Abstract: Background. We present two cases of adult rhabdomyoma in the parapharyngeal space. They are rare benign tumors with a characteristic histologic appearance.

Methods. The tumors were studied by light and immunohistochemical analysis using stains characteristic of striated muscle fibers.

Results. Cross-striation was demonstrated by phosphotungstic acid hematoxylin (PTAH), muscle specific actin, desmin, and myoglobin while dystrophin was expressed in the cell membranes. Clonal origin was confirmed by expression of myosin heavy chain-fast only. Expression of myosin-neonatal and myogenin proved slight proliferation with incipient differentiation in an otherwise mature tumor.

Conclusion. The head and neck area harbors 90% of adult rhabdomyomas and should be considered in a differential diagnosis in this region. Immunohistochemistry confirms that the tumors are almost totally mature neoplasms of clonal origin. © 2006 Wiley Periodicals, Inc. Head Neck 28: 275–279, 2006

Keywords: rhabdomyoma; parapharyngeal space; immunohistochemistry; pathology; benign

Rhabdomyomas are rare, benign tumors of striated muscle with a characteristic histologic appearance. Two types of rhabdomyomas occur, one cardiac and the other the far rarer extracardiac type. Cardiac rhabdomyoma is often associated with tuberous sclerosis and is more probably a developmental anomaly.¹ Histologically, the extracardiac rhabdomyomas are classified into fetal, genital, and adult types. The head and neck area harbors 90% of adult rhabdomyomas.¹–³ Therefore, these tumors are to be kept in mind as a differential diagnosis of tumors in this region. We report light and immunohistochemical studies of two cases of adult rhabdomyoma that were both localized in the parapharyngeal space.

CASE REPORTS

Case 1. A 65-year-old man was referred to the Department of ENT–Head and Neck Surgery, Vejle Hospital. During the previous month, he had experienced a change of sensibility in the left side of the tongue and complained about a feeling...
of occluded left external meatus acusticus. Clinical examination revealed a well-delimited tumor covered with normal mucosa in the left side of oropharynx, right behind the left tonsil but separated from it. An MRI showed tumor extension into the left side of the rhinopharynx. An aspiration biopsy from the tumor showed a smear of low cellularity dominated by large polygonal to round cells with abundant acidophilic granular cytoplasm. Uniform nuclei were distributed along the periphery of the cell. Even though the cytologic material was not conclusive, it suggested a rhabdomyoma (Figure 1).

The surgical procedure was performed using a Boyle–Davis gag. The soft palate was pulled forward with a curved suction, which enabled a fine view of the tumor area. The tumor was situated in the posterior wall of the oropharynx and rhinopharynx and was completely separated from the tonsil. It was covered with normal-appearing pharyngeal mucosa. A longitudinal incision through the mucosa was performed, and the tumor was easily mobilized by blunt dissection. A fine cleavage was found between tumor capsule and pharyngeal muscle layer. The tumor was soft in consistency and measured 2.5 × 1.5 × 0.7 cm. The histologic report confirmed the diagnosis of rhabdomyoma. The recovery was uneventful, and follow-up 1 year later showed no evidence of recurrence.

Case 2. A 66-year-old woman was admitted to the Department of ENT–Head and Neck Surgery, Odense University Hospital, with a 3-month history of an enlarged right tonsil and a burning sensation in the back of the right upper jaw. Clinical examination revealed an ulceration in the right upper alveolar ridge and an enlarged, reddish right tonsillar area. Biopsy from the ulceration showed a squamous cell carcinoma, and a CT scan visualized a maxillary tumor with destruction of the superior alveolar process and an isolated 4 × 4 × 4 cm large tumor involving the rhinopharyngeal and peritonsillar region. A partial hemimaxillectomy preceded by resection of the isolated peritonsillar tumor was planned. A Boyle–Davis gag was used, and a longitudinal mucosal incision over the tonsillar situated part of the tumor was performed. Surprisingly, the tumor seemed encapsulated and was easily removed by blunt dissection with almost no bleeding. Subsequently, the right tonsil was dissected and removed. Frozen section examination showed a rhabdomyoma, and the planned hemimaxillectomy was carried through as planned. The tumor located in the right peritonsillar area was diagnosed as a rhabdomyoma, and the tonsil was without pathology, whereas the right maxilla contained highly differentiated squamous cell carcinoma resected in healthy tissue. Postoperatively, the patient received radiotherapy. The patient was rehabilitated with an obturating prosthesis fixed with implants. Follow-up 30 months later revealed no evidence of recurrence of the malignant tumor or the benign one.

