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Case report

Caecal adenocarcinoma with rhabdoid phenotype: an immunohistochemical and ultrastructural analysis

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Summary. A polypoid caecal adenocarcinoma in a 72-year-old female was found microscopically to be composed mainly of rhabdoid cells. Deposits in the liver and lymph nodes had a similar histological appearance to the primary tumour. The rhabdoid cells were typified by abundant eosinophilic cytoplasm, eccentric nuclei and prominent nucleoli. The differential diagnosis included rhabdomyosarcoma, metaplastic carcinoma (carcinoma with sarcomatoid dedifferentiation), carcinosarcoma and extra-renal rhabdoid tumour. The rhabdoid cells showed strong immunoreactivity with cytokeratin, epithelial membrane antigen and vimentin. Ultrastructurally, cytoplasmic whorls of intermediate filaments were noted. Multiple sections, immunohistochemistry and ultrastructural examination all revealed an adenocarcinomatous component which blended with the rhabdoid areas. In one area a rhabdoid cell was present within a malignant gland. This case illustrates that the rhabdoid appearance of many tumours can be misleading and is merely a non-specific morpho-phenotypic pattern seen in extra-renal sites. In the extra-renal setting, careful search for evidence of differentiation should be undertaken.

Key words: Caecum – Adenocarcinoma – Rhabdoid phenotype

Introduction

Dedifferentiation or metaplastic change within epithelial neoplasms has led to a plethora of appellations for such lesions. Pseudosarcoma, metaplastic carcinoma, sarcomatoid carcinoma and carcinosarcoma have been used to describe this histologically peculiar entity. It is now accepted that sarcomatoid dedifferentiation of cancer cells does occur and results in a diverse array of histological patterns, including a rhabdoid appearance. Usually sarcomatoid dedifferentiation takes the form of a spindle cell component, as seen in the liver, oesophagus and kidney (Haratake and Horie 1991; Herman et al. 1983; Matsusaka et al. 1976). Carcinomas of the breast can contain sarcoma-like areas, including heterologous elements (Oberman 1987).

To the best of our knowledge, this is the first case of a caecal adenocarcinoma showing a prominent rhabdoid phenotype.

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Case report

A 72-year-old female presented with a right-sided abdominal mass and hepatomegaly. A laparotomy was performed and revealed a large right colonic mass, tumour deposits in the liver, an enlarged gastro-duodenal lymph node and regional lymphadenopathy. A right hemicolectomy and needle biopsy of the liver were performed. Three months post-operatively, the patient was lost to follow-up and is presumed dead.

Materials and methods

All specimens were received in 10% buffered formalin and processed in a routine manner. Haematoxylin and eosin sections were cut together with periodic acid-Schiff (with and without diastase predigestion), Southgate's mucicarmine and Gordon and Sweet's reticulin preparation. Immunohistochemistry was performed on the paraffin-embedded tissue using the ABC method for a panel of antibodies, which are indicated in Table 1. The non-neoplastic areas of the bowel wall served as an in-built control for the immunohistochemical markers.

Results

A right hemicolectomy specimen was received measuring 365 mm, containing a polypoid tumour 60 × 50 × 20 mm, (Fig. 1). The tumour had penetrated the entire thickness of the bowel wall, and deposits were present in the regional lymph nodes.

On microscopy the tumour was composed of sheets of large cells arranged in ill-defined nests or alveoli. Foci

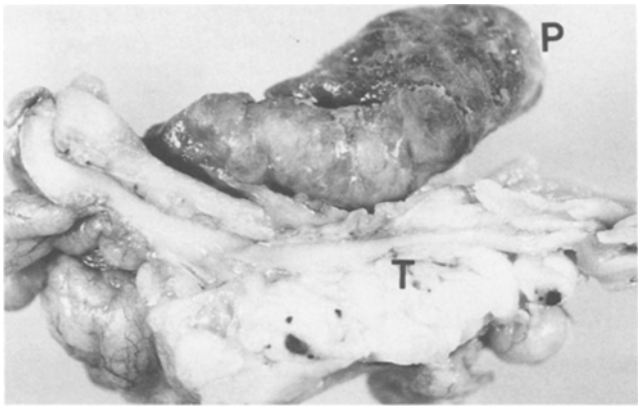

Fig. 1. Gross specimen showing the polypoid (*P*) nature of the tumour within the lumen of the caecum. The underlying bowel wall is infiltrated by tumour (*T*)

