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Case Report

## Unusual presentation of a malignant granular cell tumor of the pelvis: case report and literature review

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### Abstract

**Background.** Malignant granular cell tumors are among the rarest of soft tissue cancers, currently understood to be of Schwann cell origin. As with their benign counterparts, malignant granular cell tumors (MGCTs) have a wide anatomic distribution and carry a poor prognosis, with recurrence and metastasis typically within 1 year of diagnosis. Only a handful of MGCTs have been described in the pelvis.

**Case.** We describe a case of malignant granular cell tumor that presented as a pararectal mass associated with severe rectal pain. The patient underwent pelvic exenteration and postoperative radiation therapy. She recurred with evidence of liver metastases on imaging studies 8 months following her exenteration.

**Conclusion.** We discuss the diagnosis and prognosis of malignant granular cell tumors arising in the pelvis.

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**Keywords:** Malignant granular cell tumor; Pelvic mass

### Introduction

Granular cell tumors were initially thought to be of muscle cell origin and accordingly the entity was called a “granular cell myoblastoma” [1]. Electron microscopy and immunohistochemical studies have identified this tumor as a distinctive neural entity most likely of Schwann cell origin [2]. Intracytoplasmic lysosomes account for the granular appearance on light microscopy.

Benign granular cell tumors are relatively common, with one study reporting one case among 346 surgical specimens [2]. Although these tumors are ubiquitous in anatomic distribution, they typically present as small solitary painless

nodules in the dermis or subcutis; the tongue is the most frequently involved anatomic site [3]. The most common location in the gynecologic setting is the vulva [4].

Malignant granular cell tumors constitute less than 2% of granular cell tumors overall [2]. Fewer than 100 cases have been reported in the literature since being first described in 1945 by Ravich et al. [5]. As with their benign counterparts, malignant granular cell tumors (MGCTs) have a wide anatomic distribution and carry a poor prognosis, with recurrence and metastasis typically within 1 year of diagnosis.

### Case report

We present a case of malignant granular cell tumor arising in the pelvis. The patient is a 57-year-old Caucasian para 1 who began experiencing symptoms of rectal discomfort in the spring of 2001. She had undergone a total abdominal hysterectomy and left salpingoophorectomy for benign indications in 1993. After 3 months of rectal pain she

