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Case report

Ossified spinal epidermoid cyst: A systematic review and case report

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ABSTRACT

Background: Epidermoid cysts (ECs) are rare, benign lesions which comprise less than 1 % of all spinal tumors. Calcification of spinal ECs is rare, and EC ossification within the lumbar spine has never been documented. We report the only known congenital lumbar epidermoid tumor with ossification and a literature review of intradural lumbar ECs.
Methods: Studies meeting the following criteria were included: 1) EC as the primary tumor type, 2) intradural location, 3) involvement of the lumbar spinal level, and 4) primary presentation. Studies lacking individual patient data or published in a non-English language were excluded.
Results: A total of 172 studies were reviewed and 43 were included in analysis. Of the 83 total patients, 37 (45.1 %) were male and 45 (54.9 %) female, at an average age of 26 years. The L3 and L4 spinal levels were most frequently involved. Acquired etiology was reported in 49 (59.0 %) patients, and 24 (28.9 %) cases were congenital. Multivariate analyses demonstrated trends between decreased age and improved outcome, decreased delay in diagnosis and improved outcome, and increased extent of resection with reduced recurrence. Nine calcified spinal ECs were identified, with no previous report of EC ossification in the lumbar spine.
Conclusion: We present a case report of the only known ossified epidermoid tumor of the lumbar spine and a comprehensive literature review of 83 patients with intradural lumbar ECs. This review demonstrated trends between reduced age and improved outcome, reduced delay in diagnosis and improved outcome, and increased extent of resection with reduced recurrence.

1. Background and objective

Epidermoid tumors, or cysts, are rare, benign lesions found along the neuroaxis. These tumors are classified as congenital or

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acquired. Congenital epidermoid cysts (EC) are believed to be inclusions of cutaneous ectoderm resulting from aberrant implantation of ectodermal cells during neurulation [1–8]. In the 1950s, it was discovered that ECs can also be acquired through the displacement of epidermal tissue into the subdural space during lumbar puncture, surgical procedures, or other trauma [1,3–5,7–12]. Most epidermoid tumors are located in the cranium, while a minority arise in the spine [1,3,13,14]. EC comprise less than 1 % of spinal tumors [1,2,5,8,10,15–17] and are found most commonly in the lumbosacral spine, followed by the thoracic region [1,3,5,8,16]. These lesions are typically intradural within the spinal canal [5,8,16,17] and are associated with various types of spinal dysraphism, such as spina bifida, dermal sinuses, myelomeningocele, and diastematomyelia [1,7,10,14,17,18]. Spinal EC cases without associated congenital stigmata are typically located in the lumbar region [5,19].

The symptomatic presentation of spinal EC is dependent on the location and extent of involvement, but manifests as signs of spinal nerve or cord compression, secondary inflammation, or rupture [3,5,13,20]. The latent growth of epidermoid tumors can result in both delayed presentation and symptom manifestation years prior to diagnosis [5,21]. Magnetic resonance imaging (MRI) is the preferred imaging modality for spinal EC, and the masses are typically hypointense or isointense on T_1-weighted images and hyperintense in T_2 sequences [1,6,8,12,17,22–24].

French pathologist Cruveilhier was the first to describe ECs, which he termed *tumeurs perlées*, or pearly tumors, for their smooth capsule [6,25–27]. Epidermoid cysts are histologically characterized as well-circumscribed, encapsulated tumors with a lining of stratified squamous epithelium surrounded by an outer collagenous layer [3,6,13,17].

Due to their slow growth rate, observation is appropriate for small, uncomplicated, and asymptomatic ECs [24]. *En bloc* resection is standard of care for the surgical treatment of symptomatic ECs to reduce the risk of recurrence and prevent aseptic meningitis, which results from an inflammatory reaction to the keratinous material contained within the cyts [1,2,4,6–8,18,28,29]. Total resection can be complicated by the tendency of epidermoid tumors to adhere to critical neurovascular structures; in these cases, preservation of neurological function should be a priorty [1,8,14,18,30]. We report the first known surgical case of a lumbar epidermoid cyst with a component of mature bone formation, and the first ossified EC within the central nervous system (CNS) with pathologic images.

