Rectal cancer and Trousseau syndrome. Case report

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Abstract

Introduction: Trousseau syndrome, first described in 1865, is the relationship of venous thromboembolism and cancer. The objective of this study is to report a case with rectal cancer and Trousseau syndrome.

Clinical case: A 40-year-old female arrived at the Coloproctology Service due to painless bleeding. Diagnostic tests were ordered. Computed tomography reported a 5- to 6-cm tumor that extended up to 5 cm from the anal margin. Ultra-low anterior resection with colonic reservoir and loop ileostomy surgery was carried out. Pathological report was semi-differentiated rectal adenocarcinoma with tumor classification of T3N0M0. Within 72 h of the patient’s postoperative course, she developed sudden hypotension and painful abdominal distention. The patient was reoperated, finding necrosis of the colon from the splenic angle to the colonic reservoir with thrombi in the left colic artery, ischemia of fallopian tubes, ovaries, uterus, pelvic floor and small intestine, 40 cm before ileostomy and ileon. Left hemicolectomy and colostomy were performed. The patient was transferred to intensive care where administration of heparin was continued; however, the patient died 5 days postoperatively due to multi-organ failure.

Conclusions: The mechanism for this syndrome was unknown but there are several hypotheses, suggesting that hematological cancers present an increased risk of deep vein thrombosis. Pancreatic cancer is the most common presentation with this syndrome in 50% of cases. We suggested continuing with the standards of prevention of thromboembolism.

Key words: Trousseau syndrome, Thromboembolism.

Introduction

Trousseau syndrome is defined as a coagulopathy causing a migratory thrombophlebitis, often observed in cancer patients. According to Kakkar, in 1865 the French physician Armand Trousseau first described the relationship between venous thromboembolism and cancer, but it is recognized that the first description of deep vein thrombosis and cancer was made by Boulliard in 1823. However, according to Varki, Trousseau was not only the person who described the syndrome but also self-diagnosed it 2 years later and died due to gastric cancer.

The objective of this paper is to report a case of Trousseau syndrome in a patient who was operated on for rectal cancer.

Clinical Case

A 40-year-old female patient arrived at the Colorectal Unit of the Teodoro Maldonado Carbo Hospital in the city of Guayaquil, Ecuador with painless rectal bleeding over the last several months. Upon rectal examination, a semi-firm tumor was palpated, which occluded a third of the intestinal lumen. Sigmoidoscopy was performed. The tumor measured 6 cm and was located 5 cm from the anal margin. Histological report was tubular adenoma with focal changes of moderately differentiated adenocarcinoma. Computed tomography (CT) reported a 5 x 6 cm rectal tumor occluding the intestinal lumen. Ultra-low anterior resection was performed with colonic reservoir, with anastomosis 3 cm from the anal margin and protective ileostomy. The pathology report indicated moderately differentiated rectal adenocarcinoma, T3N0M0. The evolution of the patient was satisfactory; however, at 72 h postoperatively she suddenly experienced arterial hypotension, integumentary coldness and tachycardia. To correct the situation, the patient was administered crystalloid and colloid solutions. Hematocrit and hemoglobin were reported without significant altera-
tions. Blood pressure and heart rate were decreased. At 6 h of the event, the patient had bloating and pain that did not diminish with medication. When the arterial hypotension reappeared, surgeons decided to re-intervene. Exploratory laparotomy found free inflammatory fluid in the cavity from the splenic flexure to the colonic reservoir, without vigor, and mesothrombus (Figure 1). Also observed was the uterus, fallopian tubes and ovaries (Figure 2), purplish areas apart from the pelvis and in the small intestine, 40 cm before the ileostomy and ileum (Figure 3). Colorectal anastomosis was dismantled and a left hemicolectomy and colostomy were done. The anal canal remained normal. The patient was transferred to the intensive care unit where she continued with heparin that had been previously administered in the operating room. Improvement was relative and the patient died on the fifth day after the second surgery due to multi-organ failure.

**Discussion**

The mechanism of Trousseau syndrome is unknown; however, several hypotheses have been proposed to explain how the thrombotic state is generated by the tumor: by increased expression of the tissue factor, which is an activator of the extrinsic clotting mechanism. Activated oncogenes (K-ras) or inactivated tumor suppressors (p53) in colorectal cancer cells also induce activity in tissue factor concentrations, which has been proposed to not only encourage hypercoagulation but also tumor aggressiveness and angiogenesis.

