Differentiating intradiploic orbital dermoid and epidermoid cysts utilizing clinical features and machine learning

Andrea A Tooley, Prashant Tailor, Ann Q Tran, James A Garrity, Laurence Eckel, Michael J Link

Purpose: The purpose of this study was to characterize intradiploic dermoid and epidermoid orbital cysts to determine any differences in clinical, radiographic, or surgical features. Methods: A retrospective review was performed of patients presenting with intradiploic dermoid or epidermoid cysts. Additionally, a complete review of the literature was performed to identify cases of intradiploic orbital dermoid and epidermoid cysts. Data collected included age, sex, presenting symptoms, location of intradiploic cyst, ophthalmic findings, treatment, and follow-up. Clinical features of dermoid versus epidermoid cyst were compared. Additionally, machine-learning algorithms were developed to predict histopathology based on clinical features. Results: There were 55 cases of orbital intradiploic cysts, 49 from literature review and six from our cohort. Approximately 31% had dermoid and 69% had epidermoid histopathology. Average age of patients with dermoid cysts was significantly less than that of patients with epidermoid cysts (23 vs. 35 years, respectively; P = 0.048). There was no difference between sex predilection, presenting symptoms, radiographic findings, or surgical treatment of dermoids and epidermoids. The majority of patients (64%) underwent craniotomy for surgical removal. Machine-learning algorithms KStar and Neural Network were able to distinguish dermoid from epidermoid with accuracies of 76.3% and 69%, respectively. Conclusion: Orbital intradiploic cysts are more commonly epidermoid in origin. Dermoid cysts presented in younger patients; however, there were no other significant differences in features including ophthalmic or radiographic findings. Despite similar features, machine learning was able to identify dermoid versus epidermoid with good accuracy. Future studies may examine the role of machine learning for clinical guidance as well as new surgical options for intervention.

Key words: Machine Learning, orbital dermoid, orbital tumor

Orbital dermoid cysts – keratin-filled cyst lined by simple squamous epithelium and skin adnexal elements – and epidermoid cysts – cyst wall does not contain skin adnexal elements – are well-described benign tumors, commonly presenting in childhood as a palpable mass along the superotemporal orbit.[1] Deep orbital dermoid cysts are less common, often occurring later in life with headaches, proptosis, and signs of inflammation.[2] Less common still are intradiploic cysts involving the diploe of the sphenoid, frontal, or zygomatic bones of the orbit, which more frequently occur intracranially along the posterior fossa or cerebellopontine angle.[3,4] Patients with intradiploic orbital cysts may present with acute symptoms[5] or chronic changes including pain, headache, proptosis, or diplopia.[6] Intradiploic cysts involving the orbit include both dermoid and epidermoid histopathology, although no differentiating clinical features have been reported. Radiographically, dermoid cysts can contain fat and have a heterogenous signal on magnetic resonance imaging (MRI), while epidermoids can have densities closer to fluid, and therefore appear more homogenous with diffusion restriction. Intradiploic cysts may be more difficult to treat than non-intradiploic cysts, which are often managed with orbitotomy.[2] Surgical treatment of intradiploic cysts often involves a craniotomy to remove the extent of the cyst due to the high risk of recurrence.[6]

Herein, the authors present six cases of intradiploic orbital cysts and perform a review of the literature to characterize the clinical and radiographic features, treatment, and recurrence rates of both dermoid and epidermoid cysts occurring within the diploe of orbital bones. Additionally, the authors compare the clinical features and outcomes of dermoid versus epidermoid histopathology.