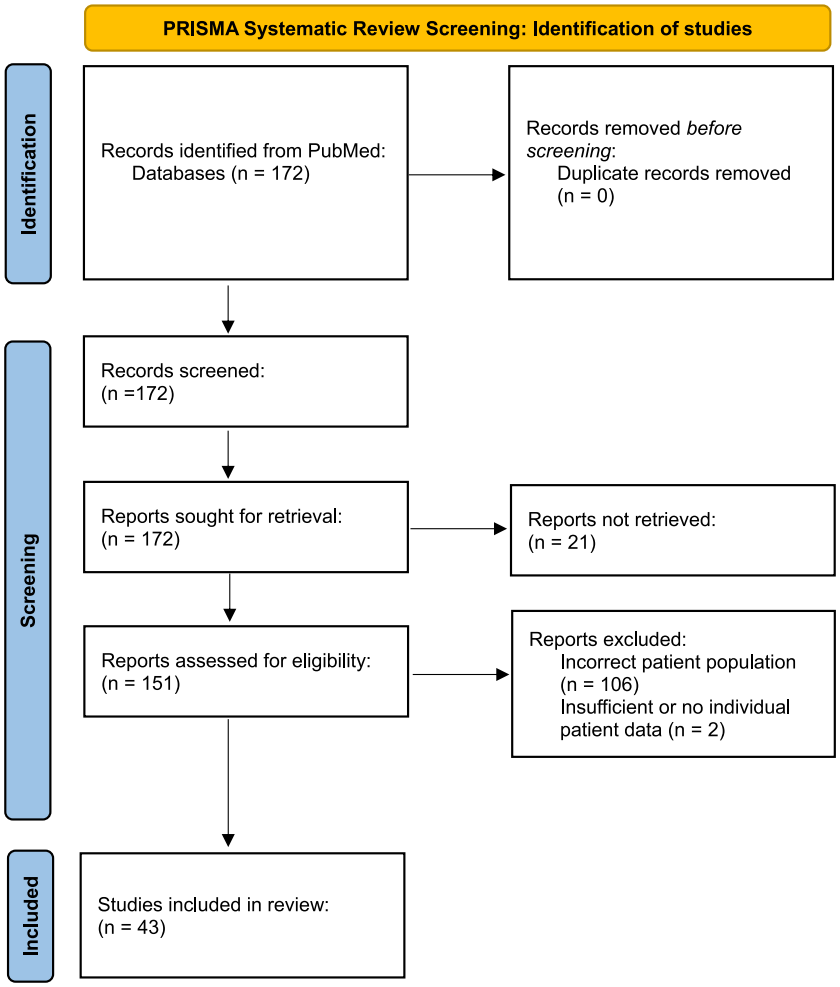

Fig. 1. PRISMA Diagram outlining Systematic Review Screening Process.

2. Methods

We present a novel case of a 55-year-old female with progressive lower back pain and paresthesia secondary to a lumbar, intradural epidermoid cyst. We also performed a literature review of the PubMed database following the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [31] using the terms "lumbar," "spine," "spinal," and "epidermoid" alone and in combination (Fig. 1). Studies that met the following criteria were included: 1) epidermoid cyst as the primary tumor type, 2) intradural location, 3) involvement of the lumbar spinal level, and 4) primary presentation. Studies were excluded if they did not report individual patient data, were published in a non-English language, or lacked an accessible full-text article. Patients with recurrent or malignant tumors were excluded. Associations between predictors and outcomes were evaluated using multivariate regression analyses. All statistical analyses were performed in RStudio [32].

2.1. Case description

Our patient was a 55-year-old female who presented with six months of severe lower back pain with left lower extremity non-dermatomal numbness, paresthesia, and non-focal subtle leg weakness with unsteady ambulation. She denied radiculopathy but reported severe bilateral pain in her feet. MRI demonstrated a 2-cm intradural, T2 mixed-intensity lesion at the level of L2-3 with a minimal focal area of contrast enhancement (Fig. 2). The patient denied any history of lumbar puncture, trauma, or spinal surgeries.

