Case Report

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Pure Intrinsic brain stem epidermoid cyst: Case report, review of the literature and new classification.

Epidermoid cysts are one of the uncommon slow growing lesions. There is some amount of controversy prevailing in the uniform understanding of these among the researchers regarding the nomenclature of these lesions. With a critical review of reported cases, author demarcated four different anatomical types of brain stem epidermoids and proposed a new classification system for a better understanding of the natural history.

Four years female child presented with insidious onset left sixth and seventh cranial nerve palsy with right hemiparesis. Radiological evaluation revealed a pure intrinsic brain stem cystic lesion. Surgical decompression of the cyst was done, and the child recovered well. Histopathological examination was an epidermoid cyst.

Brain stem epidermoids are uncommon, and there is no age or sex predilection. Based on the epicenter these tumors could be classified into four different types. Adequate surgical excision is the hallmark in the treatment.

Key words: Brainstem, Classification, Epidermoid, Intrinsic cyst, telo-velo-tonsillar approach

French pathologist Cruveilhier10 first described epidermoid cysts in 1829, and they are also called as Cruveilhian tumors. Epidermoid cysts are pearly white congenital tumors that account for 0.2 to 1.8% of all primary brain stem tumors. 45 They usually develop in the basal subarachnoid spaces like cerebello pontine angle 21 and juxta sellar areas.4,29,38 They are exceptionally slow growing tumors, commonly occur between second to the fourth decades, and appear to proliferate along the open cisternal spaces rather than infiltrating tissue parenchyma.29 42 Brain stem epidermoid cysts are rare in occurrence with only 25 cases (including present case) reported in the English literature. These cysts are a collection of pure intrinsic brain stem lesions,12,13,27,29,33,35,44 and the juxta brain stem lesion either infiltrated from surrounding cisternal spaces,5,13,17,18,20,24,45 or extending into surrounding cisternal spaces8,22-24,30-32,36. There is some amount of controversy prevailing in the pathogenesis morphological classification13,24,43, author demarcated four different anatomical types of these tumors based on the epicentre of the tumor. The author reported a case of purely intrinsic brainstem epidermoid cyst and proposed the new morphological classification for a better understanding of the natural history of these uncommon lesions.

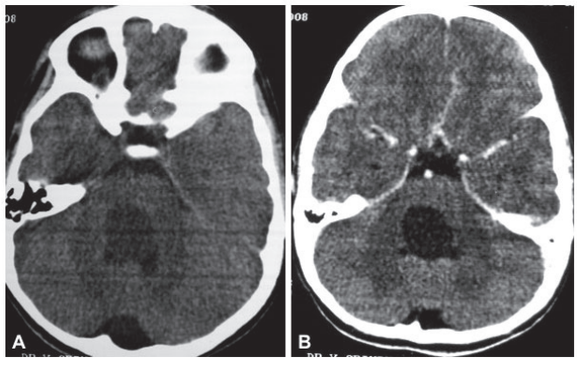

Figure 1: Pre operative CT scan images demonstrating an intra axial pontine epidermoid tumor. A: Non contrast computed tomogram (NCCT) image, B: contrast enhanced computed tomogram (CECT) image.

Case report:

Four years old girl presented to us with two months history of mild headache, diplopia and deviation of the angle of mouth towards the right. Soon she developed right hemiparesis and gait ataxia with in next two weeks. By the time she came to our hospital, she is bedridden. She never had a history of fever, neck rigidity preceding this illness.

On neurological examination, she was conscious, lethargic, and responded partly to commands. She had nystagmus, left abducent, facial nerve palsy and right hemiparesis of grade 3/5 Medical Research Council (MRC). Contrast enhanced computerized tomography (CECT) of the brain revealed non-enhancing well circumscribed, intra axial hypo dense lesion in the pons (Figure 1). There was no evidence of hydrocephalus. The lesion was predominantly hypo intense on T1- and hyper intense on T2 weighted magnetic resonance imaging (MRI) (Figure 2). Computerized tomography (CT) and MRI studies suggested a purely intrinsic non-enhancing cystic brain stem lesion possibly a neurenteric cyst, epidermoid cyst, or cystic brain stem glioma.