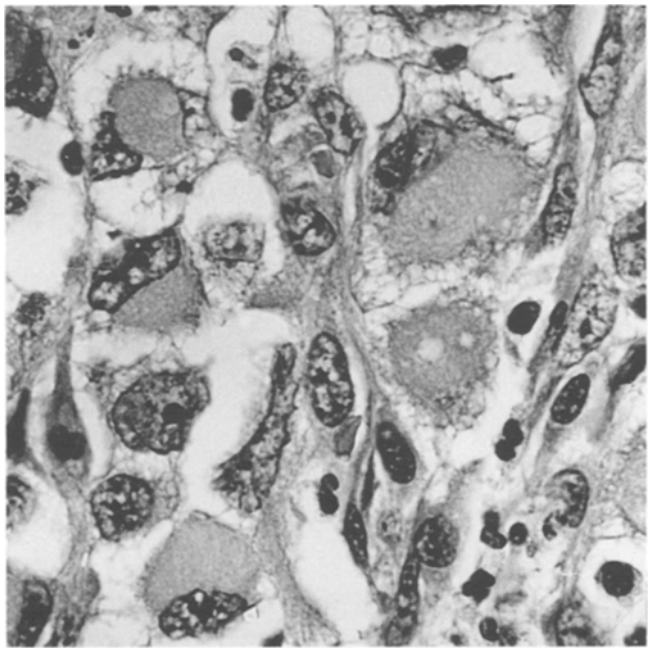

Fig. 2. Typical rhabdoid cells with intra-cytoplasmic inclusions displacing the nucleus. Some of the rhabdoid cells showed cytoplasmic retraction imparting a "spider" cell appearance. Haematoxylin and eosin, × 500

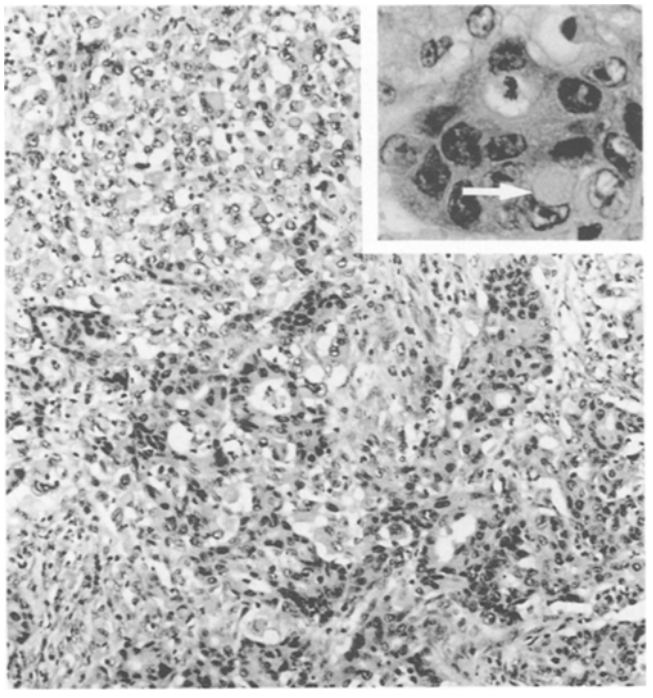

Fig. 3. Malignant glands merging with the rhabdoid areas. Haematoxylin and eosin, × 125. *Inset*: A malignant gland containing a rhabdoid cell (*arrow*). × 500

