

Simple Partial Seizures in a 70-Year-Old Female

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CASE PRESENTATION: DR. HAJI

History

A 70 year-old female presented with a history of recurrent stereotyped “spells” over the past six years. She described involuntary horizontal saccadic eye movements as the initial event. This was followed by tonic deviation of her head to the left. There was intermittent jerking of her head to the left and quivering of her lower lip and jaw. There was no loss of awareness but it was difficult for her to speak during the spells which typically lasted three to four minutes. Her speech was slurred for a further five to ten minutes. The spells had recurred approximately twice a year until a recent increase in their frequency (four episodes in three months), prompting the patient to seek medical attention.

She had a history of migraines, chronic obstructive lung disease, a 50 pack-year smoking history, and several remote minor surgeries including ureteral stenting, appendectomy, hemorrhoidectomy, and hysterectomy. She had been involved in two motor vehicle accidents, 28 years and 6 years earlier, with no recognized craniocerebral injury on either occasion. Her family history was not contributory.

Physical Examination

The patient was afebrile with a blood pressure of 150/70 mmHg, heart rate 76/min and respiratory rate 16/min. The neurological examination was normal apart from mild weakness (4+/5) of left finger extension.

Investigations

Routine bloodwork proved to be normal. Electroencephalography revealed a grade I dysrhythmia with non-specific slowing in the right hemisphere and left temporal region with no evidence of epileptiform activity.

DISCUSSANT: DR. PARRENT

The patient's episodes likely represent simple partial seizures with leftward eye deviation as an initial event. The seizures

localize to the right frontal lobe with evidence of involvement of the right eye fields (leftward eye deviation) and possibly right Rolandic cortex (lip/chin quivering and dysarthria). A right frontal lesion is also supported by the isolated finding of mild weakness of left finger extension.

The chronicity of the seizures suggests a benign and non-infectious process. It is noteworthy that the seizures began near to the time of a motor vehicle accident although no overt head trauma was evident at that time.

My differential diagnosis for this presentation would include a low grade neoplasm, namely a meningioma. Vascular possibilities would include an infarct or vascular malformation. Less likely explanations would include a traumatic cortical scar.

FURTHER INVESTIGATIONS AND MANAGEMENT: DR. HAJI

Based on semiology and electroencephalography, the patient was diagnosed with simple partial seizures originating in the right frontal lobe and she was started on Dilantin. Magnetic resonance imaging (MRI) examinations revealed a heterogeneous intra-axial mass lesion in the right frontal lobe with apparent central cystic areas and hypointensities on T1 and T2-weighted images. Susceptibility changes on gradient sequences suggested central calcification. There was substantial peri-lesional edema and associated mass effect distorting the right frontal lobe and the midline. Intense heterogeneous ring and intra-lesional enhancement was demonstrated with gadolinium as well as increased perfusion at the lesion's core on perfusion sequences (Figure 1). The patient was started on dexamethasone and neurosurgical consultation was obtained.

FURTHER DISCUSSION AND REVISED DIFFERENTIAL DIAGNOSIS: DR. PARRENT

This calcified mass is most suspicious for a vascular malformation, especially a cavernoma, although it does not have the typical “popcorn” appearance of this entity. A simple infarct or traumatic scar are not tenable considerations. I would recommend craniotomy for resection, definitive diagnosis and treatment.

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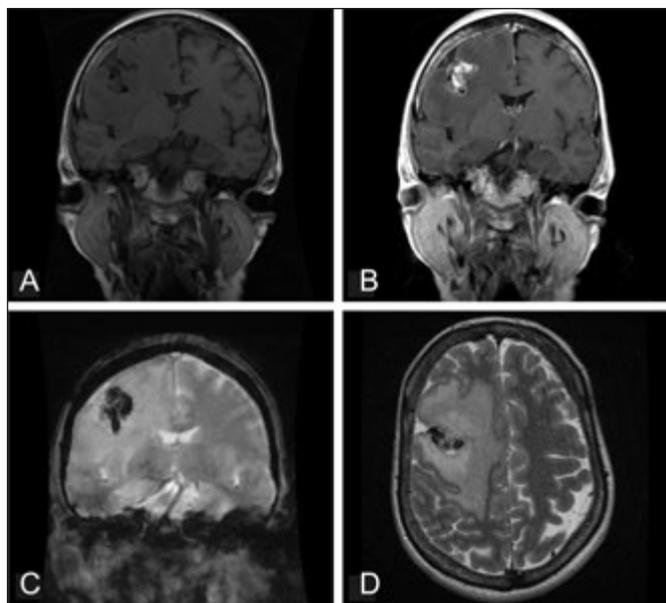