Methods

This study was approved by the Institutional Review Board, and it adhered to the tenants of the Declaration of Helsinki and Health Insurance Portability and Accountability Act. A retrospective case review was performed of intradiploic orbital dermoid or epidermoid cysts treated by the authors. Complete medical and ocular histories along with radiographic imaging of the brain and orbits were obtained for all patients prior to surgery. Additionally, a comprehensive literature

© 2022 Indian Journal of Ophthalmology | Published by Wolters Kluwer - Medknow
A comprehensive review of the literature yielded 49 cases of intradiploic orbital dermoid or epidermoid cysts. In addition, six cases from the authors were added to this cohort. Of the 55 cases, approximately 31% were dermoid and 69% were epidermoid on histopathology. Average age of patients with dermoid cysts was significantly lesser than that of those with epidermoid cysts (23 vs. 35 years, respectively; *P* = 0.048). There was no difference between sex predilection of dermoids or epidermoids [Table 1]. Common presenting symptoms included proptosis, headache, diplopia, and externally visible findings such as swelling or ulcerated skin from draining sinus tracts or fistulas. In all six patients from our cohort, both computed tomography (CT) and MRI were obtained [Fig. 1]. In a review of the literature, CT was found to be the most described imaging modality. Radiographically, boney remodeling into the orbit or intracranial space was appreciated in close to 90% of all patients, while over 50% had mass effect into the orbit. Intracranial involvement was less commonly seen (23% in dermoid cysts and 18% in epidermoid cysts). The sphenoid (29%) followed by the frontal bone (18%) were the most common sites of intradiploic cysts. Of the six Mayo Clinic patients, radiology listed dermoid or epidermoid cyst as the diagnosis in five cases (83%). The majority of patients (64%) underwent extradural craniotomy, while orbitotomy was employed in 36%.

On univariable regression analysis, features associated with an increased odd of dermoid cysts included age (odds ratio [OR] 1.031, 95% confidence interval [CI] 0.999–1.064, *P* = 0.05). There were no other significant clinical or radiographic features that were predictive of dermoid or epidermoid cysts on regression analysis.

### Results

A comprehensive review of the literature yielded 49 cases of intradiploic orbital dermoid or epidermoid cysts. In addition, six cases from the authors were added to this cohort. Of the 55 cases, approximately 31% were dermoid and 69% were epidermoid on histopathology. Average age of patients with dermoid cysts was significantly lesser than that of those with epidermoid cysts (23 vs. 35 years, respectively; *P* = 0.048). There was no difference between sex predilection of dermoids or epidermoids [Table 1]. Common presenting symptoms included proptosis, headache, diplopia, and externally visible findings such as swelling or ulcerated skin from draining sinus tracts or fistulas. In all six patients from our cohort, both computed tomography (CT) and MRI were obtained [Fig. 1]. In a review of the literature, CT was found to be the most described imaging modality. Radiographically, boney remodeling into the orbit or intracranial space was appreciated in close to 90% of all patients, while over 50% had mass effect into the orbit. Intracranial involvement was less commonly seen (23% in dermoid cysts and 18% in epidermoid cysts). The sphenoid (29%) followed by the frontal bone (18%) were the most common sites of intradiploic cysts. Of the six Mayo Clinic patients, radiology listed dermoid or epidermoid cyst as the diagnosis in five cases (83%). The majority of patients (64%) underwent extradural craniotomy, while orbitotomy was employed in 36%.

On univariable regression analysis, features associated with an increased odd of dermoid cysts included age (odds ratio [OR] 1.031, 95% confidence interval [CI] 0.999–1.064, *P* = 0.05). There were no other significant clinical or radiographic features that were predictive of dermoid or epidermoid cysts on regression analysis.

