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.


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. It is important in the genesis of the axial skeleton and normally persists in the adult as the nucleus pulposus of the intervertebral disc. 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 dorsal sella. 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. Ecchordoses are considered to be non-neoplastic hamartomas which are clinically silent lesions, and rarely, if ever, are the source of chordomas. 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. 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. 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
Figure 1 — A photograph of the ventral surface of the brainstem showing a gelatinous ecchordosis physaliphora (arrows) adherent to the arachnoid overlying the pons.

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

specimens diagnosed as chordoma and ecchordosis physaliphora over the years 1960 to 1988. Specimens labelled as ecchordoses 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 ecchordosis 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. 29

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

RESULTS

Figure 2 shows the typical light microscopic histology of ecchordosis physaliphora and chordoma. On light microscopy, both types of lesions contained typical physalipherous cells with pools of PAS positive intra- and extracellular mucin. The ecchordoses 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 ecchordoses 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 ecchordoses stained diffusely positive with CK. Similarly 90% of the chordomas were diffusely positive. A single chordoma was only focally positive. Vimentin was diffusely
positive in all cases. All the ecchordoses 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 ecchordoses and 10 chordomas. One ecchordosis 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 1856.30 These are now recognized as ecchordosis physaliphora (Figure 1).3,24 A light microscopic description was supplied in 1857 by Virchow who utilized the term ecchondrosis physaliphora sphenooccipitalis, believing they were derived from the cartilage of the sphenoooccipital synchondrosis.31 With the initial suggestion by Muller (1858) and subsequent experimental evidence provided by Ribbert (1894) consensus has arisen that ecchordoses are embryologic relics of the fetal notochord.22-23 Light and electron microscopic data confirm structural similarity between fetal notochord and ecchordosis physaliphora. Both are composed of physaliphorous cells.11,20 The electron microscopic characteristics are almost identical and include intracytoplasmic vacuoles, intermediate filaments, plasmalemmal invaginations and endoplasmic reticulum-mitochondria complexes.11,20,25

Chordomas also share histologic and ultrastructural features with both ecchordosis physaliphora and fetal notochord (Figures 2 and 3). Chordomas contain physaliphorous cells and on electron microscopy have the same features as notochord and ecchordosis physaliphora.6,7,11,16,18 Immunohistochemical staining has been reported for chordoma and notochord. As one would expect, their characteristics are similar.10,17 Both tissues express CK, EMA, vimentin and S-100.9,12,15,17,32,33 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.34

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

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

At present, the diagnosis of symptomatic ecchordosis 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 ecchordosis physaliphora.

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