Figure 1: A) T1 weighted images display a heterogeneous intraaxial lesion in the posterior mid-convexity right frontal lobe, isointense with adjacent parenchyma at its periphery and hypointense at its core. B) Post-contrast T1 weighted images display avid central enhancement of the lesion. C) Gradient echo sequences reveal susceptibility changes within the lesion consistent with calcification. D) The lesion contains hyper- and hypointense components on T2 weighted imaging, with adjacent parenchyma displaying increased signal as evidence of perilesional edema.

MANAGEMENT: DR. HAJI

Preoperative diagnostic considerations were numerous but favoured a mid- to high-grade glioma or metastasis, based on heterogeneous enhancement and abundant perilesional edema. There was no evidence of a primary systemic lesion on preoperative investigations. After discussion of surgical options, the patient was taken to the operating room for craniotomy and resection of the lesion.

Intraoperatively, the cortex overlying the lesion had a pale grey hue, deep to which a 3 x 2 x 2 cm nodular lesion of stony consistency was encountered. The lesion and adjacent parenchyma were friable and bled easily but a clear plane was found on all aspects.

The patient was neurologically intact post-operatively and had no seizure activity. She was continued on Dilantin, placed on a tapering dose of dexamethasone and discharged home on post-operative Day 3.

PATHOLOGY: DR. ALTURKUSTANI

Multiple fragments of a white to light tan, heavily calcified mass were submitted with aggregate dimensions of approximately 3 x 2 x 1.1 cm. At intraoperative consultation, the lesion was determined to be low grade in nature but of uncertain lineage.

Paraffin sections revealed a multinodular, chondromyxoid lesion that was heavily calcified and focally ossified. The majority of the mass was composed of a hypocellular mineralized core from which radial calcific deposits extended towards its perimeter. The perimeter was populated by palisading cells with fibroblastic and macrophage morphologies expressing vimentin, epithelial membrane antigen and CD68. Adjacent neural parenchyma was gliotic and studded with Rosenthal fibres (Figure 2).

The final neuropathological diagnosis was fibro-osseous pseudotumour.

DISCUSSION

Fibro-osseous lesions, also known as calcifying pseudo-neoplasms, are uncommon lesions of the neuraxis with 43 cases reported in the literature (Table). The initial description of this entity was contributed by Rhodes and Davis who described it as

