The Rarity of Rhabdomyosarcomas in the Adult
A Morphologic and Immunohistochemical Study

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SUMMARY
An analysis was made of the rhabdomyosarcomas diagnosed in the Dept. of Pathology of the University of Groningen between 1971 and 1983. Ten cases diagnosed in patients over 30 years of age were studied in detail. After review the diagnosis was discarded on morphologic criteria in all cases. In 9 cases it was changed into malignant fibrous histiocytoma (MFH) and in one case this diagnosis was favoured, but inconclusive. In 5 cases immunohistochemical studies could be performed. In all cases staining for the muscle specific intermediate filaments desmin appeared negative and for the mesenchymal intermediate filaments vimentin positive. These cases were also positive for one or more of the histiocytic markers alpha-1-antichymotrypsin, alpha-1-antitrypsin and lysozyme. It is concluded that rhabdomyosarcoma in older patients is extremely rare and the possible relationship between MFH in the adult and rhabdomyosarcoma in childhood is discussed.

Introduction
In children and young adults rhabdomyosarcoma is the most frequent soft tissue malignancy, but in older patients its relative frequency is low3, 4, 9, 10, 12, 21. Moreover, only the pleomorphic subtype appears to be diagnosed in older patients, which type is rare in children4, 5, 21. As was pointed out by Enzinger and Weiss3, the pleomorphic rhabdomyosarcoma hardly ever reveals cross-striations and is difficult to distinguish from other types of pleomorphic sarcomas, especially the malignant fibrous histiocytoma. In fact, several authors4, 5, 22 now believe that many of the previously diagnosed pleomorphic rhabdomyosarcomas in adults are in reality pleomorphic malignant fibrous histiocytomas and that also in children this subtype of rhabdomyosarcoma is rare. A more specific histogenetic classification of soft tissue tumors has been enabled by the development of several immunohistochemical markers1, and especially by the identification of different types of intermediate filaments which are more or less specific for certain cell types2, 16.

In the current study an analysis was made of the rhabdomyosarcomas diagnosed between 1971 and 1983 at the Dept. of Pathology of the University of Groningen. Those cases that were diagnosed in adults were reviewed and, where possible, were tested for the presence of mesenchymal and muscle type of intermediate filaments vimentin and desmin and for the histiocytic markers lysozyme, alpha-1-antitrypsin and alpha-1-antichymotrypsin.

Material and Methods
Patients. In 41 patients a diagnosis of rhabdomyosarcoma had been made between 1971 and 1983. The age distribution of these patients shows peak incidences in the first and seventh decades.

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(Fig. 1). Fourteen patients were over 30 years of age at the time of diagnosis, which were selected for the current study. Four cases had been referred from elsewhere and no more sections were available. The paraffin sections of the remaining ten patients were all reviewed which in all cases included haematoxylin-eosin stained sections, in 6 cases also phosphotungstic acid-haematoxylin (PTAH) and in 2 cases mucin or melanin stains. In 5 cases paraffin material was available for marker studies.

**Immunohistochemical stainings** were performed on paraffin sections applying the peroxidase-anti-peroxidase method of Sternberger, using 3-amino-9-ethylcarbazole as substrate. All cases were stained with antibodies against vimentin (raised in rabbits against calf lens vimentin) against desmin (raised in rabbits against chicken gizzard muscle desmin) and against lysozyme, alpha-1-antitrypsin (AAT) and alpha-1-antichymotrypsin (ACT; Dako). Sections stained for vimentin and desmin were preincubated overnight at 4°C, as described in detail elsewhere.

**Results**

**Morphologic evaluation.** Review of the paraffin sections did not confirm a diagnosis of rhabdomyosarcoma in any of the ten patients. In all cases large cells with strongly eosinophilic cytoplasm and irregular nuclei with very prominent nucleoli were present, which had presumably been taken for rhabdomyoblasts (Fig. 2A). However, cross-striations were never found in H&E or PTAH stained sections and the cytoplasm did not have the fibrillar appearance found in rhabdomyoblasts. In some cases cells with long extended eosinophilic cytoplasm which resembled strap cells were also present, but never revealed cross-striations (Fig. 2A). In addition a more or less prominent fibrous component was observed at least focally in all tumors. Therefore, in all but one case a diagnosis of pleomorphic malignant fibrous histiocytoma was made confidently on morphologic criteria (Table 1). In 3 cases other types of MFH were observed as well (Table 1). In cases 7 a diagnosis of MFH was favoured, but a carcinoma could not be excluded with certainty. Unfortunately, in this case, no material was available for marker studies.