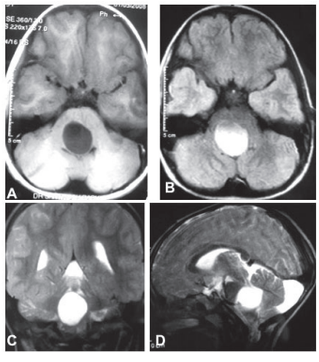

Figure 2: Pre operative Magnetic Resonance images (MRI) showing an intra axial pontine epidermoid tumor. A: Axial T1Weighted Image, B: Axial T2Weighted Image, C: Coronal T2Weighted Image, D: Sagittal T2Weighted Image.

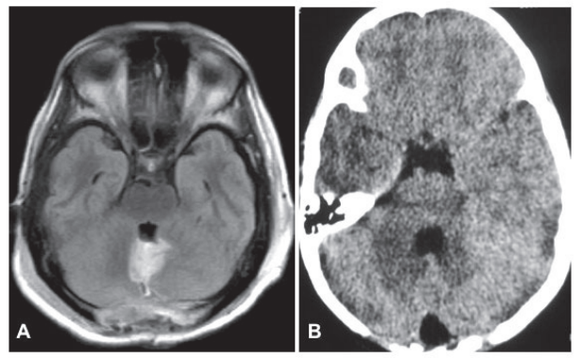

Figure3: 3A: Post operative Fluid Attenuated inversion recovery (FLAIR) MRI done on 10th post operative day showing well decompressed pontine epidermoid cyst.

3B: Post operative Non contrast computed tomogram (NCCT) image at recent follow up demonstrating no recurrence of the cyst.

Operation:

The patient underwent sub occipital craniotomy. The floor of the fourth ventricle was exposed through the telo-velo-tonsillar approach.28 The floor of the fourth ventricle appeared distended from the underlying cyst. The cyst opened through midline myelotomy at the maximum bulging point just above the facial colliculus. The cyst contained creamy, viscous fluid, with multiple small pearly white flakes. Cyst contents were aspirated completely and thoroughly irrigated to remove left out flakes. Thin rim of

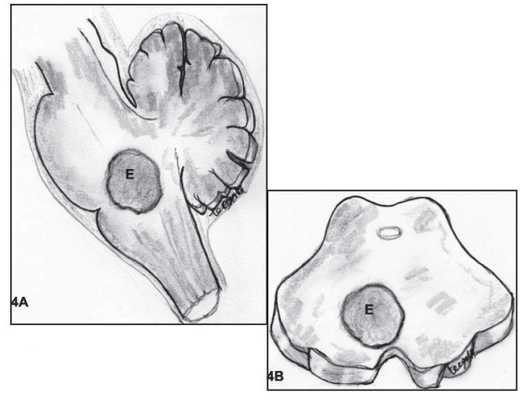

Figure 4: Illustrated diagram of type 1 brain stem epidermoid lesion showing the relations of epidermoid (E) and brain stem. (A: Sagittal view; B: Axial view)

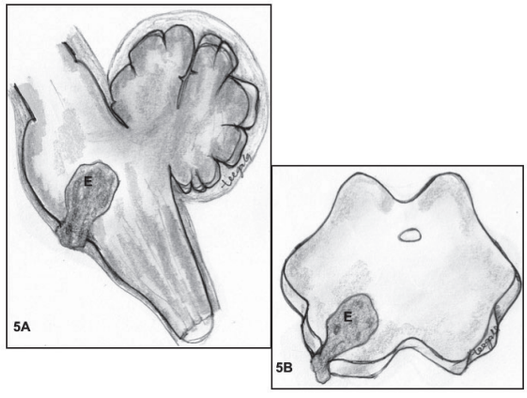

Figure 5: Illustrated diagram of type 2 brain stem epidermoid lesion showing the relations of epidermoid (E) and brain stem. (A: Sagittal view; B: Axial view)

the capsule was biopsied from the myelotomy site. Other than that, there was no well-formed capsule for removal. After complete aspiration of cyst contents, the cavity was pinkish all around. There are no hemodynamic changes during the surgery.

