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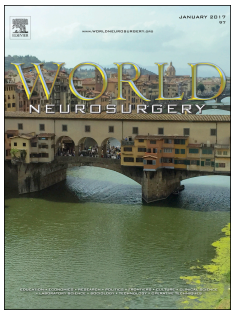

Unusual intra-parenchymal pontomedullary epidermoid cyst in a 2 year-old: case report and literature review

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Unusual intra-parenchymal pontomedullary epidermoid cyst in a 2 year-old: case report and literature review

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Abstract:

Background: Intrinsic brainstem epidermoid cysts are rare, benign, slow growing lesions. Their eloquence preclude complete excision, however subtotal resection will often result in prolonged or sometimes permanent relief of presenting symptoms and signs. We describe an unusual case and review the literature of this pathology in the paediatric population.

Case description: We report an intra-axial pontine epidermoid cyst in a 2-year-old girl who presented with developmental delay, multiple cranial nerve palsies and pneumonia. Magnetic resonance imaging (MRI) demonstrated an intrinsic pontine lesion with partial restricted diffusion and an enhancing plaque, the latter not typically seen in congenital lesions like epidermoid. However, gross surgical inspection and histopathology confirmed an epidermoid.

Conclusion: Our case, supported by the literature, shows that brain stem epidermoid cysts may have atypical radiological characteristics, and that near total resection remains safe and can improve outcome.

Key words: Epidermoid, brainstem, pons, intra-axial, congenital, cranial nerves.

Introduction:

Epidermoid cysts are rare, congenital, intracranial space-occupying lesions, which represent about 0.2-2% of all intracranial tumours[1-3]. These primarily arise in the basal subarachnoid spaces and commonly involve the cerebellopontine angle and juxta-sellar areas[4]. They usually result from inclusion of ectodermal elements during neural tube closure. These lesions classically present in middle age due to mass effect and/or hydrocephalus[5], presentation in the paediatric age group is however rarer but can occur (Table 1) . Accumulation of desquamated cell debris from the cysts' capsule increase their size. Appearances mimic cerebrospinal fluid (CSF) on computed tomography (CT) and MRI with no contrast enhancement (typically). Diffusion weighted imaging (DWI) demonstrates

restricted diffusion[2]. Brainstem epidermoid cysts in children are rare; with only fifteen cases reported to date[1, 3, 6-16]. The treatment of choice is surgical resection if the patients are neurologically symptomatic which is common at first presentation. However, due to their eloquence and adherence to brainstem, complete excision is difficult and recurrence is therefore not uncommon[3]. Although growth is typically slow and time can elapse without new symptoms; recurrence can be fatal[7]. Once diagnosed, treatment strategies including safe surgery and prolonged follow up is essential to achieve long lasting good outcomes.

Here, we describe a rare case of an intra-parenchymal pontomedullary epidermoid cyst in a 2 year-old girl who presented with general developmental delay and 5 months' history of worsening multiple cranial nerve palsies which caused aspiration pneumonia. The cyst had atypical imaging characteristics in the form of an enhancing plaque which is finding more common in pilocytic astrocytoma than epidermoid. The patient had surgery where gross surgical findings were more consistent with epidermoid and the histopathology results confirmed the diagnosis. She improved clinically after surgery. We also conduct a review of children brainstem epidermoid cysts in the literature with emphasis on MRI findings.

Case report:

This 2-year-old girl with general developmental delay, born as a twin of dichorionic, diamniotic pregnancy, presented with a 5 month history of progressively worsening strabismus, 1-week history of increasing lethargy, difficulty swallowing and decreased oral intake to both solids and liquids. She also developed hypoglycaemia (2.6mmol/l) and sepsis due to aspiration pneumonia that was treated with 3 days of intravenous ceftriaxone. On examination, her weight was within the second centile for 8 months before admission, she had left ptosis, bilateral facial palsies, bilateral sixth nerve palsy, asymmetrical chest expansion, and C - reactive protein was 60 mg/L (*N=<5mg/L*) with a low haemoglobin of 105 g/L (*N=13-15g/L*) and a normal white cell count. She was floppy, lethargic but able to

