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CASE REPORT

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Follicular thyroid carcinoma with rhabdoid phenotype

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Abstract The aim of this paper is to highlight the occurrence of an unusual histological variant of follicular carcinoma of the thyroid. Three cases are presented: each of the tumours contained a significant population of rhabdoid cells (accounting for 30–40% of the total tumour content). They were all found in female patients aged 65, 43 and 56 years, who presented with enlarged thyroid glands and were subjected to lobectomies. The tumours contained foci of well-differentiated follicular carcinoma, with areas of capsular and vascular invasion, and an accompanying rhabdoid cell component that merged with the neoplastic follicles. Immunohistochemically, the follicular component was positive with thyroglobulin, but the rhabdoid cells were negative in all three cases. The cytoplasmic aggregates in the rhabdoid cells were strongly positive for epithelial markers and vimentin. Two tumours pursued an aggressive biological course similar to other composite extrarenal rhabdoid tumours. A rhabdoid component accompanying thyroid follicular carcinomas is an adverse prognostic factor.

Key words Follicular thyroid carcinoma · Rhabdoid cells

Introduction

Rhabdoid cells are characterised by abundant deeply eosinophilic cytoplasm with eccentric, vesicular nuclei and prominent acidophilic nucleoli. They are frequently encountered outside the setting of the entity "malignant rhabdoid tumour" of the kidney, which typically occurs in childhood, and are seen as part of the histological spectrum encountered in several epithelial and mesenchymal tumours [1–6]. With rhabdoid cells being described in an ever-expanding array of tumours, a recent review attempted to bring a semblance of order to this burgeoning entity [7]. Malignant renal rhabdoid tumours were regarded as characteristic enough, from a clinicopathological viewpoint, to warrant retention as a distinct entity [7] quoted as accounting for 1.6% of all childhood renal neoplasms [7]. Two forms of extrarenal rhabdoid tumours were recognized, those composed wholly of rhabdoid cells and those containing an admixture of rhabdoid cells together with an histologically recognisable and discrete entity – the so-called composite extrarenal rhabdoid tumours [7]. Approximately 100 such cases have been documented in the literature [7].

There is merit in recognising tumours that have a significant rhabdoid component, because it has been shown that such tumours behave more aggressively than similar tumours without rhabdoid cells [5]. We describe three cases of follicular thyroid carcinoma with a large population of rhabdoid cells. Two of the tumours behaved in an aggressive fashion.

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Case reports

Case 1

A 65-year-old woman presented with thyromegaly of 1 year's duration. In the 6 months prior to admission, she had complained of dyspnoea and dysphagia. On examination, she was euthyroid but ill, with a large, soft goitre. A right lobectomy was performed with clear lines of excision. Although there was relief from the obstructive symptoms, the patient died 3 months later with disseminated malignancy to lungs and liver. No adjuvant therapy was given to the patient.

Case 2

A 43-year-old woman presented with a neck swelling of unknown duration. Clinically, a nodule within the right lobe of the thyroid was identified. The patient was euthyroid and otherwise well. No evidence of metastatic disease was noted at the time of presentation. A right lobectomy was performed, with complete removal of the lesion. The patient recovered from the operation but re-presented 7 months later with disseminated metastatic disease involving skull, lung and liver. In view of the metastatic disease no other treatment was offered. She was then lost to follow-up and is presumed dead.

Case 3

The patient, who is 56 years old, presented with a right-sided neck swelling that was localised to the right lobe of the thyroid. This had been present for about 1 year and had increased in size recently. She was otherwise well. A right thyroid lobectomy was performed. One month after the operation, the patient is alive with no evidence of metastases. Other than surgery, no other treatment has been offered to the patient.

None of these patients had other tumours, and specifically none had any tumour in the kidney, at the time of presentation.

