

# Immunohistochemistry of Ecchordosis Physaliphora and Chordoma

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**ABSTRACT:** Immunohistochemical stains for cytokeratins, vimentin, epithelial membrane antigen, carcinoembryonic antigen and S-100 were performed on nine ecchordoses and 10 chordomas. 100% of the ecchordoses were positive for cytokeratin, vimentin and epithelial membrane antigen. 78% were S-100 positive. 100% of the chordomas stained positively for cytokeratin, vimentin and S-100 and 90% were positive for epithelial membrane antigen. No ecchordosis or chordoma was carcinoembryonic-antigen positive. These findings are interesting for two reasons. First, the similar staining properties of chordoma and ecchordosis physaliphora support the embryologic hypothesis of their common origin from the fetal notochord. Second, they indicate that when an ecchordosis causes symptoms prompting surgical resection, differentiation of the lesion from chordoma with routine immunohistochemistry would not be helpful.

**RÉSUMÉ:** Immunohistochimie de l'ecchordose physaliphore et du chordome Nous avons exécuté des colorations immunohistochimiques pour les cytokératines, la vimentine, l'antigène épithélial membranaire, l'antigène carcino-embryonnaire et le S-100 sur neuf ecchordoses et dix chordomes. Cent pourcent des ecchordoses étaient positifs pour la cytokératine, la vimentine et l'antigène épithélial membranaire. Soixante-dix-huit pourcent étaient positifs pour le S-100. Cent pourcent des chordomes étaient positifs pour la cytokératine, la vimentine et le S-100 et quatre-vingt-dix pourcent étaient positifs pour l'antigène épithélial membranaire. Aucun des ecchordoses ou des chordomes n'était positif pour l'antigène carcino-embryonnaire. Ces observations sont intéressantes pour deux raisons. D'abord, les propriétés histochimiques similaires des chordomes et des ecchordoses supportent l'hypothèse embryologique de leur origine commune à partir de la notocorde foetale. Ensuite, elles indiquent que, lorsqu'un ecchordose provoque des symptômes qui motivent une résection chirurgicale, il ne serait pas coloration immunohistochimique.

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The fetal notochord is an interesting embryologic structure which is postulated to give rise to normal, vestigial and pathologic structures in the adult. In the human, the notochord forms during the third week of embryonic life.<sup>1</sup> It is important in the genesis of the axial skeleton and normally persists in the adult as the nucleus pulposus of the intervertebral disc.<sup>2,3</sup> Several other remnants of the notochord may also persist into adulthood. Heterotopic rests of notochord cells may be found outside the nucleus pulposus anywhere along the axial skeleton from the coccyx to the dorsum sella.<sup>2,4</sup> They are most common at the extreme ends of the skeleton. Chordomas are felt to arise from these ectopic rests of notochordal cells and, similar to the cell rests, they are extradural in location and most common in the sacrum or clivus.<sup>3,5-7</sup> The prognosis remains dismal with a median survival of five years from the time of diagnosis.<sup>3,5,6,8</sup> The pathological features of chordoma have been extensively studied.<sup>5-19</sup>

Another structure which is thought to be derived from the notochord and which has received less attention in the pathology literature is the ecchordosis physaliphora (Figures 1 and 2).<sup>11,20-25</sup>

These jelly-like excrescences are usually related to the clivus but may be found anywhere along the axial skeleton.<sup>2,4,21</sup> Ecchordoses are considered to be non-neoplastic hamartomas which are clinically silent lesions, and rarely, if ever, are the source of chordomas.<sup>3,8</sup> However, there are a number of reports of symptomatic ecchordoses and of patients with symptoms due to intradural lesions composed of physaliphorous cells which have all the gross features of ecchordoses although they have been larger than the usual ecchordosis.<sup>1,21,26-28</sup> A recent case of what we diagnosed as symptomatic ecchordosis led us to attempt to differentiate the lesion from chordoma, which would certainly carry a more grave prognosis.<sup>29</sup> This paper reports the results of immunohistochemical staining of ecchordosis physaliphora and chordoma. A brief discussion follows concerning the pathologic and embryologic implications of these results.