move all four limbs. The patient is being investigated yet to be confirmed to have Coffin-Siris Syndrome which is an autosomal dominant syndrome whose hallmarks include intellectual/developmental disability, delayed milestones and abnormalities of the fifth finger and toes[17]. Radiologically, a CT head (Figure 1A) revealed a large cystic posterior fossa lesion with rim enhancement posteriorly causing brainstem expansion and significant thinning of the parenchyma and mild hydrocephalus. The patient was transferred urgently to our neurosurgery centre. MRI (Figure 1B-G) demonstrated a cystic lesion within the brainstem measuring 35 x 27 x 32 mm that is hyperintense on T2 weighted imaging (T2W) sequence and of slightly higher intensity on FLAIR and hypointense on T1 weighted imaging (T1W) sequences with lower values on the ADC gradient mainly posteriorly within the cyst. The brainstem parenchyma was noted to be stretched and thinned posteriorly and anteriorly, most markedly at the lower third of the pons bulging into the floor of the fourth ventricle (Figure 1B). Post contrast images demonstrated the small enhancing nodule in the posterior right lateral aspect of the cystic lesion seen on T1W images (Figure 1 C&D). Other MRI features which may not be related directly to the epidermoid cyst included, dysgenetic and dysmorphic corpus callosum with a short midline segment. There is a sub-ependymal cyst in the right frontal horn, small septi anteriorly within the right frontal horn and underdeveloped frontal lobes. The patient underwent an urgent midline sub-occipital craniotomy. On splitting the vermis, the floor of the fourth ventricle was exposed and found to be distended posteriorly by the underlying cyst. The cyst was punctured and found to contain milky white fluid with pearly flakes. The histopathology result confirmed fibrous connective tissue and reactive astrocytes that enclosed stratified squamous epithelium. The cyst forms clefts but there are no skin appendages, which confirms the diagnosis (Figure 2). Near total resection of the nodule was achieved uneventfully. This enhancing nodule seen on MRI correlated to the histopathology findings of acute and chronic inflammatory cells infiltrating gliotic brain

tissue (Figure 2 B). The procedure was uneventful, so was the immediate post-operative period. A feeding nasogastric was kept in place due to the pre-existing poor bulbar function. Two weeks later she was started on puree diet with steady improvement in her neurological status and discharged for further rehabilitation. At 3 months, her swallowing is back to normal and she gained weight (between 9th and 25th centile), an MRI scan 3 months post operatively demonstrates no recurrence (Figure 3 C-F) and no restricted diffusion.

Discussion:

Epidermoid cysts are composed of desquamated epidermal cell debris originating from an inner epithelial lining of the glistening well-circumscribed, irregular, thin walled white cystic capsule[18]. They usually arise dorsally along the midline between the third and fifth weeks of gestation from displaced epithelial tissue during closure of the neural tube[18]. The epithelium undergoes progressive desquamation and keratin breakdown, which forms the cystic contents that include tissue debris, keratin, water, and solid cholesterol[19]. We report an intrinsic pontine cyst that has three layers, an inner layer of stratified squamous epithelium, outer layers of connective tissue and gliotic brain with infiltrative acute and chronic inflammatory cells, importantly the cyst formed clefts that did not reveal any skin appendages confirming the epidermoid diagnosis (Figure 2 A-C).

On imaging epidermoid cysts are usually homogenous, non-enhancing and hypodense on CT, hypointense on T1W MRI imaging, hyperintense on T2W and in addition to being hyperintense on DWI, an epidermoid is usually hypointense on ADC (confirming diffusion restriction rather than T2 shine-through)[20]. However, atypical characteristics have been reported in literature. In one report, cyst wall enhancement was noted in a 7 year-old girl with brainstem epidermoid cyst [15]. Moreover, nodular enhancement within the cyst wall was seen in a 2 year-old patient [16]. Interestingly, a 6 year-old girl with brainstem epidermoid cyst had atypical partial restriction on DWI sequences[16]. Uncommon features with post contrast