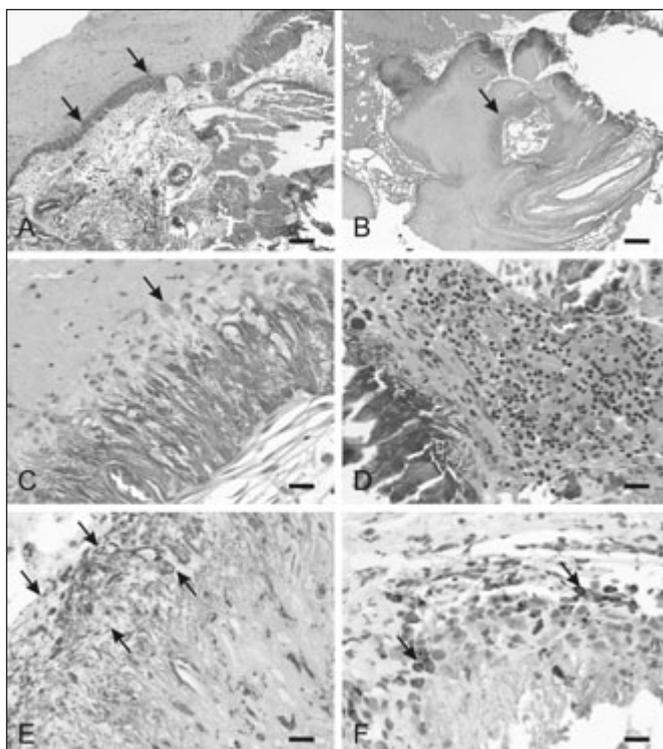


Figure 2: A) The heterogeneous lesion is outlined by a patterned calcific rim (arrows) (H&E, bar = 200 μ m). B) Focal ossification (arrow) is present at the lesion's core (H&E, bar = 200 μ m). C) The perimeter of the lesion is decorated with radial calcifications and palisading epithelioid cells. The adjacent parenchyma displays chronic gliosis with Rosenthal fibre formation (arrow) (H&E, bar = 50 μ m). D) Focal areas of chronic inflammation are present (H&E, bar = 25 μ m). E) Vimentin expression by palisading cells is abundant at the lesion's perimeter (between arrows)(anti-vimentin immunohistochemistry, bar = 25 μ m). F) Select cells at the lesion's perimeter express CD68 suggesting macrophage lineage (arrows) (anti-CD68 immunohistochemistry, bar = 25 μ m).

an unusual fibro-osseous component in intracranial lesions and proposed a metaplastic process as its origin.¹

Epidemiology

Cases have been reported in patients ranging in age from 6 to 83 years with a slight male predominance (27 males: 16 females). Twenty-seven cases were intracranial, of which 15 were intra-axial and 12 extra-axial (including one intraventricular). Sixteen spinal cases have been reported, eight in the cervical spine and four in each of the thoracic and lumbar regions. Fourteen spinal lesions were extra-dural within the spinal canal, one was intra-dural and one was intraosseous arising from the body of C2 (Table).

Clinical Presentation

The clinical presentation is largely determined by location, however several (11 of 43) were neurologically silent. Seven of the latter cases were discovered at autopsy (all intracranial) and four were incidental findings on computed tomogram (CT) scans¹⁻⁴. Of symptomatic lesions, 7 of 15 intracranial cases presented with seizures. The remainder presented with headache or focal neurological deficit. The spinal lesions predominantly presented with neck or back pain, however radiculopathy and myelopathy have also been reported⁵⁻⁹. All cases had an insidious onset with duration of symptoms ranging from months to years (Table).

Imaging

The most consistent imaging feature is hyperdensity on unenhanced CT scans, signifying the presence of calcification. In a series of six fibro-osseous lesions evaluated by MRI, Aiken et al found hypointensity on T1 and T2 weighted images in all cases, with a variable enhancement pattern; two had linear enhancement, two had ring-enhancement, one enhanced in a homogeneous pattern and one did not enhance³. This prompted the authors to conclude that fibro-osseous lesions should be considered in the differential diagnosis when a heavily calcified lesion is found on CT with hypointensity on T1-weighted and T2-weighted images, minimal linear rim or serpiginous internal enhancement, and limited to no edema^{2,3}. The present case was unusual for abundant perilesional edema but imaging features were otherwise similar to previous reports. Differences observed on imaging likely reflect differences in lesion composition, as described by Bertoni et al⁴.

Gross, Microscopic and Ultrastructural Features

Fibro-osseous pseudotumours are well-circumscribed, stony hard, somewhat granular masses that can measure up to 10 cm in diameter. Most are single discrete masses, although multiple clustered lesions with extensive reactive changes in surrounding tissues have been reported⁴.

The striking microscopic feature is the presence of focal amorphous nodules of chondromyxoid matrix surrounded by palisading spindle and/or epithelioid cells which express epithelial membrane antigen. The variably calcified and ossified matrix is composed of coarse fibrillar material in linear or anastomosing patterns. Ghost cells may be present in the lesion's core. Cellular atypia and mitotic activity are absent or minimal.

Chronic gliosis in the surrounding parenchyma may give rise to Rosenthal fibre formation. Changes reminiscent of meningio-angiomatosis have been reported in adjacent cortex⁴, raising a tenuous association with neurofibromatosis^{5,10}.

Ultrastructural examination of central hypocellular areas reveals masses of electron-dense amorphous material. These masses are largely composed of collagen¹¹ and other fine fibrillary elements¹. Palisading cells at the periphery display ultrastructural features of fibroblasts including abundant intracytoplasmic filaments, prominent rough endoplasmic reticulum and no junctional complexes. Extracellular basal lamina-like material may be present and may represent the residuum of degenerated vascular channels⁵.

