Cervical granulocytic sarcoma: report of one case and review of the literature

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Summary

Granulocytic sarcoma in the female genital tract generally has a poor prognosis. We report the case of a 52-year-old nonleukemic patient with relapsed granulocytic sarcoma at the vaginal stump after an 11-year complete remission from the uterine cervix. Magnetic resonance imaging of the pelvis showed a pear-shaped mass arising from the vagina mimicking a normal uterus. The unusual clinical presentation and the difficulties encountered in evaluation are presented. A review of the literature indicates that survival is better with multimodality management and in patients without leukemia.

Key words: Granulocytic sarcoma; Relapse; Uterine cervix.

Introduction

Granulocytic sarcoma (GS) is defined as an extramedullary myeloid tumor composed of immature myeloid cells and usually noted concurrently with or after the onset of acute myeloid leukemia (AML) or chronic myeloproliferative disorders [1]. Very rarely, patients present with GS as an isolated mass without prior or current evidence of AML; however, the vast majority of these patients develop AML within 11 months [2, 3]. The most frequent involvement sites of GS include the skin and lymphadenopathy, but it is very rare in the female genital tract [1-5]. GS generally has a poor prognosis, and complete remission has rarely been reported [6]. Herein we present the case of a nonleukemic patient with isolated cervical GS and relapse at the vaginal stump after an 11-year complete remission, mimicking a normal uterus. To our knowledge, this is the first case of GS to develop a long-term relapse tumor after complete remission. Previous literature about granulocytic sarcoma of the uterine cervix has been reviewed to define the optimal management.

Case Report

In August 1996, a 43-year-old female complained of hypermenorrhea and postcoital bleeding of one year's duration. Pelvic examination revealed a large cervical mass without vaginal or parametrial involvement. Histopathologic evaluation was consistent with a GS, but there was no evidence of leukemia on the blood smear or bone marrow biopsy. The patient received induction chemotherapy with cytosine arabinoside (Ara-C) and idarubicin in September 1996 and consolidation chemotherapy with Ara-C and idarubicin in November 1996. In February 1997 she underwent a hysterectomy; the specimen confirmed a pathologic disease-free status. Further consolidation chemotherapy with Ara-C and adriamycin was given in April 1997.

She did well until October 2007 when a hard mass over the vaginal stump was noted during an annual gynecologic examination. The Pap smear and colposcopy-directed biopsy both revealed negative findings. Magnetic resonance imaging showed a pear-shaped homogeneous mass arising from the vaginal stump mimicking a normal uterus (Figure 1). A loop electrosurgical procedure (LEEP) was used to obtain a satisfactory specimen which showed atypical primitive granulocytic cells infiltrating the stroma. The specimen was focally-positive for anti-myeloperoxidase and CD117, but negative for CLA, CD34, and TdT on immunohistochemical staining (Figure 2). The blood smears and bone marrow biopsy showed no evidence of leukemia. The patient thus received salvage chemotherapy with Ara-C and novantrone for relapsed disease in December 2007. The mass shrank based on serial sonographic measurements. An additional course of chemotherapy was administered in January 2008, but she developed sepsis and died three months after the diagnosis of relapse.

Discussion

GS involving the female genital tract is rare, and the most commonly involved organ is the ovary, followed by the cervix [1-5]. The prognosis for all patients with GS is poor [5]. Only a few cases have achieved complete remission after aggressive treatment, but relapse of disease is usually noted within two years of the initial diagnosis [7]. The risk of relapse declines three years after complete remission and such patients are considered potentially cured [8]. Only 33 cases of cervical GS have been described since 1912. The median survival of the 34 patients (including our case) in our literature review was 8.5 months (range: 6 days - 372 months), and most patients died of disease progression (Table 1) [5, 9-34]. Only six patients lived more than two years, and three patients lived more than five years including our case. The median survival is 7.5 months for patients with AML (range: 8 days - 36 months), and 24 months for patients

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Table 1. — *Characteristics of patients with granulocytic sarcoma of the cervix in the literature.*

