



## Wound Clot Used to Treat Hemorrhage from Metastatic-Encased Abdominal Vasculature in a Patient with Ovarian Cancer

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### Abstract

A 72-year-old woman with ovarian cancer, which had metastasized throughout her abdomen, experienced massive haemorrhage during surgery for bilateral salpingo-oophorectomy and to remove neoplastic tissue. The metastasis had infiltrated difficult to reach anatomy, and encased several abdominal vessels, giving rise to a bleeding site which could not be controlled with direct compression. Wound Clot Hemostatic (WCH) surgical gauze, which is effective without compression, becomes a stable gel upon contact with blood; the bio absorbable gel attracts clotting factors and facilitates coagulation. Because of the extremely heavy hemorrhage, and the irregular, haphazard tumor deposits wrapped around numerous blood vessels, the surgery was performed via a unique method of peeling the tumor from the tissues in layers; with WCH applied to the bleeding at each stage of layer removal. Once hemostasis was achieved, another layer of tumor could be removed and the process repeated. Rapid and complete hemostasis was attained with wound clot.

### Introduction

Epithelial Ovarian Cancer (EOC) is the leading cause of death due to gynecological malignancy, with nearly 15,000 deaths in the US alone in 2009 [1,2]. Incidence of ovarian cancer rises after menopause, with a median diagnosis age of 63 years. There is a 1 in 70 lifetime risk of ovarian cancer [1]. Most women present with advanced disease, following several months of abdominal pain and distension [2]. EOC typically does not spread hematogenously as do many other metastasizing tumors but para-aortic lymph nodes may be involved [1,3]. Peritoneal dissemination is the commonest mode of spread, being found in approximately 70% of patients at presentation [4]. Ovarian cancer spreads locally via direct extension to adnexal structures, the uterus and the contralateral ovary, although bilateral ovarian cancer may occur in 11% to 50% of cases. Direct infiltration of the rectosigmoid colon or bladder wall may be seen [1,3,4]. Exfoliated neoplastic cells can detach from the primary tumor and are then transported throughout the peritoneal space and abdominal cavity. This sets the stage for extensive metastatic seeding [1,3]. Pelvic and abdominal deposits of metastasis can surround and encase blood vessels, the uterus, fallopian tube, ovaries and the rectosigmoid colon. The greater momentum is almost always infiltrated by metastasis [1,4]. Other common sites include the paracolic gutters, the pouch of Douglas, the liver capsule, and the diaphragm and bowel serosa. Ascites are often present as well [4]. The current accepted treatment involves the removal of the primary tumor and its metastatic sites, known as cytoreductive surgery, combined with systemic chemotherapy. Nonetheless, the 5 year survival rate remains between 45% and 50%. Often, the surgery requires en bloc resection of the ovarian tumor, reproductive organs, and sigmoid colon, with a primary bowel reanastomosis. The goal of the surgery is to remove as much of the tumor as possible; studies have demonstrated that cytoreduction results in improved patient survival [3]. With early stage disease, this therapy can be curative; however, women with advanced disease will have recurrent disease episodes until chemo resistance occurs [2]. The tumor is rapidly proliferating, compressing visceral organs, progressing typically to death due to bowel obstruction [2]. There is an only a 30% cure rate. This high mortality rate is mainly due to the fact that the majority of patients present at an advanced stage, already having incurred widespread abdominal and pelvic metastatic disease. The cancer grows rapidly and metastasizes early, with a very aggressive course [3]. The relationship between malignancy and thromboembolic disorders is well-established [5]; therefore, it is well known that ovarian cancer patients are at a much higher risk of blood clots than the general population [6]. Additionally, more than 25 percent of patients

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undergoing chemotherapy before and after surgery for ovarian cancer develop blood clots. It has also been reported that when deep vein thrombosis occurs in cancer patients, it can involve unusual sites and tends to be resistant to standard therapy [5]. Multiple factors contribute to a higher potential for blood clots during cancer. First, malignant tumors secrete chemicals that promote blood clotting, increasing the likelihood of developing clots. Additional factors include the use of chemotherapy and decreased mobility. Surgery has also been shown to increase the risk of thromboembolism more in cancer patients than in patients with non-malignant conditions [5]. It has been suggested that patients should be treated with prophylactic blood thinners before and after surgery to decrease the incidence of blood clots and improve outcomes. If a patient develops a blood clot prior to surgery, she must be on a much higher dose of blood thinner and for a much longer time. In a study by Greco et al. [6], almost 12% of ovarian cancer patients developed clots during preoperative chemotherapy, double the number that developed postoperative clots. The problem becomes that if a patient has a clot, and is on a high dose of blood thinner, the risk of hemorrhage increases. This can affect a surgeon's decision to perform more aggressive surgery; therefore blood clots affect a surgeon's ability to treat these patients. Readmission rates rise, and survival rate goes down [6]. Conversely, it is also well known that patients with disseminated malignancies have an increased incidence of bleeding [6]. One reason, as exemplified by the case report below, is that local tumor growth can disrupt vascular integrity [5]. Also, most cancer patients develop varying degrees of Disseminated Intravascular Coagulation (DIC) [5]. DIC is a serious disorder in which the proteins that control blood clotting become overactive. In some cases, small blood clots form in the blood vessels. Some of these clots can clog the vessels and cut off the normal blood supply to organs such as the liver, brain, or kidneys. In other cases, the blood's clotting proteins are consumed, significantly increasing the risk of serious hemorrhaging, which can be spontaneous or following even minor injury. Healthy red blood cells can fragment and break up as they travel through small clot-filled capillaries. Possible complications to DIC include stroke, major organ damage and life-threatening hemorrhage. Wound Clot Hemostatic (WCH) surgical gauze is a Class III bio-absorbable non-compressional hemostatic dressing. WCH, manufactured by Core Scientific Creations, is a novel hemostat for bleeding control based on non-oxidized bio-absorbable cellulose. Its unique non-oxidation technology allows for controlling mild to severe bleeding using the actual blood flow and mucosal tissue; to self-adhere to even high volume high flow blood flow. Thus eliminating the need to apply compression to the hemorrhaging site. WCH can be utilized on multiple tissue types, including blood vessels, internal organs, bones and complex wounds. As it is bio-absorbable, it will be resorbed by the body within 7 days when left in situ. WCH is also effective for up to 36 hours post surgically if left in the body reducing oozing, seromas and forming a mechanical barrier stabilizing the crossed linked fibrin clot further thus reducing revisions, use of hemovac drains and in extension infections, blood transfusions, patient discomfort and hospital stay.