Intraoperatively, after laminectomy and dural opening, a hard lesion with a focal area of soft, flakey tumor was identified. The firm portion circumferentially encased a traversing nerve root. A trough was painstakingly drilled through the ossification using ultrasonic aspiration to release the nerve (Fig. 3). After gross total resection of the tumor (Figs. 3 and 4), the intradural space was copiously irrigated with hydrocortisone irrigation, and the dura was closed in watertight fashion. Pathology demonstrated stratified squamous epithelium and loose keratin, consistent with the contents of an epidermoid cyst. In addition, the firm tumor portion demonstrated ossification with mature bone (Fig. 5). No atypia or signs of malignancy were appreciated on histology. Postoperatively, the patient experienced resolution of her pain, normalized sensation, and improved strength and ambulation.

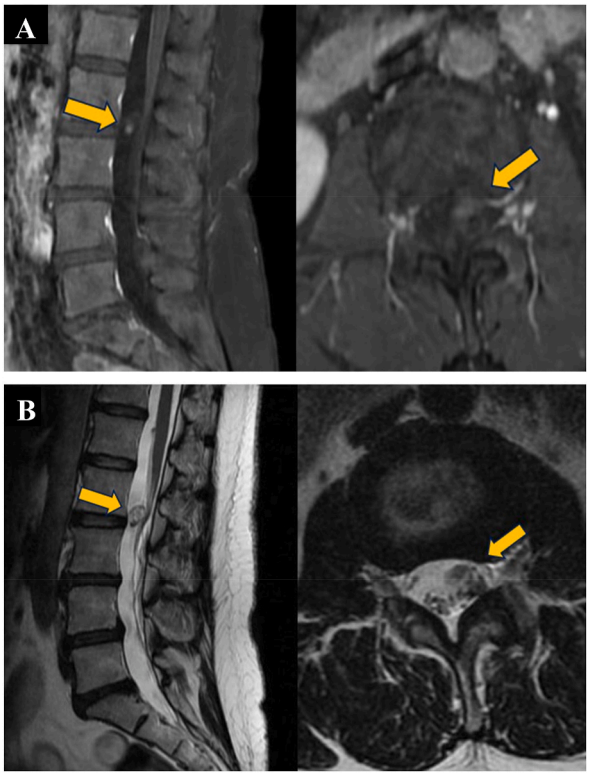

Fig. 2. (A) Preoperative T1-weighted MRI demonstrating minimal contrast enhancement on sagittal (left) and axial (right) imaging. **(B)** Preoperative T2-weighted MRI demonstrating mixed signal intensity on sagittal (left) and axial (right) imaging.