enhancement was also described in 1.5 year-old and 16 year-old girls[13]. Our patient had atypical MRI findings mimicking other low-grade tumours. In our case, axial T2WI (Figure 1 E) shows a well-defined fluid filled cystic lesion in the brainstem which was expanding the latter. There is a significant thinning of the brain parenchyma at the anterior aspect of the lesion with only a faint thread of parenchyma crossing the midline confirming an intrinsic lesion. DWI (Figure 1 F) and ADC (Figure 1 G) axial images demonstrate layering of material with increasing restricted diffusion at the posterior aspect of the lesion only. Usually a uniformed restricted diffusion on DWI is expected however only partial restriction was noted in our case perhaps reflecting a viscous fluid rather than a solid lesion. Moreover, post contrast T1W images revealed a thin plaque of enhancement at the posterior aspect of the lesion (Figure 1C, D). There is also signal intensity within the lesion, as the content changes from low T1 signal anteriorly to faintly intermediate intensity posteriorly. These findings are possibly due to variable protein concentration.

We further reviewed the literature and report 16 (including ours) cases of confirmed intra-axial brainstem epidermoid cysts in children to date[1, 3, 6-16] (Table 1). Mean age at presentation is 4.6±1.2 years (range between 1 and 16 years); however, there were 12 females with a mean age of 5.6±1.4 years and 4 males with a mean age of 1.6±0.3 years. Most of these cysts were reported in the pons with/without medulla involvement and rarely involving the medulla on its own (Table 1). Patients often have cranial nerve palsies at presentation, in addition to symptoms and signs of raised intracranial pressure and occasionally cerebellar signs. 15 patients had surgery for the cysts with one exception where the patient had a shunt only and diagnosis was confirmed post-mortem[11]. Due to the rarity of this condition in the paediatric age group, there is no consensus on the best management strategy. While surgical removal was recommended by the multidisciplinary team discussions in our unit as the best therapeutic option for the treatment of this symptomatic epidermoid cysts and total excision

was the surgical goal, subtotal excision was recommended as the cyst is adherent to the brainstem. Attempting aggressive total resection of the cyst wall poses a surgical challenge with increased risks of morbidity and mortality. Surgical judgement should ensure maximum resection while minimizing postoperative neurologic deficits. In agreement with this treatment strategy, we did a near total resection with good outcome. On reviewing the literature we found at least 7 of the brainstem epidermoid cyst cases in Table 1 had safe subtotal resection with satisfactory outcomes. On the other hand, cases with no mass effect and confirmed diagnosis can be treated more conservatively where surgery can be deferred with acceptable outcome and minimal complications[9]. We also observed that patients who had surgery whether subtotal resection or gross total excision (Table 1) did not require CSF diversion procedures and/or permanent V-P shunts whereas other posterior fossa/brainstem tumours may do.

In conclusion, intra-axial brainstem epidermoid cysts are exceptionally rare lesions in children that may mimic the appearance of cystic neoplasms. MRI with DWI sequence is helpful in diagnosis, however atypical appearances should be considered. Surgery is indicated in symptomatic patients. Although radical excision will prevent recurrence, due to their treacherous anatomical location, near total resection is a safe strategy with good outcomes as supported by the literature findings.

