Calcifying Pseudoneoplasms of the Skull Base Presenting with Cranial Neuropathies: Case Report and Literature Review

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Abstract

Objectives We report our institutional experience with calcifying pseudoneoplasms of the skull base that presented with cranial neuropathies. These lesions are also known as fibro-osseous lesions, cerebral calculi, or brain stones.

Results One patient presented with facial numbness and retro-orbital pain secondary to compression of the maxillary branch of the trigeminal nerve at the anterior portion of the infratemporal fossa. The other patient presented with occipital headaches and hypoglossal nerve palsy. This patient was found to have a calcified lesion in the posterior fossa, which eroded the left occipital condyle.

Conclusion Calcifying pseudoneoplasms are benign, slow-growing masses that are apparently cured by gross total resection. Even with incomplete tumor resection, the prognosis is considered to be favorable. We advocate a minimally invasive surgical resection of such tumors involving the cranial nerves.

Introduction

Fibro-osseous lesions, also reported as cerebral calculi, brain stones, or calcifying pseudoneoplasms of the neuraxis are extremely rare. These lesions demonstrate a characteristic histopathologic appearance. Since the first report by Miller in 1922,1 29 articles (56 cases) have been reported in the international literature.1–29 These lesions appear to be slow growing and usually carry an excellent prognosis with gross total excision.

The pathogenesis of these lesions remains unclear, but a reactive proliferative process, rather than a neoplastic one, is favored by most investigators.2–7 In addition, it is also believed that this lesion is probably an unusual expression of tumoral calcinosis. They can occur anywhere within the neuraxis, both intra-axial and extra-axial. The patients with intracranial lesion often presented with seizure, headache, or other symptoms related to local compression, whereas patients with spinal lesion commonly presented with pain in the affected area. In this report we describe our experience of calcifying pseudoneoplasms, one located in the infratemporal fossa adjacent to the foramen rotundum, and the other in the posterior fossa involving one of the occipital condyles (previously reported), both of which caused cranial nerve deficits.8 The appearance of this unusual tumor is illustrated, the radiological evaluation and pathological findings are discussed, and the literature is reviewed.
Case Reports

Case 1
A 56-year-old man with a history of chronic right-ear infections had images ordered by his primary care physician for evaluation. A computed tomography (CT) scan and subsequent magnetic resonance imaging (MRI) scan were performed. These images showed a partially calcified mass in the anterior infratemporal fossa on the right side. The patient was also having right-sided facial numbness and occasional orbital pain around the maxillary branch of the trigeminal nerve (V2). He was seen and evaluated by an otolaryngologist, who attempted a transnasal approach to the lesion. However, due to technical difficulties in gaining complete access to the lesion, the surgery was unsuccessful. The patient was referred to our institution to be considered for a skull base approach to excise the lesion.

Examination
A CT scan revealed a partially calcified mass lesion located inferior to the floor of the right anterior temporal fossa (Fig. 1A). MRI demonstrated a mass that was heterogeneous in signal (Figs. 1B, C, D). The mass measured 2.0 × 1.9 cm in greatest dimensions. It was largely hyperintense on the T2-weighted image, with multiple small-lobulated areas of hypointensity within. There were some areas of mild heterogeneous enhancement within the lesion. The mass abutted the floor of the posterior aspect of the right orbit.

Operation
A right preauricular anterior infratemporal fossa skull base approach was performed. After myocutaneous flap elevation, the anterior temporal region was well exposed. A subtemporal craniotomy was made. The V2 nerve was exposed easily at the markedly enlarged foramen rotundum with the extradural temporopolar approach. The mass was identified under the V2 nerve. The tumor was gradually elevated from the surrounding tissues with careful attention to the abducens nerve. It was a very smooth, rounded mass with a large roundish central core of calcification. Postoperative course was uneventful. His facial numbness still remained slightly, but he denied any orbital pain. Postoperative MRI demonstrated no obvious residual tumor (Fig. 1E).

Pathological Examination
Multiple pinkish-white tissue fragments and bone fragments were noted within the lesion, with an aggregate dimension of 3.5 × 3.0 × 1.0 cm. Microscopic examination showed a sparsely cellular fibromyxoid stroma containing bland fibroblastic nuclei and scattered blood vessels. It also showed a large nerve with associated ganglion cells involved by hypocellular fibrillar tissue that is partly calcified (Fig. 2A). There was no evidence of neoplasia, malignancy, or acute inflammation. There was no epidermal inclusion cyst or squamous epithelium, nor was there keratin. Immunohistochemical analysis was not performed in this case. The final histological diagnosis was consistent with a calcifying pseudoneoplasm.
Case 2
A 35-year-old man presented with a 6-month history of progressively worsening occipital headaches with some generalized fatigue, tinnitus, and dizziness.

