

Dolgotrajne, ponavljajoče, spontane, masivne krvavitve v zadnjičnem in stegneničnem področju pri pacientu s petimi primarnimi malignomi, nastalimi v različnih obdobjih

Prolonged, recurrent, spontaneous massive gluteal and femoral bleeding in a patient with five metachronous primary malignancies

Avtor / Author
Ustanova / Institute

Andrej Čretnik^{1,3}, Pia Šumer², Silva Breznik²

¹Univerzitetni klinični center Maribor, Oddelek za travmatologijo, Maribor, Slovenija;

²Univerzitetni klinični center Maribor, Radiološki oddelek, Maribor, Slovenija; ³Univerza v Mariboru, Medicinska fakulteta, Katedra za kirurgijo, Maribor, Slovenija;

¹University Medical Centre Maribor, Department of Traumatology, Maribor, Slovenia;

²University Medical Centre Maribor, Department for Radiology, Maribor, Slovenia;

³ University of Maribor, Faculty of Medicine, Department of surgery, Maribor, Slovenia;

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Izvleček

Namen: Predstavitev primera dolgotrajne, ponavljajoče, spontane, masivne krvavitve pri pacientu s petimi različnimi malignomi, nastalimi v različnih obdobjih.

Priказ primera: Predstavljamo primer 70-letnega pacienta z masivnimi, ponavljajočimi hematomi v zadnjičnem in stegneničnem področju z malignomom prostate, uretre (penisa), desne strani debelega črevesa in desnih pljuč, z mieloproliferativnim obolenjem, ki se je nedavno zaključilo z razvojem levkemije. Zaradi nastanka utesnitvenega sindroma sta bili nujni fasciotomiji z odstranitvijo hematoma, po katerih se je krvavitev vztrajno ponavljala. Kljub številnim kirurškim posegom z zatlačenjem, lo-

Abstract

Purpose: This study aimed to present the case of prolonged, recurrent, spontaneous massive bleeding in a patient with five metachronous primary malignancies.

Case presentation: A 70-year-old male patient presented with massive hematomas in the gluteal and femoral regions and a 6-year history of prostatic, urethral (penile), right colonic, and right pulmonary carcinoma, with a myeloproliferative disease that recently ended with lymphatic leukemia. Fasciotomies with the evacuation of massive hematomas were performed due to the development of compartment syndrome, which were followed by persistent recurrent bleeding. Despite several surgical

Naslov za dopisovanje / Correspondence

Corresponding author: Andrej
Čretnik M.D., Ph.D., Department
of Traumatology, University Clinical
Center Maribor, Ljubljanska 5, 2000
Maribor, Slovenia
Phone: +386 2 321 1391,
Fax: +386 2 332 4830,
e-mail: andrej.cretnik@guest.arnes.si

kalnimi sredstvi za zaustavitev krvavitve, kirurškimi šivi in selektivnimi embolizacijami s takojšnjo zaustavitvijo krvavitve je digitalna subtrakcijska angiografija po nekaj dneh vedno pokazala ponovitev krvavitve iz oddaljenega povirja notranje črevnične in globoke stegnenične arterije. Testi koagulacije in agregacije in testi za bolezenski motenj krvavitve so bili nenehno v mejah normale. Histološke preiskave niso pokazale malignega procesa v področjih krvavitve, prav tako nismo našli ponovitve malignega procesa na kontrolnih računalniških (CT) in pozitronskih emisijskih tomografijah (PET).

Zaključek: Ponavljajoče krvavitve nam je uspelo zaustaviti šele s postopno, vse agresivnejšo, neciljno embolizacijo, po čemer sta se fasciotomijski rani postopno zacelili.

interventions with packing, local hemostatic agents and sutures, and selective embolization with immediate clinical discontinuation of bleeding, the digital subtraction angiography showed recurrent bleeding from the peripheral branches of the internal iliac and deep femoral arteries always a few days after the procedures. The coagulation and aggregation parameters and bleeding disorders tests were within normal ranges. The histology showed no malignancy in the affected regions, and no relapse was reported in any regions with previously operated malignant diseases on control computed tomography and positron emission tomography scans.