## MATERIALS AND METHODS

The surgical and autopsy pathology files of the Department of Pathology at Toronto General Hospital were searched for all

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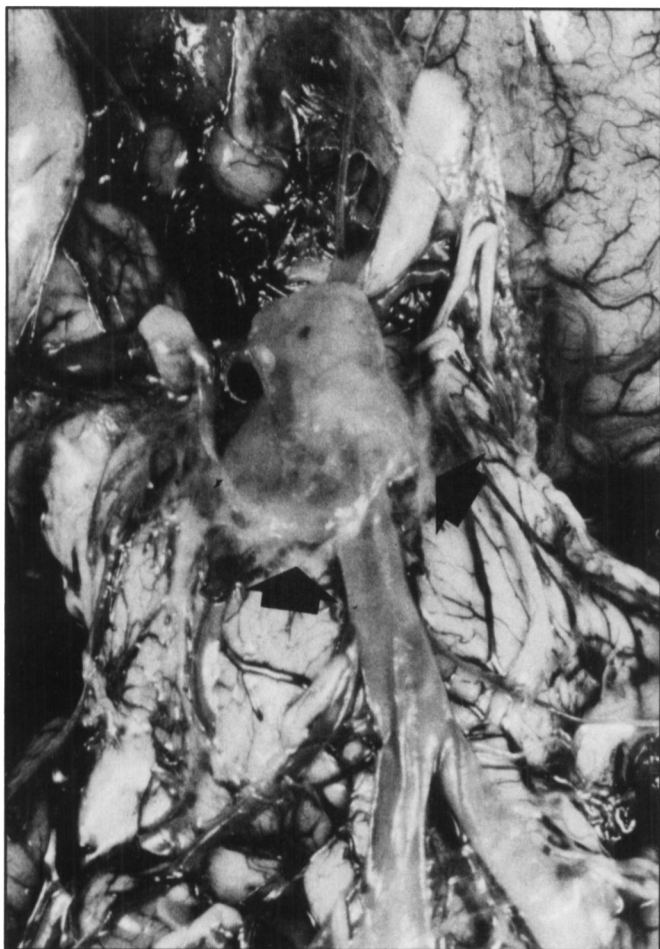


Figure 1 — A photograph of the ventral surface of the brainstem showing a gelatinous *echordosis physaliphora* (arrows) adherent to the arachnoid overlying the pons.

specimens diagnosed as chordoma and *echordosis physaliphora* over the years 1960 to 1988. Specimens labelled as *echordoses* were all, with one exception, typical gelatinous excrescences attached to the dorsal clivus whose presence was disclosed only at autopsy. The exception was a lesion with the histologic appearance of an *echordosis* which was discovered spanning the clivus from sphenoid sinus to the prepontine cistern resulting in a cerebrospinal fluid fistula in a 66-year-old woman.<sup>29</sup> The chordomas were sacrococcygeal or clival tumors diagnosed as chordomas on the basis of typical light and, occasionally, electron microscopy. Material for light microscopy was fixed in 10% formalin and embedded in paraffin. Sections of the same blocks were stained immunohistochemically for cytokeratins (CK, Hybritech pooled monoclonal antibodies to human epithelial keratins and Dako rabbit polyclonal anti-keratin), epithelial membrane antigen (EMA, Dako), S-100 (Dako), Vimentin (Histogen) and carcinoembryonic antigen (CEA, Dako). Positive controls were derived from standard blocks known to contain the appropriate antigens.

The results of staining were read as focally or diffusely positive or as negative. Classification of the particular lesion as diffusely or focally positive was made on a subjective basis. However, most samples were either obviously diffusely positive