of tumour necrosis were present. Individual cells had rhabdoid features: large vesicular nuclei with prominent acidophilic nucleoli and abundant eosinophilic cytoplasm containing whorls of paranuclear material which displaced the nucleus peripherally (Fig. 2). The cytoplasm of some cells was vacuolated, simulating "spider" cells (Fig. 2). Occasional rhabdoid cells had strap-like configurations. Multi-nucleated tumour cells were also scattered throughout the tumour. Mitoses were easily found and foci of tumour necrosis were also evident. The rhabdoid cells dominated and only after taking multiple sections were foci of obvious carcinoma discerned. The adenocarcinomatous component merged with the rhabdoid areas (Fig. 3), and in one area, a rhabdoid cell was present within an island of obvious carcinoma (Fig. 3, inset). In transitional areas, a malignant spindle cell element was noted. Metastatic tumour in the lymph

Table 1. Antibodies used and results of staining of rhabdoid cells

Antibodies	Dilutions	Source	Staining of RC
Carcinoembryonic antigen	1:10	Dakopatts, USA	–
Epithelial membrane antigen	1:10	Dakopatts	+
Cytokeratin (AE1/3)	1:400	Boehringer	+
Cytokeratin (CAM 5.2)	1:10	Becton-Dickinson	+
Myoglobin	1:25	Dakopatts	–
Desmin	1:10	Dakopatts	–
Muscle actin	1:1,600	Dakopatts	–
Smooth muscle actin	1:100	Dakopatts	–
S-100 protein	1:400	Dakopatts	–
Vimentin	1:20	Dakopatts	+