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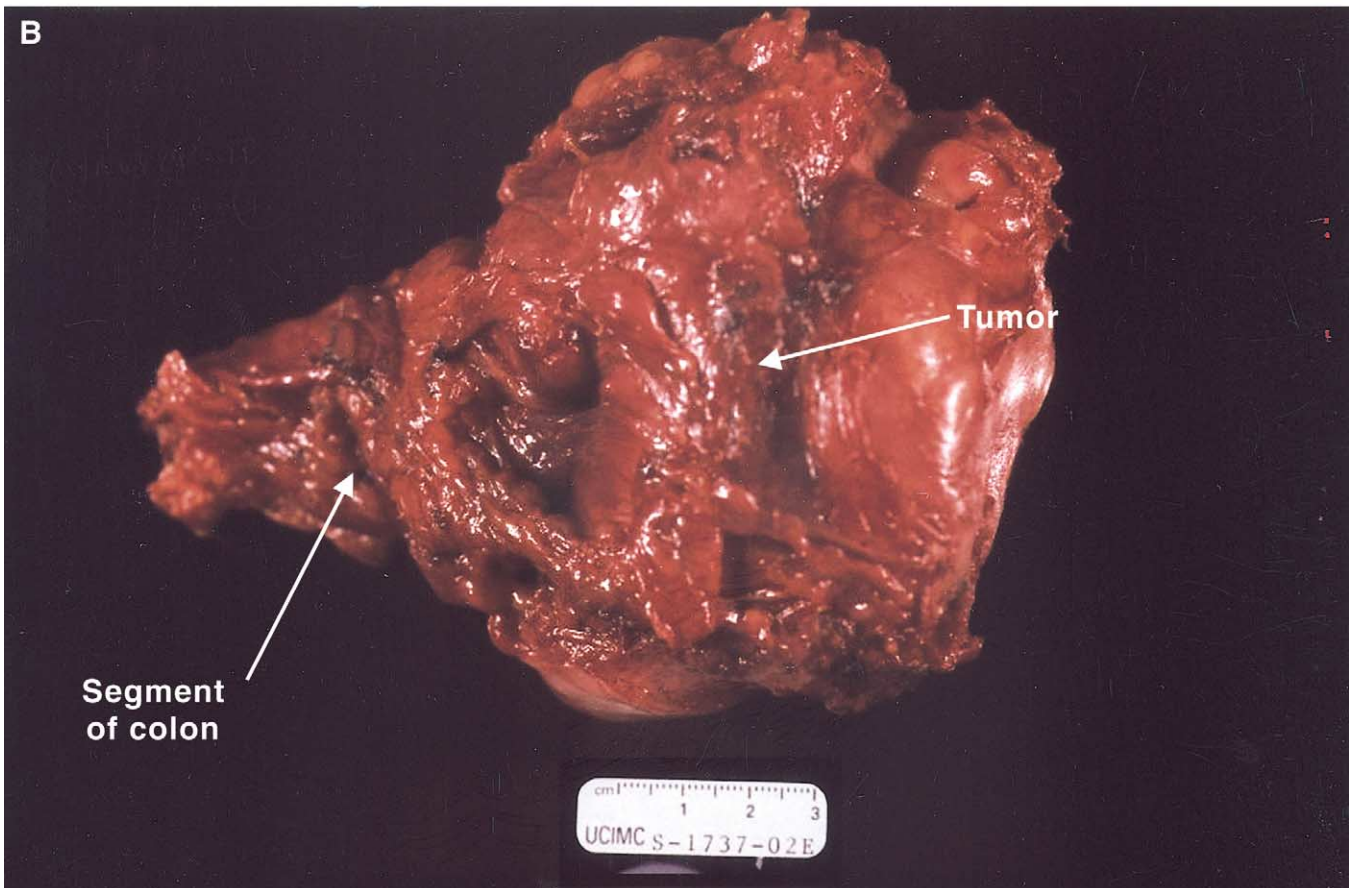
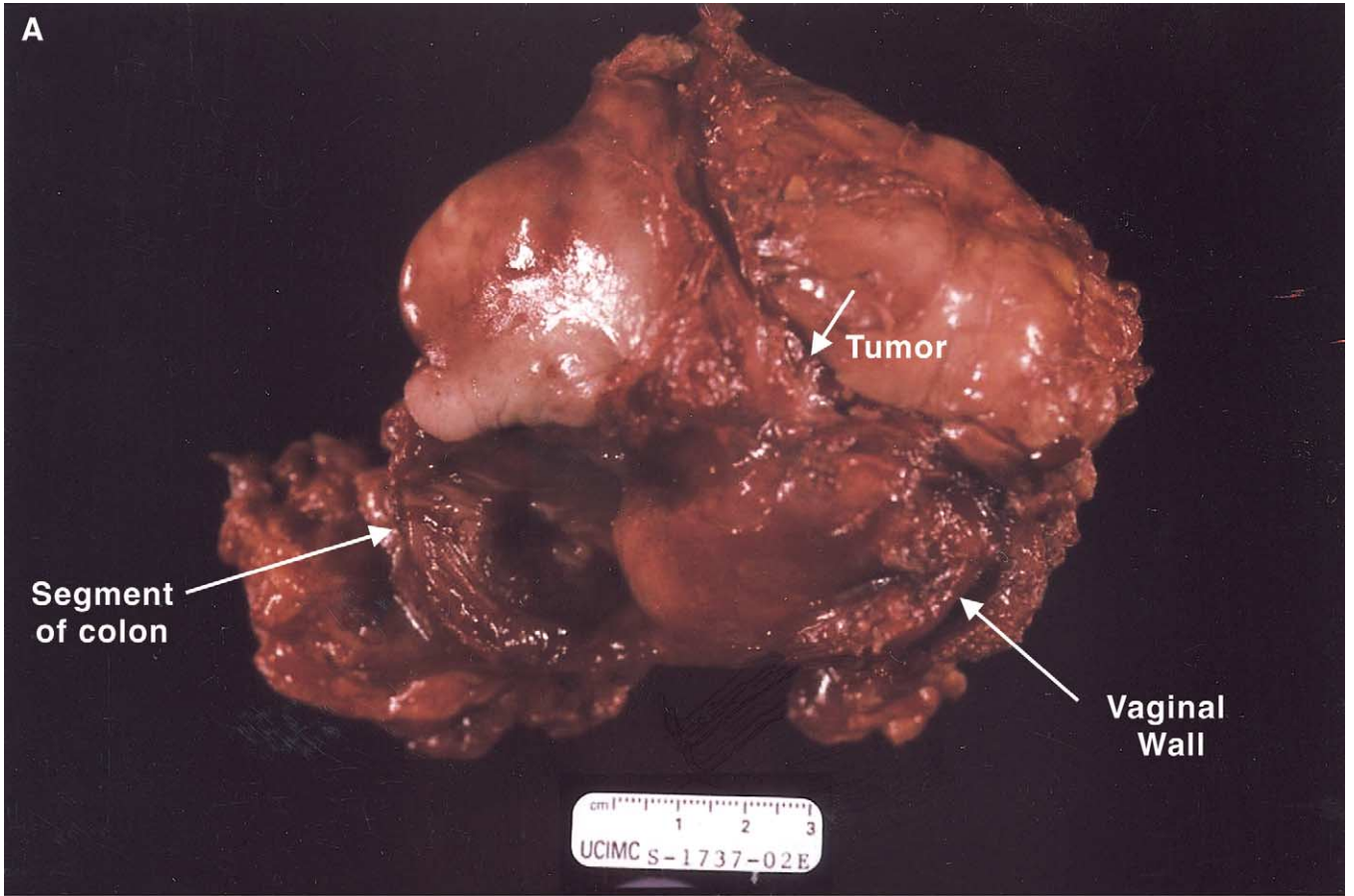


