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Persistent Ovarian Endometrial Stromal Sarcoma

Case Study

One month after terminating her fourth course of chemotherapy because of disease progression, Ms. N, a 50-year-old woman with endometrial stromal sarcoma (ESS) of the ovary complained of worsening symptoms including increased shortness of breath, increased abdominal girth, and inability to eat. She was treated immediately with thoracentesis and pleurodesis to relieve the symptoms of her malignant pleural effusions. Although her treatment history limited her possible treatment options, she requested a trial of palliative chemotherapy to improve the quality of her remaining life.

Ms. N's treatment history was long and complicated, as is often the case with persistent gynecologic malignancies. She had been diagnosed with stage III low-grade ESS approximately four years earlier after an abdominal hysterectomy and bilateral salpingo-oophorectomy for presumed endometriosis. Megestrol acetate prevented disease progression for 27 months, after which an exploratory laparotomy and biopsy revealed recurrent low-grade ESS. Tumor debulking and omentectomy were attempted, but cytoreduction was suboptimal. Treatment with nine courses of cisplatin failed to prevent disease progression, but treatment with paclitaxel produced stable disease for seven months. Ms. N subsequently was treated first with doxorubicin and then with paclitaxel again, but neither prevented further disease progression. After two rounds of surgeries and four rounds of chemotherapy, all conventional treatment options had failed. Her request for palliative chemotherapy therefore represented a clinical challenge.

Clinical Problem Solving

Addressing this challenge are Suann K. Mitchell, RN, CCRP, a research nurse in the Department of Obstetrics and Gynecology, and Linda F. Carson, MD, Patricia L. Judson, MD, and Levi S. Downs, Jr., MD, who are doctors, all at the Women's Cancer Center of the University of Minnesota in Minneapolis.

How do you treat a patient who has requested palliative chemotherapy for a terminal cancer when no conventional therapies have been effective?

In the palliative setting and in settings in which treatment is not expected to be curative, the long-term tolerability and nonhematologic toxicity of agents must be weighed against their potential to limit disease progression and palliate disease symptoms. The failure of prior regimens suggested that the Ms. N's cancer was resistant to hormone therapy, cisplatin, paclitaxel, and doxorubicin; therefore, further use of these agents was not warranted. Treatment options were assessed based on clinical experiences and results from clinical trials in related gynecologic malignancies. Although ifosfamide has shown activity in chemotherapy-naive patients with nonovarian ESS (Sutton, Blessing, Park, DiSaia, & Rosenshein, 1996), Ms. N's heavy treatment history and poor nutritional status ruled out this option. Another treatment option was topotecan (Hycamtin®, GlaxoSmithKline, Research Triangle Park, NC), which is active in the relapsed ovarian cancer setting and has shown promise in other gynecologic malignancies, including cervical (Fiorica et al., 2002) and uterine carcinomas (Finkler & Holloway, 2002). Topotecan most often has been administered by bolus IV injection at 1.5 mg/m^2 per day for five consecutive days every 21 days. However, extensively pretreated patients are especially susceptible to myelotoxicity; as a result, alternate schedules and lower-dose regimens currently are under investigation in patients with epithelial ovarian cancer (Morris & Munkarah, 2002). Lower-dose topotecan has been active and well tolerated in patients with relapsed ovarian cancer at the Women's Cancer Center of the University of Minnesota. Furthermore, topotecan's hematologic toxicity was noncumulative and this regimen generally was not associated with any severe nonhematologic toxicity, making it an appropriate choice for palliative therapy. Therefore, a compassionate use regimen of low-dose topotecan 1 mg/m^2 per day for five consecutive days in a 21-day cycle was selected.

How do you devise palliative therapy for a patient with terminal disease?

Careful observation for possible toxicities is essential, and patient feedback and input should be strongly encouraged. Although Ms. N was treated cautiously, severe symptoms emerged late during her first cycle of therapy, with grade 3 myelotoxicities (anemia, leukopenia, and thrombocytopenia), as well as coagulopathy. Admitted to the hospital because of weakness and shortness of breath, she decided to cease chemotherapy and enter a hospice program. The team followed her wishes but continued to monitor her status closely in the hospice setting. Over the ensuing three months, the hospice team noted an unusual improvement in her pain, nausea, and respiratory status. In contrast with the gradual decline in performance status and quality of life that typically are associated with terminal illness, the improvement of her physical symptoms and quality of life was both unexpected and remarkable. Moreover, the goals of patient management in the hospice setting involve comforting patients and helping them to accept the inevitability of their death; therefore, a patient who shows dramatic signs of recovery while in hospice care is a challenge to fundamental patient management strategies.

How do you treat a patient in the hospice setting who appears to be recovering?

Communication and ongoing assessment are key to effective management of patients

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with terminal cancer. When patients cease chemotherapy and surgical interventions for their cancer, improvements in quality of life may result as their bodies recover from treatment toxicities and surgical procedures. However, close attention should be paid to the patient's outlook and the etiology of any symptoms because responses to prior therapies may be delayed. Ms. N's respiratory symptoms and nausea markedly improved, but the improvement likely was not a result of recovery from the thoracentesis and pleurodesis because her symptoms had recurred after the surgery. Furthermore, the reduction in pain was not associated with any increase in analgesic usage. Therefore, reduction in tumor burden was considered as a possible cause. The improvements in symptoms were discussed with the patient, and her outlook was reassessed. Although she had chosen to cease chemotherapy and enter hospice three months earlier, her dramatic improvements gave her a new sense of hope. She believed that the improvements were the result of the low-dose topotecan and requested that therapy be reinitiated, although she chose to remain in hospice care.

Can you administer active chemotherapy to a patient in hospice?

