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General and Supportive Care

Surgical emergencies in oncology

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ABSTRACT

An oncologic emergency is defined as an acute, potentially life threatening condition in a cancer patient that has developed as a result of the malignant disease or its treatment. Many oncologic emergencies are signs of advanced, end-stage malignant disease. Oncologic emergencies can be divided into medical or surgical. The literature was reviewed to construct a summary of potential surgical emergencies in oncology that any surgeon can be confronted with in daily practice, and to offer insight into the current approach for these wide ranged emergencies.

Cancer patients can experience symptoms of obstruction of different structures and various causes. Obstruction of the gastrointestinal tract is the most frequent condition seen in surgical practice. Further surgical emergencies include infections due to immune deficiency, perforation of the gastrointestinal tract, bleeding events, and pathological fractures.

For the institution of the appropriate treatment for any emergency, it is important to determine the underlying cause, since emergencies can be either benign or malignant of origin. Some emergencies are well managed with conservative or non-invasive treatment, whereas others require emergency surgery. The patient's performance status, cancer stage and prognosis, type and severity of the emergency, and the patient's wishes regarding invasiveness of treatment are essential during the decision making process for optimal management.

Introduction

Over the past decades, there has been an increasing incidence of cancer diagnoses, resulting from changing lifestyles, aging of the population and the implementation of screening programs [1–3]. Luckily survival has improved due to earlier detection and the development of more efficient cancer specific treatment regimens. Consequently, there will be an increasing number of patients with a history of cancer presenting at the Emergency Room (ER). Cancer patients can present at the ER for various reasons; symptoms caused by malignant disease, complications of cancer treatment, or symptoms not directly related to malignant disease or treatment [4–9]. As cancer patients admitted through the ER often have advanced disease, and the frequency of visits to the ER rises near the end of life, this patient category requires special attention [10,11].

An oncologic emergency is defined as an acute, potentially life threatening condition in a cancer patient that has developed, directly or indirectly, as a result of the malignant disease or cancer treatment [12,13]. Any cancer patient can experience emergencies that require surgical consultation and possible surgical treatment, and any physician can be confronted with these emergencies. Therefore, an understanding of the pathophysiology and prognosis of the various emergencies is necessary for correct management. Many emergencies in oncology are signs of advanced, end-stage disease. To determine which procedures should be undertaken or avoided, it is essential that a surgeon is informed on the performance status of the individual patient, the cancer stage and prognosis, (need for) future cancer-treatment, and the patient's wishes regarding aggressive interventions and treatment at the end of life [14–17].

In the past decades, several reviews have been published concerning emergencies in oncology and their management in general [5,12,13,18–24]. These oncologic emergencies are mostly categorized as metabolic, hematologic, cardiovascular, infectious, and structural [5,12,21,24]. These emergencies can also be categorized as medical or surgical [15]. However, to our knowledge, no review article has been written on the surgical emergencies in oncology specifically. For this article, the literature was reviewed to construct a summary for potential surgical emergencies in oncology that any surgeon can be confronted with in daily practice, and to offer insight into the current approaches for these wide ranged

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emergencies. Guidelines for management are given, but for some cases no details of specific procedures are described, since institutions might have different protocols for execution and management.

Obstruction

Cancer patients can experience symptoms of obstruction of different structures and various causes [15]. A substantial number of obstructions is benign in nature and not caused by tumor mass [15,25].

Obstruction of the gastrointestinal tract

Obstruction of the gastrointestinal tract is the most frequent emergency seen in surgical practice and is characterized by clinical intolerance to oral intake resulting in nausea, vomiting, (abdominal) pain, and absence of stool passage [26–29]. Many patients do not experience a solitary obstruction, but concurrent intestinal obstructions [28].

Initial treatment of any obstruction in the gastrointestinal tract starts with conservative treatment; i.e. restoration of fluid and electrolyte balance, alternatives for feeding, restriction of medications that have a paralytic effect on the intestines, and nasogastric tube placement for decompression with stimulation of intestinal passage with laxatives for distal obstructions [15]. This conservative regimen will keep the patient in (the most) optimal condition and it gains time for diagnostic methods in order to identify the origin of the obstruction, staging of the malignant disease, and multidisciplinary evaluation. Minimally invasive diagnostic methods include imaging studies, endoscopy, and laboratory tests including tumor markers. The route for nutrition depends on the site of obstruction and the patient's clinical tolerance for oral intake. Options for feeding are liquid dietary supplements, a feeding tube past the obstruction if possible, or total parenteral nutrition. Nutrition for patients with obstruction of the small or large intestine should be given through the parenteral route, as a feeding tube functions poorly in case of obstruction more distally. A conservative treatment should be instituted during the diagnostic process for as long as the cause of obstruction is unknown or to see if the obstruction resolves spontaneously, but not longer than 3–7 days [15,30–32]. After this period, decisions have to be made regarding invasive therapy, (diagnostic) surgery, or refraining from any intervention and withdrawal of care. It is important that these decisions are made multidisciplinary and in deliberation with the patient and family; to provide the patient with the essential information regarding prognosis, treatment options and the expected impact, and to follow the patient's and families wishes [33,34]. The routine use of long term parenteral nutrition for patients with malignant obstruction is controversial and should be reserved for patients with minimal tumor burden who will receive surgery or chemotherapy in the near future [34]. When refraining from interventions, it must be considered that continuation of nutrition for the terminally ill patients doesn't influence survival, and may even reduce quality of life by the presence of feeding tubes or indwelling catheters. Table 1 provides a summary of causes and treatment options for the variety of obstruction symptoms.