Materials and methods

The records of the Department of Pathology were examined from 1986 to 1998 (inclusive) for all cases of thyroid malignancies. For this period, approximately 90 follicular carcinomas were accessed. None of the other carcinomas (papillary, medullary or anaplastic) were noted to contain rhabdoid cells. The specimens were fixed in 10% buffered formalin, routinely processed, and embedded in paraffin wax. Immunohistochemistry was performed on the formalin-fixed tissue using the streptavidin–biotin complex technique with DAB as chromogen following microwave antigen retrieval. The following antibodies were used: thyroglobulin (dilution 1 in 16000; polyclonal; Signet Laboratories, Dedham, USA), cytokeratins (AE1/3,1 in 1600; monoclonal; Signet Laboratories, and CAM 5.2,1 in 400; monoclonal; Becton Dickinson, San Jose, USA), CEA (1 in 2000; polyclonal; Signet Laboratories), EMA (1 in 65; monoclonal; Dakopatts, Glostrup, Denmark), vimentin (1 in 40; monoclonal; Signet Laboratories), desmin (1 in 400; monoclonal; Signet Laboratories), actin (1 in 120; monoclonal; Dakopatts), Ki-67 (1 in 10; monoclonal; Dakopatts) and S-100 protein (1 in 1200; polyclonal; Signet Laboratories).

Results

Macroscopic findings

Case 1

A lobectomy specimen weighing 193 g and measuring 9×9×6 cm was submitted for histological evaluation. A pale fleshy tumour measuring 6×3 cm with areas of necrosis, occupied most of the specimen. Extension beyond the tumour capsule was noted (pT4N0M0).

Case 2

The lobectomy specimen measured 6×3×3 cm and contained a slightly haemorrhagic tumour measuring 4×2 cm. The tumour had spread beyond the confines of the tumour capsule (pT4N0M0).

Case 3

The right lobe was received in three pieces collectively weighing 70 g. The largest piece measured 5×3×1 cm. All tissue submitted had a pale firm appearance, and grossly apparent capsular extension was noted (pT4N0M0). No thyroid tissue with a normal appearance was seen.

Microscopic findings

All three cases showed similar features. Distinct areas of follicular carcinoma with both capsular and vascular invasion were present. In case 3, multiple sections had to be examined before a follicular component was discerned. Insular areas were not evident. In addition, the rhabdoid cells constituted a major component of the tumours, accounting for 30–40% of the tumour cell population (Fig. 1). These cells were characterised by large vesicular nuclei containing prominent acidophilic nuclei and abundant eosinophilic cytoplasm with whorls of paranuclear material, imparting an eccentricity to the cell nucleus. In other areas, the rhabdoid cells appeared more hyperchromatic and displayed multinucleation and pleomorphism. Several mitoses (including abnormal forms) were identified. These cells blended with the follicular structures (Fig. 2), and within occasional follicles rhabdoid cells could be seen. The rhabdoid cells had an infiltrative growth pattern and also penetrated the capsule. The stroma appeared distinctly myxoid in some areas and contained an acute inflammatory cell infiltrate. Large areas of tumour necrosis were also evident. Both capsular and vascular invasion were found easily.

The rhabdoid cells were strongly positive for CAM 5.2 (Fig. 3), AE1/3 and vimentin. These stains highlighted the paranuclear aggregation of cytoplasmic filaments. Thyroglobulin and cytokeratin stains were positive in the well-differentiated follicular component. These cells also showed focal vimentin positivity. The rhabdoid cells were negative for thyroglobulin. Ki-67 labelling varied; within each tumour the rhabdoid cells were positive, while the follicular areas were largely unlabelled. The proliferation rate (calculated by counting the number of positive nuclei and expressing it as a percentage of the total number of cells; twenty five high-power fields were assessed) varied from 10% to a high of 30%. All other markers were negative.

Discussion

The first description of rhabdoid cells is credited to Beckwith and Palmer, who in 1978 described this rather characteristic cell type in Wilms' tumours [1]. Malignant rhabdoid tumour of the kidney was initially thought to be a variant of a "rhabdomyoid-like" tumour. Subsequent immunohistochemical and ultrastructural analyses led to the appellation "rhabdoid". The malignant rhabdoid tumour of the kidney is a distinct, but rare, clinicopathological entity that occurs more frequently in males in the first year of life and is often associated with primitive neuroectodermal tumours of the brain. It is the prototypical tumour composed of rhabdoid cells.

