Review Article

Clinical application of interventional embolization in tumor-associated hemorrhage

Yi Chen[1,2#], Yi Yang[1#], Wen-Ji Xu[3], Yu-Jing Xin[1], Ya-Nan Wang[1], Xiang Zhou[1], Xiao Li[1]

[1]Department of Interventional Therapy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China; [2]Department of Interventional Radiology, First Hospital of Shanxi Medical University, Taiyuan 030001, China; [3]Department of CT and MRI, The Hospital of Shanxi University of Chinese Medicine, Taiyuan 030001, China

Contributions: (I) Conception and design: X Zhou, X Li; (II) Administrative support: X Zhou, X Li; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Xiang Zhou, MD; Xiao Li, MD. Department of Interventional Therapy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 17 Panjiayuan Nanli, Chaoyang District, Beijing 100021, China. Email: zhou_joy4219@163.com; lixiao_drlx@sina.com.

Abstract: Recently, the main clinical treatment methods for tumor-associated hemorrhage include systemic therapy, the application of hemostatic drugs, blood transfusion, symptomatic support therapy and endoscopic interventional hemostasis. Endoscopic hemostasis is performed mainly for patients with gastrointestinal bleeding, and the procedures include hardening of the blood vessels and the injection of hemostatic drugs. Surgical hemostasis methods mainly include the surgical ligation of bleeding blood vessels or tumor resection for hemostasis. Interventional hemostasis is a new hemostasis method. With the development of interventional radiology in recent years, transcatheter arterial embolization (TAE) can quickly detect and accurately embolize arterial blood vessels. It is the preferred treatment for present tumor-associated hemorrhages.

Keywords: Intervention; embolism; tumor; bleeding; transcatheter arterial embolization (TAE)

Submitted Nov 20, 2019. Accepted for publication Feb 07, 2020.
doi: 10.21037/atm.2020.03.69
View this article at: http://dx.doi.org/10.21037/atm.2020.03.69

Introduction

At present, clinically common tumor-associated hemorrhages can be divided into the following types: epistaxis, hemoptysis, hematemesis, bloody stool, celiac hemorrhage (1,2), and hematuria, vaginal bleeding, according to the tumor location and bleeding direction. The treatment methods for tumor-associated hemorrhage mainly include the following (3): (I) systemic treatment: the application of hemostatic drugs, blood transfusion and symptomatic support treatment, but systemic treatment for a large volume of acute bleeding is often ineffective. (II) Endoscopic hemostasis: including two steps: hardening of the vessels and the injection of hemostatic drugs, this method mainly targets patients with gastrointestinal bleedings, but has a limited clinical application range. (III) Surgical hemostasis: stopping the bleeding through the surgical ligation of blood vessels or resection of tumors (4), but the application of surgical hemostasis is limited for patients who have lost the chance of surgery or cannot tolerate surgery. (IV) Interventional hemostasis: with the development of interventional radiology, transcatheter arterial embolization (TAE) can quickly identify and accurately embolize bleeding vessels (5-7), and is the first choice for the treatment of tumor-associated hemorrhage. The present study aims to summarize the clinical

application of interventional embolization in tumor-associated hemorrhage. The details of the present study are described as follows.

Clinical diagnosis of tumor-associated hemorrhage

The diagnosis of tumor-associated hemorrhage mainly depends on the patient's history (8), physical examination, laboratory examination, and imaging examination (8-12): computed tomography (CT), magnetic resonance imaging (MRI), and isotope scanning. Other diagnostic punctures, such as celiac puncture, have also been used for the rapid diagnosis of celiac hemorrhage.

Causes of tumor-associated hemorrhage

Drug-associated hemorrhage

The blood of tumor patients is usually in a hypercoagulable state, which easily forms thrombus. Some patients who stay in bed for a long time are more likely to develop lower extremity vein thrombosis (13). In the prevention and treatment of lower extremity venous thrombosis, aspirin, low-molecular-weight heparin, clopidogrel and rivaroxaban are the commonly used drugs for tumor patients in the hypercoagulable state. These anticoagulants easily induce drug-associated hemorrhage (14-18). Furthermore, anti-tumor angiogenesis drugs, such as bevacizumab, and molecular targeted drugs, such as sorafenib and apatinib, also increase the risk of bleeding (19).