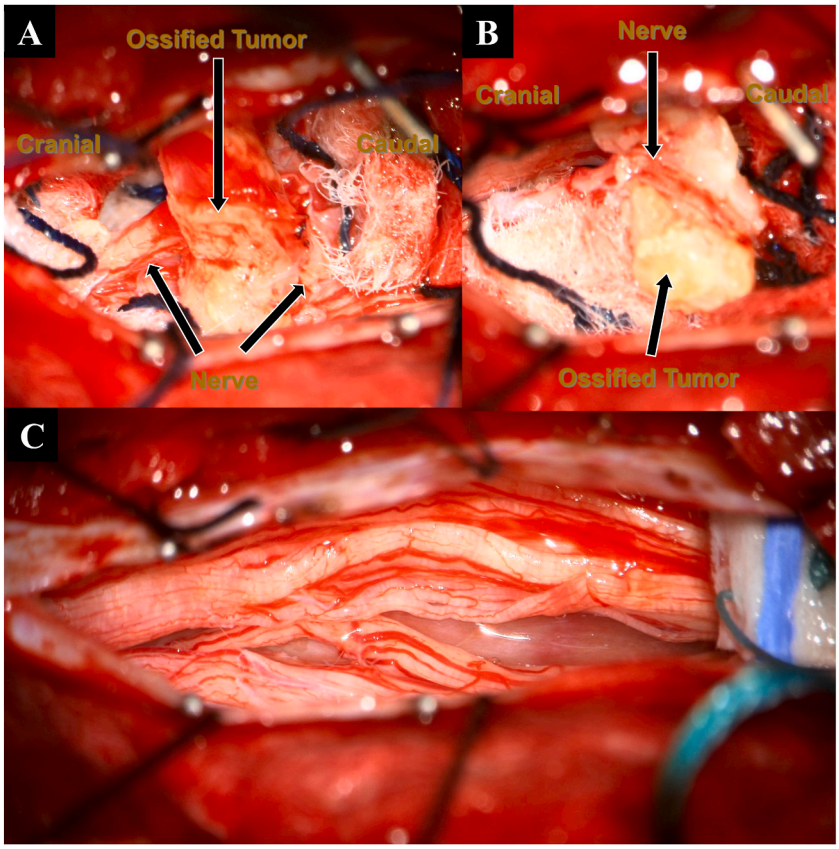

Fig. 3. **(A)** Intradural lumbar epidermoid with ossification circumferentially encasing traversing nerve root. **(B)** Intradural lumbar epidermoid with trough drilled through the ossification to release the traversing nerve root. **(C)** Gross total resection of intradural lumbar epidermoid with decompressed nerve roots.

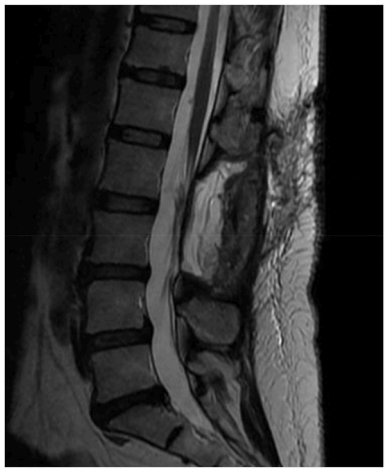

Fig. 4. Postoperative T2-weighted MRI demonstrating gross total resection on sagittal imaging.

3. Results

3.1. Intradural epidermoid cysts of the lumbar spine

Of the 172 studies returned by the literature search, 43 publications were included in analysis. Individual patient data was available

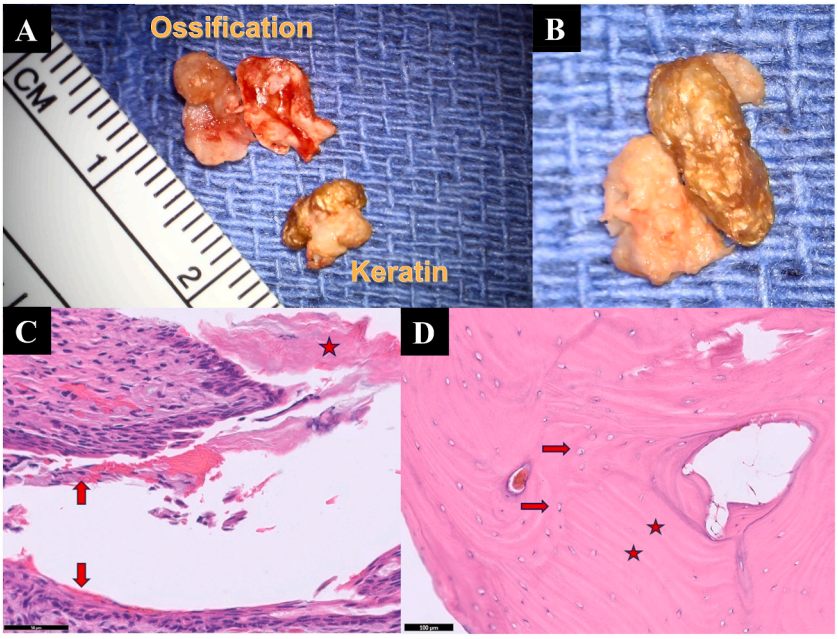

Fig. 5. **(A)** Gross pathology of soft keratin and hard ossified portions of the epidermoid. **(B)** Gross pathology of soft keratin of the epidermoid. **(C)** Histological slide at 40x shows a cyst wall lined by reactive squamous epithelium (arrows) with loose keratin (star). **(D)** Histological slide at 10x shows mature lamellar bone (stars) and lacunae with osteocytes (arrows).