## Case Presentation

A 72-year-old woman had undergone chemotherapy for ovarian carcinoma. She had metastatic tumor in a difficult-to-reach area, in the left hemiabdomen, involving mesenteric lymph nodes and vessels near the pancreas and left kidney. She was undergoing combined open surgery for bilateral salpingo-oophorectomy and tumor removal. Pre-operative prophylactic Clexane was administered in

order to reduce the risk of thromboembolic disease. The metastatic site was located between the abdominal aorta and the left renal artery. It was very highly vascularized from both the renal vessel tributaries and the vena cava; its removal resulted in heavy haemorrhage. The tumor-enmeshed vessels were primarily venous. Veins present a more difficult situation to achieve hemostasis as they do not undergo contraction when they are injured, like the vasospasm occurring in an artery. The difficult to access location of the metastatic deposits, coupled with the high vascularization due to vessels enmeshed by tumor, resulted in a hemorrhagic site that was very difficult to control with any compression; hence Wound Clot Hemostatic (WCH) surgical gauze provided the best solution for this case. Several applications of WCH surgical gauze were placed directly on the haemorrhage site. The portion of the vena cava which had been damaged during removal of the tumor was sutured and then covered with WCH gauze in order to eliminate further bleeding. Due to the extensively heavy hemorrhage, and the need to operate on irregular, haphazard deposits of tumor wrapped around major and minor blood vessels, the surgery was uniquely carried out via a method of peeling the tumor from the tissues in layers; the constant bleeding at each stage of tissue removal repeatedly interfered with the progress of the surgery. Each layer was covered with WCH until hemostasis was achieved. The product was subsequently removed in one piece, very fast and with ease, thanks to the gel stable structure and the next layer of tumor was surgically excised; the new bleeding site was then covered with WCH. This process was repeated until complete transection of the tumor was achieved.

## Discussion

When Wound Clot comes in contact with blood, a gel is formed which is designed to absorb bleeding without breaking down. The liquid absorption capability of WCH is over 2500 percent its own weight. Wound Clot's ability to absorb blood and to maintain a stable membrane allows for the pooling of active coagulation factors in significant quantities to be sequestered in the membrane. The coagulation factors attach to the surface tissue and the membrane in the presence of a patented structure incorporated into the product. This dramatically reduces the flow of blood from the wound. In turn, this process also increases adherence of the membrane to the tissue, ensuring its stability on the wound site. Once the platelets interact with Wound Clot, a molecular imbedded intrinsic clotting pathway is initiated. Wound Clot affects the coagulation process initially by transforming Hageman factor (factor XII) from inactive to active (XIIa) simulating the intrinsic mechanism using a predesigned molecular functional group which is released into the pooled coagulants starting a strong chain reaction scaling the entire coagulation process through multiplication of the gel confined coagulants and activating plasma thromboplastin antecedent (factor XI) for a longer duration when compared to other common hemostats. Simplicity of use is only one of the features and advantages of Wound Clot. The surgeon places the Wound Clot gauze onto the bleeding site; the product immediately begins to absorb blood converting to a gel consistency. The stability of WCH's proprietary gel status of WCH permits easy removal when warranted, and the ability to coagulate venous blood with relative ease, as the product works with, enhances and locally accelerates, the natural clotting mechanism of the body, resulting in rapid hemorrhage control. Intra abdominal venous hemorrhage can present a very challenging situation. Vasoconstriction of an artery or arteriole decreases the radius, increasing resistance and pressure, but decreasing flow. Venospasm, on the other hand, has a very

different outcome. The walls of veins are thin but irregular; thus, when the smooth muscle in those walls constricts, the lumen becomes more rounded. The more rounded the lumen, the less surface area the blood encounters, and the less resistance the vessel offers. Vasoconstriction increases pressure within a vein as it does in an artery, but in veins, the increased pressure actually increases flow. So bleeding veins, due to their thinner and less elastic walls, do not constrict or retract as do arteries. Nonetheless, this is not a complicating factor for Wound Clot, which creates a hemodynamic environment that captures the coagulants and optimises the clotting mechanism to enhance the coagulation cascade, without the need for applying pressure that may further increase blood flow in veins. Furthermore, Wound Clot not only allows for a very flexible configuration, which is very important in abdominal, soft tissue or vascular surgery, but it is extremely strong at the same time. At the conclusion of the surgery the injured sites were covered with WCH and the area was sutured closed. Each bleeding site achieved hemostasis within less than 2 minutes and no rebleeding was detected either during surgery or after product removal. The surgeon who performed this operation is Prof. Boris Yoffe from Barzilai Hospital in Ashkelon, where he serves as the head of general vascular surgery.

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