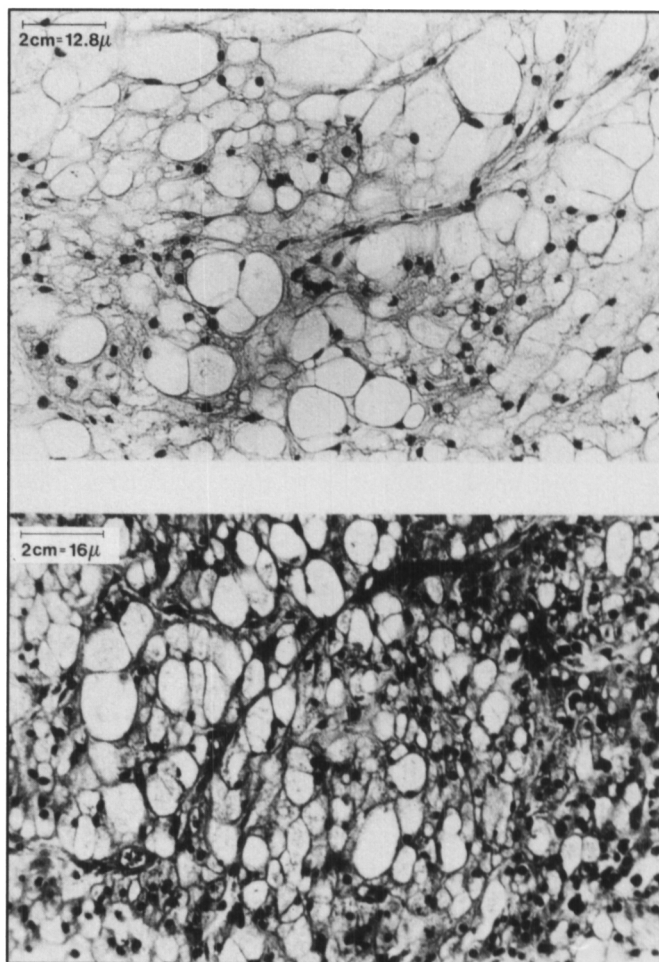


Figure 2 — Photomicrographs of an *echordosis physaliphora* (upper) and of a chordoma (lower) showing prominent physaliphorous cells in both lesions. The chordoma is more cellular and pleomorphic than the *echordosis*. Hematoxylin and eosin.

or entirely negative; patchy and irregular staining specimens were uncommon.

## RESULTS

Figure 2 shows the typical light microscopic histology of *echordosis physaliphora* and chordoma. On light microscopy, both types of lesions contained typical physaliphorous cells with pools of PAS positive intra- and extracellular mucin. The *echordoses* were generally less pleomorphic and cellular than the chordomas although an attempt to quantify this difference was not made.

The results of immunohistochemical staining of 10 chordomas and nine *echordoses* are shown in Table 1 and Figure 3. Focal or diffuse positive staining is recorded as positive in the table. Staining with monoclonal and polyclonal CK stains produced identical results, hence the single CK column in the table. All the *echordoses* stained diffusely positive with CK. Similarly 90% of the chordomas were diffusely positive. A single chordoma was only focally positive. Vimentin was diffusely

**Table 1: Table showing the number of specimens staining positively for the various immunohistochemical markers**

Lesion	Cytokeratins	Vimentin	EMA	CEA	S-100
Echordosis (N = 9)	9	9	9	0	8
Chordoma (N = 10)	10	10	9	0	10

positive in all cases. All the echordoses were EMA positive whereas only nine chordomas were positive, seven of them diffusely and two focally. No specimen showed CEA reactivity. Positive diffuse staining with S-100 was observed in seven echordoses and 10 chordomas. One echordosis was focally positive for S-100 and one was negative.