Rhabdoid cells are increasingly encountered in the extrarenal setting. Wick and colleagues suggested dividing these tumours into those consisting exclusively of rhabdoid cells and those in which rhabdoid cells are combined with another defined morphological entity –

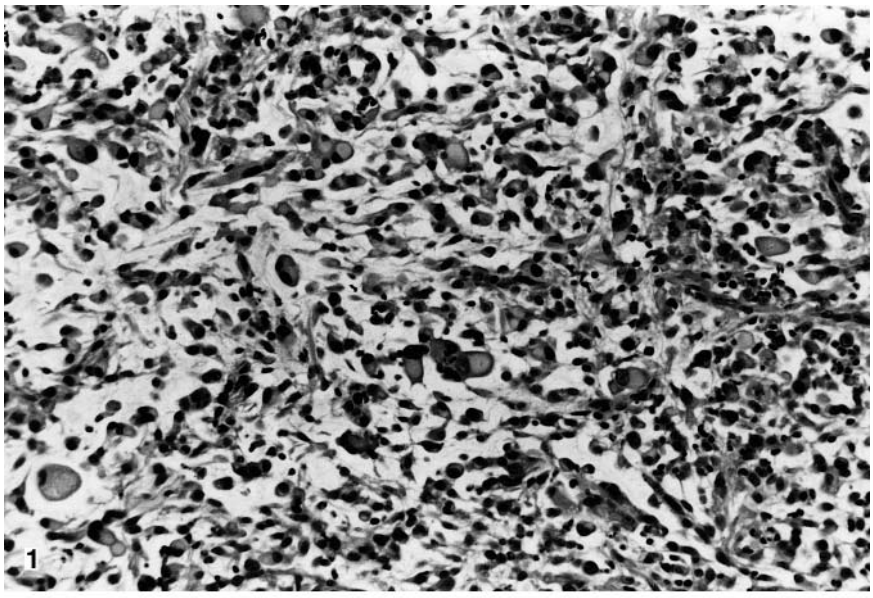

Fig. 1 Sheets of rhabdoid cells, forming a large component of the tumour. These cells are admixed with acute inflammatory cells within a myxoid stroma. H&E, ×200

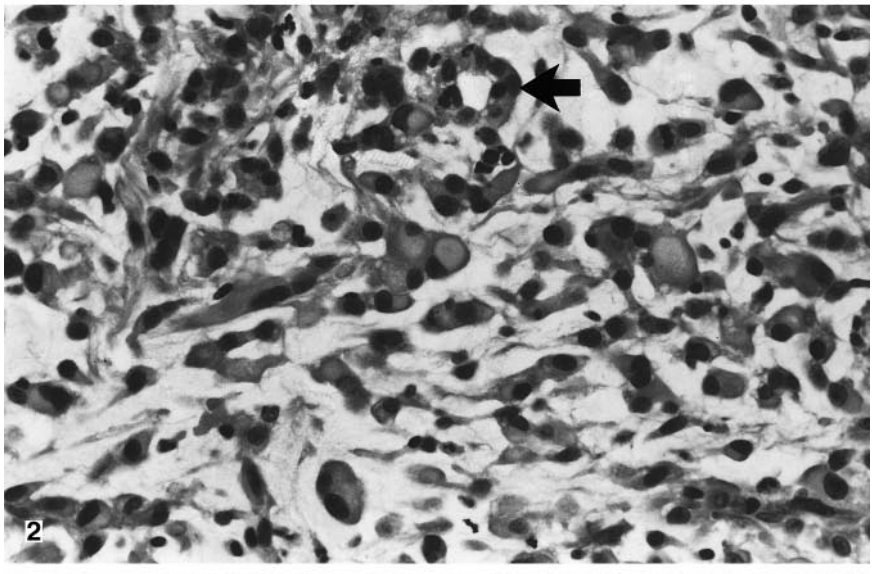

Fig. 2 Occasional follicular structures (*arrow*) blending with the diffuse infiltrate of rhabdoid cells. In addition to the cytoplasmic paranuclear eosinophilic aggregation, there is associated nuclear atypia, with binucleation of some cells noted. H&E, ×400