### Table 1: Demographics of intradiploic orbital dermoid versus epidermoid cysts

|                                | Dermoid (n=17) | Epidermoid (n=38) | P   |
|--------------------------------|----------------|-------------------|-----|
| Age (years)                    | 23±20          | 35±20             | 0.048* |
| Sex (m)                        | 9 (53%)        | 22 (40%)          | 0.732 |
| Presenting symptoms            |                |                   |     |
| Headache                       | 3 (18%)        | 8 (21%)           | 0.770 |
| Proptosis                      | 7 (41%)        | 19 (50%)          | 0.545 |
| Pain                           | 1 (6%)         | 5 (13%)           | 0.424 |
| Decreased vision               | 0 (0%)         | 2 (5%)            | 0.335 |
| Diplopia                       | 3 (18%)        | 5 (13%)           | 0.663 |
| Globe displacement             | 1 (6%)         | 3 (8%)            | 0.791 |
| External skin changes          | 7 (41%)        | 12 (32%)          | 0.489 |
| Incidental finding             | 1 (6%)         | 5 (13%)           | 0.424 |
| Radiographic findings          |                |                   |     |
| Bony erosion                   | 15 (88%)       | 34 (89%)          | 0.921 |
| Mass effect into the orbit     | 9 (53%)        | 19 (50%)          | 0.848 |
| Intracranial involvement       | 4 (23%)        | 7 (18%)           | 0.453 |
| Bony involvement               |                |                   |     |
| Sphenoid                       | 5 (29%)        | 11 (29%)          | 0.684 |
| Zygomatic                      | 2 (12%)        | 2 (5%)            | 0.482 |
| Frontal                        | 3 (18%)        | 10 (36%)          | 0.244 |
| Temporal                       | 1 (6%)         | 1 (3%)            | 0.552 |
| Ophthalmic findings            |                |                   |     |
| Reduced vision                 | 2 (12%)        | 9 (24%)           | 0.253 |
| Abnormal extraocular motility  | 7 (41%)        | 10 (26%)          | 0.618 |
| Proptosis                      | 7 (41%)        | 19 (50%)          | 0.545 |
| Surgery                        |                |                   |     |
| Craniotomy                     | 7 (41%)        | 22 (40%)          | 0.251 |
| Orbitotomy                     | 7 (41%)        | 9 (24%)           | 0.187 |
| Follow-up (years)              | 3.0±2.8        | 3.1±3.7           | 0.759 |

### Table 2: Machine-learning classifiers to predict tumor histology

| Classifier (10-fold ‑CV) | Accuracy | ROC  |
|--------------------------|----------|------|
| KStar                    | 76.30%   | 0.746|
| Neural Network            | 69%      | 0.687|
| Logistic Regression       | 61.80%   | 0.634|
| Gradient Descent          | 65%      | 0.571|
| Naive Bayes               | 69%      | 0.582|
| Decision Tree             | 63%      | 0.385|

CV: Cross validation

Postsurgical complications were not documented in a majority of reports in the literature. Of the six cases at Mayo Clinic, vision remained excellent postoperatively, extraocular motility improved, and no complications were noted over an average 2.5 years (range 3 months–7 years) of follow-up. Over half of the patients (four/six) underwent MRI 3 months postoperatively, which showed complete resection of the cyst without any operable complications.

Utilizing data aggregated during the comprehensive literature search, machine-learning classifiers were developed...
to predict tumor histologic classification. Age, sex, bone involved, motility changes, vision changes, proptosis >2 mm present, globe displacement, ptosis present, osseous changes on imaging, and mass effect on imaging were used as features to predict the tumor histological classification (dermoid vs. epidermoid). Two models had particularly strong performances (KStar and Neural Network with accuracies of 76.3% and 69%, respectively). Furthermore, AUC-ROC curves for both classifiers were 0.746 and 0.687, respectively [Table 2].