Conclusion: We could stop the bleeding only with more aggressive, nontarget gradual embolization. Subsequently, hemostasis was achieved, with gradual healing of incisions.

INTRODUCTION

An increase in overall life expectancy, improved cancer therapies and follow-up, and more sensitive detection modalities have allowed an increase in the reported frequency of multiple primary tumors in the range of 2%–17% (1,2). The term multiple primary malignancies commonly includes two large categories: if they are diagnosed simultaneously or within 6 months, they are called synchronous neoplasms, and if second- or higher-order malignancies follow at least 6 months after the previous one, they are called metachronous neoplasms (2).

Massive soft-tissue hematomas can occur acutely or can be chronic, with an increase in size for more than a month after the initial hemorrhagic event (3-5). In most cases, these hematomas are associated with trauma, surgery, and bleeding disorders (3-7). Bleeding can be ex-

acerbated by medications and can vary from single episodic bleeding, which can be stopped and spontaneously resolved by hemostatic mechanisms, to catastrophic bleeding, possibly with compartment syndrome or even exsanguination (4,7). Besides surgical treatment, the embolization of bleeding vessels has been proven to be successful in treating prolonged and recurrent bleeding in patients (7,8).

CASE PRESENTATION

A 70-year-old male patient visited the emergency department due to pain in the chest and in the left lower extremity for some days, with a “hot feeling” in the hip region.

His medical history revealed prostatic enlargement with elevated levels of prostate-specific antigen 9 years ago. The prostatic biopsy showed adenocarcinoma three years later, but the patient could not decide on the operative therapy. During the follow-up, a planocellular tumor of the urethra in the penile region was found on cystoscopy 2 years later. First partial and then total amputation of the penis with neo-urethrostomy was performed due to disease progression. Two years later, anemia and, consequently, adenocarcinoma of the right colon were found. Hence, a right hemicolectomy was performed (T3, N0, M0, R0). Additional biopsy of the bone marrow was performed due to the high suspicion of myelofibrosis, which was not confirmed at that time (and a year later), but was confirmed with an additional biopsy and genetic tests 3 years later, when enlarged spleen was detected, which recently progressed to leukemia. With scintigraphy, planocellular carcinoma of the right lung was found a year after the adenocarcinoma of the colon. Therefore, right inferior pulmonary lobectomy was performed (T3, N0, M0, R0). During the further follow-up, positron emission tomography scans showed some reactive nodes in the thorax, but with no signs of local relapse of any malignant diseases. Therefore, chemotherapy was added to the therapy, which ended 5 months before problems in the hip region occurred.

The routine laboratory tests and electrocardiogram showed no abnormalities and infection. Hence, traumatic, coronary, and thromboembolic events were excluded, and the patient was discharged with symptomatic therapy.

Eight days later, a palpable mass and hematoma were confirmed in the gluteal region on ultrasonography. The hemoglobin level dropped to 84 g/L. Other routine laboratory tests, including bleeding (aggregation and coagulation) tests, showed no abnormalities. Mini incision and evacuation of the gluteal hematoma, with transfusion of red blood cells and compression dressing, were performed. The patient was discharged 3 days later, as he reported no signs of bleeding or other problems.

Three days later, he returned to the clinic, with the same

anamnesis of a “hot feeling” a night before, recurrent palpable mass in the gluteal and femoral regions, and a drop in the hemoglobin level to 81 g/L. The bleeding tests, including rotational thromboelastometry, were again without abnormalities, and computer tomography angiography showed no active bleeding. Magnetic resonance imaging (MRI) was performed, showing massive hematomas in the gluteal and femoral regions (Fig. 1).



Figure 1. MRI (pelvic and femoral region, antero-posterior plane); central areas of massive hematomas in the gluteal and femoral regions are marked with arrows.