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Figure legends

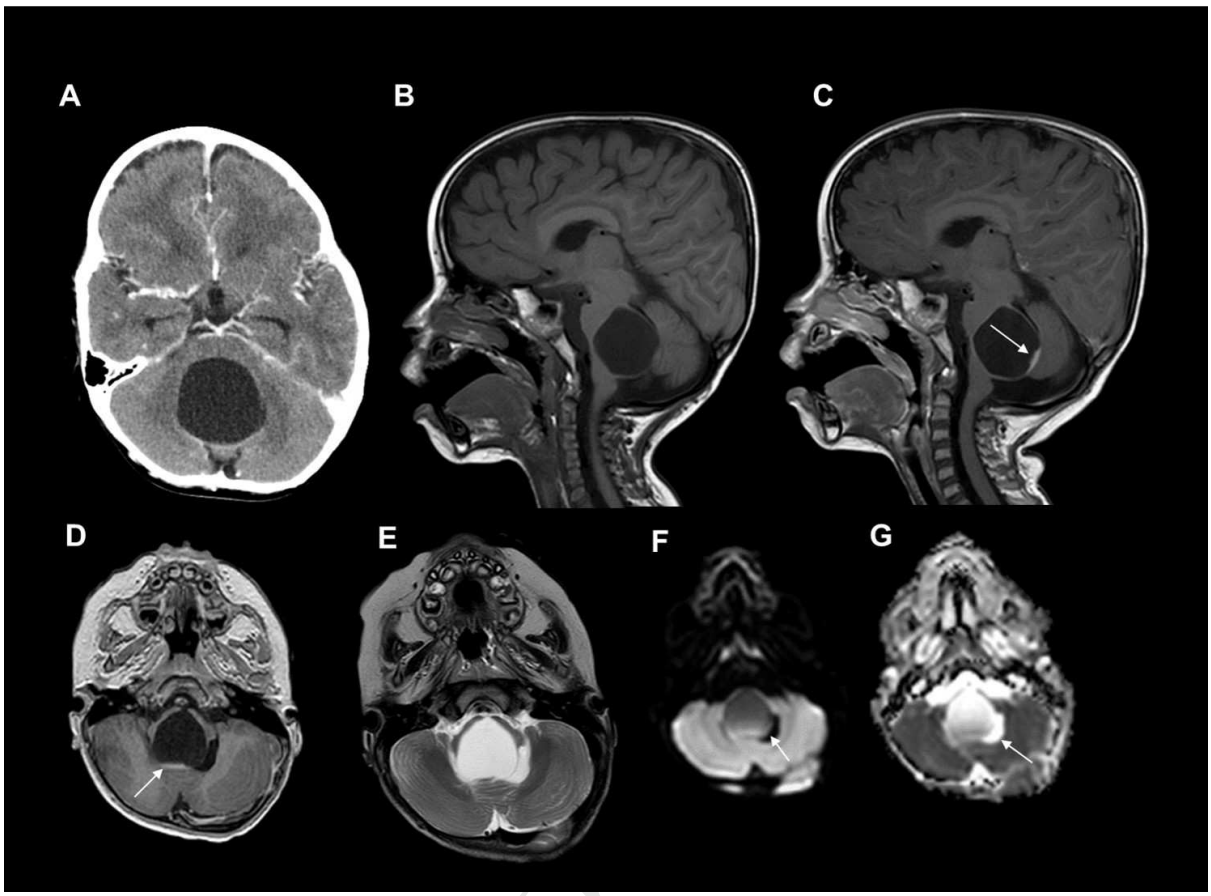
Figure 1 Pre-operative images. A An axial post contrast CT image showing the cyst with rim enhancement. B A sagittal T1WI demonstrating the epidermoid cyst with very thin pontine parenchymal tissue. C & D Post contrast sagittal and axial T1WI showing the enhanced nodule of the cyst (arrow). E An axial T2WI showing hyperintense and well-defined fluid rich cystic lesion in the brainstem expanding the latter. F DWI & G ADC axial images demonstrating restricted diffusion (arrows) at the posterior aspect of the lesion only.