Fig. 1. Gross specimen. The tumor is shown with portions of the vaginal wall and colon.

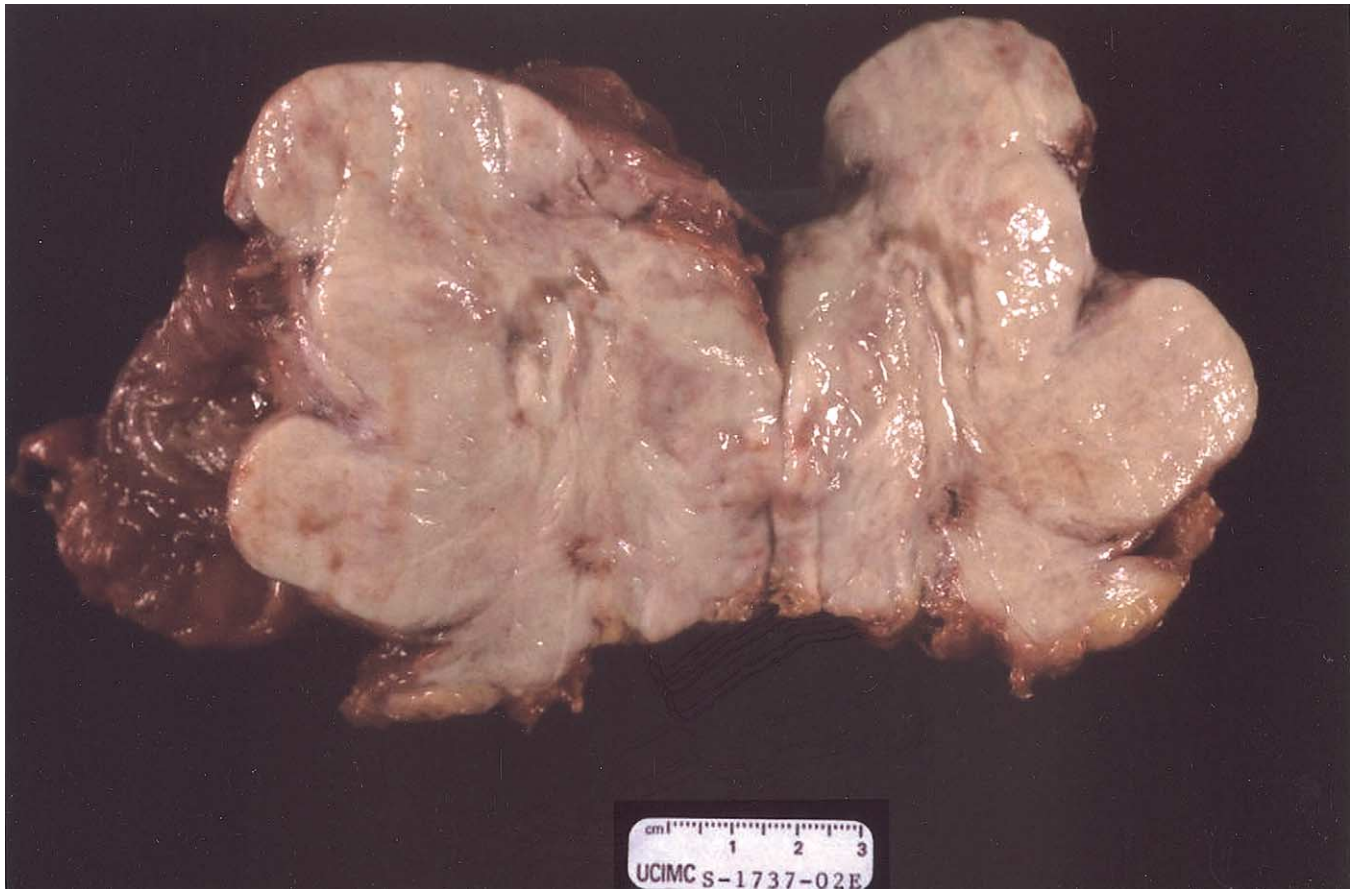


Fig. 2. Cut surface, showing multifocal areas of hemorrhage.

was referred to a gastroenterologist for a colonoscopy which revealed an extrinsic mass compressing the colonic lumen. A spiral CT scan of the pelvis revealed a  $9 \times 8 \times 6.5$ -cm soft tissue mass contiguous with both the left aspect of the rectum and vaginal cuff, in close proximity to the left pelvic sidewall with stranding in the perirectal fat. A fine-needle aspiration of the mass was nondiagnostic, showing only a few clusters of atypical cells. A CT-guided pelvic core biopsy subsequently showed an organized pattern of cells separated by smooth muscle fibers. The individual tumor cells had bland-appearing nuclei with no evidence of nucleoli and abundant eosinophilic staining granular cytoplasm characteristic of granular cell tumors. Rare mitotic activity was seen. The tissue was S-100 positive and PAS positive. These features were consistent with a granular cell tumor. Clear-cut features of malignancy were not present.

The patient was seen in consultation by the gynecologic oncology service at the University of California, Irvine Medical Center, where she complained of severe rectal pain, pressure that prevented her from sitting, constipation, and urinary frequency. The vagina was compressed and elevated by the posterior and lateral mass, precluding a speculum examination. Bimanual and rectovaginal examination revealed a hard, irregular 12-

14-cm tumor mass which was fixed to the left pelvic wall and which extended to the level of the anus. There was no clinical evidence of lymphadenopathy. The upper abdomen was radiographically normal on computerized tomography. Despite concern regarding respectability, the patient was not considered a candidate for preoperative radiation given the large tumor volume and absence of mitoses, both of which were considered adverse factors when considering possible benefits of this modality. The patient was taken to surgery where intraoperative findings revealed a  $10 \times 15$ -cm solid, irregular mass completely filling the left pelvis and crossing the midline. No disease was present outside of the pelvis. The patient underwent a posterior extenteration including a complete perineal resection, end sigmoid colostomy, and left pelvic lymph node dissection, with a rectus abdominus myocutaneous flap employed to reconstruct the pelvic floor.

The  $12.5 \times 9.5 \times 9$ -cm tumor at excision (Figs. 1 and 2) consisted of a yellow pink soft tissue mass attached to the vaginal wall and segment of colon, with separate specimens from the left pelvic sidewall. Cut surface showed multifocal areas of hemorrhage.

Microscopic examination revealed a poorly circumscribed tumor consisting of cells that were rounded, polyg-