Discussion

Intradiploic orbital dermoid and epidermoid cysts are rare, benign tumors, with only 49 cases reported in the literature.\(^{[3-51]}\) Orbital dermoid cysts are far more common and are most often periocular, with several large series reporting over 80% presenting as a subcutaneous mass.\(^{[1,52]}\) Deep orbital dermoid cysts, also referred to as endophytic cysts, have also been reported, and are more often present later in life with orbital inflammation.\(^{[53]}\) These cysts, which may be dermoid or epidermoid, are rarely intradiploic in nature. Histopathologically, dermoid and epidermoid cysts are congenital rests from primitive ectoderm; dermoid cysts contain dermal and possible mesodermal elements, while epidermoids are composed completely of epithelium.\(^{[47]}\) Despite these histopathological differences, the authors found the presentations, treatment, and recurrences of dermoid and epidermoid intradiploic orbital cysts to be nearly identical, with age being the only significant difference between groups. Given the failure of logistic regression and univariate analysis to identify unique factors between groups, we utilized
machine learning not for clinical classification, but to identify any multidimensional interactions across factors through prediction. Our machine-learning analysis showed that higher-order interactions are likely to occur across features that can distinguish between dermoid and epidermoid lesions. While at this time, preoperative differentiation of dermoid versus epidermoid cyst would likely not change the medical decision-making, machine learning demonstrates a difference, which may become clinically relevant over time as we encounter more of these cases.

While non-intradiploic deep orbital dermoids may present in similar fashion to intradiploic cysts, these may be managed by orbitotomy over craniotomy. Intradiploic cysts are more likely to involve the cranial space, and therefore, craniotomy is the most common treatment. With advances in surgical techniques, minimally invasive options may continue to expand. Nevertheless, the outcomes of craniotomy for intradiploic cyst removal are excellent, with no patients in the Mayo Clinic series suffering any complications related to surgery.

Traditional statistical analysis showed only age to be statistically significant between dermoids and epidermoids, although both may occur in younger patients. Radiology reads correctly identified dermoid/epidermoid histopathology 83% of the time, but does not consistently differentiate between the two. The accuracies of the top two machine-learning models to predict histology were unexpected, given the clinical and radiographic similarities. It is possible that statistical testing was underpowered, given the relatively low sample size due to the rarity of these tumors. The classifiers were chosen to represent the available demographics and clinical and radiographic features of the cases reported in the literature as well as the Mayo Clinic series. These models demonstrate that in a multidimensional feature space, there are distinct differences between dermoids and epidermoids. With additional cases, the characteristic differences between these two groups can be further elucidated, which is likely to improve the classification accuracy.

Limitations to this study include its retrospective nature, which relies on the accuracy of the medical record, as well as the inherent publication biases present in literature reviews. There was wide variability in the amount of clinical information, including the oculic exam and radiographic features, about the cases reported in the literature. Additionally, a case series of deep orbital dermoids likely included several intradiploic cysts, but clinical information including cyst location was not provided for each individual case, therefore these were not included. Regarding radiology interpretations, given the similar clinical presentations and treatments, radiologists have not historically prioritized differentiating between dermoid and epidermoid; therefore, we are unable to determine if the machine-learning algorithms would perform to the same level as trained radiologists, should emphasis be placed on distinguishing dermoid versus epidermoid histopathology. Complications were infrequently reported as well; however, in all six cases from Mayo Clinic, patients did very well without any postsurgical complications.

