CASE REPORT

The Role of Laparoscopy in the Diagnosis and Treatment of Peritoneal Carcinomatosis: A Case Report

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A patient presented with deep venous thrombosis and an elevated CA-125 level, but normal pelvic ultrasound and abdominal and pelvic CT scans. Laparoscopy revealed diffuse carcinomatosis and a diagnosis of stage IIIc, poorly differentiated epithelial ovarian carcinoma was made. Laparoscopy may provide an alternative means of diagnosis when conventional imaging fails, and may facilitate the placement of catheters for subsequent intraperitoneal therapy.

INTRODUCTION

Transcoelomic spread resulting in peritoneal metastases is a common feature of tumors within the abdomino-pelvic cavity. However, malignant ascites may not be apparent, and this presents a diagnostic problem for conventional imaging techniques [1]. Laparoscopy can be used to identify peritoneal carcinomatosis in such cases. The primary tumor is ovarian in 35 percent of cases, colonic in 30 percent, and gastric in 10 percent. CA-125 antigen is a high molecular weight mucin-like glycoprotein whose serum level is elevated in a variety of conditions, notably ovarian epithelial carcinoma. Its increased levels in several benign conditions suggest it is not a tumor specific antigen. CA-125 can

be produced by mesothelial cells lining the adult pleura, pericardium, peritoneum, and can be considered as a marker of peritoneal involvement [2]. Its role has been well documented for the assessment and prognosis of ovarian carcinoma and identification of recurrent disease [3].

CASE REPORT

A 59-year-old morbidly obese woman presented with a primary episode of deep vein thrombosis. Investigation revealed thrombosis from the right popliteal vein extending to the inferior vena cava, but pelvic ultrasound, CT scan of the abdomen and pelvis, and a chest X-ray were all normal. Occult neoplasia was suspected and

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Received: September 1, 2000; Returned for revision: December 5, 2000; Accepted: January 5, 2001.

tumor markers were requested; the CA-125 was elevated (11300 IU/l; N < 35 IU/l) and the CA-15.3 was elevated (460 IU/l; N < 60 IU/l). Work up for breast, GI, and pancreatic tumors was negative.

A diagnostic laparoscopy with biopsy demonstrated extensive peritoneal carcinomatosis, ovarian in nature, involving the pelvic organs, both paracolic gutters, the greater omentum, and the diaphragm. The procedure was then converted to a laparotomy and a hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy, omentectomy, and tumor debulking were performed. The histology confirmed a poorly differentiated ovarian carcinoma, stage IIIc.

Surgery was followed by treatment with chemotherapy. First chemotherapy was cisplatin (Platinol, Bristol-Myers Squibb) $(50 \text{ mg/m}^2, \text{ days } 1 \text{ to } 3)$ and cyclophosphamide (Endoxan, ASTA Medica) $(600 \text{ mg/m}^2, \text{day 1})$. This regimen was discontinued after three cycles for plateauing CA-125 levels (31,000 IU/l before treatment and 27,200 IU/l after treatment). Second line treatment was cyclophosphamide with paclitaxel (Taxol, Bristol-Myers Squibb) (135 mg/m²) but progression of disease was suspected after three cycles with rising CA-125 levels, thus treatment was changed to topotecan (Hycamtin, Smithkline Beecham) (1.25 mg/m^2 , days 1 to 5). A CT scan during the course of topotecan showed the presence of ascites and thickened folds of peritoneum. The patient was admitted before her fifth cycle of topotecan for treatment of a bowel obstruction. She underwent laparoscopy, which revealed continued diffuse peritoneal carcinomatosis. The laparoscope was then used to position an intraperitoneal catheter through which chemotherapy was administered for palliative therapy. The patient died one month later.

DISCUSSION

Peritoneal carcinomatosis complicates approximately 35 percent of ovarian carcinomas. Ovarian cancer is the second most common gynecological malignancy in the United States, with an annual incidence of roughly 25,000 and annual death rate of nearly 15,000. Its prognosis has improved slightly over the past two decades, although in two-thirds of patients the disease has already spread beyond the pelvis at the time of presentation. The diagnosis of ovarian cancer is often mismanaged because of understaging [4]. Young et al. [5] described a series of 100 patients in which 31 were understaged at the time of original diagnosis, 23 of which were stage III.

Ultrasound has been found useful in the diagnosis of peritoneal carcinomatosis, but its sensitivity in detecting seedling implants is highly variable, ranging from 8 to 63 percent [1]. CT scanning has similar limitations, specifically when scanning the pelvis. MRI scanners have a sensitivity of 82 percent for recurrent disease at the primary site when the tumor mass is greater than 2 cm in diameter, but this drops to 35 percent sensitivity for smaller lesions. Sensitivity for peritoneal deposits is poor, with lesions of 3 cm diameter often missed. Clearly another method of diagnosis is indicated.

Laparoscopy can provide a sensitive means of diagnosing peritoneal carcinomatosis. It is preferable to laparotomy in most cases because it is safer for the patient. Post-operative complications of laparotomy include wound infections, prolonged ileus, small intestinal obstructions, and intestinal injury. Improvements in laparoscopic techniques have indeed made laparoscopy a safer and viable option to laparotomy. It has been shown to have a positive predictive value of 100 percent and a negative predictive value of 86 percent [6]. However, post-operative adhesions from previous operations often make laparoscopy more difficult to identify residual disease, in which case conversion open laparotomy is indicated. to Laparoscopy may also have a role in second-look procedures, though these have historically been controversial [7]. It is useful in reviewing the effectiveness of chemotherapy by allowing directed biopsies to be taken and in vitro sensitivities to be assessed. Chemotherapy can be administered via intraperitoneal catheters or implant capsules, and can be positioned accurately through the laparoscope at the same time as the second look assessment.