for 83 patients with intradural lumbar ECs. The average patient age was 26 years (range: 4 months to 69 years), with a slight female preponderance (55 % female, 45 % male). The most frequently involved spinal levels were L3 and L4, each with 38 (25.9 %) cases. On presentation, 44 (53.0 %) patients reported back pain, 43 (51.8 %) lower extremity pain (including hip pain), 41 (49.4 %) sensory or motor neurologic deficit, 21 (25.3 %) bowel/bladder dysfunction, and 11 (13.3 %) with gait dysfunction.

Acquired etiology was reported in 49 (59.0 %) patients, and there were 24 (28.9 %) cases of congenital origin. The tumor etiology was unclear in 10 (12.0 %) patients. Spinal dysraphism or other associated congenital anomalies were recorded in 13 (15.7 %) individuals. Prior lumbar puncture was noted in 43 patients (51.8 %), lumbar surgery in six (7.2 %) cases, and lumbar discography in one (1.2 %). The average time from lumbar puncture to diagnosis in relevant cases was 77.5 months (median of 72.0 months). Adherence to nearby structures was observed during the operation in 30 (36.1 %) cases. No cases of associated ossification were identified. One (1.2 %) patient in the cohort presented with chemical meningitis secondary to ruptured EC and died before undergoing resection. The remaining patients all underwent surgical resection as the primary treatment.

The average delay to diagnosis (time from onset of symptoms to diagnosis) was 24.6 months (median: nine months, range: 0.1–180 months), and the average last follow-up visit was at 48.7 months (median: 32.0 months, range: 0.5–209 months). No significant association was found between outcome and age, spinal level, adherence, or delay in diagnosis. However, trends were noted between decreasing age and improved outcome ($p = 0.031$), reduced delay in diagnosis and improved outcome ($p = 0.095$), and increased extent of resection with reduced recurrence ($p = 0.058$).

3.1.1. Calcified or ossified epidermoid cysts along the neuroaxis

In a 2023 query of the full-text English literature in PubMed, calcification was noted in 49 cases of intracranial ECs and nine cases of spinal ECs. Of the spinal calficiations, no cases involved the cervical spine, two involved thoracic levels, six involved the lumbar region, and one was solely located within the sacrum (Table 1) [23,33–40]. Only two documented instances of CNS epidermoid cysts with ossification were identified, both appearing in the same 1986 case series. The first was a 54-year-old woman who presented with progressively worsening leg pain and weakness, and a T10-11 extradural mass with intradural erosion was identified. The resected mass was histologically consistent with an epidermoid cyst and was reported to have “perivascular ossification.” The second patient was a 55-year-old woman with six months of leg weakness who was found to have an extradural T11 lesion. Pathology was described as having “ossifying debris, similar to that seen in Patient 1.” However, no ossification was noted on the published pathology image.

4. Discussion

We present a novel case of an intradural lumbar epidermoid cyst with mature bone formation. Calcified epidermoid cysts are rare, with a vague incidence due to lack of large studies. The combined incidence of cranial and spinal ECs with calcified components ranges from 4 to 25 %, with a predominance of calcification in cranial rather than spinal EC [37,41–46]. We identified a total of nine spinal ECs with calcified components in the English literature to date.

