatment	Follow-up
1	Daly et al, ⁴ 1957	42	M	V2/V3 trigeminal pain with progressive numbness	Right gasserian ganglion and V2 and V3	NA	NA	Mostly within nerve capsule with small component outside; 50% trigeminal nerve bundles replaced by amyloid	Craniotomy with extensive resection of amyloidoma around nerve fibers	After surgery, resolution of pain with complete numbness of V1, V2, and V3; complete V3 motor weakness
2	Plogsties, ⁹ 1964	54	M	Numbness and trigeminal pain	Right gasserian ganglion	NA	NA	Within nerve capsule	Craniotomy for biopsy of infiltrated ganglion	NA
3	Borghi and Tagliabue, ² 1961	58	F	V1/V2/V3 incomplete numbness, trigeminal pain, and motor weakness	Right Meckel's cave	NA	NA	Lesion at Meckel's cave but ganglion and nerve not identified	Craniotomy for complete tumor resection	At 2 years, complete sensory loss V1–3, complete V3 motor weakness, and resolution of pain
4	DeCastro et al, ⁵ 1976	59	M	Numbness and minimal pain V2 and V3 progressing to V1	Right gasserian ganglion	NA	NA	Lesion with components outside of nerve and within nerve without discrete nerve capsule	Craniotomy for complete tumor resection	After surgery, complete V2 and V3 sensory loss, resolution of pain, transient weakness V3 motor
5	Bornemann et al, ³ 1993	32	F	Numbness and pain V2 and V3; atrophy of muscles of mastication	Left gasserian ganglion	Normal	NA	Lesion within Meckel's cave	Craniotomy for resection without other details	After surgery, resolution of pain, but at 9 years' follow-up, sensory and motor deficits were unchanged
6	Bornemann et al, ³ 1993	49	F	V1/V2/V3 numbness and pain	Left Meckel's cave to V2 and V3 branches	Normal	Uniform enhancement	Lesion within Meckel's cave	Craniotomy for resection without other details	After surgery, improvement of pain, but at 1 year continued numbness with atrophy of muscles of mastication
7	Bornemann et al, ³ 1993	45	F	V1/V2/V3 numbness	Left Meckel's cave	Enhancement of lesion	Slight marginal enhancement	Lesion within Meckel's cave	Craniotomy for resection with further details	After surgery, pain resolved

(Continued)

Table 1 (Continued)

Patient No.	Reference	Age	Sex	Symptom	Location per Symptoms or Imaging	CT	MRI	Tumor Location at Surgery	Treatment	Follow-up
8	O'Brien et al, ⁸ 1994	49	F	*Left decreased sensation V1-V3, weak V3 motor, left V2 trigeminal pain, right V3 numbness	Left gasserian ganglion and trigeminal branches	NA	Uniform enhancement	Within nerve capsule	Craniotomy for biopsy of infiltrated ganglion	NA
9	Kirch et al, ⁶ 1998	34	M	*Bilateral numbness V1 > V2 or V3, microbial keratitis	Bilateral gasserian ganglion masses	NA	Hypointense on T1-weighted, heterogeneous on T2-weighted imaging; uniform enhancement	Within nerve capsule	Craniotomy for biopsy of infiltrated ganglion	NA
10	Vorster et al, ¹⁰ 1998	46	F	V2/V3 numbness progressing to trigeminal pain	Right gasserian ganglion and V1, V2, and V3	NA	Isointense on T1-weighted, hypointense on T2-weighted imaging; uniform enhancement	Outside and within nerve capsule	Craniotomy for subtotal resection; tumor intermingled with trigeminal branches unable to be resected	At 1 month, complete resolution of pain with complete anesthesia of V1 and V2, normal V3 motor function with minimal V3 anesthesia
11	Matsumoto et al, ⁷ 1999	41	F	V2/V3 numbness	Left Meckel's cave	Isodense	Isointense on T1-weighted, heterogeneous on T2-weighted imaging; uniform enhancement	Outside of nerve capsule	Craniotomy for total resection	At 2 months, improved sensation
12	Yu and de Tilly, ¹¹ 2004	62	M	Trigeminal pain	Left Meckel's cave	NA	Isointense on T1-weighted, hypointense on T2-weighted imaging; uniform enhancement	Within nerve capsule	Craniotomy for biopsy of infiltrated ganglion	NA
13	Current case, 2007	64	M	V2/V3 numbness	Right lateral cavernous sinus into Meckel's cave and V2 and V3 trigeminal nerves	NA	Isointense on T1-weighted, hypointense on T2-weighted imaging; uniform enhancement	Outside and within nerve capsule	Craniotomy for resection of amyloidoma outside capsule compressing nerve and decompression of foramen	At 2 months, improved sensation