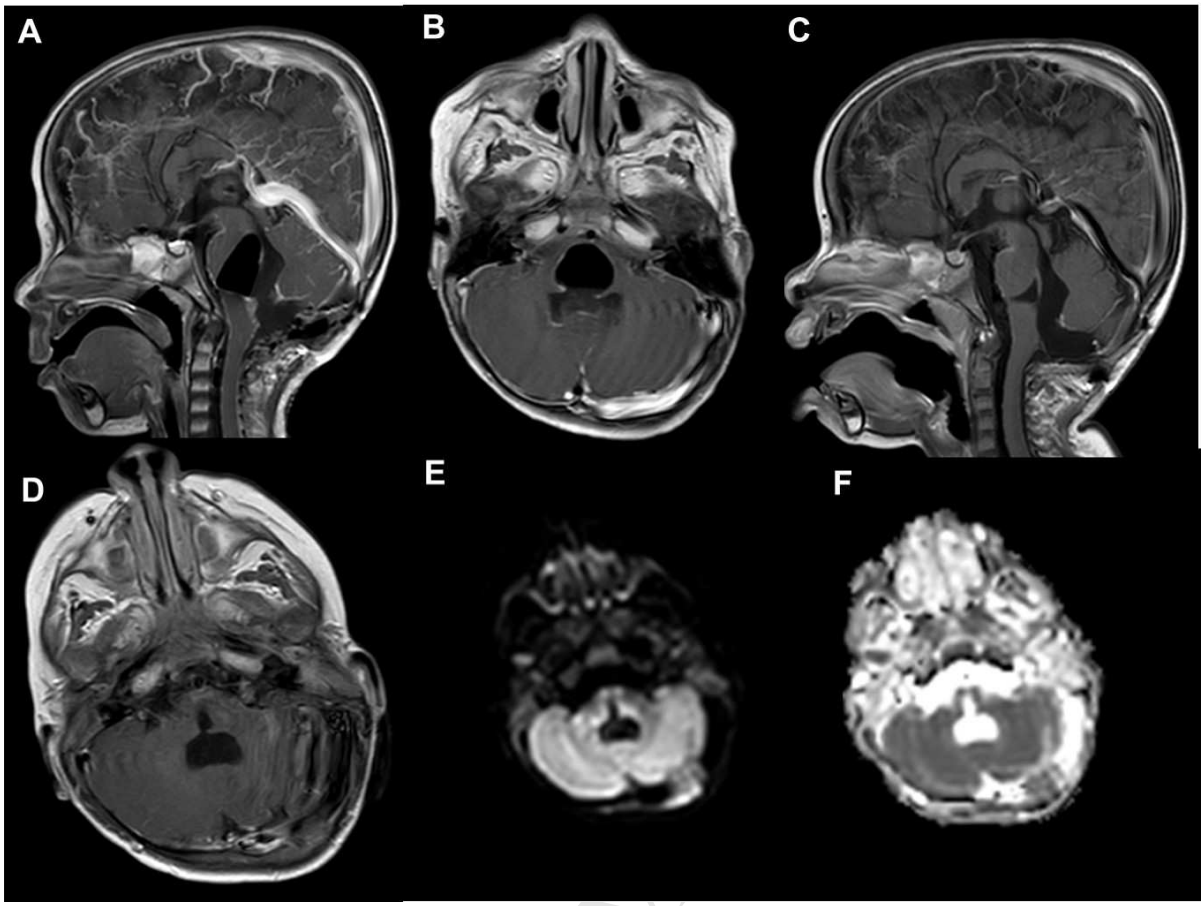
Figure 2 Histopathology of the cyst. A The cyst has three layers, an inner layer of stratified squamous epithelium and outers layers of connective tissue and gliotic brain. Haematoxylin and eosin. B. The cyst is focally ulcerated and inflamed. Haematoxylin and eosin. C The cyst forms clefts but there are no skin appendages. Haematoxylin and eosin. Objective lens magnification 20x, scale bar = 100 microns.

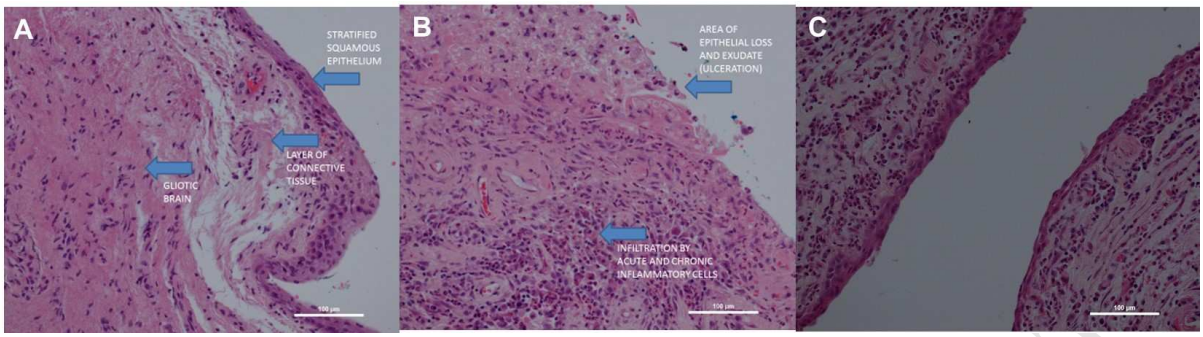
Figure 3 A & B Post contrast T1WI (sagittal and axial) showing decompressed cyst with intracranial air (same day after surgery). C & D Post contrast T1WI (sagittal and axial) demonstrates satisfactory follow up appearance at 3 months with no recurrence. E DWI & F ADC axial images shows no restricted diffusion at 3 months follow up MRI scan.