METHODS

After resection, the tumors were fixed in neutral-buffered formaldehyde. Four-micrometer sections were cut from paraffin-embedded tissue blocks and stained with hematoxylin–eosin, periodic acid Schiff (PAS) with and without digestion with diastase, and phosphotungstic acid hematoxylin (PTAH). Immunohistochemistry was performed on deparaffinized sections using antibodies as shown in Table 1. Sections from normal skeletal muscle served as positive controls. Negative controls were performed by omitting the primary antibody.

Pathologic Findings. The two tumors measured 2.5 × 1.5 × 0.7 cm and 7.0 × 3.5 × 2.0 cm, respectively. They were well circumscribed, coarsely lobulated, and reddish brown. The tumors, which were histologically identical, consisted of large polygonal cells forming sheets divided by thin, fibrous septae with small vascular channels. The tumor cells had abundant acidophilic finely

FIGURE 1. Large cells with abundant granular cytoplasm and the nuclei located peripherally (May-Grunwald-Giemsa stain, original magnification ×400). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
granular cytoplasm and peripherally located vesicular nuclei with prominent nucleoli, resembling that of striated muscle. PAS-positive material could be demonstrated within the cytoplasm; PAS staining was negative after digestion with diastase. The cells often appeared vacuolated, because intracellular glycogen had been removed during processing (Figure 2). Cross-striation of the cells was most obvious after histochemical staining with PTAH.

**Immunohistochemical Findings.** The tumor cells exhibited some cross-striation and intense granular cytoplasmic staining for myoglobin, desmin, and muscle-specific actin (Figure 3). The tumor cells also expressed dystrophin, which is located

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**Table 1. Antibodies used for immunohistochemistry.**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Antibody</th>
<th>Clone</th>
<th>Firm</th>
<th>Code no.</th>
<th>Detection</th>
<th>Epitope retrieval</th>
<th>Dilution/ incubation for 60 min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTIN PAN</td>
<td>Actin, HHF35 - pan-muskel</td>
<td>HHF35</td>
<td>DakoCytomation</td>
<td>M0635</td>
<td>EnVision+</td>
<td>MBO/TEG* 15 min.</td>
<td>1 + 200</td>
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<tr>
<td>MYOGENIN</td>
<td>Myogenin, F5D</td>
<td>F5D</td>
<td>DakoCytomation</td>
<td>M3559</td>
<td>EnVision+</td>
<td>MBO/TEG* 15 min.</td>
<td>1 + 200</td>
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<tr>
<td>DYS-ROD</td>
<td>Dystrophin, MAB 1692 - Rod Domain</td>
<td>DY4/6D3</td>
<td>Chemicon</td>
<td>MAB1692</td>
<td>PowerVision+</td>
<td>Protease MBO technique 2</td>
<td>1 + 10</td>
</tr>
<tr>
<td>DYS-C</td>
<td>Dystrophin, MAB 1694 - Carboxy Terminus</td>
<td>DY8/6C5</td>
<td>Chemicon</td>
<td>MAB1694</td>
<td>PowerVision+</td>
<td>MBO/TEG 15 min.</td>
<td>1 + 10</td>
</tr>
<tr>
<td>MHCd</td>
<td>Myosin developmental, NCL-MHCd</td>
<td>RNMy2/9D2</td>
<td>Novocastra</td>
<td>NCL-MHCd</td>
<td>PowerVision+</td>
<td>Protease MBO technique 3</td>
<td>1 + 10</td>
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<tr>
<td>MHCf</td>
<td>Myosin fast, MY32</td>
<td>MY-32</td>
<td>Sigma</td>
<td>M-4276</td>
<td>PowerVision+</td>
<td>MBO/TEG* 15 min.</td>
<td>1 + 8000</td>
</tr>
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<td>MHCn</td>
<td>Myosin neonatal, NCL-MHCn</td>
<td>WB-MHCn</td>
<td>Novocastra</td>
<td>NCL-MHCn</td>
<td>PowerVision+</td>
<td>Protease MBO technique 2</td>
<td>1 + 10</td>
</tr>
<tr>
<td>MHCS</td>
<td>Myosin slow, WB-MHCs</td>
<td>WB-MHCs</td>
<td>Novocastra</td>
<td>NCL-MHCs</td>
<td>PowerVision+</td>
<td>Protease MBO technique 2</td>
<td>1 + 100</td>
</tr>
</tbody>
</table>

*Abbreviations: DYS-ROD, dystrophin rod domain; DYS-C, dystrophin C-terminus; MHCd, myosin heavy chain developmental; MHCf, MHC fast; MHCn, MHC neonatal; MHCS, MHC slow.
* MBO/TEG 15 min.: Microwave treatment for 15 minutes in a solution of 10 mM Tris + 0.5 mM EGTA, pH 9.
† Protease MBO technique 2: Proteolytic pretreatment in protease type 14 (0.002% in TBS) at room temperature for 8 minutes followed by MBO/TEG for 15 minutes.
‡ Protease MBO technique 3: Microwave treatment for 15 minutes in 10 mM citrate buffer followed by proteolytic treatment in protease type 14 (0.05% in TBS) at 37°C for 2 minutes.