*Bilateral amyloidomas on imaging. Note: None of these patients had any evidence of systemic amyloidosis, underlying malignancy, or inflammatory disease. CT, computed tomography; MRI, magnetic resonance imaging; NA, not available.

an amyloidoma through an extradural skull base approach and found the tumor located between the lateral wall of the cavernous sinus and the V2 and V3. The tumor adhered slightly to the trigeminal nerve but was easily removed so that gross total resection was obtained. In a similar surgery, Vorster and coworkers¹⁰ resected an amyloidoma located medial to the gasserian ganglion, which was clearly distinguishable from it. However, amyloid was intermingled with the V1, V2, and V3 branches. The surgical plane was lost where the lesion was intimately involved with these nerves. Thus, a subtotal resection was performed to spare the function of the nerves. In contrast to the patient described by Matsumoto et al, their patient suffered an increase in numbness from the surgery. In another two reports,^{2,5} it was difficult to differentiate lesion from nerve. Gross total resection was attempted, but both patients had increased sensory loss and weakness after surgery. Finally, the patient described by Daly and coworkers⁴ underwent an extensive piecemeal resection of all of the abnormal tissue intermingling with the nerve fibers within the nerve capsule. After surgery, the patient had complete trigeminal numbness in all distributions and V3 motor weakness. Overall, decompressive surgery with debulking of tumor outside the capsule was associated with improvement or resolution of trigeminal pain and numbness, while extensive resection within the nerve capsule was associated with worse trigeminal dysfunction.^{2,4,5,10}

In the current case, the tumor located outside the nerve was resected completely through an extradural approach similar to two of the cases above^{7,10}; however, the tumor within the nerve capsule involving the nerve fibers was biopsied but not resected. The V2 and V3 branches were markedly enlarged; thus, we decompressed the foramina rotundum and ovale. The tumor within the trigeminal nerve was not resected to preserve function. This surgical strategy offers immediate symptomatic relief from trigeminal pain and dysesthesia without increasing sensory loss or V3 motor dysfunction. Long-term imaging has not been reported from any of the 12 cases. Therefore, the natural

history of the disease and whether the lesion has the capacity to regrow and cause symptoms after subtotal resection are unknown. In one report,³ two patients with postoperative deficits were followed for 1 and 9 years, without a clinical recurrence of symptoms.

This case demonstrates that, in addition to meningiomas, schwannomas, malignant cavernous sinus tumors, and inflammatory disorders, amyloidomas should be considered as a possibility in the differential diagnosis of a cavernous sinus lesion or of a lesion arising from the gasserian ganglion or within Meckel's cave.