Examination
Initial neurological examination showed a slight asymmetry of the soft palate and the tongue deviation toward the left side. Neither obvious tongue atrophy nor any fasciculations were noted. He had a subtle left dysmetria and a negative Romberg's sign. He eventually underwent CT and MRI scans. The CT scan demonstrated a large calcified mass in the left posterior fossa that appeared to arise from the left occipital condyle, causing mass effect onto the brainstem and cerebellum. MRI imaging demonstrated a 4.3 × 2.9 × 2.9 cm mass that involved the left posterior aspect of the clivus and extended exophytically into the posterior fossa (Fig. 3A, B). A majority of the mass projected intradurally. There was rightward deviation of the brainstem and narrowing of the inferior aspect of the fourth ventricle.

Operation
A left far-lateral transcondylar approach was performed along with a retro-infralabyrinthine mastoidectomy. During the partial mastoidectomy, the left sigmoid sinus was found to be occluded. The mastoidectomy was followed anteriorly until the facial nerve was identified. The lateral suboccipital craniotomy was then performed and the foramen magnum was opened. The tumor had eroded through the bone into the foramen magnum. The condyle then was partially resected. The condyle was filled with tumor, which was mostly calcified; the presence of large balls of calcium made us think that this might have been a meningioma. The dura was involved with the tumor. Underneath, a hard bony mass was found,
Calcifying, fibro-osseous lesions known as calcifying pseudoneoplasms of the neuraxis, cerebral caluli, or brain stones are extremely rare and are usually seen at the cranial base, commonly adjacent to the dura mater or the arachnoid.1–20 However, they can occur anywhere within the neuraxis.2,3,5 It has been suggested, but not proven, that calcifying pseudoneoplasms may develop as a healing response to an array of inciting factors, which can account for the variations in histopathologic features.3,5,7 Although the histopathologic characteristics of this unusual lesion are not yet understood, a reactive rather than a hamartomatous process has been favored.3,5

Our review of the literature revealed 29 reported articles with 56 cases of these lesions (►Table 1). Articles were identified via PubMed search using the key words "fibro-osseous lesion," "calcifying pseudoneoplasm," "pseudotumor," "cerebral caluli," "brain stone," "neural axis," "neuraxis," "central nervous system (CNS)," "intracranial," "brain," and "spine" alone and in combination.

The first reported case was described as "calci within the brain" by Miller in 1922.2 The terms "calcifying pseudoneoplasms of the neural axis" was used by Bertoni et al at first in 1990. There have been 30 male and 23 female patients (gender unknown in three cases) reported, with ages ranging from 6 to 83 years (mean age 46.1 years). These lesions most often arose from intracranial space (intracranial type: 37 cases; 66.1%) followed by spine (spine type: 15 cases; 26.8%) and craniovertebral junction (CVJ type: four cases; 7.1%). The mean age of intracranial type, CVJ type, and spine type were 44.6, 52.8, and 47.7 year respectively.

The patients with intracranial type most commonly presented with seizure (31.6%) followed by headache (13.2%) and cerebellar sign (5.3%).1–23 Three patients (8.1%) were found incidentally, and seven cases (18.9%) were autopsy findings. Only four cases out of 37 presented with symptoms related to CN involvement.2,3,17 Over half of the intracranial type lesions were seen in the supratentorial region (54.1%). Infratentorial lesions were seen in 29.7% of them (not described in six cases). The patients with CVJ type most commonly presented with neck pain (75%), followed by headache (25%), facial pain (25%) and lower-extremity stiffness.3,5,20,24 Three of four cases were mainly located at the foramen magnum and another at the clivus to the upper cervical spine.

The patients with the “spinal” type commonly presented with pain in the affected area (86.7%; back pain; seven cases, neck pain; four cases, hip pain; two cases; and leg pain, one case) and gait disturbance (20.0%) or sensorial disturbance (13.3%).3,5,25–29 Only one case (6.6%) was found incidentally. The lesions were seen at the cervical spine (46.7%), lumbar spine (33.3%), and thoracic spine (20%). Among them, C2, T-10, and L4-L5 were the most commonly affected levels. Interestingly, 86.7% of the spine type lesions were found at the extradural location near the intervertebral disc level (one case in the subarachnoid space), whereas all cases except for one (97.7%; not described in one case) of intracranial type and all of CVJ-type lesions occurred in the intradural space. Only two cases out of 57 reported cases had suffered a recurrence a couple of years after the initial excision, however, the outcome is often considered to be excellent even if the tumor was not resected completely.3,25