Causes

Proximal esophageal and gastric outlet obstruction can lead to the initial presentation of esophageal or gastric cancer, or be a symptom of recurrence of locally advanced disease [15,35–37]. It may be caused by intraluminal tumor presence, intraluminal invasion, or extrinsic compression by tumor mass. Benign causes of esophageal obstruction are treatment-related edema, initial worsening of obstructive symptoms due to chemo- or radiation therapy, and anastomotic strictures after surgery. With the exception of (postoperative) gastroparesis, gastric outlet obstruction is malignant in nature and usually a sign of advanced, incurable disease [38].

Patients with a history of cancer, frequently experience symptoms of small intestine obstruction [15,27]. Benign causes have been reported to account for about 18% up to 55% of cases of small intestine obstruction, including postoperative adhesions, intestinal strangulation or hernia, and structures following radiation therapy [27,32,39–41]. Malignant causes can be intraluminal tumor presence, intraluminal invasion, or extrinsic compression by tumor in primary disease, local recurrence, and peritoneal carcinomatosis [25,27,31,32,42]. Small intestinal obstruction due to recurrent cancer is commonly seen in colorectal cancer, ovarian cancer, gastric cancer and melanoma, and is often a sign of end-stage disease [12,31,42]. The time of the occurrence of obstruction symptoms after surgery tends to be shorter for malignant causes (within three years after the initial surgery), compared to benign causes (median time five years) [25,27,43]. Incomplete obstruction, non-permanent pain, the presence of ascites and a known cancer recurrence prior to the obstruction seem to be indicative for malignant small intestinal obstruction [25,27].

For patients with colorectal obstruction 80% of cases is malignant, and 10–30% of patients with colorectal cancer present with symptoms of obstruction [44]. Malignant colorectal obstruction is often caused by intraluminal tumor presence in cases of colorectal cancer, with the majority located in the left side of the colon [45,46]. Other malignant causes can be metastatic disease of other origin, and pelvic tumors causing obstruction through extrinsic colorectal compression or invasion [45,47]. A pseudo-obstruction, Ogilvie's syndrome, may mimic a mechanical obstruction [15,45,48]. Other forms of benign colorectal obstruction can be volvulus, diverticulitis, intussusception, and anastomotic strictures developed after surgery [45]. Colorectal obstruction becomes life-threatening when the presence of a competent ileocoecal valve leads to a closed-loop situation with distention of the colon and subsequent risk of colonic perforation [4,15,46].

Management

For proximal obstructions in locally advanced esophageal cancer, there is no indication for palliative surgical resection or bypass [15]. In contrast, some patients with gastric outlet obstruction and a good performance status, may benefit from surgery, e.g. bypass gastrojejunostomy, or distal gastrectomy [15,38,49,50]. Less invasive interventions to establish nutrition in patients with proximal obstruction and poor performance status are endoscopic stent placement, percutaneous gastrostomy or surgical jejunostomy for feeding past the obstruction, [15,35,36,51–55]. Esophageal stent placement and percutaneous gastrostomy should be reserved for patients with fair prognosis, e.g. benign strictures or patients who receive treatment with curative intent, since it is associated with a high complication rate [56–58]. For gastric outlet obstruction, surgery has the potential of causing less long term morbidity dependant on the life expectancy of the patient, by reducing the risk of re-obstruction compared to stent placement. Surgery may be considered for patients with a short tumor length, a single site obstruction, and a life expectancy greater than 60 days [34,59]. Endoscopic ablative techniques are available to reduce proximal obstruction; however, these techniques have a substantial risk of bleeding or perforation and decreased peristaltic motility [36,60,61].

Conservative treatment with stimulation of intestinal passage appears ineffective in many cases of (benign and malignant) obstruction of the small intestine as the obstruction symptoms often reoccur in 47% up to 72% of patients within one year after

Table 1
Possible locations, causes, and treatment options for symptoms of obstruction in cancer patients.