Surgical bleeding

Surgery is an important method of the treatment for early and middle stage tumors, and bleeding is often one of the most common complications of surgery (20). The complication of massive hemorrhage caused by surgery often endangers the life of patients, and needs timely hemostasis treatment (21-24).

Other iatrogenic hemorrhage

Invasive operations, such as tumor biopsy, ablation and endoscopy, also easily cause iatrogenic bleeding. Percutaneous biopsy and endoscopic minimally invasive operations, such as biopsy and mucosal peeling, are important methods for minimally invasive diagnosis and treatment, but the common complication for these is bleeding (25). Ablation is an important means of local treatment for tumors. For some tumors, such as liver tumors, kidney tumors and thyroid tumors, it can achieve a radical effect, but these methods can also cause local bleeding (25).

Hemorrhage after radiotherapy

Radiotherapy is a common technique in tumor treatment. During radiotherapy, there is a risk of damaging the blood vessels around the tumors, which easily causes hemorrhage after radiotherapy (26). Clinically, the common ones are hemorrhages after radiotherapy for cervical cancer, bladder cancer, nasopharyngeal cancer and esophageal cancer (27-30).

Hemorrhage caused by tumor invading blood vessels

Most tumors represented by liver cancer have an abundant blood supply (31). In the process of tumor invasion and metastasis, vascular invasion or tumor compression of the peripheral blood vessels may lead to tumor-associated hemorrhage (32), such as hemoptysis caused by lung cancer (33), gastrointestinal hemorrhage caused by gastrointestinal cancer (34,35), hematuria caused by bladder cancer and renal cancer, and vaginal bleeding caused by cervical cancer (36,37).

Interventional therapy of tumor-associated hemorrhage

Characteristics of angiography

As a minimally invasive interventional therapy technology, TAE can accurately and quickly identify the bleeding vessels. Besides, TAE can effectively embolize these bleeding vessels, and has the advantages of rapid hemostasis, significant curative effect, and less related complications. Therefore, interventional therapy has become the first choice of treatment for tumor-associated hemorrhage (3,5,7).

At present, digital subtraction angiography (DSA) manifestations of bleeding in patients are usually divided into five categories) In clinical practice, the DSA manifestations of patients with tumor-associated hemorrhage are summarized and divided into five categories (At present, there is no classification of angiographic manifestations of patients with bleeding in clinical practice.

This is the author's summary based on a large number of observations, which is original): (I) extravasation in early staining: in the early arterial phase, obvious contrast agent extravasation could be observed. It suggests that the bleeding rate of these patients is fast, and the amount of bleeding is large. Therefore, this kind of patients need fast hemostasis to save lives. (II) Extravasation in late staining: the extravasation of the contrast agent can be observed in the late arterial phase. It suggests that the bleeding rate of this kind of patients is slightly slow, and it needs to be in the late arterial phase or parenchymal phase to observe the contrast agent extravasation. (III) Abnormal vascular morphology: the angiography reveals abnormal vascular masses, aneurysms, or thickening of the diameter of the blood vessels. (IV) Hyperchromatism of the tumor: for these patients, the tumor staining can be only observed in the parenchymal phase. Although there is no obvious extravasation of the contrast medium, the tumor is deeply stained. (V) Normal staining, negative findings: the angiogram of these patients is basically normal.

Selection of interventional embolic agents

In clinic, the appropriate embolic agent would be selected according to the different bleeding sites and angiographic manifestations of patients. For example, patients with early extravasation bleeding have a faster bleeding rate and a larger volume of bleeding. Hence, it is usually necessary to use a spring coil or a large-particled gelatin sponge to embolize the bleeding vessels. Patients with late extravasation bleeding have a relatively slow bleeding rate, and they can choose gelatin sponge particles, microspheres, polyvinyl alcohol (PVA) and spring coils for embolization. Bleedings caused by abnormal vascular morphology, such as abnormal vascular morphology, obvious thickening of the diameter of blood vessels when compared with normal blood vessels, and aneurysm (38), can be treated with spring coil, particles (5) and covered stent, and the bleedings caused by hyperchromatism can be treated by embolization with an embolic spring coil (39), iodized oil, microspheres (40), PVA and gelatin sponge particles.