Ultimately, patients must decide the course of treatment that they would like to receive, but the healthcare team has a responsibility to decide whether therapy is feasible. After discussion with the patient and hospice staff, the oncology team decided that the potential side effects of low-dose topotecan 0.75 mg/m^2 (a slight reduction from her prior dose) would be safe and manageable in the hospice setting. Therefore, Ms. N's request for further compassionate use treatment with low-dose topotecan was honored.

Clinical Outcome

After Ms. N had reinitiated low-dose topotecan therapy, scans revealed a partial response of her measurable disease. Two months after low-dose topotecan was reinitiated, she was symptom-free and discharged from hospice care.

Because her initial courses of low-dose topotecan were well tolerated, the dose was increased to topotecan 1.0 mg/m^2 with standard growth factor support with recombinant human erythropoietin and granulocyte colony-stimulating factor. The dose was escalated further to topotecan 1.25 mg/m^2 after her seventh course. Ms. N ultimately received 20 courses of topotecan, during which time she maintained a partial tumor response for 24 months and enjoyed a good quality of life that included travel to Europe. She finally died from disease-related complications 2.5 years after her initial admission to the hospice program.

Advanced or recurrent gynecologic malignancies are rarely curable; therefore, in a palliative setting, improving patient quality of life and controlling disease symptoms while minimizing treatment toxicity are important goals of therapy. Treatment of rare cancers may require more individualized and adaptive therapy. All treatment options and their associated toxicities should be discussed with the patient.

References

Finkler, N.J., & Holloway, R.W. (2002). A phase I/II trial of weekly topotecan in the treatment of advanced recurrent metastatic endometrial carcinoma [Abstract]. *Proceedings of the American Society of Clinical Oncology, 21,* 171b.

Fiorica, J., Holloway, R., Ndubisi, B., Orr, J., Grendys, E., Boothby, R., et al. (2002). Phase II trial of topotecan and cisplatin in persistent or recurrent squamous and nonsquamous carcinomas of the cervix. *Gynecologic Oncology, 85,* 89–94.

Morris, R., & Munkarah, A. (2002). Alternate dosing schedules for topotecan in the treatment of recurrent ovarian cancer. *Oncologist, 7*(Suppl. 5), 29–35.

Sutton, G., Blessing, J.A., Park, R., DiSaia, P.J., & Rosenshein, N. (1996). Ifosfamide treatment of recurrent or metastatic endometrial stromal sarcomas previously unexposed to chemotherapy: A study of the Gynecologic Oncology Group. *Obstetrics and Gynecology, 87,* 747–750.

Clinical Highlights: Endometrial Stromal Sarcoma

Definition: Endometrial stromal sarcoma (ESS) of the ovary is a rare Müllerian tumor variant that is very aggressive and poorly differentiated.

Incidence: Gynecologic malignancies are a significant source of morbidity and mortality among women in the United States, with approximately 26,800 deaths anticipated in 2004 (Jemal et al., 2004). Although the majority (53%) of these deaths is attributed to ovarian cancer, other gynecologic malignancies, including rarer forms, also contribute to patient mortality. ESS of the ovary is exceptionally rare, but uterine ESS is slightly more common and accounts for 0.2% of all uterine malignancies (Doctor's Doctor, 2004).

Diagnosis: The most common symptoms of ESS are abdominal swelling and pain (Young, Prat, & Scully, 1984). Perhaps because of these nonspecific symptoms or the rarity of this malignancy, almost half of the women with ovarian ESS are not diagnosed until after the cancer has spread (Young et al.). Furthermore, ESS often is misdiagnosed, most commonly as leiomyoma (fibroids), which can delay the enactment of cancer treatment strategies.

Natural history and treatment: Ovarian ESS is rare and therefore impossible to study in prospective, randomized clinical trials. Because these cancers are generally hormone-receptor positive, hormonal therapies may slow disease progression.

Patients with high-grade ESS appear to follow a clinical pattern similar to, albeit more aggressive than, that observed in women with epithelial ovarian cancer (Burke, Eifel, & Muggia, 2001), raising the possibility that cytotoxic agents active in epithelial ovarian cancer may prove beneficial in ESS of the ovary. Platinum-based agents form the cornerstone of systemic treatment of advanced gynecologic malignancies and are active against ovarian sarcomas (Sood et al., 1998). However, platinum-based therapies can cause severe nonhematologic toxicities, and their application in patients with persistent disease is limited by cumulative toxicities (Dunton, 2002).

Burke, T.W., Eifel, P.J., & Muggia, F.M. (2001). Cancers of the uterine body. In V.T. DeVita, Jr., S. Hellman, & S.A. Rosenberg (Eds.), *Cancer: Principles and practice of oncology* (6th ed., pp. 1573–1594). Philadelphia: Lippincott Williams and Wilkins.

Doctor's Doctor. (2004). Endometrial stromal tumors. Retrieved April 7, 2004, from http://www.thedoctorsdoctor.com/diseases/endometrialstromaltumors.htm

Dunton, C.J. (2002). Management of treatment-related toxicity in advanced ovarian cancer. *Oncologist, 7*(Suppl. 5), 11–19.

Jemal, A., Tiwari, R., Murray, T., Samuels, A., Ghafoor, A., Samuels, A., et al. (2004). Cancer statistics, 2004. *CA: A Cancer Journal for Clinicians, 54,* 8–29.

Sood, A.K., Sorosky, J.I., Gelder, M.S., Buller, R.E., Anderson, B., Wilkinson, E.J., et al. (1998). Primary ovarian sarcoma: Analysis of prognostic variables and the role of surgical cytoreduction. *Cancer, 82,* 1731–1737.

Young, R.H., Prat, J., & Scully, R.E. (1984). Endometrioid stromal sarcomas of the ovary. A clinicopathologic analysis of 23 cases. *Cancer, 53,* 1143–1155.