Locations	Causes	Treatment options
Esophagus	– Intraluminal tumor presence or invasion – Extrinsic compression by tumor mass – Treatment-related edema – Initial worsening of obstructive symptoms due to chemo- or radiation therapy	– Conservative treatment (restoration of fluid and electrolyte balance, alternatives for feeding) – Endoscopic stent placement or ablation – No indication for surgery
Stomach	– Intraluminal tumor presence or invasion	– Conservative treatment (nasogastric decompression, restoration of fluid and electrolyte balance, alternatives for feeding) – Endoscopic stent placement – Surgical bypass or gastrectomy
Small intestine	– Postoperative adhesions – Postradiation strictures – Strangulation or hernia – Intraluminal tumor presence or invasion – Extrinsic compression by tumor mass – Peritoneal carcinomatosis	– Conservative treatment (nasogastric decompression, stimulation of stool passage, restoration of fluid and electrolyte balance, parenteral nutrition) – Laparotomy for adhesiolysis, bypass, bowel resection, or ileostomy
Colon/rectum	– Intraluminal tumor presence or invasion – Extrinsic compression by tumor mass – Pseudo-obstruction (Ogilvie's syndrome) – Volvulus – Diverticulitis – Intussusception – Anastomotic strictures after surgical resection	– Conservative treatment (nasogastric decompression, stimulation of stool passage, restoration of fluid and electrolyte balance, parenteral nutrition) – Endoscopic detorsion, stent placement, decompression, or ablation – Laparotomy for bowel resection, bypass, or ileocolostomy
Biliary tract	– Intraluminal tumor presence or invasion – Extrinsic compression by tumor mass – Postradiation strictures – Anastomotic strictures after surgical resection	– Percutaneous transhepatic or endoscopic (external or internal drainage) of biliary system – Endoscopic balloon dilatation or stent placement – Sphincterotomy – Surgical biliary-enteric bypass – Cholecystectomy or percutaneous cholecystostomy
Urinary tract	– Extrinsic compression by retroperitoneal or pelvic mass – Intraluminal tumor presence or invasion – Postsurgical fibrosis, structures, pelvic inflammatory disease – Catheter induced edema – Postradiation strictures	– Percutaneous nephrostomy catheter – Endoscopic ureteric stent placement – Suprapubic or transurethral bladder catheter – No indication for laparotomy
Airway	– Foreign body aspiration – Airway edema, hemorrhage, angioedema or infection – Tracheal stenosis – Intraluminal tumor presence or invasion – Extrinsic compression by tumor of head, neck, and lung	– Tracheotomy/-stomy, intubation – Bronchoscopy with tumor debulking, ablation, or stent placement – Steroids – Chemotherapy or external beam radiation therapy – No indication for extensive surgical exploration
Spinal cord	– Compression, displacement, or encasement of dural sac by epidural metastases or locally advanced cancer	– Glucocorticoids – External beam radiation therapy – Hormonal therapy, chemotherapy – Surgical decompression by laminectomy

initial relief [30,31]. When the cause of the obstruction is benign, one should not hesitate to perform a laparotomy for adhesiolysis or bowel resection [25,27,31,42]. In the case of radiation enteritis, it is important to resect the entire diseased bowel segment to reduce recurrence, postoperative complications and mortality [62–66]. In cases of malignant origin, surgical interventions such as bowel resection, bypass, or ileostomy, may seem to provide in good palliation by reduction of symptoms and obstruction recurrence in progressive disease, but depend on the extend of disease in the individual patient [15,27,32,42]. The invasiveness of surgery is associated with high treatment related morbidity and mortality rates. Thus, in case of malignant obstruction, surgery for malignant obstruction should be reserved for patients with resectable disease, good performance status (ECOG > 1), and a life expectancy of more than 6 months [26,34,50]. Surgery for patients with peritoneal carcinomatosis is associated with a 30-day mortality of 21–40% and high recurrence rates [59]. Non-invasive treatment with palliation of discomfort remains the best treatment for patients with incurable disease with peritoneal metastases, and for those who are not fit for surgery [25,31,32,42]. The acrimonious aspect of obstructions of the small intestine is that in many cases, the origin of the obstruction is only identified by surgical exploration and/or the final pathology report.

The treatment of colorectal obstruction depends on the cause and the clinical severity of the presentation. Benign causes with presence or risk of ischemia, perforation, or volvulus require emergency surgery [45]. For less emergent presentations, endoscopic detorsion or stenting must be considered as alternatives for surgery.

In cases of malignant colorectal obstruction, the urgency of treatment depends on the risk of perforation and subsequent complications [67]. For relief of the obstruction, the most optimal treatment would be surgical resection, bypass, or ileo-/colostomy with or without subsequent staged resection [26,45,47,67,68]. Surgery is reported to be successful for control of obstruction symptoms in 42–80% of procedures [69–71]. Surgical options for obstruction of malignant origin depend primarily on the location of the tumor, extend of the disease, and clinical performance status of the

patient [46,72,73]. When determining the appropriate surgical procedure for palliative cause, the risks and consequences of treatment-related complications and the burden of an ileo-/colostomy should be taken into account. The focus of surgery should be on the clinical outcome, i.e. short term relieve of the obstruction, long term reduction of morbidity and mortality and establishing optimal quality of life [26,47]. Presence of total obstruction or ascites seems to be associated with worse outcome and a reduced rate of palliation of symptoms after emergency surgery [69].