The diameters of the tumor embolic agents range within 50–1,000 μm. Different embolic agents should be used according to different conditions and the doctor's experience. The end point of embolization is the disappearance of abnormal vessels and the end of abnormal staining. Attention should be given to the embolization of hollow organs. In particular, the embolization of hollow organs with a single blood supply needs special care. It is required to select the location of the diseased vessels, and use short-term embolic agents, such as gelatin sponge particles, as far as possible.

Determining blood vessels of bleeding

For patients with tumor-associated hemorrhage, it is very important to quickly, accurately and comprehensively find these bleeding vessels. Therefore, finding all these bleeding vessels and embolizing these vessels is an important guarantee for the success of the interventional embolization. The general blood vessels of hemorrhage are summarized, which are as follows: the bleeding vessels of nasopharyngeal carcinoma are the branches of the external carotid artery, which include the middle meningeal artery, facial artery and maxillary artery; the bleeding vessels of hemoptysis of lung cancer include the intercostal arteries, bronchial arteries, internal thoracic artery and septal artery (41); the general bleeding vessels of esophageal cancer are bronchial arteries, intercostal arteries, left gastric artery, thyrocervical trunk and left gastric artery; the bleeding vessels of liver cancer include the hepatic artery, superior mesenteric artery, phrenic artery and internal thoracic artery; the most general bleeding vessels of bladder cancer include the superior vesical artery and internal iliac artery branch; the common bleeding vessels of cervical cancer are the uterine artery and ovarian artery; the main bleeding vessel of gastric cardia and fundus carcinom is the left gastric artery; the main bleeding vessel of duodenal cancer is the duodenal artery; and the main bleeding vessel of rectal cancer is the inferior rectal artery.

Side effects of the treatment of interventional infection

After all, interventional therapy is an invasive procedure, which inevitably has some side effects. The common side effects include perioperative infections, damage to the vascular lining, secondary hematoma formation, and limb ischemia.

In summary, interventional therapy plays an important role in the treatment of tumor-associated hemorrhage. This can not only quickly identify the bleeding sites and affected blood vessels, but also allow for the selection of different embolic agents for precise embolization, according to the different sites and bleeding properties. At present, this has become the first choice for the treatment of tumor bleeding and hemostasis.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this article and any accompanying images.