Intraperitoneal chemotherapy, popular in the 1950s [8], has again found a role in patients with persistent intraperitoneal tumors after debulking surgery and aggressive chemotherapy with first- and second-line drugs. Larger volumes of fluid (1500-2000 ml) are now being used to distribute the drugs more evenly [9], and safer and more effective drug delivery systems have been developed [10]. These two advances have made intraperitoneal chemotherapy more beneficial, and hence popular again. Studies have shown that it is most effective with small deposits no greater than 2 mm in diameter [11]. This method yields response rates of up to 55 percent, of which 30 percent result in complete remission. These results that can be achieved even when a tumor has shown resistance to intravenous chemotherapeutic agents.

The role of serum antigen CA-125 as a marker in monitoring the management of ovarian carcinoma has been extensively studied and several clinical research teams concur on its predictive value [12]. Indeed, there does seem to be a correlation between the rate of decline of serum CA-125 and the prognosis of disease [13]. However, its value in screening programs has yet to be confirmed. Although a strongly elevated CA-125 level indicates a high likelihood of ovarian carcinoma, as in this case, moderately elevated levels can be present in benign conditions such as liver disease, pancreatitis, peritonitis, endometriosis, benign ovarian tumors, benign ascites, and pregnancy. The simultaneous use of other markers such as CEA, CA-19, and CA-15.3, which by themselves are not very specific, may, in conjunction with CA-125, improve the diagnostic accuracy of the study [2].

CONCLUSION

Imaging techniques have been disappointing in the diagnosis and follow-up of peritoneal metastases, especially in diffuse peritoneal carcinomatosis. Conversely, laparoscopy provides a more accurate assessment with the advantage of direct vision, which allows directed biopsies to be taken and, when appropriate, the positioning of peritoneal chemotherapy deliverv systems. The sensitivity of laparoscopy has been shown to be 100 percent, thus a positive finding would clearly indicate the need for laparotomy and postumor debulking or salvage sible chemotherapy. As laparoscopic techniques improve, the diagnosis of difficult cases complicated by severe adhesions will be made possible by laparoscopy, saving patients from the often complicated postoperative course of laparotomy.

ACKNOWLEDGMENTS: Special thanks to Dr. Melanie Snyder, a fellow in the Gynecologic Oncology department at the Yale University School of Medicine, who reviewed this paper.

REFERENCES

- Rioux, M. and Michaud, C. Sonographic detection of peritoneal carcinomatosis: a prospective study of 37 cases. Abdom. Imaging 20:47-51, 1995.
- 2. Stenman, U.-H., Alfthan, H., Vartiainen, J., and Lehtovirta, P. Markers supplementing CA-125 in ovarian cancer. Ann. Med. 27:115-120, 1995.
- 3. Folk, J.J., Botsford, M., and Musa, A.G. Monitoring cancer antigen 125 levels in induction chemotherapy for epithelial ovarian carcinoma and predicting outcome on

second-look procedure. Gynecol. Oncol. 57:178-182, 1995.

- 4. McGowan, L., Lesher, L.P., and Norris, H.J. Misstaging of ovarian cancer. Obstet. Gynecol. 65:568, 1985.
- 5. Young, R.C., Decker, D.G., and Wharton, J.T. Staging laparotomy in young early ovarian cancer. JAMA 250:3072, 1983.
- Clough, K.B., Ladonne, J.M., Nos, C., Renolleau, C., Validire, P., and Durand, J.C. Second look for ovarian cancer: laparoscopy or laparotomy? A prospective study. Gynecol. Oncol. 72:411-417, 1999.
- Skret, A., Kluza, R., and Fabisiak, W. The place of second-look laparoscopy in monitoring treatment of advanced malignant ovarian neoplasms. Ginekol. Pol. 68:193-198, 1997.
- Green, T.H. Hemisulfur mustard in the palliation of patients with metastatic ovarian carcinoma. Obstet. Gynecol. 13:383, 1959.
- 9. Dunnick, N.R., Jones, R.B., and Doppren, J.L. Intraperitoneal contrast infusion for assessment of intraperitoneal fluid dynamics. AJR 133:221, 1979.

- Jenkins, J., Sugarbaker, P.H., and Gianola, F.J. Technical considerations in the use of intraperitoneal chemotherapy administered by Tenckhoff catheter. Surg. Gynecol. Obstet. 154:858, 1982.
- Nelson, R.C., Chezmar, J.L., Hoel, M.J., Buck, D.R., and Sugarbaker, P.H. Peritoneal carcinomatosis: preoperative CT with intraperitoneal contrast material. Radiology 182:133-138, 1992.
- Rustin, GJ., Gennigs, J.N., and Nelstrop, A.E. Use of CA-125 to predict survival of patients with ovarian carcinoma. J. Clin. Oncol. 7:1667, 1989.
- 13. Ron, I.-L., Inbar, M., Gelernter, I., Lewysohn, O., Ayalon, D., Dale, J., and Chaitchik, S. Use of CA 125 response to predict survival parameters of patients with advanced ovarian carcinoma. Acta Obstet. Gynecol. Scand. 73:658-662, 1994.