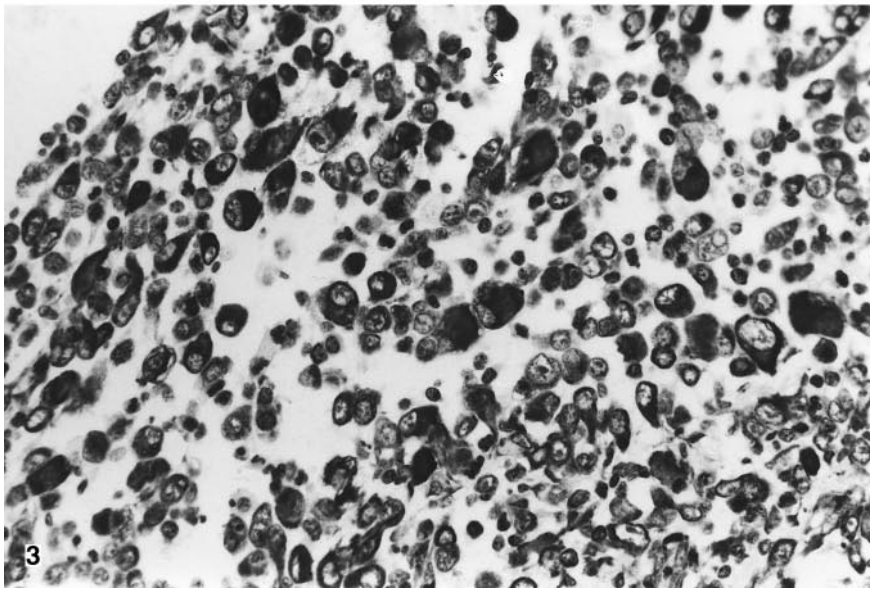

Fig. 3 The rhabdoid cells stain intensely with CAM 5.2 (a low-molecular-weight cytokeratin marker). This stain highlights the cytoplasmic aggregates of intermediate filaments with resultant eccentricity of the tumour cell nuclei. CAM 5.2, ×400

so-called composite extrarenal rhabdoid tumours [7]. It is in this latter category that the three follicular carcinomas described here would best be classified. A comprehensive list of both epithelial and mesenchymal tumours falling under the rubric of composite extrarenal rhabdoid tumours is provided in the detailed review by Wick et al. [7].

The merit of identifying a significant proportion of rhabdoid cells within a tumour is that these cells confer a more aggressive behaviour on the tumours. An important question to address at this juncture is, what is deemed "significant" for the rhabdoid component? A large, controlled study comparing the different percentages of rhabdoid cells has not been performed. The random figure of 10% has been used in two studies [3, 5]. However, the range of rhabdoid cells encountered in both these studies varied from a minimum of 10% to a maximum of 90% of the total tumour population. Although not commented on specifically, it appears that most composite extrarenal rhabdoid tumours have at least 10% of the tumour population made up of these cells. It must be emphasised that tumours containing cells with eosinophilic cytoplasmic inclusions but lacking the nuclear features (vesicular nuclei, prominent acidophilic nucleoli and nuclear atypia) should not be categorised as rhabdoid tumours.

The three follicular carcinomas reported in this paper contained a high percentage of rhabdoid cells, and two (thus far) followed an aggressive clinical course. Although all three cases were treated with lobectomies only (which was inadequate for T4 thyroid tumours), the rapid spread and dissemination is still unusual. This behaviour is in keeping with that of the majority of other composite extrarenal rhabdoid tumours from diverse sites. The coexistence of areas of typical follicular carcinoma is also important. Rhabdoid cells often represent the phenotypic endpoint of tumours that heralds a high-grade, more aggressive biological state. This is paralleled in the thyroglobulin staining, where the well-differentiated follicular component was positive while the rhabdoid cells were negative, attesting to their dedifferentiated state. A differentiated component is often only found after multiple sections have been examined, as was demonstrated in case 3 [4]. In two tumours, a differentiated follicular component was easily found. In view of the blending of typical follicular carcinoma cells and rhabdoid cells, a dedifferentiation or transformation process into a poorly differentiated form is favoured. It is also possible that rhabdoid cells have been encountered in thyroid malignancies previously (although not documented), but these may have been labelled anaplastic carcinomas, especially the so-called sarcomatous variety. Indeed, "rhabdomyomatous" areas have been seen within anaplastic thyroid carcinomas, and these could possibly conform to the rhabdoid component described in this paper. It is felt that the rhabdoid cells herald the onset of de-differentiation, the endpoint of which is an anaplastic carcinoma. Whether these tumours should be categorised as anaplastic carcinomas rather than follicular carcinomas is uncertain. The presence of rhabdoid cells within follicular structures tends to favour these tumours being follicular carcinomas. It is probable that at the endstage, where the follicular component is barely discernible, they would be called anaplastic.

In the context of the biological behaviour of follicular thyroid carcinoma, we propose that a rhabdoid phenotype (constituting at least 10% of the total tumour cell population) should be considered as conferring an adverse prognosis. Once these lesions resemble anaplastic carcinomas, they are more than likely to behave in the same way as other anaplastic carcinomas lacking rhabdoid cells. In addition, this is the first report of rhabdoid cells occurring in follicular carcinoma of the thyroid gland.

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