References

1. Gon Y, Todo K, Mochizuki H, et al. Cancer is an independent predictor of poor outcomes in patients following intracerebral hemorrhage. Eur J Neurol 2018;25:128-34.
2. Wang J, Packer CD. Acute abdominal pain after intercourse: adrenal hemorrhage as the first sign of metastatic lung cancer. Case Rep Med 2014;2014:612036.
3. Johnstone C, Rich SE. Bleeding in cancer patients and its treatment: a review. Ann Palliat Med 2018;7:265-73.
4. Shabunin AV, Bagateliya ZA, Korzheva IY, et al. Urgent surgical care for patients with colon cancer complicated by hemorrhage. Khirurgiia (Mosk) 2017;12:46-51.
5. Seki A, Shimono C. Transarterial chemoembolization for management of hemoptysis: initial experience in advanced primary lung cancer patients. Jpn J Radiol 2017;35:495-504.
6. Han K, Yoon KW, Kim JH, et al. Bronchial Artery Embolization for Hemoptysis in Primary Lung Cancer: A Retrospective Review of 84 Patients. J Vasc Interv Radiol 2019;30:428-34.
7. Ugras S, Gemignani ML, Connolly PH, et al. Endovascular approach to acute hemorrhage in locally advanced breast cancer. Breast J 2015;21:189-91.
8. Han H, Qiao P, Jiang XW, et al. Acute flank abdominal pain as the chief complaint of spontaneous adrenal hemorrhage secondary to metastatic lung cancer. Urol Case Rep 2017;16:65-8.
9. Jung SI, Jeon HJ, Park HS, et al. Multiparametric MR imaging of peripheral zone prostate cancer: effect of postbiopsy hemorrhage on cancer detection according to Gleason score and tumour volume. Br J Radiol 2018;91:20180001.
10. Ku YK, Wong YC, Fu CJ, et al. Timely Antecedent CT or MRI Can Help Predict Hemorrhage Site of Posttreatment Head and Neck Cancer, With Digital Subtraction Angiography Used as the Reference Standard. AJR Am J Roentgenol 2016;206:829-36.
11. Pellino G, Simillis C, Qiu S, et al. Social media and colorectal cancer: A systematic review of available resources. Plos One, 2017;12:e0183031.
12. Casal Núñez JE, Vigorita V, Ruano Poblador A, et al. Presacral venous bleeding during mobilization in rectal cancer. World J Gastroenterol 2017;23:1712-9.
13. Staub Y, Nishiyama A, Suga Y, et al. Clinical Characteristics Associated With Lenvatinib-induced Fistula and Tumor-related Bleeding in Patients With Thyroid Cancer. Anticancer Res 2019;39:3871-8.
14. Bauersachs R, Lee AYY, Kamphuisen PW, et al. Renal Impairment, Recurrent Venous Thromboembolism and Bleeding in Cancer Patients with Acute Venous Thromboembolism-Analysis of the CATCH Study. Thromb Haemost 2018;118:914-21.
15. Zakai NA, Walker RF, MacLehose RF, et al. Impact of anticoagulant choice on hospitalized bleeding risk when treating cancer-associated venous thromboembolism. J Thromb Haemost 2018;16:2403-12.
16. Ording AG, Horvath-Puho E, Adelborg K, et al. Thromboembolic and bleeding complications during oral anticoagulation therapy in cancer patients with atrial fibrillation: a Danish nationwide population-based cohort study. Cancer Med 2017;6:1165-72.
17. van der Hulle T, den Exter PL, Planquette B, et al. Risk of recurrent venous thromboembolism and major hemorrhage in cancer-associated incidental pulmonary embolism among treated and untreated patients: a pooled analysis of 926 patients. J Thromb Haemost 2016;14:105-13.
18. Hambley BC, Norsworthy KJ, Jasem J, et al. Fibrinogen