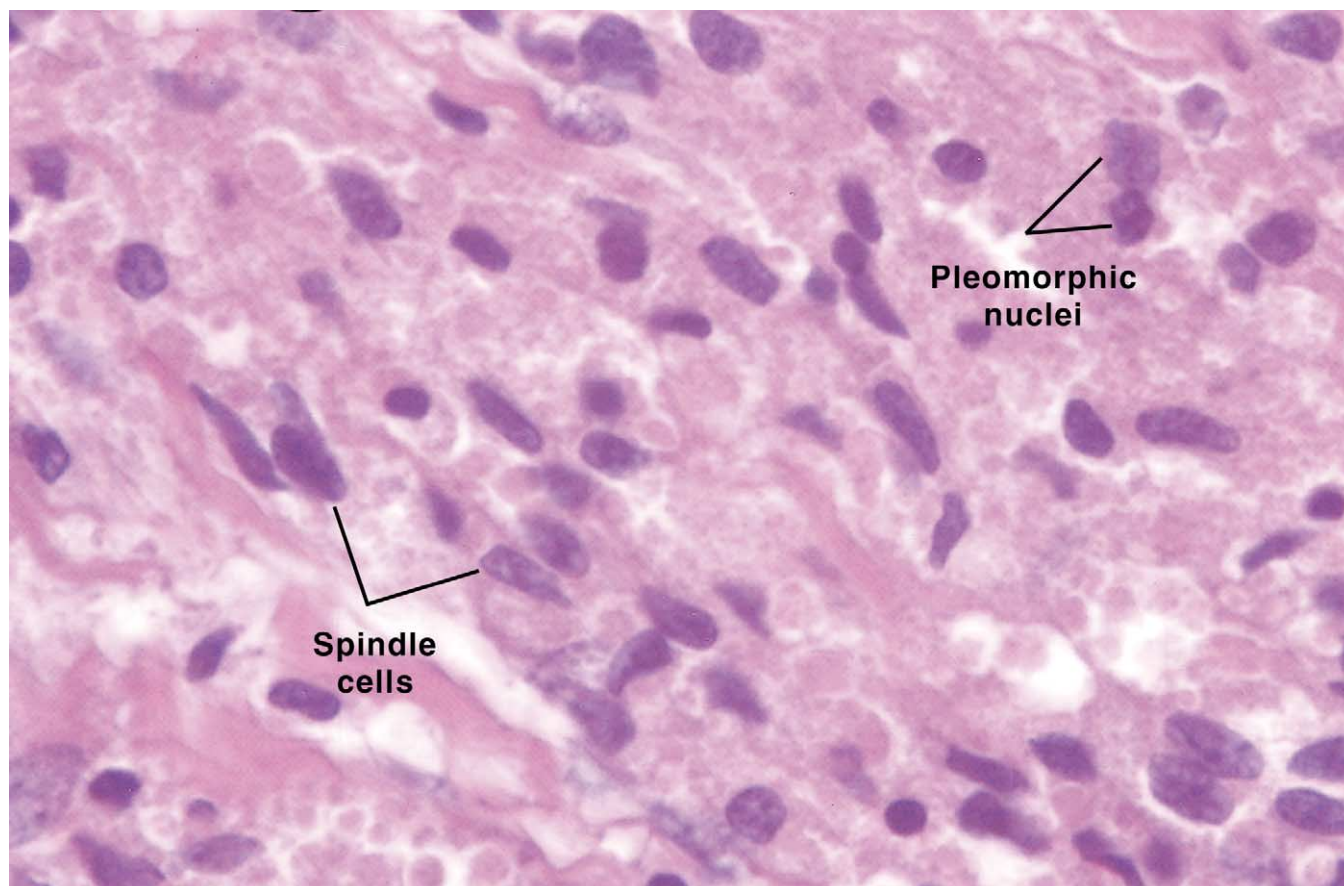


Fig. 3. High-power hematoxylin and eosin stained-micrograph of tumor showing pleomorphic nuclei, elevated nuclear/cytoplasmic ratio, and spindled tumor cells.

onal, and in many areas spindled (Figs. 3 and 4). They were arranged in nests and ribbons, and some areas had an infiltrative growth pattern. The tumor cells had an eosinophilic coarsely granular cytoplasm characteristic of granular cell tumors. Many cells had vesicular nuclei and prominent nucleoli. Some of the tumor cells had a high nuclear/cytoplasmic ratio and nuclear pleomorphism. In some areas tumor necrosis and vascular proliferation were noted. Zero mitotic figures were seen per 10 high-power fields (0/10 HPF). The tumor cells were present at the soft tissue margins and in the submucosa of the vaginal wall (Fig. 5). Ten pelvic lymph nodes were examined and found to be benign. Immunohistochemical staining revealed S-100-positive, PAS-negative tissue.

The patient initially did well following her pelvic exenteration, with reduction in her pain to the point where she could sit comfortably. She underwent whole-pelvis radiation therapy which was well tolerated. She recurred with evidence of liver metastases on imaging studies 8 months following her exenteration and remains alive with disease 11 months after surgery.