In the next 5 days, the hemoglobin level continuously dropped and symptoms of compartment syndrome developed. Therefore, two separate fasciotomies and evacuation of massive hematomas in the gluteal and femoral regions were performed, with no obvious source of bleeding found. In the following days, the drop in the hemoglobin level and hematomas were found on ultrasonography again. Subsequently, another operative revision with packing and topical local hemostats and digital subtraction angiography (DSA) were performed. Large-caliber peripheral arteries (Fig. 2) with minor extravasation were found. Hence, selective peripheral em-

bolization was conducted, with no bleeding found at the end of the procedure.

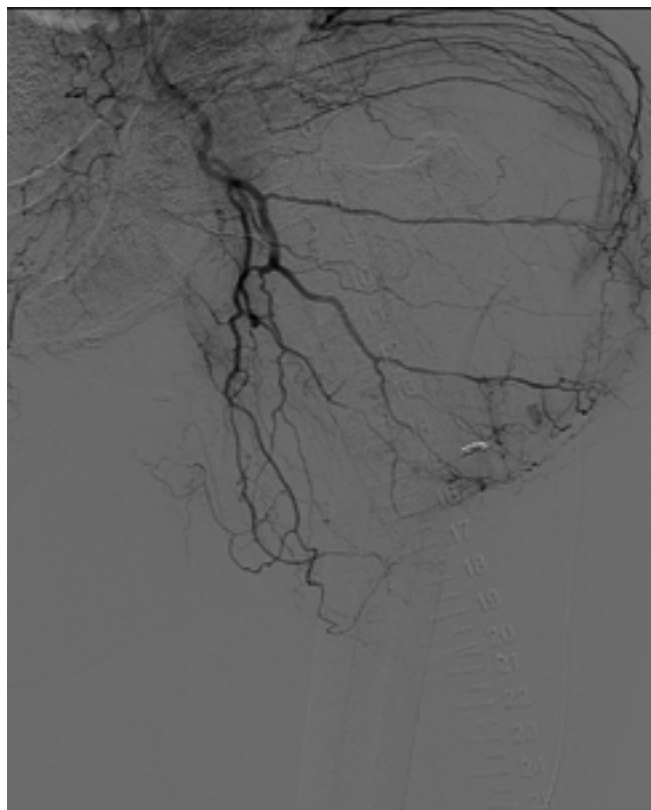


Figure 2. DSA (femoral region, AP plane); large-caliber peripheral arteries are seen, together with extravasation and (previous) peripheral (selective) embolization with coils, gelfoam, microspheres, and polyvinyl alcohol particles.

Unfortunately, new hematomas, bleeding, and the same anamnesis of “hot feeling” recurred almost every 3–5 days. A multidisciplinary approach involving a consultation with a hematologist, an oncologist, a transfusionist, a microbiologist, a pathologist, a specialist in infective diseases, and an interventional radiologist was chosen. However, the bleeding, genetic, autoimmune, and hormonal tests, including tumor markers, showed no abnormalities. Therefore, the same therapy of repeated surgical revisions with packing and less and less selective interventional embolization with bigger and bigger coils (up to 4 mm), gelfoam, microspheres, and polyvinyl alcohol particles (up to 1200 µm) was performed. The bleeding in the gluteal region stopped after the fourth interventional embolization. However, in the femoral region, seven procedures of embolization were needed. Aggressive, nontarget proximal emboliza-

