

COMPLETE RESPONSE WITH ALTERNATIVE COMBINATION CHEMOTHERAPY IN ENDODERMAL SINUS TUMOR CASE OF THE OVARY

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SUMMARY

A 20 year old female with endodermal sinus tumor of the ovary, Stage III, underwent cytoreductive surgery and combination chemotherapy at Ankara Maternity Hospital, Ankara, Turkey. The patient was initially treated with Vincristine, Actinomycin and cyclophosphamide. The patient was followed by Alpha-feto-Protein which demonstrated a rise in titer which was then managed by Vinblastine, Bleomycin and CIS-platinum. The patient was documented to be in complete clinical and surgical remission by a "second-look" laparotomy. This is the first patient with an advanced germ cell tumor treated by aggressive surgery and multi-agent chemotherapy in Turkey.

INTRODUCTION

Endodermal Sinus Tumor (EST) of the ovary is a rare and highly malignant germ cell neoplasm, affecting primarily young women. Prior to the introduction of combination chemotherapy, the reported two-year survival rates were less than 10 %.

Currently newer treatment protocols emphasize cytoreductive surgical procedures, monitoring with Alpha-Feto-Protein as a tumor marker and combination chemotherapy. This has resulted in improved survival rates. This report documents a patient with endodermal sinus tumor who received combination chemotherapy. She had a recurrence of the disease and received a second multi-agent chemotherapy protocol which induced a complete and durable remission.

This was the first case of an endodermal sinus tumor which was managed by aggressive surgery and chemotherapy. The management plan, associated morbidity and outcome now serves as the standard of care.

CASE REPORT

A 20 year old single, para 0, was admitted to the Ankara Maternity Hospital on May 12, 1986 with a three-month history of progressive abdominal distention, pain, weight loss and fatigue.

The physical examination revealed a poorly nourished, wasted female with respiratory distress. The pertinent findings on the physical examination were of massive ascites which precluded an adequate pelvic examination. The patient underwent an abdomino-pelvic ultrasound which documented ascites and a cystic and solid right pelvic mass which measured 20 x 10 x 10 centimeters in length.

The patient underwent an exploratory laparotomy on May 12, 1986 which revealed six liters of ascitic fluid and a 20 centimeter friable right ovarian mass. Disseminated tumor was noted on the serosa of the uterus, small bowel, bladder peritoneum, omentum and diaphragm, and significant retroperitoneal adenopathy was detected. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, node dissection, omentectomy and cytoreductive surgery. No residual tumor greater than two centimeters remained following the operative procedure. The tumor histopathology was reported as a pure endodermal sinus tumor, of stage III. An Alpha-Feto-Protein level was obtained following surgery and reported as 1112 ng/ml. The beta subunit of the hCG molecule was reported as negative. The first cycle of intravenous chemotherapy was initiated on May 29, 1986.

The patient received Vincristine 1.5 mg per meter squared, Actinomycin 5 mg and Cyclophosphamide 7 mg/kg. The Vincristine was administered on Day 1 and then weekly for twelve weeks. The Actinomycin and Cyclophosphamide were given intravenously for five

days every four weeks. The patient developed severe nausea and vomiting and was treated with an antiemetic protocol. The Alpha-Feto-Protein levels decreased precipitously with the chemotherapy (Figure 1). After the third cycle of chemotherapy the Alpha-Feto-Protein level was 0. The Alpha-Feto-Protein level following the fifth course of therapy was reported as 420 mg. This increase in the Alpha-Feto-Protein level was interpreted as progressive disease. The physical examination revealed no evidence of disease. An ultrasound of the abdomen and pelvis showed no evidence of disease. The interpretation was of recurrent and progressive disease and the patient was started on a protocol of Vinblastine, Bleomycin and CIS-platinum therapy. The first cycle was initiated on December 25 and consisted of Vinblastine 0.2 mg/kg. The Vinblastine was given 0.2 mg/kg in two divided doses on Days 1 and 2. The Bleomycin was administered at 20 units per meter squared, weekly, and CIS-platinum 75 mg per meter squared on Day 1. After two courses of VBP therapy the Alpha-Feto-Protein level returned to normal (Table 1). The patient received a third course on February 16, 1987. The patient then underwent a "second-look" laparotomy on, April 20, 1987 which consisted of peritoneal cytology, bilateral pelvic and para-aortic lymph node sampling, biopsy of the diaphragm, ileum, jejunum and residual omentum. No persistent tumor was documented in any, of the cytopathologic or histopathologic specimens. The patient received one further course of VBP therapy. During the course of the VBP therapy there was no morbidity other than that associated with severe nausea and vomiting which was controlled by metoclopramide regimen of therapy. The patient, when last seen in May of 1991, was clinically disease free and with no sequelae of therapy, five years after the initial surgery.

DISCUSSION

The endodermal sinus tumor is the second most frequent histologic type of malignant germ cell tumor (1). The median age for patients with endodermal sinus tumor is 19 years. The Alpha-Feto-Protein is consistently found in association with these tumors. Endodermal sinus tumors are characterized by aggressive behaviour and poor prognosis. Kurman and Norris reported 71 patients with endodermal sinus tumor 9 of 65 patients with adequate follow up surviving three years. The introduction of combination chemotherapy has been responsible for an increase in survival. Kurman and Norris reported longterm survival in three of four patients with Vincristine, Actinomycin -D and cyclophosphamide (2). Subsequent reports have shown the efficacy of combination (3) chemotherapy using CIS-platinum, Bleomycin and Vinblastine. The currently accepted regimen consists of Vinblastine, Bleomycin and CIS-platinum.

This case of disseminated endodermal sinus tumor which was treated by initial aggressive cytoreductive surgery, then Vincristine, Actinomycin and cyclophosphamide, with an initial response and then recurrence as documented by Alpha-Feto-Protein and subsequent treatment with chemotherapy with Vinblastine, Bleomycin and CIS-platinum, demonstrates the efficacy of this therapeutic approach. The ability to perform this chemotherapy at the Ankara Maternity Hospital in Ankara, Turkey has demonstrated that this program can be carried out with minimal morbidity to the patient with excellent outcome. This first case managed now serves as a standard of care for metastatic germ cell tumors of the ovary.

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