RC, rhabdoid cells

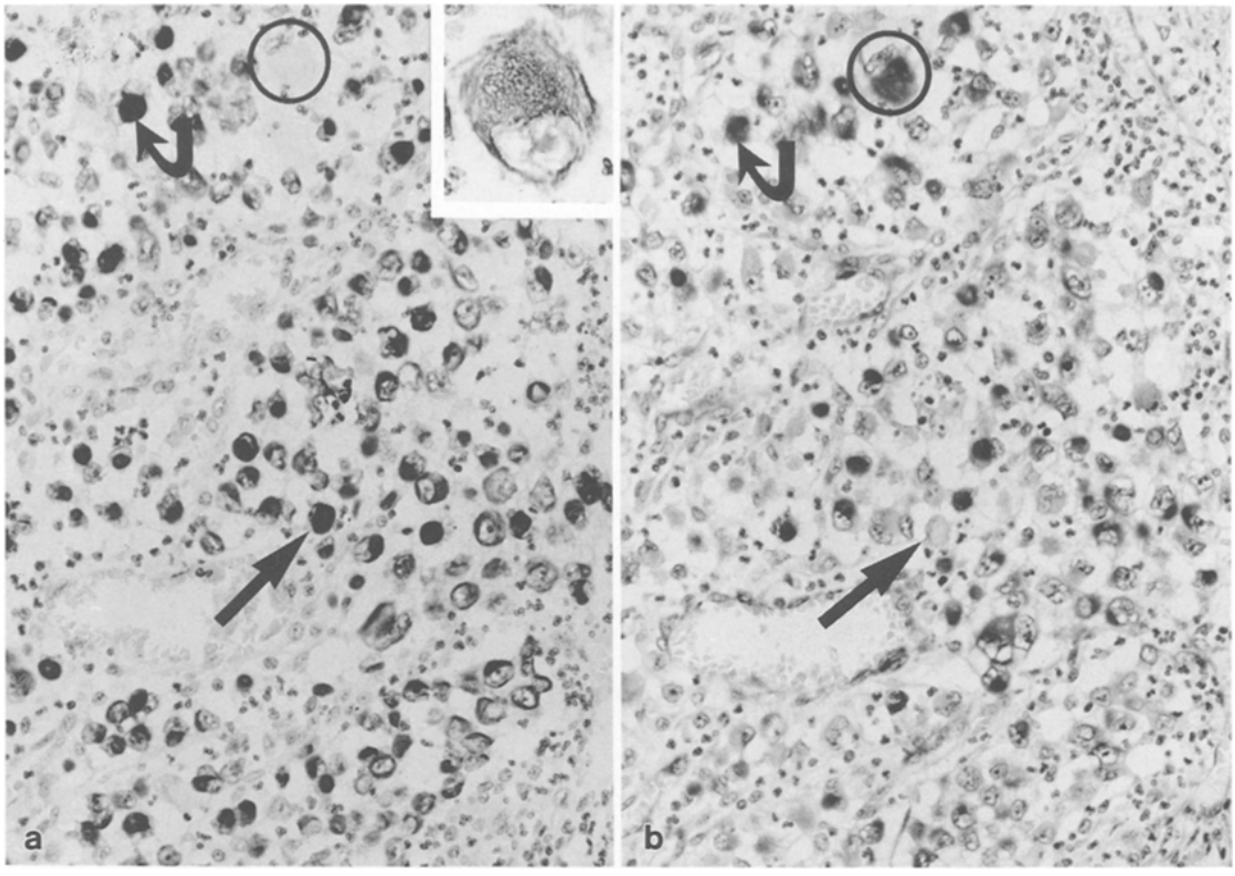

Fig. 4a, b. Co-expression of cytokeratin and vimentin was not seen in every rhabdoid cell. Some cells were positive for CAM 5.2 but negative for vimentin (*straight arrows*). Similarly, vimentin was expressed in some cells that were negative for CAM 5.2 (*circled cells*). However, a large proportion of the cells co-expressed both markers (*curved arrows*). *Inset*: Intracytoplasmic whorls of intermediate filaments reacting strongly for CAM 5.2. ×500. **a** CAM 5.2 ×200, ABC method. **b** Vimentin ×200, ABC method

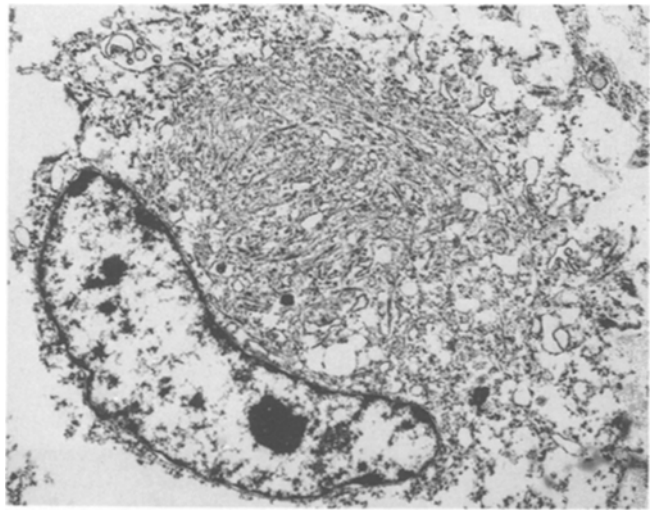

Fig. 5. Intermediate filaments arranged in characteristic whorls in a paranuclear location. ×5360

nodes and liver was also made up of sheets of rhabdoid cells. Little glycogen and mucin was found in the rhabdoid cells, while intra-cytoplasmic mucin was detected in the well differentiated adenocarcinomatous foci.

The rhabdoid cells were strongly positive for CAM 5.2, vimentin (Fig. 4a, b), AE1/AE3 and epithelial membrane antigen (Table 1). Co-expression of both vimentin and cytokeratin was frequently observed in the same cells. The majority of rhabdoid cells were cytokeratin positive. At the same time, a proportion of cells reacted positively with only one of vimentin or cytokeratin. The obviously adenocarcinomatous component showed a similar staining reaction. In addition, the normal mucosa and malignant glands revealed membrane and weak cytoplasmic positivity for the carcinoembryonic antigen (CEA). The rhabdoid cells were strikingly negative for CEA. All other antibodies were negative in the rhabdoid areas.