When considering the differential diagnosis for calcifying intra-axial or extra-axial lesions, the uniform T1 and T2 hypointensity without solid enhancement is a key distinguishing feature.2 The primary differential considerations for the extra-axial calcifying pseudoneoplasms at the skull base are meningioma, chordoma, chondrosarcoma, and vestibular schwannoma. Specifically, the uniform T2 hypointensity without enhancement would be unusual for chordoma, chondrosarcoma, or vestibular schwannoma. Important differential diagnosis considerations for intra-axial calcified masses include such tumors as gangliogliomas and oligodendrogliomas, vascular lesions such as cavernous malformations and even infections such as tuberculosis.2,3 The differential diagnosis for spine lesions included disc herniation, synovial cyst, epidural abscess, meningioma, or possibly an old calcified hematoma.26

• Calcifying pseudoneoplasms are composed of fibro-osseous tissue with an amorphous calcification mixed with spindle and giant cells palisading generally around the chondroid or calcifying material.2–7 Microscopically, the differential diagnosis of calcifying pseudoneoplasms includes a variety of reactive lesions such as granulomatous disease, herniated disk material, and even neoplastic lesions like chondroid chordoma, chondroma, chondrosarcoma, metastatic meningioma, or calcified primary parenchymal central nervous system tumors.6 In most cases, immunohistochemistry findings for
| Author/Year               | Description                        | Age/Sex | Symptoms     | Location     | Intracranial | CVJ | Spine | Intra- | Extra-Dural |
|--------------------------|------------------------------------|---------|--------------|--------------|--------------|-----|-------|--------|-------------|
| Miller 1922              | calculi within the brain           |        |              | brain        | +            |     |       |        |             |
| Swartenbroekx 1962       | brain stones                       |        |              | brain        | +            |     |       |        |             |
| Tiberin and Beller 1963  | brain stones or cerebral calculi   |        |              | brain        | +            |     |       |        |             |
| Averback 1977            | brain stones                       | 30M     | seizure      | frontal      | +            |     |       |        |             |
| Rhodes and Davis 1978    | fibro-osseous component            | 27F     | HA           | frontal      | +            |     |       |        |             |
|                          |                                    | 55F     | autopsy finding | brain, dura  | +            |     |       |        |             |
|                          |                                    | 60M     | autopsy finding | cerebellum   | +            |     |       |        |             |
|                          |                                    | 74F     | autopsy finding | brain, dura  | +            |     |       |        |             |
|                          |                                    | 46M     | autopsy finding | 4th ventricle | +            |     |       |        |             |
|                          |                                    | 62M     | autopsy finding | pineal meninges | +      |     |       |        |             |
|                          |                                    | 83M     | autopsy finding | brain, dura  | +            |     |       |        |             |
| Jun and Burdick 1984     | fibro-osseous lesion               | 55M     | HA           | corpus callosum | +     |     |       |        |             |
| Maruki et al. 1984       | brain stone                        | 43F     | seizure      | temporal     | +            |     |       |        |             |
| Hashimoto et al. 1986    | brain stone                        | 29M     | seizure      | temporal     | +            |     |       |        |             |
| Nitta et al. 1987        | brain stone                        | 28F     | vertigo, nausea | cerebellum   | +            |     |       |        |             |
| Garen et al. 1989        | fibro-osseous lesion               | 44M     | facial pain  | Meckel's cave | +            |     |       |        |             |
| Bertoni et al. 1990      | calcifying pseudoneoplasm          | 31M     | hoarseness, JF syndrome | CPA, JF | +            |     |       |        |             |
|                          |                                    | 50M     | neck pain    | FM           | +            |     |       |        |             |
|                          |                                    | 48M     | XI CN palsy  | cerebellar tonsil | +     |     |       |             |
|                          |                                    | 23M     | back pain    | spine, T10   | +            |     |       |        |             |
|                          |                                    | 58M     | back pain    | spine, C2-C3 | +            |     |       |        |             |
|                          |                                    | 32M     | seizure      | frontal      | +            |     |       |        |             |
|                          |                                    | 45F     | autopsy finding | skull base | +            | ND  |       |        |             |
|                          |                                    | 58M     | hoarseness, hearing loss | JF | +            |     |       |        |             |
|                          |                                    | 12M     | neck pain    | spine, C6    | +            |     |       |        |             |
|                          |                                    | 32M     | back pain    | spine, L4-L5 | +            |     |       |        |             |
|                          |                                    | 33F     | back pain    | spine, T9    | +            |     |       |        |             |
|                          |                                    | 68F     | hip pain     | spine, L4-L5 | +            |     |       |        |             |