**Intermediate filaments.** In all 5 cases available for marker studies the staining for desmin appeared entirely negative, whereas vimentin was positive in many of the tumor cells (Table 2, Fig. 2C, D).

![Fig. 1. Age distribution of patients in which a rhabdomyosarcoma was diagnosed.](image-url)
Table 2. Results of marker studies. + strongly positive cells, throughout the tumor tissue; ± focal or weak positivity. * positivity largely confined to granulocytes, partly phagocyted by tumor cells

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<th>Pat.</th>
<th>Desmin</th>
<th>Vimentin</th>
<th>α1-Anti-trypsin</th>
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**Histiocytic markers** (Table 2). In all 5 cases ACT appeared to be positive in at least some of the tumor cells (Fig. 2B). AAT was positive in 4 cases, but generally showed a weaker staining. Lysozyme appeared to stain granulocytes strongly, including those phagocyted by tumor cells, but gave only weak cytoplasmic staining reaction in tumor cells and was entirely negative in one case.

**Discussion**

The current study analysed the rhabdomyosarcomas diagnosed in our Department in the years 1971 through 1983. Similar to older studies rhabdomyosarcomas had been diagnosed most frequently in young children and older adults. However, after review this diagnosis was rejected in all cases of patients over 30 years of age and MFH could be diagnosed confidently on morphologic criteria in all but one cases. In the remaining case this diagnosis was favoured, but carcinoma could not be excluded with certainty. It is of interest to note that all cases were diagnosed before 1978, around which time the diagnosis of MFH became generally accepted. The current findings confirm the suppositions of other authors, which, however, were not systematically studied, that many of the older cases of adult rhabdomyosarcomas are in reality pleomorphic MFH's. They are also in keeping with the findings of Enjoji et al. that approximately 7% of MFH's were previously labeled rhabdomyosarcoma.

Immunohistochemical studies in 5 of the current cases confirmed the mesenchymal nature of the tumor by positivity for the vimentin type of intermediate filaments. The myogenic type of intermediate filaments, desmin, was consistently negative. Since the desmin type of intermediate filaments has been shown to be less sensitive for fixation procedures than the vimentin type, the negativity for desmin in these vimentin-positive cases cannot be attributed to fixation artifacts. Moreover the anti-desmin antiserum has been tested extensively on normal and tumor tissues. Although childhood rhabdomyosarcomas are generally desmin positive, negative cases have been reported as well. However, a recent study from our laboratories dealing with 21 cases of childhood rhabdomyosarcomas and using the same technique demonstrated that only very primitive tumors were desmin negative. In all cases which contained round rhabdomyoblasts, which resemble the large eosinophilic cells observed in the current cases, most of these cells were positive. The desmin negativity of the current tumors may therefore be considered additional proof of their non-malignant origin. Their staining pattern for ACT, AAT and lysozyme is compatible with a fibrohistiocytic origin.

The extreme rarity of rhabdomyosarcomas later in life is also interesting from a histogenetic point of view. A comparison of morphologic features and of intermediate filament patterns in childhood rhabdomyosarcoma and normal myogenesis suggests that these tumors arise from primitive mesenchymal cells which are capable of muscle differentiation. In contrast to fibroblasts, muscle cells lose their proliferative capacity later in life, which might also render them less sensitive to stimuli resulting in uncontrolled proliferation, i.e. tumor development. It is conceivable that the ubiquitously present pool of primitive mesenchymal cells which lasts throughout life, may respond to carcinogenic stimuli in a way which parallels their most probable normal development at that stage of life, i.e. myogenic early in life and fibroblastic later in life (cf. also Stern). The origin of the histiocyte has been long debated, but this cell might well arise from this same primitive mesenchymal cell. The wide variety in histologic features and in marker patterns observed in MFH presumably reflects the various cell types arising from the primitive mesenchymal cell proliferating in different combinations and in different proportions to each other. It is tempting to consider the possibility that MFH in the adult and rhabdomyosarcoma in childhood arise from a common type of primitive mesenchymal cell and that MFH represents the adult counterpart of rhabdomyosarcoma.

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