On electron microscopy the dominant feature was the presence of intra-cytoplasmic whorls of intermediate filaments which contained entrapped organelles (Fig. 5). These findings were in keeping with the ultrastructural features of rhabdoid cells.

Discussion

The morphological appearances encountered in this tumour suggest several diagnostic possibilities: adenocar-

cinoma with sarcomatous metaplasia or dedifferentiation, a true carcinosarcoma, a metastatic sarcoma within a pre-existing carcinoma, and a poorly differentiated adenocarcinoma showing prominent rhabdoid phenotype. We favour the last possibility in view of the immunohistochemistry and ultrastructure of the tumour.

Adenocarcinomas can manifest a variety of metaplastic changes including squamous and spindle cell differentiation. Heterologous mesenchymal elements have been described in breast carcinomas of ductal origin (Oberman 1987). Transitions between carcinoma and heterologous elements, without an intermediate spindle cell population, have also been described (Oberman 1987). Large bowel tumours consisting of sheets of cells with little or no glandular differentiation have been designated "undifferentiated" carcinomas (Gibbs 1977). Whilst the constituent cells have prominent nucleoli, the abundant eosinophilic cytoplasm with intracytoplasmic inclusions of rhabdoid cells is missing.

Malignant rhabdoid tumour was first described in the kidney as a variant of a rhabdomyoid-like tumour. Subsequent immunohistochemistry and ultrastructural analysis led to the appellation rhabdoid tumour. Since then phenotypically similar rhabdoid tumours have been described in several extra-skeletal sites as detailed in the review by Berry and Vujanic (1992). There is growing evidence that extra-renal rhabdoid tumours, especially in adults, are a group of heterogenous, poorly differentiated tumours (Weeks et al. 1989). In the extra-renal setting, every effort should be made to find some evidence of differentiation. Several soft tissue tumours contain rhabdoid cells (Tsuneyoshi et al. 1987), and epithelial tumours have also been noted to have this distinctive phenotype (Ekfors et al. 1985; Harris et al. 1987; Kumar et al. 1992). In the study by Kumar et al. (1992), rhabdoid cells were found in situ in the bladder. This points towards epithelial differentiation of the rhabdoid cells in this particular tumour. These authors also found desmin-positivity in these cells. However, we were unable to demonstrate reactivity with any of the muscle antibodies employed. Furthermore, desmin is not consistently expressed in rhabdoid tumours (Berry and Vujanic 1992). Perhaps the increasing number of extra-renal rhabdoid tumours is due to lack of an assiduous search for features of a differentiated neoplasm. It is therefore essential to distinguish between rhabdoid (due to intracytoplasmic aggregation of cytokeratin intermediate filaments causing the hyaline inclusion-like appearance) and rhabdomyoid (showing evidence of skeletal differentiation). Phenotypic variation within a poulation of cells from the same clone or indeed, progenitor cell, is a characteristic feature of normal tissue, especially tissues that are constantly turning over and regenerating (Hall and Watt 1989). Heterogeneity within tumours can be ascribed to one of two possibilities. The various cell populations visualized could arise from more than one progenitor cell or from the formation of cell hybrids by fusion. The alternative is that cellular heterogeneity reflects normal mechanisms of generating differentiated progeny. Furthermore, additional or new molecular defects may account for variability in morphological appearances (Hall 1992) and rhabdoid change may be a manifestation of such events.

The degree and extent to which this phenotypic expression occurs in a given tumour varies, and in some may completely dominate the histological picture. Most of the rhabdoid tumours encountered in childhood tend to be very aggressive and rapidly fatal. This tumour had a short history (about 6 months) and showed widespread dissemination. Whether this behaviour is a reflection of the rhabdoid cell content is conjectural.

This case provides further morphological, immunohistochemical and ultrastructural evidence supporting the concept that rhabdoid change in many extra-renal tumours is a characteristic but non-specific phenotype that can be encountered in many tumours.

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