Nature/Origin

Given the favourable clinical outcomes and morphological features, most authors have proposed a non-neoplastic proliferative or reactive etiology with which we concur. Other proposed explanations include an unusual expression of tumour calcinosis or abortive membranous bone formation, with osseous metaplasia. Various cells of origin have been proposed including: i) arachnoid cap cells; supported by a common location of this lesion in the CNS (i.e., dural or leptomeningeal) and epithelial membrane antigen or vimentin immunoreactivity, ii) fibroblasts or other mesenchymal cells; supported by ultrastructural studies and examples arising outside the neuraxis, and, iii) astrocytes; supported by glial fibrillary acidic protein immunoreactivity among palisading cells in a single case⁶. In one report, a concurrent calcifying pseudoneoplasm and ependymoma were described¹². In the latter case the ependymoma was low-grade and displayed prominent reactive changes in the form of piloid gliosis at its periphery. The latter case also lent support to the suggestion that calcifying pseudoneoplasms may be part of an exuberant reaction to an underlying pathologic process, such as inflammation or neoplasia.

Differential Diagnosis and Treatment

Heavy lesional calcification engenders a wide differential diagnosis including chronic inflammatory and infectious entities, granulomatous lesions, low grade tumours (pilocytic astrocytoma, ganglioglioma), chordoma, chondrosarcoma, chondroblastoma, meningioma, longstanding intracerebral hematomas, aneurysms and vascular malformations¹³. In most cases the imaging is not conclusive, necessitating tissue sampling for definitive diagnosis.

The recognition of this distinctive pseudotumour has practical importance in the avoidance of aggressive diagnostic, surgical or therapeutic measures. Excision appears to be curative with only one reported case treated by partial excision that recurred three years later⁴. In all other cases of gross total or subtotal resection, patients were asymptomatic post-operatively with no evidence of recurrence or progression on follow-up imaging. Morbidity appears to be primarily associated with lesion location⁴.

CONCLUSION

At six-week follow-up, the patient was neurologically intact with no further seizure activity. Three months after craniotomy, MRI examinations revealed no definite residual or recurrent tumour.

