

Epilepsy Due To Idiopathic Subcortical Calcification; Treatment by Lesionectomy

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Abstract : Two young male patients with increasing frequency of seizures unresponsive to anti-epileptic drugs are reported. The focal electroencephalographic findings and the lesions revealed by magnetic resonance and x-ray computed tomographic images were compatible with the clinical features of the seizures. Removal of the lesions was performed without the guidance of electrocorticography. Histological examination revealed focal calcifications

but could not specify the exact nature of these although extensive clinical and laboratory investigations were performed. The minimal vascular abnormality detected in the centre of the lesions must have triggered the lesions.

Key Words : Epilepsy, Surgical treatment, Cerebral calculi, Calcification, Vascular lesion

INTRODUCTION

Patients with partial epilepsy who do not respond adequately to proper medical management, should be considered as candidates for surgical treatment, especially if seizures are the most troublesome symptoms. These patients usually harbour intracranial lesion; such as slow growing tumours, arteriovenous malformations or calcifications (4). Basically, two different surgical procedures are possible in the treatment of focal epilepsy: either the epileptic focus is eliminated directly by partial lobectomy for direct resection of a pathological lesion (16,18) or the pathways are severed from the limbic system (5,17,19,21); so that the propagation of epileptic activity is interrupted.

Intracranial calcifications may be physiological or pathological, diffuse or focal. They can be revealed using direct radiological techniques. Besides normal calcium deposition in the plexus choroideus, pineal body, falx and Pacchionian bodies; many pathological conditions may also result in calcification.

Characteristics of the lesion such as localization, multiplicity and associated radiological findings usually lead to a diagnosis.

CLINICAL MATERIAL AND METHOD

Case 1 : A 19 year old medical student was admitted to our clinic with convulsions on the left side together with a feeling of nausea in the aura state but without losing consciousness, at a frequency of 1 to 3 times a year. The seizures were intractable, unresponsive to first line antiepileptic drugs (AED) for about 4 years, and increasing gradually.

Case 2 : A 16 year old male patient was admitted with convulsions on the right side of his face and right arm for the past 2 years, with a frequency of twice a month. The seizures were intractable, unresponsive to AED and associated with short unconscious periods.

Medical History: No birth or post natal trauma, head trauma, tuberculosis, parasitic infection or febrile seizures were not recorded for either patient. All families were investigated in detail and no clinical dysmorphic characteristics, intracranial calcification, psychological problems or seizures were encountered.

Physical Investigation : The patients had no retinal abnormality, they had a normal stature and

dental formation with no abnormality of the extremities, skin or nails. Physical, neurological and mental signs were normal.

Laboratory Investigation : Serum electrolyte, glucose, cholesterol levels, hepatic tests, CBC and urine analysis, CSF survey consisting of serology, serum calcitonin - inorganic phosphate - ionized calcium - alkaline phosphatase, creatinin, Fe, Fe binding capacity, ceruloplasmin and Cu levels were normal. Toxoplasma dye test and cytomegalovirus antibodies were negative.

Serum protein electrophoresis, immunoglobulin G,A and M levels, erythrocyte sedimentation rate, anti-DNA activity, complement C3 and C4 levels, rheumatoid factor, antinuclear factor, LE cell investigations were all negative. Parathormon levels and calcium-phosphate output in the urine were normal. Tuberculosis-syphilis and hydatid cyst were all ruled out using appropriate tests. Consecutive serum anticonculsant levels were also in the therapeutic range.

Imaging Results : MRI scans were obtained with extensive coronal cuts to evaluate the temporal lobes, the orbitofrontal cortex and the insulae. The lesions revealed non homogenous high signal intensity on the T1 weighted images and on the contrary, low signal intensity in the T2 weighted images which was compatible with partial haemosiderin accumulation and focal calcification. CT scans with enhancement, angiographies and SPECT scans were also obtained. Case 1 was shown to have a right frontal subcortically placed 2 cm diameter calcified mass with clear borders (Fig 1). The mass was surrounded by a hypodens area, reflecting the gliosis of the epileptic region, without any sign of ventricular distortion. Case 2 had a left temporally placed 1 cm diameter calcified mass with pure subcortical localization. The focus was not in the motor or speech cortex (Fig. 2,3,4).

