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The bright side of ascites in ovarian cancer

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Epithelial ovarian cancer (EOC) is the leading cause of gynecologic cancer-related deaths in Western countries. Main reason is that the disease is frequently asymptomatic in its early stage and is found only when cancer has already spread outside the pelvis and disseminated throughout the abdominal cavity. As the disease progress, many EOC patients have accumulation of fluid in the peritoneal cavity corresponding to malignant ascites formation. This condition may be an extremely distressing complication for the patient, which may need repetitive palliative drainage to relieve pain and discomfort.

Mechanism involved in the production of excessive peritoneal fluid is still unclear. Under physiological condition, the high concentration of protein inside the capillary vessels creates an oncotic pressure and promotes fluid reabsorption from the interstitial space into the vessels. Main hypothesis in favor of peritoneal fluid formation are an impaired drainage of the peritoneal cavity due to the obstruction of lymphatic system by tumor cells or an increased filtration rate to the peritoneal cavity due to the increased microvessels membrane-surface lining the peritoneal cavity. In addition, malignant ascites contain high protein and albumin concentration reducing the ratio plasma to peritoneal oncotic pressure and leading to fluid leak into the peritoneal cavity.[1]

Malignant ascites generally resolve when the underlying disease is successfully treated. EOC is managed by cytoreductive surgery followed by platinum-based chemotherapy and the expected response rate of primary therapy is more than 70%. However, most of these women will experience recurrence 12–18 months later and progressively a chemoresistant disease will occur. These patients may present a progression of ascites, which may become a major clinical challenge in palliative care setting requiring repetitive paracentesis to alleviate symptoms (pain, anorexia, respiratory distress, fatigue, insomnia, lower extremity edema). Serial paracentesis provide relief of symptoms but also promote loss of proteins, hypovolemia and potential spread of cancer cells to site of drainage.

Alternative approach to traditional palliative paracentesis is the "concentrated ascites reinfusion therapy" (CART).[2] This procedure is approved by the Japanese national insurance scheme since 1981 and is suggested as a therapy tailored for EOC patient having intractable ascites. To date, there is low level of evidence in the literature supporting that this therapy reduce the progression of disease or improve the quality of life, however it is considered by some investigators as safe since all cellular components such as blood cells and cancer cells are removed.

However, malignant ascitic fluid is generally considered as a contributor to the disease progression by facilitating multifocal dissemination of ovarian tumors cells on peritoneal surface. Indeed, it contains angiogenic and growth factors, cytokines, chemokines and extracellular matrix components which are known factors contributing to cell growth, tumor invasion and resistance to TNF-related apoptosis-inducing ligand.[1] On the other hand, acellular fraction of ascites also contains antiangiogenic factors[3] and factors that promote apoptosis[4] which may reduce cancer cells proliferation and survival. Thus, the acellular fraction of ovarian cancer ascites could affect the tumor microenvironment but the mechanisms involved in these tumor-modulating properties are still debated and data are limited to in vitro studies. Recently, chick chorioallantoic membrane (CAM) was used as an in vivo model to study the effect of ascites fluid in combination with taxol on ovarian cancer growth.[4] The results from the CAM assay demonstrated that acellular fraction of ascites potentializes the taxol effect on tumor regression. This data supports the hypothesis that the association of CART and chemotherapy has the potential to improve survival of patients with advanced EOC.[5] Because tumor cell invasion and dissemination largely depend on the peritoneal microenvironment, the role of CART and factors acting on this environment should be more explored.

Finally, ascites represents an accessible and valuable source of material to identify signals that influence tumor growth and to develop new treatment strategy to improve quality of life and survival of EOC patients.

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