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REFERENCES

1. Laeng RH, Altermatt HJ, Scheithauer BW, Zimmermann DR. Amyloidomas of the nervous system: a monoclonal B-cell disorder with monotypic amyloid light chain lambda amyloid production. *Cancer* 1998;82:362-374
2. Borghi G, Tagliabue G. Primary amyloidosis in the gasserian ganglion. *Acta Neurol Scand* 1961;37:105-110
3. Bornemann A, Bohl J, Hey O, et al. Amyloidoma of the gasserian ganglion as a cause of symptomatic neuralgia of the trigeminal nerve: report of three cases. *J Neurol* 1993; 241:10-14
4. Daly DD, Love JG, Dockerty MB. Amyloid tumor of the gasserian ganglion. *J Neurosurg* 1957;14:347-352
5. DeCastro S, Sparks JR, Lapey JD, Freidberg SR. Amyloidoma of the gasserian ganglion. *Surg Neurol* 1976;6:357-359
6. Kirch IE, Beaver HA, Lee AG, Green LK, Tang RA. Microbial keratitis as the manifestation of trigeminal amyloidoma at initial presentation. *J Neuroophthalmol* 1998;18:192-195
7. Matsumoto T, Tani E, Fukami M, Kaba K, Yokota M, Hoshii Y. Amyloidoma in the gasserian ganglion: case report. *Surg Neurol* 1999;52:600-603
8. O'Brien TJ, McKelvie PA, Vrodo N. Bilateral trigeminal amyloidoma: an unusual case of trigeminal neuropathy with a review of the literature. Case report. *J Neurosurg* 1994; 81:780-783
9. Plogsties HR. On amyloid tumors of the gasserian ganglion [in German]. *Acta Neurochir (Wien)* 1964;12:120-130

10. Vorster SJ, Lee JH, Ruggieri P. Amyloidoma of the gasserian ganglion. *AJNR Am J Neuroradiol* 1998;19:1853–1855
11. Yu E, de Tilly LN. Amyloidoma of Meckel's cave: a rare cause of trigeminal neuralgia. *AJR Am J Roentgenol* 2004;182:1605–1606
12. Love S, Bateman DE, Hirschowitz L. Bilateral lambda light chain amyloidomas of the trigeminal ganglia, nerves and roots. *Neuropathol Appl Neurobiol* 1997;23:512–515
13. Gandhi D, Wee R, Goyal M. CT and MR imaging of intracerebral amyloidoma: case report and review of the literature. *AJNR Am J Neuroradiol* 2003;24:519–522
14. Bauer WH, Kuzma JF. Solitary "tumors" of atypical amyloidoma (paramyloid). *Am J Clin Pathol* 1949;19:1097–1112
15. Eriksson L, Sletten K, Benson L, Westermark P. Tumour-like localized amyloid of the brain is derived from immunoglobulin light chain. *Scand J Immunol* 1993;37:623–626
16. McKechnie S, Yang F, Harper CG, et al. Amyloidoma of a spinal root. *Neurology* 2003;61:834–836
17. Consales A, Roncaroli F, Salvi F, Poppi M. Amyloidoma of the brachial plexus. *Surg Neurol* 2003;59:418–423; discussion 423
18. Pizov G, Soffer D. Amyloid tumor (amyloidoma) of a peripheral nerve. *Arch Pathol Lab Med* 1986;110:969–970

Commentary

This is an interesting case with a concise and comprehensive review of amyloidoma involving the trigeminal ganglion. The lesion is rare and almost indistinguishable from other lesions in the parasellar

area that the authors have included in the differential diagnosis. Interestingly, no other cranial nerve ganglia were reportedly involved by this pathology. This is another reason that the results of radiation without a tissue diagnosis are unreliable. I commend the authors for bringing this case to our attention and for reviewing the current literature.

Chandranath Sen, M.D.¹

Commentary

The authors have described a rare condition involving the lateral wall of the cavernous sinus and trigeminal nerve. Because of the patient's symptoms and the location involved, the lesion could be mistaken for a trigeminal schwannoma or chondrosarcoma. However, the radiological features appeared to be quite distinct—the lesion was hypointense or isointense on T2-weighted MRI, in contrast to these other two tumors. The authors' strategy of extraneural resection and nerve decompression appears to be a good one, especially if the diagnosis can be made by frozen section, and the tumor is distinguished from malignant lesions such as adenoid cystic carcinoma.

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