**Conclusion**

Intradiploic orbital dermoid and epidermoid cysts are rare benign tumors that often present with proptosis, diplopia, pain, or visible external changes including swelling, ulcerative lesions, or draining fistula tracts. While dermoid cysts are more common in younger patients, no other clinical or radiographic feature differentiates dermoid from epidermoid histopathology, and both lesions are successfully managed with craniotomy and/or orbitotomy. Machine-learning algorithms may allow us to further characterize intradiploic orbital cysts to aid in future diagnosis and treatment strategies. Further studies are needed to obtain more cases and to test tumor classification in a prospective manner.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Bajric J, Griepentrog GJ, Mohney BG. Pediatric periorbital dermoid cysts: Incidence, clinical characteristics, and surgical outcomes. Ophthalmic Epidemiol 2019;26:117-20.
2. Vahdani K, Rose GE. Presentation and treatment of deep orbital dermoid cysts. Ophthalmology 2020;127:1276-8.
3. Eijpe AA, Koomneef L, Verbeeten BJ, Peeters FL, Zonneveld PW, Bras J. Intradiploic epidermoid cysts of the bony orbit. Ophthalmology 1991;98:1737-43.
4. Bilmaz K, Cosar M, Bek S, Gokduman CA, Arslan M, Iplikcioğlu AC. Intradiploic epidermoid cysts of the skull: A report of four cases. Clin Neurol Neurosurg 2005;107:262-7.
5. Lee BG, Chen Y, Rajak S, Selva D. Intradiploic epidermoid cyst of the orbital roof: A case report. Orbit 2019;38:81-3.
6. Adelstein LJ. Intradiploic epidermoid tumors (cholesteatoma of the skull). Am J Surg 1949;78:480-5.
7. Pollard ZF, Calhoun J. Deep orbital dermoid with draining sinus. Am J Ophthalmol 1975;99:310-3.
8. Wakan S. Intradiploic epidermoid tumor of the lateral orbital wall–Case report. Neurol Med Chir (Tokyo) 1983;23:577-9.
9. White AK, Jenkins HA, Coker NJ. Intradiploic epidermoid cyst of the sphenoid wing. Arch Otolaryngol Head Neck Surg 1987;113:995-9.
10. Ciappetta P, Artico M, Salvati M, Raco A, Gagliardi FM. Intradiploic epidermoid cysts of the skull: Report of 10 cases and review of the literature. Acta Neurochir (Wien) 1999;110:33-7.
11. Sargent EW, Garcia P, Paniello RC, Spector GJ. Giant intradiploic epidermoid cyst of greater sphenoid wing causing unilateral proptosis and optic nerve compression. Skull Base Surg 1993;3:55-9.
12. Arana E, Latorre FF, Revert A, Menor F, Riesgo P, Llano F, et al. Intradiploic epidermoid cysts. Neuoroadiology 1996;38:306-11.
13. Niederhagen B, Reich RH, Zentner J. Temporal dermoid with intracranial extension: Report of a case. J Oral Maxillofac Surg 1998;56:1352-4.
14. Chawda SJ, Moseley IF. Computed tomography of orbital dermoids: A 20-year review. Clin Radiol 1999;54:821-5.
15. Meyer DR, Lessner AM, Yeatts RP, Linberg JV. Primary temporal fossa dermoid cysts. Characterization and surgical management. Ophthalmology 1999;106:342-9.
16. Posey LA, Sterman BA. Quiz case 2. Intradiploic epidermoid cyst. Arch Otolaryngol Head Neck Surg 1999;125:913, 915.
17. Blanco G, Esteban R, Galarrreta D, Saornil MA. Orbital intradiploic giant epidermoid cyst. Arch Ophthalmol 2001;119:771-3.
18. Holds JB, Anderson RL, Mamalis N, Kincaid MC, Font RL. Invasive squamous cell carcinoma arising from asymptomatic...
choristomatous cysts of the orbit. Two cases and a review of the literature. Ophthalmology 1993;100:1244-52.
19. Schonauer C, Conrad M, Barbato R, Capuano C, Moraci A. Traumatic rupture into frontal sinus of a frontal intradiploic epidermoid cyst. Acta Neurochir (Wien) 2002;144:401-2.