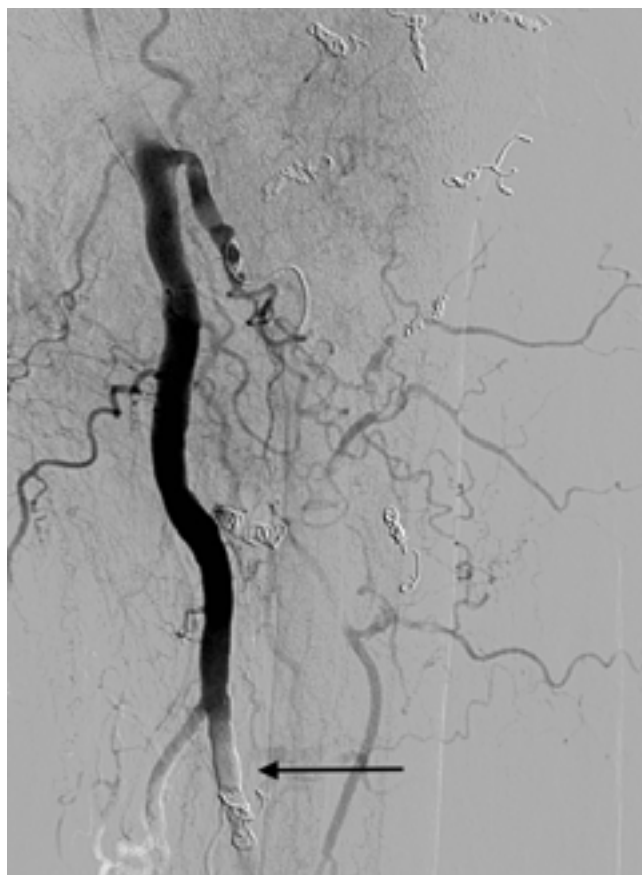


Figure 3. DSA (femoral region, AP plane); proximal nontarget embolization of deep femoral artery (marked with an arrow) is seen, together with previous proximal nontarget embolization of the internal iliac artery and more selective (peripheral) embolization of branches with coils, gelfoam, microspheres, and polyvinyl alcohol particles.

tion of the deep femoral artery with a plaque of 7 mm was conducted until hemostasis was achieved (Fig. 3). Minor skin edge ischemia in the femoral region occurred at the end of all the procedures, which healed using negative-pressure dressings in the following months. The tissue samples from the bleeding regions were sent several times for microbiologic and histologic examinations. A network of enlarged capillaries (and peripheral vessels) with signs of inflammation was found, with no signs of infection or malignant growth. The patient received 91 doses of red blood cells, and it took 167 days until he was discharged home.

DISCUSSION

We presented the case of a patient with five primary malignancies in whom the exact mechanism of bleeding could not be clearly explained. We could not detect any traumatic event, bleeding (hematologic) disorders, coagulopathy, markers for autoimmune conditions, or medication (anticoagulant) history. No such case was reported earlier.

During surgical revisions and DSA, we found a capillary network that continuously formed and bled, with a greater diameter of vessels, as in histologic samples. The activation and recruitment of macrophages and neutrophils (leukocytes) in inflammation processes and under hypoxic conditions, as in compartment syndrome or due to the iatrogenic embolization of the bleeding vessels, contribute to the changes in vascular permeability and secretion of proangiogenic growth factors (including Fibroblast Growth Factor - FGF and Vascular Endothelial Growth Factor - VEGF), stimulating neoangiogenesis and changes in vascular properties (9).

This mechanism is well known as tumor-induced local and systemic impacts on blood vessel function, not only in the local tumor microenvironment but also at other sites, in a patient with cancer (5,9), which might

be related to patient's bleeding problems. However, this needs further investigation. Finally, the bleeding was stopped with more aggressive, nontarget gradual embolization with a combination of different embolic materials because embolization with coils only was associated with a greater occurrence of recurrent bleeding or could cause the occlusion of nontarget vessels with coil migration (8). More aggressive, nontarget embolization could successfully stop the bleeding and thus reduce the risks of massive blood loss, compartment syndrome, and necrosis due to massive hematomas with compression effect. Necrosis with potential infection could arise due to the ischemic effect of embolization. Therefore, a multidisciplinary approach with benefits outweighing the risks could be a reasonable approach in such cases.

CONCLUSION

The proposed multidisciplinary approach with surgical interventions, less selective embolization, and full supportive (replenishment) therapy was proved in our case to be effective, as hemostasis was successfully achieved with no adverse effects.

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