## Discussion

Malignant granular cell tumors are similar in epidemiology to their benign counterparts. Both occur most commonly from age 40 to age 69, are found twice as often in women as men, and have been reported to show a predominance in African-Americans [2]. Larger tumor size and advanced age at presentation correlate with a worse prognosis [2].

Malignant granular cell tumors were first thought to be of myogenic origin. After immunohistochemistry revealed an absence of myogenic material, other cell types proposed as the possible cell of origin include histiocytes, primitive mesenchymal cells, and primitive neurofibroblasts [3]. The Schwann cell is currently believed to be the cell of origin based on S-100 positivity and supportive electron microscopy [3]. Myelin figures and axon-like structures have been found within cytoplasmic lysosomes [2].

At times it can be difficult to diagnose a granular cell tumor as malignant based on histologic criteria alone. Indeed, the earliest review of MGCTs noted two categories of malignancy: one based on clinical presentation and corre-

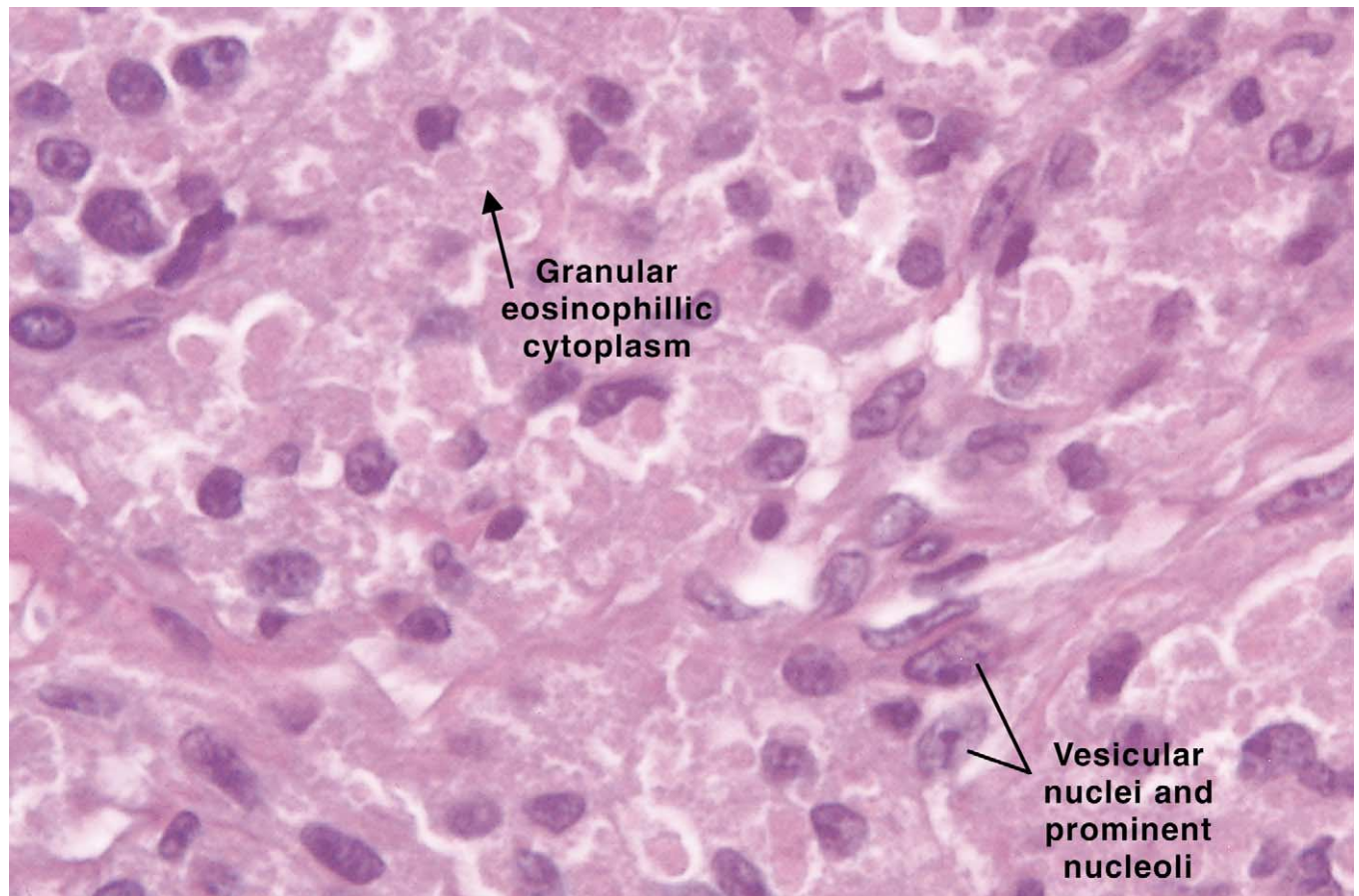


Fig. 4. High-power hematoxylin and eosin stained-micrograph of tumor showing pleomorphic nuclei, elevated nuclear/cytoplasmic ratio, and spindled tumor cells.

lating histologic criteria, the other with metastasis as the only evidence of malignancy [6]. To avoid overlooking potentially malignant but histologically benign lesions, both pathologic evidence and clinical evidence are often employed in the diagnosis of MGCT. Clinical features such as increased tumor size (>5 cm), advanced age