No	Age	AML history	Chief complaint	Pelvic examinations	PB smear	BM exams	Management	Recurrence	Outcome	Survival	Reference
1	26	No	Weight loss, night sweats, cough	NA	NA	NA	None	NA	Dead	2 weeks	[9]
2	39	No	Vaginal bleeding	Cervical mass	NA	NA	RT	NA	Dead	5 months	[10]
3	44	No	Vaginal bleeding	Cervical mass	NA	NA	OP	NA	Dead	3 months	[11]
4	75	No	Vaginal bleeding	Uterine tumor	NA	NA	RT/CT	NA	Dead	2 months	[11]
5	65	No	Vaginal bleeding	Cervical mass	Negative	NA	RT	Breast	Dead	31 months	[12]
6	58	No	Vaginal bleeding	Cervical mass	Positive	Positive	CT	NA	Dead	9 months	[13]
7	36	No	Vaginal bleeding	Cervical ulceration	Positive	Positive	OP	NA	NA	NA	[14
8	39	No	Abdominal pain, fever	Uterine tumor	NA	NA	None	NA	Dead	6 days	[15]
9	35	No	Groin tumor, paresis, leg pain	Cervical mass	NA	Positive	None	NA	Dead	8 days	[16]
10	59	No	Vaginal bleeding	Cervical mass	NA	NA	RT	NA	Dead	5 months	[16]
11	34	No	Vaginal bleeding	Cervical mass	NA	NA	CT/OP/herb	NA	Dead	17 months	[17]
12	48	No	Vaginal bleeding	Uterine tumor	NA	NA	OP/RT	NA	Dead	7 weeks	[18]
13	71	No	Vaginal bleeding	Cervical mass	NA	NA	CT/RT	NA	NA	NA	[18]
14	53	Yes	Vaginal bleeding, abdominal pain	Paracervical mass	NA	Negative	RT/CT	NA	Dead	19 months	[19]
15	32	No	Vaginal bleeding	Cervical mass	NA	NA	RT/CT	NA	Alive	11 months	[20]
16	66	No	Vaginal bleeding	Cervical ulceration	NA	Positive	CT	NA	Dead	2 months	[21]
17	36	Yes	Vaginal bleeding	Cervical mass	Negative	Negative	CT	Bone marrow	Dead	36 months	[22]
18	51	No	Vaginal bleeding	Cervical mass	Positive	Positive	CT	NA	Alive	13 months	[23]
19	48	No	Vaginal bleeding	Waxy, green cervix	NA	NA	OP/CT	NA	Dead	24 months	[24]
20	48	No	NA	NA	Negative	Negative	CT	NA	Dead	24 months	[24]
21	20	No	Vaginal bleeding	Cervical mass	Negative	Negative	CT	Right adnexa	Alive	58 months	[25]
22	33	No	Vaginal bleeding	Cervical mass	Positive	Positive	None	NA	Dead	< 1 month	[26]
23	41	No	Vaginal bleeding	Cervical mass	Positive	Positive	OP/CT	NA	Dead	< 2 months	[27]
24	49	No	Vaginal bleeding, Dyspareunia	Cervical mass	NA	Positive	RT/CT	NA	NA	NA	[28]
25	67	Yes	Abdominal pain	Cervical mass	Negative	Positive	CT	CNS	Dead	13 months	[29]
26	48	No	NA	NA	Negative	Negative	CT/BMT	Bone marrow	Dead	10 months	[30]
27	30	Yes	Vaginal bleeding	Cervical mass	Negative	Negative	CT	NA	Alive	6 months	[31]
28	30	Yes	Vaginal bleeding	Cervical mass	Positive	Negative	CT	NA	Alive	8 months	[32]
29	33	No	Vaginal bleeding	Cervical mass	Negative	Positive	CT	NA	Alive	7 months	[5]
30	37	No	Vaginal bleeding	NA	Negative	Negative	CT	NA	Alive	2 months	[33]
31	34	No	Dysmenorrhea	NA	Negative	Negative	CT	NA	Alive	12.5 years	[33]
32	43	No	Vaginal bleeding	NA	Negative	Negative	CT	Nasal fossa	Alive	31 years	[33]
33	50	Yes	Abdominal pain	Cervical mass	Positive	Positive	CT	NA	NA	NA	[34]
Our case	42	No	Vaginal bleeding	Cervical mass	Negative	Negative	CT/OP	Vaginal stump	Dead	11 years	

AML; acute myeloid leukemia; CT: chemotherapy; NA: not available; OP: operation; RT: radiotherapy.

without AML (range: 6 days - 372 months) (Figure 3A). The patients with cervical GS without AML apparently responded better to the treatment than those with AML.

Because the vast majority of nonleukemic patients with GS developed acute leukemia within a matter of months, it is now generally accepted that GS should be treated as systemic disease with chemotherapy which could prolong the duration of nonleukemic stage and improve the prognosis [35]. Evidence has also shown that anti-AML therapy is associated with higher rates of disease-free and overall survival in GS than in AML [8]. From our review (Table 1), the median survival is less than one month for patients without any treatment, four months for patients with only local treatment including radiotherapy or hysterectomy (range: 7 weeks - 5 months), 9.5 months for patients with only chemotherapy (range: less than 2 months - 372 months), and 17.5 months (range: 2 months - 122 months) for patients with chemotherapy and local treatment (Figure 3B). However, because the number of treated patients is so limited, the role of local treatment