Postoperative course:

Postoperatively patient did well, and hemiparesis improved fully. The sixth, seventh cranial nerve palsies were also improved before she was discharged from the hospital on the 10th postoperative day.

Histopathological examination revealed epidermoid cyst. Cyst fluid culture for bacteria, fungus, and mycobacterium did not yield any positive report.

MRI done at the time of discharge (Figure 3A) did not reveal any residual cyst. A follow CT scan (Figure 3B) done in the recent follow up at six years, did not show any recurrence of the tumor and child is healthy.

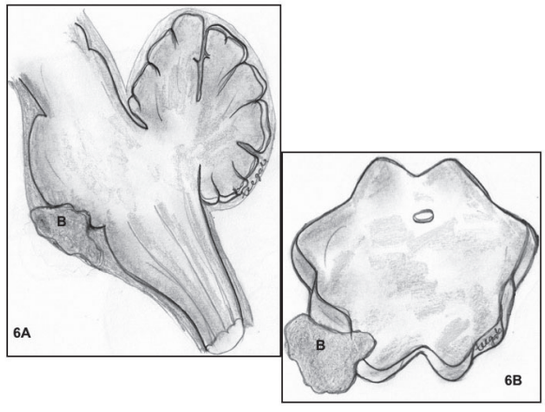

Figure 6: Illustrated diagram of type 3 brain stem epidermoid lesion showing the relations of epidermoid (E) and brain stem. (A: Sagittal view; B: Axial view)

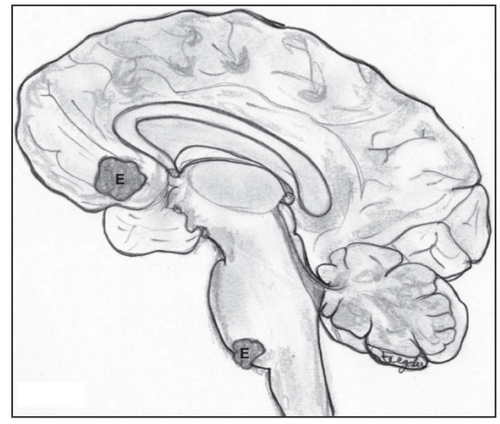

Figure 7: Illustrated diagram of type 4 brain stem epidermoid lesion showing the relations of epidermoid (E) and brain stem. (A: Sagittal view)

Discussion:

Since the first report of brain stem epidermoid by Leal et al22 in 1978, many case reports added to the literature describing the clinical features, embryogenesis, pathology, radiology and surgical management. With the advancements in the imaging modalities and surgical techniques, the diagnosis and management of these lesions became easy with a better outcome. The aetiology is not clear, and there is always been a controversy.9,24,43

Pathogenesis and rationale for the classification:

The exact pathogenesis of brain stem epidermoid cysts is always been speculative.12,26,41,44 There are many hypotheses whitch are explaining the pathogenesis of these uncommon lesions in the English literature. Few important ones among them are:

Epidermoid tumors probably develop from the inclusion of ectodermal elements during the neural tube closure between 3rd and 5th week of embryonic development.29,43 The median location of the epidermoid tumors seen in few cases can be explained by this hypothesis where, separation of neuroectoderm from the cutaneous counterpart occurring dorsally along the midline.4,24,31,43,45

The proliferation of pluripotent embryonic remnants along the otic and optic cerebral vesicles can explain the occurrence of the majority of cranial epidermoids either in Cerebello pontine angle (CPA) or sellar areas.4,14,24,43

Migration of embryonic ectodermal remnants along the Virchow-Robin spaces around the brain microvasculature.11,13,43 This hypothesis can explain the occurrence of intrinsic brain stem epidermoid tumors even in the later part of the life.17,43,45

Type of Epidermoid classification	Description	Number of cases reported in the Literature
Table 1	Purely intrinsic / intra axial brain stem tumors	8
Table 2	Brain stem epidermoids having predominant intra axial component with slight extension to the surrounding cisternal spaces	8
Table 3	Brain stem epidermoids having predominant extra axial cisternal component with slight intra axial brain stem infiltration	7
Table 4	Multiple intracranial epidermoid cysts involving the Brain stem	2

Table 1: Classification of brain stem epidermoid tumors

Ziyal et al. 45 reported that the tumor extends from the cisternal space into the brain stem, and is usually demonstrated as an exophytic lesion in the ventral brain stem cisterns. Over a period, the brain parenchyma may cover the cyst contents and may give the appearance that the lesion is intra axial.