20. Aiyama H, Utsunomiya A, Suzuki S, Hirano T, Suzuki I, Nimura T, et al. [Case of enlargement of an intradiploic epidermoid cyst by a head contusion]. Brain Nerve 2009;61:707-10.
21. Berti AF, Lovaas GC, Santillan A, Berti AF 2nd. Primary intradiploic pterional epidermoid cyst. South Med J 2010;103:87-9.
22. Lelli GJ, Levy RL. Epidermoid cyst masquerading as dacryocystocele: A rare cause of proptosis. Br J Ophthalmol 1990;74:445-6.
23. Ormond DR, Omesi I, Abrahams J. Uncommon presentation of an intradiploic orbital epidermoid tumor: Case report. Oral Maxillofac Surg 2011;15:163-67.
24. Akbaba M, Karsloglu S, Damluck A, Karcoglu ZA. Intradiploic epidermoid cyst of frontal bone with spontaneous fistulization to eyelid. Ophthalmic Plast Reconstr Surg 2012;28:e15-7.
25. Bonavolonta G, Strianse D, Grassi P, Comune C, Tranfa F, Uccello G, et al. An analysis of 2,480 space-occupying lesions of the orbit from 1976 to 2011. Ophthalmic Plast Reconstr Surg 2013;29:79-86.
26. Samdani S, Kalra GS, Rawat DS. Posttraumatic intradiploic epidermoid cyst of frontal bone. J Craniofac Surg 2013;24:e128-30.
27. Adulkar NG, Arunkumar MJ, Kumar SM, Kim U. Unusual case of epidermoid cyst presenting as oculomotor nerve palsy. Indian J Ophthalmol 2014;62:1032-4.
28. Yildiz K, Sagir HO, Tosuner Z, Canter HI, Guneren E. Asymptomatic intradiploic epidermoid cyst eroding frontal bone in a patient with craniosynostosis. J Craniofac Surg 2015;26:e58-9.
29. Burnham JM, Lewis K. Intracranial extension of an orbital epidermoid cyst. Ophthalmic Plast Reconstr Surg 2016;32:e135-6.
30. Arko LT, Berry CT, Desai AS, Weaver M. Intradiploic epidermoid tumors of the cranium: Case report with review of the literature. J Neurol Surg A Cent Eur Neurosurg 2017;78:167-79.
31. Kumar R, Vyas K, Jaiswal G, Bhargava A, Kundu J. Deep orbital dermoid cyst bulging into the superior orbital fissure: Clinical presentation and management. J Ophthalmic Vis Res 2017;12:110-2.
32. Mukherjee B, Banerjee M, Agarkar S. Orbital dermoid cyst presenting as chronic osteomyelitis. J AAPOS 2018;22:480-1.e1
33. Prior A, Anania P, Facetti M, Secchi F, Ravegnani M, Pavanello M, et al. Dermoid and epidermoid cysts of scalp: Case series of 234 consecutive patients. World Neurol Surg 2018;120:119-24.
34. Barkley AS, Sussarla SM, Lee A. Frontotemporal dermal sinus tract with 2 connected intradiploic dermoid cysts: A rare case and review of the literature. World Neurosurg 2019;127:350-3.
35. Diniz SB, Chahud F, Cruz AAV. Orbital extension of a frontal bone intradiploic epidermoid cyst. Ophthalmic Plast Reconstr Surg 2019;35:e158.
36. Ma J, Jia G, Jia W. Primary intradiploic epidermoid cyst: A case report with literature review. Clin Neuropathol 2019;38:28-32.
37. Mukherjee B, Desai A. A giant dermoid cyst of the orbit. Orbit 2019;38:158-61.
38. Bajric J, Harris GJ. The spectrum of orbital dermoid cysts and their surgical management. Orbit 2020;39:266-75.
39. Concepcion-Torio K, Park JW, Woo KI, Suh YL, Kim YD. Pilosebaceous malignant transformation of dermoid cyst in the orbit. Ophthalmic Plast Reconstr Surg 2020;36:e103-5.
40. Hatcher J, Sarma A, Sobel R, Padovani-Claudio D. Sphenofrontal intradiploic epidermoid cyst with cutaneous dural sinus tract. J AAPOS 2021;25:56-9.
41. Pushker N, Meel R, Kumar A, Kashyap S, Sen S, Bajaj MS. Orbital and periorbital dermoid/epidermoid cyst: A series of 280 cases and a brief review. Can J Ophthalmol 2020;55:167-71.
42. D’Andrea M, Musio A, Fuschillo D, Mongardi L, Riccioni L, Tosatto L. Epidermoid cyst of the anterior clinoid process: Report of a unique finding and literature review of the middle cranial fossa locations. Clin Neurol Neurosurg 2021;200:106381.