As the patient's condition is often very poor in the emergency setting, especially for patients with end-stage disease, emergency surgery is associated with a treatment related morbidity up to 61%, 30-day mortality of 9.8%, and overall mortality of 15–37% [45,69,74]. Endoscopic alternatives for surgery include tumor ablation and decompression by stent placement [45,46,75]. Endoscopic techniques are also associated with complications such as stent migration, stent stenosis, reocclusion, or bowel perforation with subsequent tumor spread [44,76,77]. When the patient's condition allows surgery, emergency surgery leads to better clinical relief for malignant colorectal obstruction compared to stent placement alone (98.84% clinical success vs. 78.05%, $p = 0.001$), without significant differences in mortality and morbidity [44,76]. However, endoscopic stent placement does have the benefit of lower pain scores shortly after the procedure, shorter procedure time and hospital stay, and minimal blood loss. Endoscopic stent placement can serve as a bridge to surgery at later stage or as palliative therapy, when surgery in the acute setting is not expected to be beneficial for the patient [45,75–79]. Previous studies are inconclusive in the long term advantages of the systemic use of stent placement to create elective opportunities for surgical resection [74,76–81]. It seems to provide in an increased primary anastomosis and decreased permanent stoma rates for left-sided obstruction, but there is no effect on the occurrence of anastomotic leakage, morbidity, and overall survival.

For patients with inoperable bowel obstruction, poor performance status (ECOG > 2) and short cancer-related life expectancy, refraining from invasive procedures and discharge from the hospital with palliation of nausea, vomiting and pain may be the best management at the end of life. The definition of a short life expectancy remains an ethical discussion point.

Obstruction of the biliary tract

Malignant obstruction of the biliary tract can be due to intraluminal tumor presence, local invasion of primary disease, or due to metastases of cancers of distant origin [15,82]. Biliary obstruction can result in secondary cholangitis [82]. Symptomatic cholangitis is characterized by jaundice, pruritus, fever, and abdominal pain and it can cause fibrosis, cirrhosis, and ultimately liver failure. Malignant biliary obstruction is most often caused by mass lesions due to either adenocarcinoma of the pancreatic head, periampullary neoplasms, intra- or extrahepatic cholangiocarcinoma, and metastatic lymphadenopathy in the hepatoduodenal ligament [82,83]. It can also be caused by strictures developed after radiation therapy or surgery. The overall prognosis of malignant biliary obstruction is poor; many patients who are symptomatic already have advanced disease and palliative treatment is often the only option [82,83]. Symptomatic hyperbilirubinemia, resulting in pruritus, cholangitis, or sepsis, are indications for emergency drainage [15,82]. In absence of cholangitis, immediate decompression is not necessary and there is time for staging and the evaluation of options for resection [15].

Management

Possible interventions for biliary obstruction are percutaneous transhepatic or endoscopic (external or internal) drainage of the biliary system, balloon dilatation, or stent placement [15,82,84]. Further alternatives are endoscopic sphincterotomy, and – the most invasive option – surgical biliary-enteric bypass [15,82,83]. As these procedures may lead to secondary infection and obstructive cholangitis, surgical treatment should only be performed in case of relatively fair oncological prognosis [15,83]. For patients with obstruction at the level of the common hepatic duct or higher, poor oncological prognosis, or poor performance status, placement of an external percutaneous biliary drainage catheter is most effective for palliation or to gain time for definitive treatment [15,82,83]. Possible complications of percutaneous biliary drainage are catheter dislodgement or obstruction, cholangitis, bile leak, extrahepatic hemorrhage, abscess formation, pneumothorax, and hemobilia [82,83] Stent placement provides better quality of life for patients with incurable disease and relatively fair life expectancy, when compared to the presence of external drainage catheters [82]. Technical success is reported to be more than 90% and the clinical success 77–98% [85]. A frequently occurring complication of stent placement (5–25%) is stent occlusion [82]. This is treated by stent replacement or placement of a percutaneous transhepatic internal–external drainage catheter. Galbladder outlet obstruction can be treated by cholecystectomy or percutaneous cholecystostomy, dependant on the ability of the patient to undergo surgery [15].

Urinary tract obstruction

Patients with retroperitoneal or pelvic malignant lesions can develop urinary tract obstruction [12,13,86]. Pelvic cancers such as prostate carcinoma, cervical cancer, and bladder carcinoma can cause bladder outlet obstruction [12,13]. Retroperitoneal malignancies, such as lymphoma, sarcoma, and metastatic lymphadenopathy from pelvic cancers, can cause ureteric obstruction. Large pelvic masses, such as ovarian carcinoma and pelvic sarcoma can result in bilateral ureteric obstruction. Obstruction is caused by either extramural compression or direct tumor invasion of the ureters, most frequently distal to the level of the common iliac vessels [12]. Benign causes for acute obstruction of the urinary tract in cancer patients can be fibrosis or pelvic inflammatory disease after surgery, catheter induced edema, or strictures after radiation therapy [86].

Patients with urinary tract obstruction present with flank pain and sudden anuria, sometimes alternating polyuria and progressive rise in serum creatinin [13]. Obstruction of the urinary tract can lead to hydronephrosis and subsequent infection and/or renal failure [13,86]. Patients with malignant obstruction are usually in poor condition with advanced metastatic disease, and palliative decompression can be performed [87].