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**FIGURE 2.** Rhabdomyoma composed of large polygonal cells with peripheral nuclei and abundant cytoplasm with cross-striation (hematoxylin–eosin stain, original magnification ×200). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

**FIGURE 3.** Intense, granular cytoplasmic staining for muscle-specific actin (actin stain, original magnification ×200). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
in the membranes (Figure 4). Further immunohistochemical investigation revealed intense positivity for myosin heavy chain-fast (MHCf), whereas staining for MHC-slow (MHC) was negative in all cells. Both MHC-neonatal (MHCn) and myogenin were positive in some cells. No cells expressed MHC-developmental (MHCd).

Myosin is a contractile muscle-specific protein composed of two MHCs and four myosin light chains (MLCs). Slow-type I MHCs and fast-type II MHCf MHC-containing fibers are found in adult human muscle. MHCs and MHCf are expressed in mature muscle cells. MHCd and MHCn are isoforms of heavy chain myosin. They are present during the fetal and neonatal period, because they are important for development of skeletal muscle. MHCd and MHCn are not found in mature muscle cells. MHCn reappear transiently after induction of necrosis and denervation. Regenerating muscle fibers can be identified by MHCn; they are seen as small recently formed fibers suggesting proliferation. Myogenin plays an important role in the differentiation of rhabdomyoblasts; it occurs in proliferating cells and disappears in mature muscle cells.

**DISCUSSION**

The two tumors presented were benign rhabdomyomas of adult extracardiac type, and they were both located in the parapharyngeal space. These tumors favor the head and neck region, because they arise from the musculature of the third and fourth branchial arches. Symptoms, which are nonspecific, depend on the localization and the size of the tumor. In the first case, the tumor was mistaken for a salivary gland tumor, and in the second case, the tumor was found coincidently during an operation for a squamous cell carcinoma of the upper alveolar ridge. Both patients were in their sixth decade, and adult rhabdomyomas generally occur in the elderly (median age, 60 years). Although rare in children, these tumors have been described in patients of all ages from 5 weeks to 82 years of age. The tumors are more common in men than in women (up to 6:1). The treatment of rhabdomyoma is complete excision. Recurrence may be as high as 42%, and in one case, three recurrences have been reported within a period of 35 years after primary resection. This is probably due to incomplete excision or multifocality, which is seen in 14% to 26% of the cases. None of our patients showed evidence of recurrence or tumor at other sites. Rhabdomyomas have no malignant potential. Since Gibas et al demonstrated clonal chromosome abnormalities, the adult rhabdomyoma is considered a true neoplasm rather than a hamartoma. Immunohistochemically, our results also confirmed a clonal origin, because the tumors stained intensely positive MHCf and were completely negative for MHCs, suggesting origin from a single clone. Dystrophin is a very large molecule located in the cell membrane. Both the terminal (Dys-A) and the middle (Dys-ROD) part of the molecule were expressed in the two tumors, suggesting they were mature. The expression of dispersed positive MHCn cells shows that a slight proliferation takes place, and thus the tumors are not totally mature, but differentiation is demonstrated, because myogenin was positive in these few cells. Electron microscopic investigations have found similar various degrees of myofibril differentiation in adult rhabdomyomas. Granular cell tumors, hibernomas, oncocytomas, and paragangliomas are the most important differential diagnoses. All these tumors can be distinguished from a rhabdomyoma by conducting immunohistochemistry; these tumors also do not exhibit cross-striation, and they do not contain glycogen. Surely one must always have the malignant counterpart in mind, the rhabdomyosarcoma, but this tumor will exhibit nuclear polymorphism and a lot of mitoses.

**CONCLUSION**

Adult extracardiac rhabdomyoma is a rare, benign, slow-growing tumor. It is best treated by
radical surgery. It can recur, but it never turns malignant. Immunohistochemistry confirms that it is a practically mature, true neoplasm of clonal origin. Ninety percent of rhabdomyomas arise in the head and neck region. Therefore, rhabdomyomas should be considered in a differential diagnosis in this region.

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REFERENCES