Fig. 1

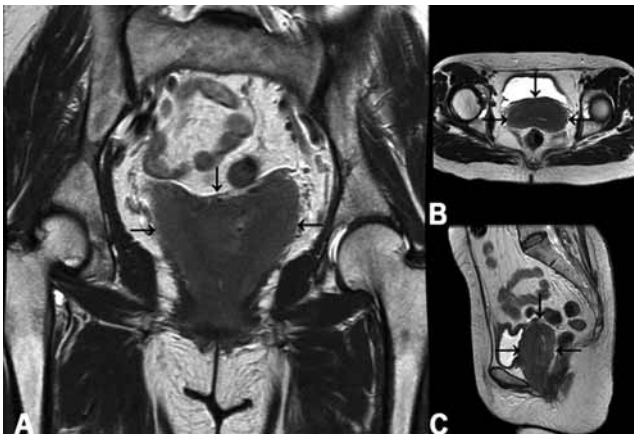


Fig. 2

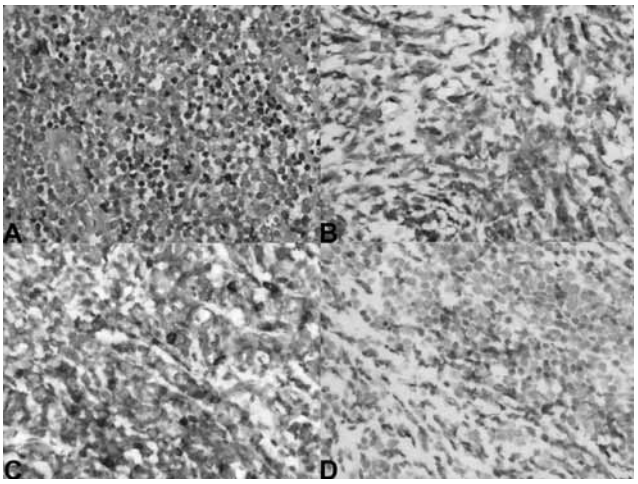
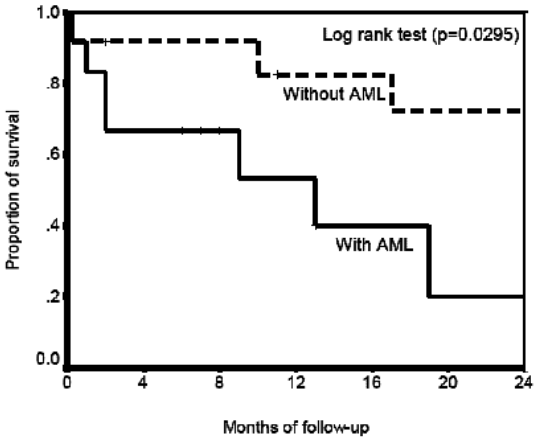


Figure 1. — MRI images of the relapsed vaginal stump mass (about 8 x 5 x 4 cm) mimicking a normal uterus in the pelvis. A: Coronal view; B: Axial view; C: Saggital view.
Figure 2. — Microscopic pictures showing the atypical primitive granulatic cell infiltration in the stroma. A: Hematoxylin/eosin stain, 400 X; B: Immunohistochemical stain, positive for MPO, 400 X; C: Immunohistochemical stain, focally positive for CD117, 400 X; D: Immunohistochemical stain, negative for TdT, 400 X.



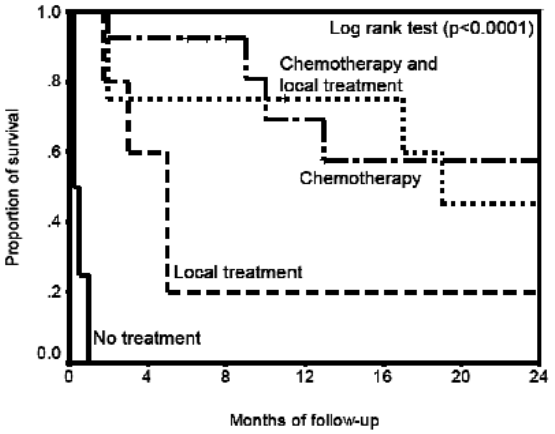


Figure 3. — Kaplan-Meier survival analysis of overall survival in patients with cervical granulocytic sarcoma in the literature. A: Overall survival of patients without AML was significantly longer than for those with AML (log rank test, $p = 0.0295$). B: Overall survival of patients receiving chemotherapy or combined local treatment and chemotherapy was significantly longer than for those with only local treatment or without any treatment (log rank test, $p < 0.0001$).

remains controversial. Nonetheless the extra-medullary foci are often chemoresistant with resulting relapsed or persistent disease, so multimodality management, including local treatment, is reasonable.

Our case presented an unusual course of local relapse without developing acute leukemia after achieving an 11-year complete remission. She had an asymptomatic mass above the vaginal stump mimicking a uterus, which could have easily been misdiagnosed as normal without a thorough examination. Even though relapsed disease was highly suspected, a Pap smear and colposcopic biopsy failed to obtain tissue verification, which may reflect the accumulation of immature myeloid cells in the stroma beneath the unaffected epithelium. Thus an adequate depth of specimen is critical for pathologic confirmation. Our clinical experience and the literature review suggest that anti-AML therapy is highly effective in patients with nonleukemic cervical GS. Therefore, an accurate initial diagnosis of GS in a nonleukemic patient and appropriate and timely chemotherapy may reduce the risk of subsequent AML. In addition, the unusual late relapse also emphasizes the need for careful follow-up, which should include imaging studies and tissue biopsies whenever clinical suspicion exists.

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