at diagnosis, and local recurrence are reported to be associated with an increased potential for malignant behavior; however, because benign and malignant granular cell tumors have similar clinical presentations, histologically proven metastatic disease is the only certain clinical feature unique to MGCT

[7]. DNA ploidy has proved an inconsistent tool in making this diagnosis [8]. A more recent analysis has examined the growth pattern of benign granular cell tumors as a guide to predict later aggressive behavior, citing an infiltrative pattern even in the presence of negative surgical margins as predictive of local recurrence [4].

Because MGCT is so rare and because benign-appearing tumors sometimes behave in a malignant fashion, reliable criteria for histologic diagnosis have been difficult to establish. Morphologic criteria that might help predict malignant behavior include spindling of tumor cells, increased nu-

Table 1  
Cases of malignant and atypical granular cell tumor in the pelvis

Authors	Year	Maximum size (cm)	Site	Primary intervention	Outcome
1. Ravich et al. [5]	1945	Unknown	Urinary bladder	Surgical resection	DOD, 17 months
2. Shimamura et al. [10]	1984	9	Sciatic nerve	Surgical resection	DOD, 13 months
3. O'Donovan et al. [11]	1988	6	Pelvis (pouch of Douglas)	Unknown	Unknown
4. Rosenthal et al. [12]	1989	10	Buttock	Surgical resection	NED, 4 years
5. Fanburg-Smith et al. [8]	1998	8.5	Buttock	Unknown	AWD, 2 years
6. Cruz-Mojarrjeta et al. [13]	2001	15	Pelvis, deep soft tissue	Surgical resection	DOD, 17 months

Note. DOD, dead of disease; NED, no evidence of disease; AWD, alive with disease.