Management

The aim of decompression is to secure renal function [88]. There is no indication for invasive laparotomy in cases of urinary tract obstruction. Decompression of the obstruction can be achieved by percutaneous nephrostomy catheters or an ureteric stent for obstructions of the upper urinary tract, and a suprapubic or transurethral bladder catheter in case of lower urinary tract obstruction [12,13,87,88]. When patients have a short life expectancy of only a few days or weeks and already significant renal failure, palliative pain control and refraining from any interventions may be the only suitable treatment [15].

Airway obstruction

Benign causes of the upper or lower airways in cancer patients include food or foreign body aspiration, airway edema or hemorrhage, angioedema, tracheal stenosis, and infections [13].

Malignant causes are intraluminal tumor growth or by extrinsic compression of the airway by tumors of the head, neck, and lung [13,21,23,89]. Dyspnea, cough, and wheezing are commonly the only early symptoms of airway obstruction [13,21,23]. If dyspnea occurs at exercise, the intraluminal diameter of the airway is usually decreased to about 8 mm [13]. However, if dyspnea occurs in rest, usually accompanied by stridor and/or retraction, and use of accessory muscles, immediate action is necessary since the airway diameter is expected to be critically narrow and less than 5 mm [13,21].

Management

A tracheotomy can be lifesaving in the acute setting for patients with an obstruction proximal to the larynx [13]. Semi-acute tracheostomy or intubation may be necessary [23,89]. Bronchoscopy with tumor debulking, ablation, or stenting are options for relief of more distal obstructions [13,89]. Steroids, chemotherapy or external beam radiation therapy may be helpful as well [13,21,23,89]. In case of extrinsic compression, stent placement is the preferred method of palliation [13,21,89]. Extensive surgical exploration of the obstruction is seldom performed because of the invasiveness of the procedure and the very poor prognosis in case of malignant airway obstruction [89]. For the same reasons, in cases of malignant obstruction, one should consider to refrain from any intervention or artificial ventilation, since many of them seem too invasive in cases of advances disease.

Malignant spinal cord compression

Malignant spinal cord compression (MSCC) is defined as compression, displacement, or encasement of the dural sac by spinal epidural metastases or locally advanced cancer and occurs in about 5–10% of all cancer patients [5,18,21]. MSCC is an oncologic emergency that becomes life threatening when it involves level C3 or higher, and requires immediate treatment to relieve pain and preserve neurological function [5,19,21].

Metastases from breast, renal, prostate and lung cancer are reported to account for the most common causes [5,18,19,21,23]. Symptoms of MSCC include local or radicular pain, worsening when lying down or during percussion of the vertebral bodies [5,18,19,23]. In a later stage, symptoms can be accompanied with neurological signs such as incontinence and loss of sensory function. Most patients will show abnormalities on plain radiographs of the spine, but the gold standard for assessing MSCC is magnetic resonance imaging (MRI).

Management

Management is effective in 90% of cases of early diagnosis and includes administration of high dose intravenous glucocorticoids with external beam radiation therapy, hormonal therapy, or chemotherapy [5,21,90]. The optimal dose and schedule of glucocorticoids and radiation therapy remain controversial in the literature [18,19]. Surgical decompression by laminectomy is indicated when pain and neurological symptoms are progressive despite initial treatment or spinal instability is present [5,18,19,21,23].

Infection

Patients with cancer frequently suffer from malnutrition and immune deficiency secondary to the disease or its treatment [82,91]. These factors can result in an increase in frequency, severity, and duration of infections, and also the development of infections caused by non-common pathogens [91].

Neutropenia is seen as a result of chemotherapy for leukemia, further, diminished function of T-lymphocyte and mononuclear phagocyte function is seen in patients with Hodgkin's and non-Hodgkin's lymphoma or in those receiving corticosteroids or chemotherapy. Alterations in B-lymphocyte function are seen in multiple myeloma, chronic lymphocytic leukemia, and secondary to chemotherapy. Typical manifestations of infections often change and may be masked due to immune deficiency [91,92]. In other cases, infections may manifest as severe life-threatening conditions, such as septic shock [91]. Immune deficient patients can develop infections of the gastrointestinal tract, such as perianal or perirectal abscesses, severe mucositis, candidiasis, neutropenic enterocolitis and other intraabdominal infections [29,91,92].

Neutropenic enterocolitis is a life threatening condition and has been associated with acute lymphatic leukemia and chemotherapy [29,92,93]. It is a transmural inflammatory condition of the right colon and particularly the cecum, in the setting of myelosuppression and profound neutropenia [15,29,93]. However, it is also reported to affect the transverse and descending colon, and even the rectum [94]. It is thought to be caused by ischemia due to distention, leukemic infiltration of the bowel wall, direct toxic effects of chemotherapy, and bacterial invasion of the bowel wall after change in bowel flora [15,29]. The cecum is a poorly vascularised, often most dilated part of the bowel, and therefore at greatest risk to be affected in case of increased intraluminal pressure [15,93]. Symptoms include abdominal distention, diarrhea, fever and right lower quadrant tenderness and it may mimic acute appendicitis [15,29,95]. Characteristic findings on computed tomography are thickened bowel wall and also occasionally pneumatosis of the bowel wall [15,29,92]. Neutropenic enterocolitis can lead to bowel necrosis with perforation and sepsis [93,96].