Chandler et al9 suggested that epidermoid cysts seem to develop when the neural tube closes and divides from cutaneous ectoderm, rests of cells are left on the inner or outer surface, or within the neural tube ectoderm. This would explain the occurrence of intraventricular epidermoid tumors.[19] This hypothesis can explain the rare possibility of multiple intra cranial epidermoid cysts.[24,26]

Another hypothesis suggesting that, the epidermoid cysts appear to grow in cleavage planes between nerve fibers, extending along vessels into the subarachnoid space.24 39 From there, they usually take the path of least resistance and fill the subarachnoid space before displacing neurovascular structures.39,43

Series (Author & Year)	Age	Sex	Site of lesion	Clinical features	Duration of symptoms	Treatment	Follow up & Outcome
Weaver EN,[39] 1979	1year	M	Pons & Medulla	Bulbar features with 6th & 7th palsy	2weeks	Operated twice	-6 Months -Morbidity
Fournier D,[11] 1992	14 months	M	Pons & Medulla	Gait ataxia, quadraparesis 7th and lower cranial nerve palsy	2 months	Operated trice	Expired
Yoshizato K,[42]1996	69 Years	F	Pons	Hemiparesis, gait ataxia,7th nerve palsy	2 years	Operated Once	-2 Years -Good recovery
Radha VVK, [25]1992	13Years	F	Pons	Bulbar features	NA	Operated Once	Expired
Recinos P,[27] 2006	17 months	F	Ponto medullary	Hemiparesis, 7th nerve palsy, gait ataxia	18monhs	Operated twice	-2 Years -Good recovery
Sinha AK,[31] 1999	37 years	F	Pontine	Gait ataxia and vomiting	4yrs	Operated Once	-NA -Good recovery
Gopalakrishnan CV[12],2012	2 Years	M	Pons-Medulla	Right Hemiparesis	2 months	Operated Once	-6 Months -Good recovery
Present case	4 years	F	Pontine	6th, 7th , Hemiparesis, ataxia	2 months	Operated Once	-4Years -Good recovery

Abbreviations: NA, Not available

Table 2: Reported cases of Type1 brain stem epidermoid cysts in the literature

Authors	Age	Sex	Site of lesion	Clinical features	Duration of symptoms	Treatment	Follow up & Outcome
Leal O,20 1978	2years	F	Pons & Medulla	Infection, bulbar features, left hemiparesis	2-3 days	Operated Twice	-2 Months -Expired
Obana WG,22 1991	27 Years	F	Medulla	Headache, Diplopia Hemiparesis	3 years	Operated Once	-3 years -Good Recovery
Sari A,28 2005	18 Years	M	Pons & pre pontine cisterns	Neck pain	2 year	Operated Once	-NA -Good recovery
Caldarelli M,7 2001	18 months	F	Pons & pre pontine cisterns	Neck pin and non specific symptoms	NA	Operated Twice	-3 years Good recovery
Sener RN,30 2004	39 Years	F	Pons & pre pontine	Headache, 7th palsy	NA	Operated Once	-NA -Good recovery
Malcolm GP,21 1996	25 Years	M	Ponto medullary & pre pontine	Headache, gait ataxia Multiple cranial nerve palsy	3 months	Operated Once	-1 year -Good recovery
Takahashi M,34 2007	10 years	F	Ponto medullary & pre pontine cisterns	B/L 6th nerve,	3 weeks	ETV, 4 times Suboccipital craniotomy	-16 months -Good recovery
Schwartz,29 1978	13 months	F	Pons & pre pontine cisterns	Recurrent meningitis	18 months	No surgery	Dead