Table 1 Literature review of brainstem epidermoid cysts in children. Post contrast MRI, Y= enhancement, N= no enhancement, N/A= data not available.

Report	Age/ Sex	Location	Presentation	MRI Characteristics			Treatment	Outcome
				T1WI	T2WI	Post Contrast MRI (Y/N/NA)		
Bhatia et al 1978	3½Y/ F	Pons, medulla	CN V,VI ,VII palsies, hemiparesis, papilloedema	No MRI, Ventriculogram only			Surgery	Died
Schwartz et al 1978	14mo/F	Pons	Meningitis, CN VII palsy, hemiparesis	No MRI, CT only			V-P shunt	Died
Leal et al 1978	3½Y/ F	Medulla	Facial palsy, drowsiness, hemiparesis	No MRI, Ventriculogram only			Surgery twice	Died
Weaver et al 1979	1Y/M	Pons	CN VI & CN VII palsy,	No MRI, CT only			Aspiration, subtotal excision	Survived
Fournier, et al., 1992	14mo/M	Pons, medulla	CN VII palsy, quadriparesis, spastic/ataxic gait, swallowing problems	MRI details N/A			Surgery 3 times	Died
Kuzeyli et al 1996	2Y/M	Pons	Headache, CN VII palsy, behaviour problem	MRI details N/A			Subtotal resection	Survived
Caldarelli et al 2001	18mo/F	Pons, medulla	Unsteadiness, behaviour problems,	Hypointense	Hyperintense	Y (Rim)	Subtotal resection	Survived
Caldarelli et al 2001	16Y/F	Pons, medulla	Headache, CN VI&VII palsies	Hyperintense	Hypointense	Y (Rim)	Subtotal resection	Survived
Ziyal et al 2005	5Y/F	Medulla	Dysphagia, lower CN palsies	Had MRI but not mentioned characteristics			Subtotal resection	Survived
Recinos et al 2006	17mo/F	Pons, medulla	CN VII palsy, hemiparesis, loss of balance, headache	Hypointense	Hyperintense	N	Surgery twice	Survived
Takahashi et al 2007	7Y/F	Pons, medulla	Dysphagia, vomiting	N/A	N/A	Y Rim enhancement	Surgery twice	Survived
Gopalakrishnan et al 2012	6Y/F	Pons, medulla	Headache	Hypointense	Hyperintense	N (partial DWI restriction)	Subtotal resection	Survived
Gopalakrishnan et al 2012	2Y/M	Pons, medulla	Hemiparesis	Hypointense	Hyperintense	Y (nodular enhancement)	Gross total resection	Survived
Mishra et al 2014	15Y/ F	Pons, medulla	Quadriparesis with multiple cranial nerve palsies (V, VI, IX, X, and XII)	Hyperintense	Hypointense	Y	Gross total resection	Survived
Patibandla et al	5Y/F	Pons, medulla	Headache, swallowing	Hypointense	isointesne	N	Subtotal resection	Survived







Highlights:

Manuscript title: Unusual intra-parenchymal pontomedullary epidermoid cyst in a 2 year-old: case report and literature review

Manuscript type: Case report and Literature Review

- Intra-axial brainstem epidermoid cyst in a child.
- Atypical radiological characteristics.
- Subtotal resection is safe and improves the outcome.

Abbreviation in this article:

Magnetic resonance imaging: MRI

T2 weighted imaging: T2WI

T1 weighted imaging: T1WI

Diffusion weighted imaging: DWI

Computed tomography: CT