Tissue factor contains membrane fragments or microvesicles produced by tumor cells that may appear as the most likely cause of distant thrombosis.

Tumorous cysteine protease excretion by the tumor, referred to as a tumor procoagulant, directly activates factor X, independent of factor VII. This activity was later reported in some human tumors. For more than a decade we conducted a clinical study to evaluate prothrombotic markers and their relationship to the concentration of cysteine-proteinase in the blood of patients with gastrointestinal adenocarcinomas with or without metastases. The data suggest that cysteine-proteinase is just a minor risk factor for deep vein thrombosis in these patients. Producing mucinous carcinomas are heavily glycosylated large molecules and usually carry sialoglycans, fucosilates and sulfates that can act as selectin ligands.

Virchow’s triad includes stasis, vascular trauma disease, and hypercoagulability of the blood itself. In the pathophysiology of venous thromboembolism, the hemostatic system and the coagulation cascade take action. Most cancer patients have elevated levels of coagulation factors V, VIII, IX and XI and an increase in markers of coagula-
tion activation (thrombin, antithrombin, prothrombin fragment).\textsuperscript{13} Furthermore, patients with metastases are shown to have poor activity of von Willebrand factor protease (AD-AMTS13), which is an adhesive protein involved in primary hemostasis.\textsuperscript{14}

Early epidemiological studies suggested that hematologic, lung and gastrointestinal cancers have a substantial risk of deep venous thrombosis. Cancers associated with a high incidence of deep vein thrombosis–pulmonary embolism include lung, kidney, stomach, pancreas, brain, ovarian and lymphoma. In contrast, cancers of the head and neck, bladder, breast, esophagus, uterus and cervix are associated with a relatively low degree of deep vein thrombosis.\textsuperscript{15} Cancers commonly associated with Trousseau’s syndrome are pancreas, lung, prostate, stomach and colon cancer; pancreatic cancer is shown in 50\% of these cases.\textsuperscript{16}

It is suggested that in Trousseau syndrome the effect of the oncogenic mutations in cancer cells is produced by the activation of the oncogene tract, which can result in a direct or indirect perturbation of coaguloma and, finally, Trousseau syndrome.\textsuperscript{17}

The indirect effect (non-specific) in oncogenic events in Trousseau syndrome can occur through known consequences of increased aggressiveness of the tumor and vascular invasion, metastasis, hemorrhage, vascular permeability and angiogenesis.\textsuperscript{18}

Treatment of patients with this syndrome is with heparin because coumarin anticoagulants are resistant and thus constitute the activation mechanism of antithrombin,\textsuperscript{19} heparin cofactor 72\textsuperscript{20} and inhibitor of protein C.\textsuperscript{21} Treatment should be continued until removal of the underlying cancer that resolves the hypercoagulable state. There are several reports that low molecular weight heparins can be as effective as heparin and reduce the incidence of thrombocytopenia.\textsuperscript{22}

There may be cases where a patient begins with an unexplained thrombosis with an undiagnosed cancer. In this case, positive emission tomography (PET) helps to identify the primary tumor site and carry out a directed biopsy.\textsuperscript{23}

In this case, the patient presented with sudden nonspecific symptoms of migratory venous thrombosis despite receiving immediate postoperative low molecular weight heparin (LMWH). In the immediate pre-, intra- and postoperative period, a continuous pressure system was used in the extremities and sudden hypotension was sustained for 72 h after surgery. The patient experienced severe abdominal pain for 6 h after initially having it been controlled. Postoperative evolution of the exploratory laparotomy was torpid and without response to the heparin infusion administered in the intensive care unit. The patient died on the fifth postoperative day due to multi-organ failure.

In conclusion, the mechanism of this syndrome is unknown but there are several hypotheses: it is suggested that patients with blood cancers are at a high risk of deep vein thrombosis. Pancreatic cancer is associated with this syndrome in 50\% of the cases. It is suggested to continue with the appropriate standards for prevention of thromboembolism.

References

Trousseau syndrome