Repeated interictal scalp EEG recordings revealed stable epileptiform discharges consistently localized to the same side and area of the lesion as shown on the tomographical images. There was focal paroxysmal presence of 4-7 cycle/sec. slow waves together with spike discharges and evidence of spread to the cortical surface which provided direct and essential evidence. The focal clinical features of the seizures were also compatible with the EEG focus.

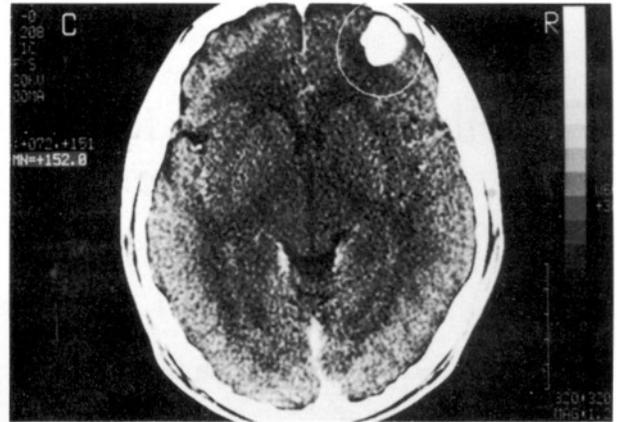


Fig 1 : CT scan showing dense calcification at the right frontal pole (Case 1).



Fig 2 : Axial CT displaying left temporal calcification which could easily have been reported as a partial volume effect (Case 2).



Fig 3 : Coronal CT slice of the same calcified lesion showing the relation between the lesion and the temporal bone (Case 2).

Surgical Removal of Lesions : Craniotomies were performed under general anaesthesia using enflurane, nitrous oxide and oxygen. The pia, arachnoid of the lobe was coagulated with bipolar

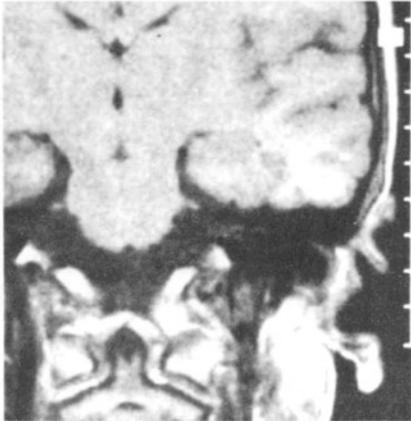


Fig 4 : Coronal MRI scan displaying the subcortical localization of the lesion (Case 2).

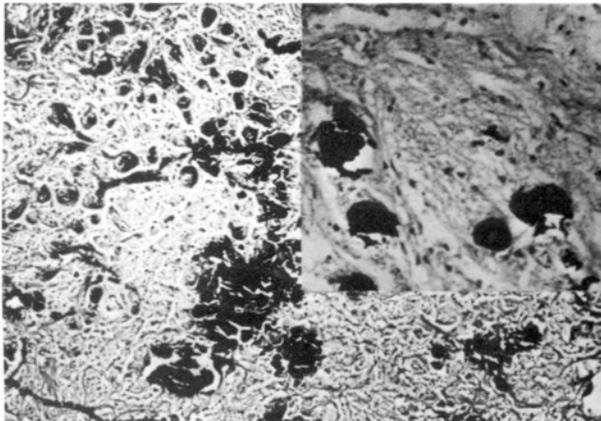


Fig 5 : Section showing the border between the lesion and peripheral brain tissue. HE, after decalcification, 80 X.
Inset : Vascular areas displaying concentric hyalinosis located at the lesion centre. HE, after decalcification, 200 X.

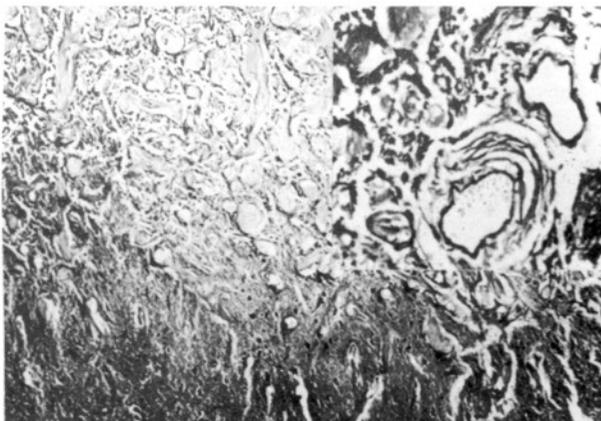


Fig 6 : At the lesion centre; vascular formation with thickened walls, psammoma bodies and irregular calcifications are observed. HE, 80 X.
Inset : Focal calcifications located at the lesion periphery and the surrounding brain. Van Kossa, 200 X.

forceps and opened with microscissors. Horsley's subpial dissection was employed to remove the

slightly hard and yellow tissue en bloc as extensively as possible under an operating microscope and without the guidance of Electro Cortico Graphy which was not available. Since seizure activity does not arise from the lesion itself, but from the damaged adjacent epileptogenic cortex and as it is known that gliotic scar conducts electric current well or amplifies electrophysiological activity (7,8), the neighbouring cortex was removed with a small suction tip.