Table 1
Spinal epidermoid cysts with calcified component in the literature with patient history and treatment outcome. These cases were identified from articles selected from the PubMed database according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Patient Demographics														
Author, Year	Age (yr)	Gender	Level	Congenital/ Acquired	Prior LP	Time from LP (mo)	Presenting Symptoms	Delay to Diagnosis (mo)	Treatment	Extent of Resection	Adherence	Follow-up (mo)	Outcome	Recurrence
Willinsky, 1986[70]	54	F	T10-T11	a	No	–	LEP, MD, SD	72	resection	–	–	–	PR	–
Demaerel, 1994[16]	9	M	L1-L3	a	Yes	96	BP	–	resection	–	–	–	GR	–
Lai, 2005[33]	49	M	L1-L3	–	No	–	LEP, MD	192	resection	STR	Yes	–	–	–
Miyake, 2005[38]	61	F	L4	a	Yes	168	BP, SD	180	resection	GTR	Yes	–	–	–
Morita, 2012[39]	45	F	L4	a	Yes	120	LEP, SD	–	resection	GTR	Yes	52	WR	No
Mishra, 2015[37]	14	M	T5	c	No	–	BP, MD, SD, BBD	4	resection	STR	Yes	6	–	–
Agrawal, 2019[1]	32	F	L1-L3	c	–	–	MD, BBD	12	resection	–	Yes	6	PR	Yes
Phuyal, 2020[56]	36	M	sacral	a	No	–	BP, LEP, BBD	–	biopsy	–	–	–	–	–
Katayama, 2022[29]	24	F	L5-S1	c	No	–	BP, SD	3	resection	GTR	No	24	–	–

yr, year; a, acquired; c, congenital; LP, lumbar puncture; mo, month; BP, back pain; LEP, lower extremity pain; MD, motor deficit; SD, sensory deficit; BBD, bowel/bladder dysfunction; STR, subtotal resection; GTR, gross total resection; PR, partial recovery; GR, good recovery; WR, worse recovery.

It is essential to differentiate the processes of calcification and ossification. Calcification involves the accumulation of calcium salts within tissue, whereas ossification pertains to new bone formation [47–49]. These processes are challenging to distinguish on imaging due to subtle deviation in structure, particularly when using MRI [47–50]. Ossification itself is characterized by distinct mechanisms of bone formation, termed endochondral and intramembranous ossification. Endochondral ossification involves the formation of a cartilage matrix, which is calcified to form mature bone [47,51–53]. In intramembranous ossification, bone is formed without a cartilage template; mesenchymal cells differentiate into osteoblasts, which secrete bone matrix and eventually develop into osteocytes [47,54,55]. Pathologic ossification seen in tumors not derived from bony tissue is termed heterotopic ossification, or bone formation outside the skeleton [56]. Theories of heterotopic ossification include tumor factor driven metaplasia of pluripotent stem cells into osteoblasts (epithelial-mesenchymal transition, or EMT) and osteoblastic metaplasia of tumor cells [56–58]. However, the etiology of ossification within epidermoid cysts is unclear.

5. Literature review

Individual data was available for 83 patients with intradural lumbar ECs.

Of the lesions with reported spinal level, 52 % involved the L3 and/or L4 level. The predominance of the L3 and L4 levels is supported by the association of lumbar puncture with the etiology of iatrogenic ECs [1,9,11,59], along with the findings that a majority (67 %) of our cases were acquired and 52 % of patients underwent prior lumbar puncture. The percentage of patients with iatrogenic ECs in our cohort is somewhat higher than previously reported values of around 40 % [1,11]. The reason for this is unclear, however may stem from a late 20th-century emphasis on lumbar puncture as an iatrogenic etiology of EC, followed by other causes of iatrogenic EC, such as trauma or surgery. The average time from lumbar puncture to diagnosis in our review was 6.5 years, which is consistent with an average of six years in a report by Manno et al. [11].

Few patients (16 %) in our cohort had associated congenital anomalies such as spinal dysraphism, which is consistent with previous reports. While spinal ECs are associated with spinal dysraphism [1,7,10,14,17,18], those without congenital anomalies are commonly located in the lumbar region [5,19]. Rupture of the cyst can result in an inflammatory reaction [20,24,28,29,60], and potentially fatal meningitis. This can occur spontaneously or during resection; to prevent iatrogenic meningitis, *en-bloc* resection of the tumor is recommended [1,61,62]. However, epidermoid cysts have a tendency to adhere to critical anatomy [30,63–65], which may preclude total resection and increase the risk of recurrence [1,8,14,18,30,63,64,66]. In our case, the epidermoid tumor was circumferentially encasing a traversing nerve root. Adherence was reported in 36 % of the cases in our literature review.