Abbreviations: NA, Not Available

Table 3: Reported cases of Type2 brain stem epidermoid cysts in the literature

There has always been a speculation in naming these lesions whether pure brainstem lesions or extension of these lesions into brain stem from the surrounding cistern. Based on the pathogenesis and relevant hypotheses, the author proposed four different anatomical types of brain stem epidermoid tumors, which can explain their natural history. (Table 1 & Figures 4,5,6,7)

Including the present case, there are 25 cases reported in the literature. According to this classification, eight each cases merits type 112,13,27,29,33,41,44 (Table 2) and type28,22-24,30-32,36 (Table 3) variants. There are seven type 35,13,17,18,20,24,45 (Table 4) and two type 424,26 (Table 5) lesions. According to the classification, the present case is a type 1 lesion, as it is a pure intrinsic brain stem epidermoid.

This classification system helps in assessing the natural history and uniform understanding among researchers. Based on the classification type, one can plan the surgical corridor for easy removal of these complex lesions.2,23

Clinical features:

Epidermoid cysts develop slowly, and the onset of neurological symptoms is usually gradual. Patients are harbouring these cysts typically become symptomatic between the ages of 20 and 40 years.8,39 Evaluation of the reported cases in the literature showed that the age ranged from one to 69 years with an average age of 20.9 years. There are 13 cases younger than ten years; two cases in the range of 11-18 years and 10 cases are above the age of 18 years. This distribution clearly shows that the paediatric age cases outnumber the adults. (Tables 2-6). Among the intrinsic brain stem (Type 1) epidermoids, 75% of cases are paediatric age group12,13,27,29,41. Unlike the previous reports29 suggesting that the paediatric brain stem epidermoids are uncommon, this report clearly showed that 60% 5,8,12,13,20,22,27,29,31,36,41,45of total reported cases are in paediatric age group.

Patients presenting with brain stem epidermoid tumors commonly exhibit symptoms related to compression

Authors	Age	Sex	Site of lesion	Clinical features	Duration of symptoms	Treatment	Follow Up & Outcome
Obana WG,[22] 1991	37	M	CPA, interpeduncular cisterns Infiltrating in to pons & medulla	Hearing loss Lower cranial nerve involvement Hemiparesis	5 years	Operated Twice	-7 years -Partial recovery
Kachhara R,[17] 2000	55	M	CPA, pons	Neck pain, gait ataxia Hemiparesis	10 years	Operated once	-9 Months -Good recovery
Bhatia,[4]1978	3.5 yrs	M	Ponto medullary	NA	NA	Operated once	Expired
Kuzeyli K,[19] 1996	2 years	M	Pons	Right 7th and facial nerve palsy	2 months	Operated once	-5 Months -Good recovery
Iihara K,[18] 1989	32	M	Pre pontine cisterns, pons & 4th ventricle	Head ache, ataxia, right 7th palsy, Hemiparesis	NA	Operated once	-NA -Good recovery
Ziyal IM,[43] 2005	5 years	F	Pre medullary cisterns & medulla	Lower cranial nerve palsy	3 Months	Operated once	-NA -Good recovery
Gopalakrishnan CV,[12] 2012	6	F	Ventral to pons & medulla	Headache	10 months	Operated once	-3 Months -Good recovery

Abbreviation: NA, Not Available

Table 4: Reported cases of Type 3 Brain stem epidermoid cysts in the literature.

Authors	Age	Sex	Site of lesion	Clinical features	Duration of symptoms	Treatment	Follow Up & Outcome
Obana W,[22] 1991	27	M	Pre pontine cisterns Pons	Head ache, Gait ataxia	2 years	Operated Twice	-1 year -Recurrence
Ogawa T,[24] 1985	38	F	Middle fossa & pons	Multiple cranial nerve palsy, Hemiparesis, ataxia	3 years	Operated Once	Expired at 3 months post operative period

Table 5: Reported cases of Type 4 brain stem epidermoid cysts in the literature.