Another cause of right lower quadrant pain can be appendicitis [29,92,97]. Typical symptoms and ultrasound findings of appendicitis can be masked in immune deficient patients, and thus, symptomatic patients may already have developed peritonitis [29]. A similar infection that can develop in cancer patients is acute cholecystitis, either resulting from immune deficiency, as complication of locoregional treatment of hepatic cancer, or cholelithiasis [82,92]. Due to masking of symptoms, acute cholecystitis may develop into gangrenous cholecystitis, emphysematous cholecystitis or even gallbladder perforation [82].

Management

Broad spectrum antimicrobial therapy is the initial management of choice for any infection in immune deficient patients and should be continued until neutropenia resolves or for a minimum of 10–14 days [91].

For neutropenic enterocolitis, initial therapy should be conservative with bowel rest, nasogastric suction, broad spectrum antibiotics, administration of fluid and electrolytes, and total parenteral nutrition [15,29,92]. Patients should improve as their white blood cell count returns to normal [29]. Many patients who are treated successfully with conservative treatment may develop a relapse of neutropenic enterocolitis during a next course of chemotherapy [15,29,93,95,98]. In the past some authors have recommended prophylactic bowel rest with total parenteral nutrition during consecutive chemotherapy and even elective right hemicolectomy to prevent recurrence [95,98]. Prophylactic surgery is not common practice given the low incidence rates of fatal enterocolitis, the success rates of conservative treatment, the delay surgical interventions cause in chemotherapy cycles, and the invasiveness of the procedure [15]. If a patient doesn't improve after 2–3 days of conservative treatment, surgical resection of the right colon with primary or secondary anastomosis should be considered to prevent perforation [15,29,96]. Given the risks of surgery-related complications in patients with neutropenia, the consequences of a primary anastomosis after bowel resection and even the benefit of any

surgical procedure must be questioned for patients who are septic and severely ill.

Uncomplicated acute appendicitis and cholecystitis treated by appendectomy and cholecystectomy have been reported to have unproblematic postoperative course [92,97]. However, for high-risk, immune deficient or severely ill patients, less invasive image guided percutaneous cholecystostomy must be considered as a bridge to surgery or as definitive treatment for cholecystitis [82]. In the presence of ascites, the transhepatic approach should be executed for percutaneous drainage, given the risk of leakage of bile and ascites with subsequent peritonitis for the transperitoneal approach. Indications for surgical drainage of perianal infections in patients with neutropenia is usually based on the white blood cell count and the development of an abscess, since this is dependent on the presence of leukocytes, and associated with better wound healing, fewer complications, and lower mortality [92].

Patients with an acute abdomen require immediate surgery for survival [29,96,97]. Even though mortality is high for immune deficient patients, mortality in immune deficient patients with peritonitis who are treated conservatively is reported to be 100%.

Perforation

When there is clinical evidence of pneumoperitoneum, perforation of a hollow organ must be suspected [12]. Regardless of treatment, perforation of the gastrointestinal tract with the concomitant infectious complications is a serious life-threatening emergency with mortality up to 100% in case of an uncontrolled perforation [15,99,100]. In addition, perforation of primary tumor in the gastrointestinal tract is associated with a high risk on spread of tumor cells into the peritoneal cavity, worsening the patient's prognosis [15,99].

Perforation of the intestine can occur in cancer patients after prolonged obstruction [12,15,67,99]. Furthermore, it can result from localized intestinal wall replacement by tumor with subsequent tumor necrosis or from lack of normal mucosal integrity [15,99]. In tumors that are sensitive to chemotherapy, such as lymphoma, treatment responses in full-thickness intestinal wall tumor deposits with rapid necrosis of the malignant cells can lead to perforation [15]. Colorectal carcinoma and gastrointestinal lymphoma are malignancies that are associated with spontaneous perforation [12]. Perforation may result from complications of medicinal treatment such as steroids, NSAIDs, or from complications of chemotherapy, for example neutropenic enterocolitis and severe dehydration resulting in decreased bowel perfusion [15]. Last, some systemic agents, serving as anti-angiogenesic drugs such as bevacizumab for colorectal cancer, or sunitinib and imatinib for gastrointestinal stromal tumors (GIST), have been associated with intestinal perforation [12,15,101]. The evidence in the literature on the treatment of perforation induced by anti-angiogenic drugs is based on case series and there is no common approach for this emergency [102].

Perforation of other intraabdominal structures is also possible. Comparable to intestinal perforation, esophageal and gastric perforation can occur due to perforation of primary tumor, and due to secondary causes such as ischemia or treatment responses in gastrointestinal stromal tumors [15,38,103]. Malignant perforation of gastric cancer is often indicative of advanced disease [103].