The brain areas were "dispensable", their removal was not likely to lead to a new neurological deficit. The remainder of the resection margin was the white matter. The postoperative course of both patients was uneventful without any infection or persisting focal neurological deficit. They were discharged 2 weeks after operation with postoperative imaging data displaying total removal of the lesions and were followed up as outpatients.

Follow-up Study : At present, one of the patients is still receiving medical anticonvulsant treatment at preoperative levels without any seizures in the postoperative 2-year period. The other patient who has been completely free of seizures for a period of 3 years started a six-month tapering off of antiepileptic medication. EEG has revealed only non specific paroxysmal presence of slow waves without any evidence of spreading spikes.

Pathological Examination : Both preoperative and postoperative evaluation revealed a marked margin but not a capsula (Fig 5). Peripheral brain was oedematous with focal calcifications (Fig 6, inset). The lesion centre consisted of thick walled vessels and calcifications irregular in some areas and psammoma body shaped in others. When this region was decalcified; vascular malformations were more marked in some areas and displayed concentric hyalinosis (Fig 5, inset). Von Kossa stain was positive for Calcium and Gomori stain for Fe was sparse and focal.

Histopathological examinations could not specify the nature of the calcifications. They were therefore labelled idiopathic.

DISCUSSION

Results of the treatment of cases with medically refractory epilepsy favour ablative surgery, especially when the focus is in the non-dominant

hemisphere (16). There are more "excellent" responders in this group than in the stereotactic group. Rasmussen analysed the results of operations for the treatment of focal epilepsy (other than originating in the temporal lobe) in 1145 patients. 64% had complete or nearly complete elimination of seizures (18).

Furthermore, in cases with the most circumscribed foci; excellent results could be expected up to 90% (22). These results favour early recognition of surgical candidates before the spread of epileptic activity occurs and therefore; radical resections may be necessary as stereotactic operations may not be optimally effective.

Our cases had partial seizures with elementary symptoms persisting despite vigorous therapy for 2 years (6) and were treated surgically before adulthood so as to prevent possible devastating effects on development, socialization and education (12).

Recurrent seizures are associated with ongoing neuronal damage in a chronic experimental animal model (9). Secondary independent epileptic foci develop in about one-third of human cases with continuing seizures even when the pathological process is likely to be unilateral. Moreover, there is increased occurrence of sudden death with recurrent seizures (10).

Statistically, the most common cause of intracranial calcification is the primary brain tumours (14). On the contrary, metastatic masses have radiologically shown calcifications in only 1%. Chronic calcifications observed in non-neoplastic lesions are called "brain stone" or "cerebral calculi". Some are reported to occur due to the organization process of intracerebral-extradural or subdural-haematomas and brain abscesses. 6% of tuberculomas are calcified and occur as a single focus (15). In multiple sclerosis, multiple lesions are found in close relation with ventricles. Giant aneurysms and AVMs have curvilinear calcifications while telangiectatic hamartomas or cavernous haemangiomas exhibit big and dense lesions, generally situated in the peripheral regions of the brain (20). Fibrous lesions of unknown aetiology can also occur with calcifications and they have a very slow progression rate (11).

The incidence of hypoparathyroidism or pseudohypoparathyroidism is 70-80% in patients with cerebral calculi(13).

Also exhibiting cerebral calcification are toxoplasmosis (2), systemic lupus erythematosis or lymphocytic leukaemia and similar systemic diseases (1); toxins like CO-radiation-anoxia and cytomegalovirus infections Albright's hereditary osteodystrophy, Hallervorden-Spatz disease, Kearns-Sayre syndrome, Fahr syndrome (3), Sturge-Weber syndrome, Down's syndrome, Dyskeratosis congenita, Morgagni-Morel syndrome, Urbach-Wiethe syndrome and Cockayne syndrome are clinical entities that cause cerebral calcification.