Table: Literature review summary

Reference	Pt #	Age	Sex	Location	Presentation	Calcification	Multiplicity	Therapy	Follow-up
Rhodes & Davis 1978 ¹	1	27	F	Intra-axial, R frontal	H/A	Yes	Multiple	Excision	7 years, NR
	2	55	F	Extra-axial, Parafalcine/R convexity dura	Autopsy Finding	N/A	Multiple	None	Incidental
	3	60	M	Intra-axial, L cerebellum	Autopsy Finding	N/A	Single	None	Incidental
	4	74	F	Extra-axial, R convexity dura	Autopsy Finding	N/A	Multiple	None	Incidental
	5	46	M	Intra-axial, 4th ventricle choroid plexus stroma	Autopsy Finding	N/A	Single	None	Incidental
	6	62	M	Extra-axial, Pineal leptomeninges	Autopsy Finding	N/A	Single	None	Incidental
	7	83	M	Extra-axial, Dural based	Autopsy Finding	N/A	Multiple	None	Incidental
Jun et al. 1984 ¹⁴	8	55	M	Intra-axial, Corpus callosum	H/A, N/V	Yes	Single	Excision	1 year, NR
Garen et al. 1989 ¹¹	9	44	M	Extra-axial, Dura of Meckel's cave	Atypical Facial Pain	Yes	Single	Excision	11 years, NR
Bertoni et al. 1990 ⁴	10	31	M	Extra-axial, Jugular foramen	H/A, Hoarseness	N/A	N/A	Excision, debulking (recurrent)	Deceased*
	11	50	M	Extra-axial, Foramen magnum	Neck Pain	N/A	N/A	Debulking	3yrs 6mo, NR
	12	48	M	Extra-axial, Skull base/cerebellum	R CN XI Palsy	N/A	N/A	Wide excision	19 years, NR
	13	23	M	Spinal Extra-dural, T10	Back Pain	N/A	N/A	Marginal excision	Lost to F/U
	14	58	M	Spinal Extra-dural, C2-3	Back Pain	N/A	N/A	Marginal excision	9yrs 4mo, NR
	15	32	M	Intra-axial, L frontal	Seizure	N/A	N/A	Wide excision	30 years, NR
	16	45	F	Extra-axial, Skull base	CN Palsy	N/A	N/A	None	Autopsy
	17	58	M	Extra-axial, Skull base	Hoarseness	N/A	N/A	Intralesion excision	Lost to F/U
	18	12	M	Spinal Extra-dural, C6	Neck Pain	N/A	N/A	Curettage	3yrs 3mo, NR
	19	32	M	Spinal Extra-dural, L4-5	Back Pain	N/A	N/A	Intralesional excision	7 years, NR
	20	33	F	Spinal Extra-dural, T9	Back Pain	N/A	N/A	Intralesion excision	Lost to F/U
	21	68	F	Spinal Extra-dural, L4-5	R hip pain	N/A	N/A	Marginal excision	Lumbar DJD 13m
	22	20	F	Spinal Extra-dural, C2	Incidental	N/A	N/A	Curettage	Lost to F/U
	23	56	F	Spinal Extra-dural, L4-5	Back Pain	N/A	N/A	Curettage	Lost to F/U
Smith et al. 1994 ¹²	24	48	M	Spinal Intra-dural, L2-3	Sciatica	N/A	Single	Subtotal removal	N/A
Tsugu et al. 1999 ¹⁵	25	22	F	Intra-axial, R parietal	Seizures	Yes	Single	Total removal	8 years, NR
Qian et al. 1999 ⁵	26	33	F	Intra-axial, L temporal	Developmental Delay	Yes	Single	Excision	2yrs 7mo, NR
	27	49	M	Spinal Extra-axial, C1 and clivus	Weakness	N/A	Single	Excision	7yrs 6mo, NR
	28	59	M	Spinal Extra-axial, C1-2	Shuffling Gait	N/A	Single	Excision	3yrs 10mo, NR
	29	47	F	Intra-axial, Frontal	Seizures	Yes	Single	Excision	3 years, NR
Shrier et al. 1999 ²	30	32	F	Intra-axial, Temporal	Incidental	Yes	Single	Total removal	1 year, NR
	31	59	M	Extra-axial, Foramen magnum	Neck Pain	Yes	Single	Total removal	2 years, NR
Chang et al. 2000 ¹⁶	32	60	M	Spinal, Intraosseous arising from C2	Neck Pain	Yes	Single	Subtotal removal	2 years, NR
Mayr et al. 2000 ⁸	33	58	M	Spinal Extradural, T10-12	Thoracic Myelopathy	Yes	Single	Subtotal removal	4 years, NR
	34	63	M	Spinal Extradural, C3-4 (dorsal)	Cervical Myelopathy	Yes	Single	Subtotal removal	5 years, NR
Tatke et al. 2001 ¹⁷	35	6	M	Intra-axial, L temporal	Seizures	Yes	Single	Subtotal removal	6 months, NR
Liccardo et al. 2003 ⁷	36	40	M	Spinal Extradural, T8-9	Thoracic Myelopathy	Yes	Single	Total removal	3 years, NR
Aiken et al. 2009 ³	37	16	M	Extra-axial, Temporal horn	Incidental	Yes	Single	Total removal	N/A
	38	35	M	Intra-axial, R temporal	Seizures	Yes	Single	Total removal	N/A
	39	49	F	Intra-axial, L hippocampus	Seizures	Yes	Single	Total removal	N/A
	40	59	M	Intra-axial, R parietal	L Arm Numbness	Yes	Single	Total removal	N/A
Park et al. 2008 ⁹	41	59	F	Spinal Extradural, C7-T1	L C8 Radiculopathy	N/A	Single	Total removal	N/A
Rodriguez et al. 2008 ⁶	42	67	F	Intra-axial, R cerebellum	Incidental	Yes	Single**	Total removal	N/A
Haji et al.	43	70	F	Intra-axial, R frontal	Partial Seizures	Yes	Single	Total removal	6 weeks, NR

N/A=Not available, NR=No Recurrence, DJD=Degenerative Joint Disease, H/A=Headache, N/V=nausea and vomiting, CN=cranial nerve, F/U=follow-up, CVA=cerebrovascular accident; *Patient died of CVA 13 yrs after initial operation; ** Lesion found adjacent to an epidymoma.

This case demonstrated many typical clinical, radiographic and histopathological features of a fibro-osseous pseudotumour. The present case was atypical for the presence of abundant perilesional edema on imaging. Although uncommon, awareness of this entity and its inclusion in the differential diagnosis of long-standing calcified lesions along the craniospinal axis has practical importance in directing optimal investigations and treatment.

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