Gallbladder perforation can be a complication of cholecystitis due to cholelithiasis, prolonged obstruction of the cystic duct, after biliary stent-placement, or locoregional ablation of hepatic cancer [82]. It is rarely associated with primary malignancy or metastases of the gallbladder. Symptoms can be similar to uncomplicated cholecystitis such as right upper quadrant pain or acute generalized peritonitis. Most gallbladder perforations are subacute with abscess formation or drainage into adjacent organs with fistula formation.

Management

Treatment of perforation of any organ depends on whether contents of the organ are spilled into the abdominal cavity, the patient's white blood cell count, and physical status [15,68,100]. It is based on drainage and control of the perforation with minimal stress for the patient, and following oncological principles.

Antimicrobial control is essential and broad spectrum antibiotics should be administered in any case. Urgent laparotomy is often necessary for the patient's survival in case of (suspection of) an uncontrolled perforation [15,46,99,103]. When there is a contained perforation with abscess formation and the absence of generalized peritonitis or sepsis, image-guided percutaneous drainage may be more suitable management [4,15]. In case of a primary non-metastasized tumor perforation of the intestine or stomach, surgery is justified and a formal resection with primary anastomosis or temporary ileo-/colostomy could remove both the primary tumor as well as the entire perforated segment [4,15,99]. Perforation of gallbladder is best treated by percutaneous drainage by cholecystostomy catheter or by directly draining the fluid collection as bridge to cholecystectomy [82].

For patients with poor performance who are septic and severely ill, and who are not expected to be fit for extensive surgical resections, a laparotomy with lavage of the peritoneum with or without proximal diversion by ileo-/colostomy, or an external drainage catheter is more appropriate [15,38]. This could allow resection at later stage. In case of perforation of intraabdominal structures during chemotherapy and subsequent neutropenia, mortality is very high due to infectious complications, even with aggressive broad spectrum antimicrobial therapy and surgical exploration [15]. Palliative care should be instituted for patients who are septic and have multi organ failure, who are not expected to benefit from surgery.

Bleeding

Hemorrhagic events in cancer patients may be caused by malignant disease or medical treatment [15,24,104]. Patients with visible bleeding can present with hematemesis, hemoptysis, hematochezia, melena, hematuria, vaginal bleeding, echymoses, petechiae, epistaxis, or ulcerated skin lesions [104]. Occult bleeding, i.e. intraperitoneal or retroperitoneal hemorrhage, can also develop [12]. Bleeding can occur in various stages of malignant disease and vary in severity [4,104]. It can originate from tumor invasion, local vessel damage, treatment response of tumor, or radiation injury. It can also result from coagulopathies or abnormalities in platelet function or number, induced by systemic therapy.

Severe intraabdominal bleeding can be caused by solid tumors, such as hepatocellular carcinoma, renal carcinoma, and melanoma [12]. Spontaneous rupture of the spleen caused by lymphoma or leukemia can also result in severe intraabdominal bleeding [12]. Bleeding can occur from solid malignancies of the gastrointestinal tract and other hollow organs such as the bladder, as a result of tumor invasion into the organ or mucosa [24]. Risk factors for bleeding from solid tumors include large tumor size, peripheral or subcapsular location, and increased vascularity [12]. Direct vascular invasion, increased intratumoral pressure, increased venous pressure or portal hypertension, and decreased autoregulatory mechanisms within the tumor vessels, can cause spontaneous bleeding [12].

Some chemotherapeutic agents and anti-angiogenic targeted therapies, are associated with increased bleeding tendency, decreased

wound healing, and gastric perforation [13,24]. Patients receiving radiation therapy for pelvic malignancies can develop lower gastrointestinal bleeding, and this may occur months to years after treatment [24]. NSAIDs, which are taken by many cancer patients as pain medication, are associated with an increased risk of gastrointestinal bleeding [24,104]. Coagulopathies, such as hyperviscosity syndrome or disseminated intravascular coagulation are possible causes of spontaneous bleeding in cancer patients [5,15,20,21,24]. Last, quantitative or qualitative platelet defects induced by liver failure, chemotherapy, hematological malignancies, or anticoagulants can be the underlying cause.

Management

In the acute setting, initial management of hemorrhage is based on hemodynamic monitoring, establishment of intravenous access, and fluid resuscitation or even transfusion of blood products if necessary [4,24,104]. Agents that advance bleeding or inhibit coagulation should be eliminated, and definite treatment of solid bleeding tumors should be initiated [24]. Prior to any intervention, if possible, identification of systemic abnormalities and localization of the bleeding source by (interventional) angiography or endoscopy is preferable [4,104].

Systemic interventions for bleeding include correction of underlying coagulopathies and platelet defects by administration of clotting factor, vitamin K, vasopressin, somatostatin analogs, antifibrinolytic agents or blood products [82,104]. Applying local pressure, hemostatic or vasoconstricting agents and dressings may provide in temporary measures for local bleeding from skin lesions, nose, vagina or rectum [104].