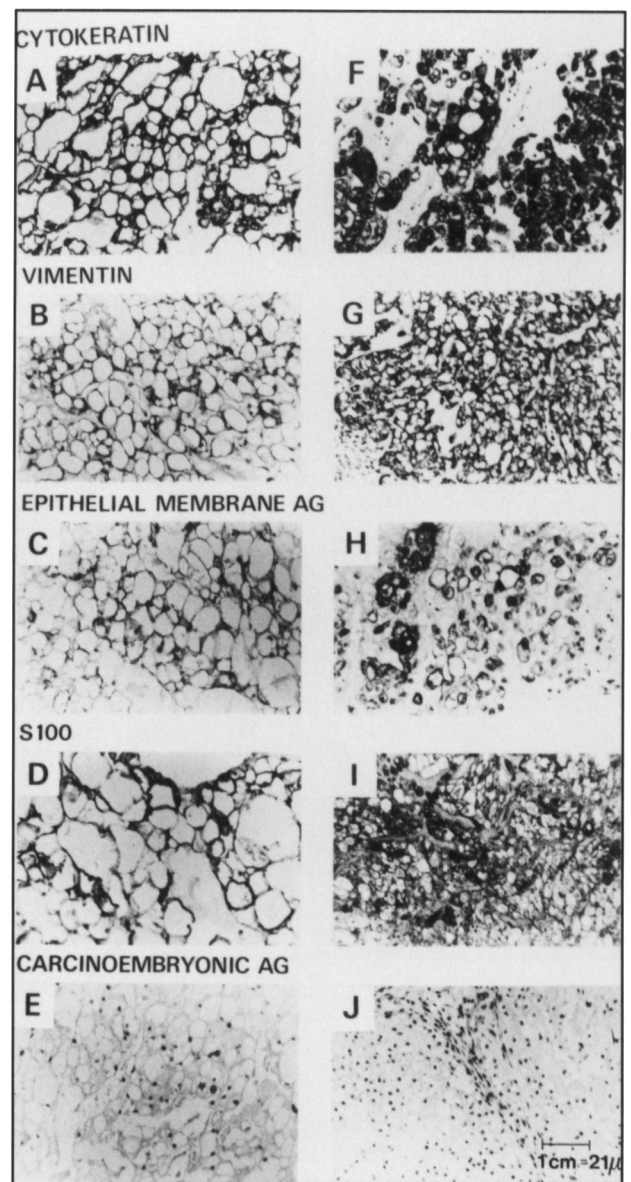
### DISCUSSION

Small gelatinous masses of tissue applied to the dorsal aspect of the clivus were first described by Luschka in 1856.<sup>30</sup> These are now recognized as echordosis physaliphora (Figure 1).<sup>3,24</sup> A light microscopic description was supplied in 1857 by Virchow who utilized the term *echondrosis physaliphora sphenooccipitalis*, believing they were derived from the cartilage of the sphenooccipital synchondrosis.<sup>31</sup> With the initial suggestion by Muller (1858) and subsequent experimental evidence provided by Ribbert (1894) consensus has arisen that echordoses are embryologic relics of the fetal notochord.<sup>22,23</sup> Light and electron microscopic data confirm structural similarity between fetal notochord and echordosis physaliphora. Both are composed of physaliphorous cells.<sup>11,20</sup> The electron microscopic characteristics are almost identical and include intracytoplasmic vacuoles, intermediate filaments, plasmalemmal invaginations and endoplasmic reticulum-mitochondria complexes.<sup>11,20,25</sup>

Chordomas also share histologic and ultrastructural features with both echordosis physaliphora and fetal notochord (Figures 2 and 3). Chordomas contain physaliphorous cells and on electron microscopy have the same features as notochord and echordosis physaliphora.<sup>6,7,11,16,18</sup> Immunohistochemical staining has been reported for chordoma and notochord. As one would expect, their characteristics are similar.<sup>10,17</sup> Both tissues express CK, EMA, vimentin and S-100.<sup>9,12-15,17,32,33</sup> There are few reports of differences between these tissues although Bottles and Beckstead found 5'-nucleotidase activity on the plasma membrane of chordoma and not on fetal notochord.<sup>34</sup>

The immunohistologic features of echordoses have not been previously reported but our results using routine immunohistochemistry confirm that echordoses, like chordomas, express CK, EMA, S-100 and vimentin (Figure 3). These findings provide further support for the embryologic derivation of echordoses from the fetal notochord.<sup>2,3,23</sup>

These results are important because of the occasional need to differentiate pathologically between chordoma and echordosis physaliphora. A number of cases of symptomatic echordoses which may be pathologically similar to chordomas have been reported.<sup>21,26-29</sup> Some authors have used the term intradural or benign chordoma for such echordoses.<sup>1,5,27</sup> Unlike true chordomas, however, these cases have presented with apoplexy and only rarely with compressive neurologic symptoms. The prognosis of symptomatic echordosis is better than for chordoma as they are surgically resectable and they do not invade bone. Hence the need for pathologic distinction.<sup>1</sup> However, routine



**Figure 3** — Photomicrographs showing the immunohistochemical staining of echordosis physaliphora (left, A to E) and chordoma (right, F to J). Both lesions express cytokeratin (A and F), vimentin (B and G), epithelial membrane antigen (C and H) and S-100 (D and I) as shown by the dark staining. There is no positive staining with carcinoembryonic antigen (E and J). (AG; antigen. The calibration bar on photomicrograph J applies to all photomicrographs in this illustration).

light and electron microscopy and, from this study, immunohistochemistry, fail to aid in this distinction.

At present, the diagnosis of symptomatic echordosis must rest on the clinical and radiologic features combined with a consistent pathologic lesion. In the future new markers and diagnostic methods may aid in distinguishing chordoma and echordosis physaliphora.

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