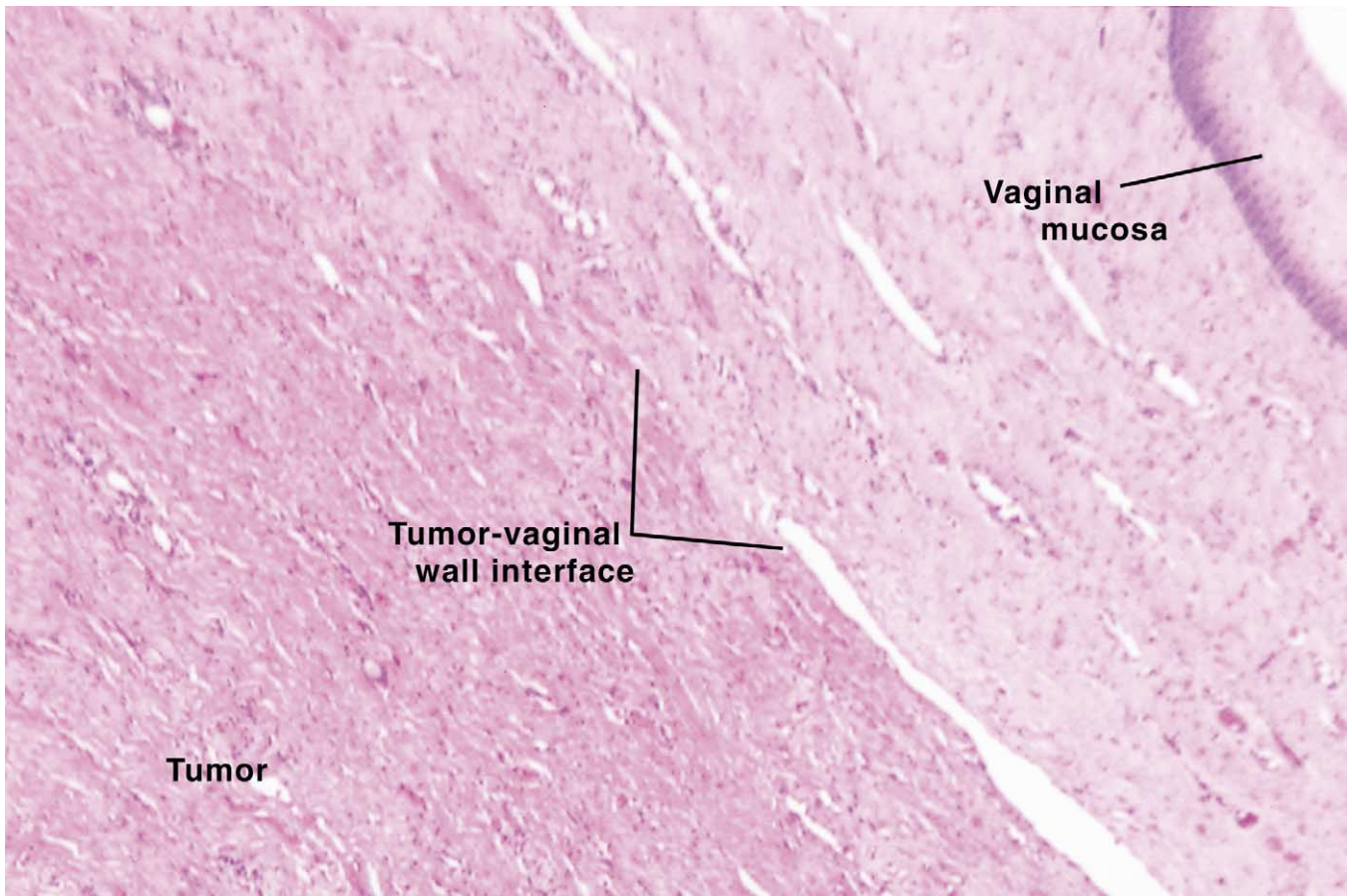


Fig. 5. Low-power hematoxylin and eosin-stained micrograph of tumor (lower left) and vaginal mucosa (upper right).

clear/cytoplasmic ratio, vesicular nuclei with large nucleoli, pleomorphism, necrosis, and increased mitotic activity [8]. Of these criteria, spindling of tumor cells, increased nuclear/cytoplasmic ratio, and vesicular nuclei with large nucleoli appear to be most significantly related to malignant behavior [8].

The tumor we report here had a maximum size of 12.5 cm, invaded into the vaginal mucosa and pelvic sidewall, and met the histologic criteria of malignancy established by Fanburg-Smith et al. [8]. Pleomorphism, increased nucleus/cytoplasmic ratio, spindling of tumor cells, vesicular nuclei with large nucleoli, and presence of necrosis were found throughout the tumor with only scattered mitotic figures seen. The absence of more than two mitoses per high-powered field is the only histologic finding described by Fanburg-Smith et al. not seen in this tumor. It is likely that vascular invasion was present focally in the original tumor, accounting for her subsequent recurrence in the liver. Thus our case is classified as malignant based on a constellation of both clinical and pathologic findings.

As with benign granular cell tumors, MGCTs are anatomically ubiquitous; however, only a handful of MGCTs have been described in the pelvis. Interestingly, the first published case report of a MGCT arose in the urinary

bladder of a 31-year-old woman who died of metastatic disease 17 months after surgical removal [5]. Those cases reported to arise in the pelvis are listed in Table 1.

The early occurrence of liver metastases in this case is consistent with the aggressive biological behavior reported by others. The two largest studies to date of this entity report mortality rates of 39% at 3 years [8] and 48.6% at no specified time interval [9]. Indeed, it is surprising that the primary tumor reached such a large size without metastases occurring earlier. The aggressive surgical approach employed reflected uncertainty regarding the biological behavior of this tumor and the need to palliate the patient's debilitating pain.

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