In our patients, all these causes were ruled out by clinical-pathological or laboratory data. They could be labelled "idiopathic" since pathological investigation did not reveal any haematoma, cystic cavity, hydatid cuticles or macroscopic vascular malformations. In several sections; no parasitic infection, tumours, haematoma or abscess formation was present. The minimal vascular abnormality in the centre of the lesions consisting of thick walled vascular formations must have triggered the present lesion in these patients.

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REFERENCES

1. Anderson JR: Intracerebral calcifications in a case of SLE with neurological manifestations. *Neuropathol Appl Neurobiol* 7:161-166, 1981
2. Dyke CG, Wolf A, Cowen D: Toxoplasmic encephalomyelitis, significance of roentgenographic findings in the diagnosis of infantile or congenital toxoplasmosis. *Am J Roentgenol* 47:830, 1942
3. Fahr T: Idiopathische Verkalkung der Hirngefasse. *Zentralblatt Allgemeine Pathologie* 50:129-133, 1930
4. Fisher RS, Uematsu S: Surgical therapy of complex partial epilepsy. *Johns Hopking Med J* 151:332-343, 1982
5. Ganglberger JA: New possibilities of stereotactic treatment of temporal lobe epilepsy (TLE). *Acta Neurochir Suppl, Wien* 23:211-214, 1976
6. Gestaut H: Clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 11:102-113, 1970
7. Glötzner FL: Membrane properties of neuroglia in epileptogenic gliosis. *Brain Res* 55:159-171, 1973
8. Harris AB: Degeneration from experimental seizures. *Neurosci Abstr* 2:246, 1976.
9. Grossman RG, Rosman LJ: Intracellular potentials of inexcitable cells in epileptogenic cortex undergoing fibrillary gliosis after a local injury. *Brain Res* 28:181-201, 1971
10. Jay GW, Leetsma JE: Sudden death in epilepsy: A comprehensive review of the literature and proposed mechanisms. *Acta Neurol Scand Suppl.* 82:1-66, 1981

11. Jun C, Burdick B: An unusual fibrous lesion of the brain. *J Neurosurg* 60:1308-1311, 1980
12. Lindsay J, Glaser G, Richards P: Developmental aspects of focal epilepsies of childhood treated by neurosurgery. *Dev Med Child Neurol* 26:574, 1984
13. Loewenthal A, Bruyn GW: Calcification of the striopallidodentate system. In *Handbook of Clinical Neurology*: vol 5: Diseases of basal ganglia. Amsterdam: North Holland, 1970:703-725
14. Martin F Jr, Lemmen LJ: Calcification in intracerebral neoplasms. *Am J Pathol* 28:1107-1131, 1952
15. Mudd R, Pearlmutter I, Strain RE: Calcified intracranial tuberculoma with report of a case. *AJR* 73:19-22, 1955
16. Pendl G, Grunert P, Graf M, Czech T: Surgical treatment of epilepsy. *Neurochirurgica* 23 Suppl 1, 27-29, 1990
17. Ramamurthi B, Kalyanaraman S: Stereotactic targets for epilepsy. Schalterbrand G, Walker AE (Ed), in *Stereotaxy of human brain*. Stuttgart: Georg Thieme, 1982:653-660
18. Rasmussen T: Cortical resection for medically refractory focal epilepsy: Results, lessons and questions. Rasmussen T, Marino R (Ed), in *Functional Neurosurgery*. Vol 9, New York: Raven, 1979:253-269
19. Spiegel AE, Wycis HT, Szekely EG: Stimulation of Forel's field during stereotactic operations in the human brain. *Electroenceph Clin Neurophysiol* 16:537-548, 1964
20. Voigt K, Yaşargil MG: Cerebral cavernous haemangiomas or cavernomas. Incidence, pathology, localization, diagnosis, clinical features and treatment. Review of the literature and report of an unusual case. *Neurochirurgica (Stuttg)* 19:59-68, 1976
21. Walker AE: General principles of stereotactic surgery for epilepsy. Schalterbrand G, Walker AE (Ed), in *Stereotaxy of The Human Brain*. Stuttgart: Georg Thieme, 1982:645-652
22. Wieser HG: Selective amygdalo-hippocampectomy: Indications, investigative techniques and results. Symon L (Ed), in *Advances and Technical Standards in Neurosurgery*. Vol 13, Wien: Springer, 1985:39-133