(Continued)
| Author/Year          | Description                | Age/Sex | Symptoms                        | Location                  | Intracranial | CVJ | Intra-Dural | Extra-Dural |
|---------------------|----------------------------|---------|---------------------------------|---------------------------|--------------|-----|-------------|-------------|
| Smith et al. 1994   | fibro-osseous lesion       | 48M     | hip pain, leg pain              | spine, L2-L3              | +            | +              |
| Tokunaga et al. 1995| brain stone                | 72F     | tinnitus, ataxia               | cerebellum                | +            | +              |
| Qian et al. 1999    | fibro-osseous lesion       | 33F     | developmental delay            | temporal                  | +            | +              |
| Shrier et al. 1999  | fibro-osseous lesion       | 32F     | incidental finding             | temporal                  | +            | +              |
| Tsugu et al. 1999   | calcifying pseudotumor     | 22F     | seizure                        | parietal                  | +            | +              |
| Chang et al. 2000   | calcifying pseudotumor     | 60M     | neck pain                      | spine, C2                 | +            | +              |
| Mayr et al. 2000    | calcifying pseudoneoplasm  | 58M     | LE jerkiness                   | spine, T10-T12            | +            | +              |
| Albu et al. 2001    | fibro-osseous lesion       | 53F     | HA, visual loss                | frontal-parietal          | +            | +              |
| Tatke et al. 2001   | calcifying pseudoneoplasm  | 6M      | seizure                        | temporal                  | +            | +              |
| Ghosal et al. 2007  | cerebral calculi           | 26F     | seizure                        | lateral ventricle         | +            | +              |
| Park et al. 2008    | calcifying pseudoneoplasm  | 59F     | neck pain, radiculopathy       | spine, C7-T1              | +            | +              |
| Rodriguez et al. 2008| calcifying pseudoneoplasm | 67F     | incidental finding             | cerebellum                | +            | +              |
| Aiken et al. 2009   | calcifying pseudoneoplasm  | 35M     | seizure                        | temporal                  | +            | +              |
| Montibeller et al. 2009| calcifying pseudoneoplasm | 49F     | seizure                        | hippocampus               | +            | +              |
| Mohapatra et al. 2010| calcifying pseudoneoplasm | 59M     | UE numbness                    | parietal                  | +            | +              |
| Tong et al. 2010    | calcifying pseudoneoplasm  | 67F     | back pain, inability to walk   | spine, L4-L5              | +            | +              |
| Hodges et al. 2011  | calcifying pseudoneoplasm  | 34M     | HA, dizziness                  | CPA                       | +            | +              |
| Ozdemir et al. 2011 | calcifying pseudoneoplasm  | 53M     | facial pain                    | FM                        | +            | +              |

CPA, cerebellopontine angle; CVJ, craniovertebral junction; FM, foramen magnum; HA, headache; JF, jugular foramen; LE, lower extremities; ND, not described; UE, upper extremities.
vimentin were positive, with negative staining for glial fibrillary acidic protein and 5–100. Vimentin immunoreactivity was noted in peripheral palisading cells, but the intensity varied from case to case. EMA was sometimes positive for the spindle, stromal, and epithelioid cells surrounding the matrix and was negative in some other cases. However, unfortunately, immunohistochemical findings have not contributed significantly in determining the histogenesis of calcifying pseudoneoplasms.

The classic histopathologic features in calcifying pseudoneoplasms include a distinctive set of common elements: (1) typical chondromyxoid matrix in a nodular pattern; (2) palisading spindle to epithelioid cells; (3) variable amounts of fibrous stroma; (4) calcification, osseous metaplasia, and scattered psammoma bodies; and (5) foreign-body reaction with giant cells. However, not all classic histopathologic signs are present in all calcifying pseudoneoplasms. The presence of each component is highly variable in individual lesions. In our reported cases, the pathological examination (second case) demonstrated the typical characteristics of a calcifying pseudoneoplasm; however, the first case we reported showed only some of these features.

**Conclusion**

Calcifying pseudoneoplasms appear to be slow-growing lesions that tend to present secondary to local compression or irritation of adjacent tissues. Cases with spinal lesion presented with pain, gait disturbance, radiculopathy, or myelopathy related to the affected area, and other intracranial lesions presented with seizure, headache, and cerebellar signs caused by tumor compression. Our two cases demonstrated apparent CN deficits with encasement or involvement with tumor.

Although calcifying pseudoneoplasms are histopathologically benign, surgical outcome depends on the tumor location, tumor extension, and the degree of adhesion. Surgical technique to preserve the involved CNs and vasculature is essential. Given that the prognosis is favorable even with subtotal resection, we do not recommend performing an extensive or morbid surgical procedure. It may be sufficient to debulk the tumor just enough to decompress the neural elements.

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