Epidermoid cysts exhibit a latent growth pattern with a gradual onset of signs and symptoms, which are characterized by symptoms of nerve or cord compression. The wide range of differential diagnoses for these symptoms often precludes prompt diagnosis of an EC. The average delay to diagnosis in our review was two years, similar to the findings reported by Sirbu et al. in a 2020 review of 139 spinal ECs [1]. The most common symptoms in our review were back pain (53 %), lower extremity pain (52 %), neurologic deficits (49 %), and bowel/bladder dysfunction (25 %). The average last reported follow-up period for our review was four years (median of three years). However, follow-up data was reported in only 50 (60 %) patients, and the follow-up period may be an underestimate, as most of the included articles were case reports. Authors tend to publish case report findings soon after the patient encounter, rather than wait for a significant follow-up period.

No significant predictive factors were identified for outcome or recurrence. This is likely due to insufficient data, resulting in reduced sample sizes for the studied correlations. In addition, the characterization of outcomes likely played a role, as most patients in the cohort had a full recovery in the postoperative period. It is unclear if this indicates an inclination to publish cases with favorable outcomes, or if this observation is a reflection of the latent growth pattern of ECs and a good prognosis with resection. Nevertheless, trends were noted between decreased age and improved outcome, reduced delay in diagnosis and improved outcome, and increased extent of resection with reduced recurrence. Future studies with larger sample sizes, more specific reporting and characterization of postoperative outcomes, and more complete data on long-term outcomes of patients should be performed to validate these trends towards correlation.

A correlation between calcification and recurrence has been documented in prior studies [45], which may be related to a potential association between adherence and calcification. Our intraoperative observations and previous reports suggest that there is a tendency for the dense calcified/ossified component of an EC to adhere to nearby structures [39,67,68]. However, it is unclear if this can be distinguished from the adherent qualities of ECs at baseline, or if other factors involved in the calcification process independently increase the risk for recurrence.

Multiple theories have been postulated regarding the development of calcification within epidermoid cysts. This calcification has been thought to be due to either saponification of cystic components causing dystrophic calcification, or high protein content secondary to liquefactive necrosis [37,39,42]. Complete ossification of ECs have also been reported at other sites. There are many reports of calcification and ossification of scrotal ECs resulting in calcinosis cutis, thought to result from dystrophic calcification of an epidermoid tumor involving chronic inflammation and eventual rupture of the cyst [24,69–71]. Cutaneous ossification of ECs has also been reported [72–75], with proposed etiologies of anomalous mesenchymal cell differentiation into osteoblasts (metaplasia) or displaced embryonic cells resulting in hamartoma formation [73,75]. It is unclear if ECs of different primary sites undergo the same process of heterotopic ossification. Further molecular analysis of ECs from various tissue sites is required to determine the true mechanism(s) of ossification in epidermoid tumors.

The presented case is unique due to the rarity of spinal epidermoid cysts and the presence of ossification with mature bone within the cyst, which has only been vaguely reported once before in the neuroaxis, and never with accompanying pathological slides. Future research should be conducted to elucidate the etiology of ossification within ECs. Large-scale studies are required to evaluate the trends

identified in our review and better define the incidence, prognostic factors, and long-term outcomes of calcified or ossified epidermoid cysts.

6. Conclusion

We report the first known case of a lumbar spinal epidermoid cyst with a component of mature bone formation, and the first ossified EC within the CNS with pathologic images. A review of the available literature demonstrated trends towards association between younger age and improved outcome, reduced delay in diagnosis and improved outcome, and increased extent of resection with reduced recurrence. Early diagnosis and gross total resection should be the aim in the management of epidermoid tumors. The finding of complete ossification calls for future investigation to determine the etiology and significance of mature bone formation within these rare tumors.

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Competing interests & disclosures

All authors declare that they have no personal, financial, or institutional conflict of interest.

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CRediT authorship contribution statement

Gabrielle E.A. Hovis: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Anubhav Chandla:** Writing – review & editing, Project administration, Methodology, Funding acquisition. **Steven E. Kolker:** Validation, Resources, Investigation, Data curation. **Isaac Yang:** Validation, Supervision, Resources, Funding acquisition. **Daniel T. Nagasawa:** Writing – review & editing, Validation, Supervision, Resources, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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