Type of Epidermoid (Classification)	Total Number of cases reported in Literature	Age (Years)		Sex		Average Duration of Symptoms (Months)	Recurrence rate (Percentage)	Mortality rate (Percentage)
		Average	Median	Male	Female			
1	8	16	3	3	5	13.8	12.5	8
2	8	15.4	14	2	6	13.6	12.5	8
3	7	20	6	5	2	60.7	4	4
4	2	32.5	32.5	1	1	30	4	4
Total	25	20.9	13	11	14	29.5	33	24

Table 6: Comparative analysis of clinical features according to the type of brain stem epidermoid

of associated structures. The average duration of the symptoms was 29.5 months. In paediatric cases, the duration of symptoms are only 1½ months, whereas in adults it is 42 months. The age and sex distribution, duration of symptoms according to the classification are summarized in Table 6. On the evaluation of clinical features, it was observed that the most common signs are hemiparesis (64%), cranial nerve palsy (64%) and gait ataxia (32%). This child presented with left 6th and 7th cranial nerve palsy along with gait ataxia and left hemiparesis. The child became lethargic and bedridden two weeks before surgery. Following the surgery, she recovered quite well.

Radiological features:

Typical intrinsic epidermoid cyst as seen in the present case has the characteristic appearance on conventional MR imaging sequences (Figure 2). They appear hypointense on T1 – weighted MR imaging and hyperintense on T2 – weighted MR imaging6,34,37 compared to Cerebro spinal fluid (CSF). The relative composition of cholesterol and keratin contributes to the MR signal. Cholesterol in the solid state contributes to the hypointense signal on MR imaging.1,25 T1 and T2 weighted MR imaging can also show variable signal intensity depending on the protein, free water, lipid, calcification, fibrosis, and paramagnetic cyst contents.25 Hyperintensity of the epidermoid cyst could be due to the high protein contents of the cyst.25 The hyperdensity can be attributed to the calcification of the keratinized debris and saponification of debris of calcium.7 The hyperdensity may be attributable to traumatic or spontaneous intra cystic micro bleeding.15,16 Epidermoid typically appears as hyperintense on diffusion-weighted imaging due to the precise organization of the epithelial cells and their preference to grow in layers, so the anisotropy restricts diffusion.34 Special MR sequences like FLAIR, CISS- 3D, ADC, and MR spectroscopy, helps to differentiate typical epidermoid cysts from few atypical epidermoid cases and other brain stem lesion like arachnoid cyst, neurenteric cyst, and cystic gliomas.3,6,40

Treatment:

Despite their eloquent location in the brain stem, surgical removal is the best treatment. Except one31 , out of 25 reported cases were managed surgically. Although the cyst contents can be removed easily, radical excision of the cyst wall can be extremely difficult at times because of the firm adherence to the surrounding neurovascular structures.24 Attempts at a radical remove of the capsule especially in Type 1 lesions could be dangerous as demonstrated by analysis of the experiences reported in the literature.13,24,33 Even in the present case, it was not possible to remove the capsule entirely, as it was ill defined. A major concern after a conservative resection is a recurrence. The recurrence rate is nearly 33%8,12,22,24,29,36,41 out of all the reported cases (Table 5). The incidence of recurrence is common among type 1 and type 2 cases. Although the tumor recurrence is expected to follow in partial or incomplete resection, the symptom-free interval before recurrence can be unusually long. Six of 25 reported cases died, among them five5,12,22,26,27 cases were operated. Three of these expired cases were treated before the availability of the CT scan. The cases reported after 1992, did not encounter mortality. Delayed diagnosis, aggressive surgical removal, and post-operative complications14,44 might have contributed to the poor outcome in CT and pre-CT scan era. All patients who had a decent surgical outcome had undergone total removal of the cyst contents and subtotal removal of the nonadherent cyst wall. The author also believe that radical resection of the cyst wall tends to produce poor outcome irrespective of the type of epidermoid cyst. This child is asymptomatic with out recurrence for the last six years. During the surgery, one should be careful to avoid the spillage of the cyst contents into the subarachnoid space to avoid chemical meningitis and adhesions.13,31,44

Conclusion: Brain stem epidermoids are rare tumors with uncertain pathogenesis. The age distribution of the reported cases ranged from one to 69 years with slight paediatric predominance. Based on the morphological features these tumors could be divided into four different types for a better understanding of the natural history and clinical spectrum. Typical brainstem epidermoid tumors can be diagnosed appropriately with MRI. Wherever feasible, adequate surgical excision is the hallmark in the treatment of these lesions.

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