Endoscopy is an effective minimally invasive method for bleeding in the gastrointestinal tract, lungs, and bladder [4,24,104]. It can be used for localization, but also for hemostasis using injection of sclerosing agents, heater probe, electro- or photocoagulation. Nevertheless, sometimes it can be difficult to identify the location of the bleeding, and bleeding often recurs when it originates from the tumor site. Angiography and interventional radiologic embolization of blood vessels is minimal invasive, can be very effective, also for localization, and limits the need for laparotomy [4,104]. However, it is limited by multiple factors [104]; presence of a bleeding disorder, accessibility of the target blood vessels, subsequent ischemia of important non-target organs, and the availability of appropriate expertise. Radiation therapy can be considered for hemoptysis, bleeding from skin lesions, vagina, rectum and bladder and may be effective in 60–85% of cases [90,104].

Emergency surgery may be required to control severe bleeding with persistent hemodynamic instability despite attempts of resuscitation, failure of other therapy, and recurrent bleeding [4,24,103,104]. However, surgery is often difficult after a long trial of conservative treatment due to clinical deterioration after great blood loss or coagulopathies.

Pathological fractures

Bone injury can result from primary bone tumors or metastases from lung, prostate, breast, kidney, thyroid cancer and all kinds of other malignancies [15,105–107]. After radiation therapy, bone tissue can become hypovascular, hypocellular and hypoxic, and the bone has a decreased ability to replace the normal collagen and cellular losses [106]. Furthermore, androgen deprivation therapy, for example in the treatment of prostate cancer, is associated with development of osteoporosis [108]. Bone injury in cancer patients becomes emergent in case of pathological fractures, spinal cord compression, hypercalciemia, bone marrow infiltration and severe bone pain [105,107].

Management

Studies on the use of bisphosphonates have shown to have a positive effect on prevention of skeletal-related events in patients with bone metastases originating from breast or prostate cancer, and multiple myeloma (up to 10% absolute risk reduction) [108–110]. Acute cancer related fractures are an indication for surgery and are treated with internal fixation or joint prostheses dependent on the fracture type and underlying malignant cause (i.e. primary tumor or metastatic) [15,107]. However, healing rates of pathological fractures are dependent on the type of malignancy and have been reported to be between 0% and 67% [107]. Whatever fixation device is used, it is recommended to use a device that will last as long as the life expectancy of the patient, and stabilizes the entire diseased bone at once. Additional radiation therapy is often indicated for local control and quality of life. Opinions differ on the best radiation scheme for bone metastases. Single dose regimens have been compared to multifraction regimens and no differences were noted for symptomatic improvement. Different regimens may be indicated for patients with short or longer life expectancy. For palliation of severe bone pain, radiation therapy and bisphosphonates may be effective [15,107,109]. The exact mechanism of action of radiation therapy on bone pain is unknown [107].

Patient selection, palliative care, and quality of life

No cancer patient is equal in potential to recover from extensive procedures in the acute setting. There are many factors which can't be measured or compared in randomized studies that play a role in the process of decision making concerning treatment for surgical emergencies. The patient's performance status, cancer stage and life expectancy, type and severity of the emergency, and – most importantly – the patient's and families wishes regarding invasiveness of treatment, are major determinants for the choice of therapy and clinical outcome [15,104]. These determinants are individually diverse and it is difficult to define prognostic factors and the right treatment for cancer patients in an emergency setting [111]. When possible, in any emergency situation it is important to create the opportunity for diagnostic methods in order to identify the cause of the emergency, and for multidisciplinary evaluation.

In the absence of curative treatment options, the aim of palliative therapy should be to reduce symptoms without reducing the quality of life [83]. The risk of intervention related complications may be greater than a beneficial outcome and may even reduce survival. When interventions are insufficient in patients with poor condition, refraining from invasive therapy with palliation of discomfort will be the only appropriate option left [15]. Therapy for any emergency depends on the individual case and ethical considerations regarding extensive procedures, quality of life, and continuation of treatment [112]. It is essential to inform the patient and family about the prognosis of the condition, treatment options, and the expected impact and benefit of treatment. Personalized policies and a multidisciplinary approach are necessary for optimal treatment and/or palliation, to suffice the patient's and families wishes, and to prevent unnecessary invasive procedures at the end of life.

Summary

To our knowledge, this is the first review on surgical emergencies in oncology. There are various surgical emergencies that can occur in cancer patients and these can have either benign or malignant origin. The most frequent surgical emergency experienced by cancer patients is obstruction of the gastrointestinal tract. Obstruction can also develop in other structures, such as the urinary tract, airway, or spinal cord. Other surgical emergencies

include perforation of the gastrointestinal tract, bleeding events, infections due to immune deficiency, and pathological fractures. The patient's performance status, cancer stage and prognosis, type and severity of the emergency, and – most importantly – the patient's wishes regarding invasiveness of treatment are essential during the decision making for optimal management. The complications of the oncologic emergency can be more life threatening than the risks of an intervention, whereas for others, the intervention itself can cause worse outcome and shorten survival. The institution of palliative (terminal) care may be more appropriate for some patients. Personalized policies and a multidisciplinary approach are necessary for optimal treatment and/or palliation, to suffice the patient's and families wishes, and to prevent unnecessary invasive procedures at the end of life.

Conflict of interest

None declared.

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