consumption and use of heparin are risk factors for delayed bleeding during acute promyelocytic leukemia induction. Leuk Res 2019;83:106174.
19. Zhu X, Tian X, Yu C, et al. Increased risk of hemorrhage in metastatic colorectal cancer patients treated with bevacizumab: An updated meta-analysis of 12 randomized controlled trials. Medicine (Baltimore) 2016;95:e4232.
20. Nagai M, Sho M, Akahori T, et al. Risk Factors for Late-Onset Gastrointestinal Hemorrhage After Pancreatoduodenectomy for Pancreatic Cancer. World J Surg 2019;43:626-33.
21. Ohta H, Miyake T, Shimizu T, et al. The impact of pharmacological thromboprophylaxis and disease-stage on postoperative bleeding following colorectal cancer surgery. World J Surg Oncol 2019;17:110.
22. Wang X, Zhou L, Li X, et al. Analysis of the common hemorrhage sites during laparoscopic rectal cancer surgery. Zhonghua Wei Chang Wai Ke Za Zhi 2017;20:675-9.
23. Kamio Y, Hiramatsu H, Kamiya M, et al. Cerebellar Hemorrhage due to a Direct Carotid-Cavernous Fistula after Surgery for Maxillary Cancer. J Korean Neurosurg Soc 2017;60:89-93.
24. Lian JJ, Chen SY, Zhou PH, et al. Hemorrhage-prevention value of second-look endoscopy after endoscopic submucosal dissection for early gastric cancer:a meta-analysis. Zhonghua Wei Chang Wai Ke Za Zhi 2019;22:673-7.
25. Sag AA, Brody LA, Maybody M, et al. Acute and delayed bleeding requiring embolization after image-guided liver biopsy in patients with cancer. Clin Imaging 2016;40:535-40.
26. Yanazume S, Karakida N, Higashi R, et al. Tumor bleeding requiring intervention and the correlation with anemia in uterine cervical cancer for definitive radiotherapy. Jpn J Clin Oncol 2018;48:892-9.
27. Chen CS, Park S, Shin JH, et al. Endovascular treatment for the control of active vaginal bleeding from uterine cervical cancer treated with radiotherapy. Acta Radiol 2018;59:1336-42.
28. Aggarwal V, Chuprin A, Aggarwal A, et al. Bleeding after interstitial brachytherapy for cervical cancer requiring embolization. Radiol Case Rep 2018;13:1141-5.
29. Kimura K, Tomita N, Shimizu A, et al. A case of severe hemoptysis after stereotactic body radiotherapy for peripherally located stage I non-small cell lung cancer. Jpn J Radiol 2015;33:370-4.
30. Lu Q, Chen L, Zeng J, et al. Clinical Features of Liver Cancer with Cerebral Hemorrhage. Med Sci Monit 2016;22:1716-23.
31. Sonoo T, Inokuchi R, Yamamoto M, et al. Severe Hemorrhage from Cervical Cancer Managed with Foley Catheter Balloon Tamponade. West J Emerg Med 2015;16:793-4.
32. Lim JH, Ryu JS, Cho SY, et al. Small-cell Lung Cancer Presenting as Fatal Pulmonary Hemorrhage. Open Med (Wars) 2018;13:64-6.
33. Martiniuc A, Grasu M, Dumitru R, et al. Gastric Cancer, Hemophilia A and Angiodysplasia - An Unreported Association with Clinical Implications in a Patient with Digestive Hemorrhage. Chirurgia (Bucur) 2018;113:857-66.
34. Tsuchihashi K, Shimokawa H, Takayoshi K, et al. Regorafenib-induced retinal and gastrointestinal hemorrhage in a metastatic colorectal cancer patient with liver dysfunction:A case report. Medicine (Baltimore) 2017;96:e8285.
35. Kawahara Y, Nagai T, Abe T, et al. Spurting Hemorrhage in a Patient with Colon Cancer. Intern Med, 2016;55:3069-70.
36. Eleje GU, Eke AC, Igberase GO, et al. Palliative interventions for controlling vaginal bleeding in advanced cervical cancer. Cochrane Database Syst Rev 2019;3:CD011000.
37. Higashiyama M, Suzuki H, Watanabe C, et al. Lethal hemorrhage from duodenal ulcer due to small pancreatic cancer. Clin J Gastroenterol 2015;8:236-9.
38. Aksoy Ş, Akçe B, Kılıçkesmez Ö, et al. Transcatheter Arterial Embolization for Controlling Severe Bleeding From Recurrent Locally-Advanced Breast Cancer. J Breast Health 2016;12:137-40.
39. Nieuwkamp DJ, de Wilde A, Wermer MJ, et al. Long-term outcome after aneurysmal subarachnoid hemorrhage-risks of vascular events, death from cancer and all-cause death. J Neurol 2014;261:309-15.
40. Orii T, Karasawa Y, Kitahara H, et al. Efficacy of Self-Expandable Metallic Stent Inserted for Refractory Hemorrhage of Duodenal Cancer. Case Rep Gastroenterol 2016;10:151-6.
41. Zhu LZ, Yang RJ, Zhu X. Role of inferior phrenic artery in the interventional treatment of lung metastases tumor: A report of 11 cases. J Cancer Res Ther 2018;14:61-7.

Cite this article as: Chen Y, Yang Y, Xu WJ, Xin YJ, Wang YN, Zhou X, Li X. Clinical application of interventional embolization in tumor-associated hemorrhage. Ann Transl Med 2020;8(6):394. doi: 10.21037/atm.2020.03.69

