Abdominal Complications Following Hematopoietic Stem Cell Transplantation
We use the term hematopoietic stem cell transplantation (HSTC) better than bone marrow transplantation because cells may come from bone marrow, peripheral blood stem cells or umbilical cord blood.

**Indications**

- **Malignant hematologic disorders:**
  - Acute myeloid leukemia (AML)
  - Acute lymphoblastic leukemia (ALL)
  - Chronic lymphocytic leukemia (CLL)
  - Myelodysplastic syndrome (MDS)
  - Hodgkin lymphoma (HL)
  - Non-Hodgkin lymphoma (NHL)
  - Multiple myeloma (MM)

- **Nonmalignant hematologic disorders**

- **Immunologic disorders**

- **Solid tumors**

- **Genetic disorders**
Types of transplantation
- Autologous: minor risk for developing complications/higher relapse rates of tumor
- Allogenic: genetically different (matched/mismatched) in terms of histocompatibility
- Syngenic: an identical twin

Conditioning regimen
- Myeloablative conditioning
- Non-myeloablative “mini” conditioning
- Non-myeloablative conditioning
There are three periods defined with concrete risk factors based on the immune status:

- **The pre-engraftment phase**: lasts for 15 to 30 days following transplantation. It is characterized by pancytopenia and severe neutropenia.

- **The early posttransplantation phase**: among the 30 and 100 days after transplantation. Persistent cellular and humoral deficiency that increases the risk of viral infections.

- **The late posttransplantation phase**: begins 100 days after transplantation. A progressive recovery of cellular and humoral immune function.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Introduction. Current state

Complications following stem cell transplantation:

- Pulmonary (40-60%)
- Abdominal (60-80%): Hepatobiliary, Gastrointestinal, Genitourinary
- Head and neck
- Muculoskeletal

Hepatobiliary complications

Hepatic toxicity caused by drugs

Hepatic veno-occlusive disease (VOD)

Acute hepatic graft versus host disease (GVHD)

Infections

Cholangitis
Hepatobiliary complications

Hepatic VOD

Pathology: obstruction of hepatic sinusoids with subsequent fibrosis and portal hypertension. Most often occurs following myeloablative conditioning.

Incidence: 54% of patients receiving allogenic transplants and <50% of patients receiving autologous transplants. Frequent among the first and fifth week posttransplantation.

Clinical: painful hepatomegaly, jaundice, unexplained weight gain (Seattle’s criteria), ascites.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Hepatic VOD

Ultrasound (US)
- Gallbladder wall thickening
- Ascites
- Narrowed hepatic veins (HV)

Doppler US
- Hepatofugal portal venous flow
- Monophasic flow pattern in the HV
- Increased hepatic artery resistance (>0.8)
- Paraumbilical circulation

Transabdominal US (a,b) and color doppler US portal vein (c), hepatic vein (d) hepatic artery (e) in a 25 year-old man with AML 18 days post allogenic HSCT with proven biopsy of hepatic VOD with minimal ascites (arrow) as the only finding
Transabdominal US, color doppler US hepatic vein and portal vein in a 32 year-old man with HL 15 days post allogenic HSCT. Diffuse gallbladder wall thickening (a); narrowed and monophasic flow in right hepatic vein (b); reversal of flow in portal vein (c). Findings suggestive of hepatic VOD.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Hepatic VOD

CT:

• Periportal edema
• Diffuse heterogeneous liver parenchyma attenuation
• Narrowed hepatic veins
• Ascites

RM:

• Heterogeneous hyperintense T2W signal.
• Narrowed hepatic veins
• Periportal edema
• Marked hyperintense signal in T2W of the gallbladder’s wall

Axial contrast enhanced CT in a 22 year-old patient with NHL, 20 days post allogenic HSCT. Diffuse hypodense liver parenchyma, not visualized hepatic veins, periportal edema and ascites. Proven biopsy of hepatic VOD
Axial T2-weighted, T1-weighted and gadolinium enhanced MRI of a 45 year-old patient with MM. Diffuse hyperintense signal of hepatic parenchyma, narrowed hepatic veins, edema of gallbladder wall, splenomegaly. Heterogeneous enhancement of the liver parenchyma on the arterial phase image. Proven biopsy of hepatic VOD.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Definitive diagnostic: biopsy

Hepatic VOD

Hepatic GVHD
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Hepatic GVHD

**Incidence:** 9-50% allogenic transplants. Among 2°-10° post-transplant week

**Clinical:** painful hepatomegaly, jaundice, nausea, vomit

<table>
<thead>
<tr>
<th>VOD</th>
<th>GVHD</th>
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<tr>
<td><strong>Time frame</strong></td>
<td><strong>1-5 wk</strong></td>
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<tr>
<td>Periportal edema</td>
<td>++</td>
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<tr>
<td>Ascites</td>
<td>+++</td>
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<tr>
<td>Narrowed HV</td>
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<tr>
<td>Small bowel wall thickening</td>
<td>+/-</td>
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<td>Doppler</td>
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Axial contrast enhanced CT of a 42 year-old patient with Myelodisplastic Syndrome. 45 days post allogeneic mismatched HSCT. Skin, gastrointestinal tract and liver acute GVHD. Thickening of the gallbladder wall and minimal periportal edema.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Hepatic infections

Bacterial and fungal

Clinical: fever, painful hepatomegaly

At neutropenic phase it is possible that alterations are not detected. The exploration should be repeated if clinical suspicion persists.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hepatobiliary complications

Hepatic infections

Ultrasound: hypoechoic, bull’s eye, wheel in wheel lesions

CT: hypoattenuating lesions with hyperattenuating ring
Sometimes arterial phase shows them better

MR: hypointense in T1W and hyperintense in T2W
Enhancing ring after gadolinium contrast
Transabdominal US in a 22 year-old patient with NHL. 15 days post autologous HSCT. Disseminated candidiasis. Small hypoechoic lesion with central hyperechoic area ("bull’s eye") (arrows)
Axial contrast enhanced CT in a 22 year-old patient with NHL. Pre-engraftment phase, oral and hepatosplenic candidiasis. Small hypodense lesions in the liver with peripheral enhancement in some of them compatible with abscesses.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Gastrointestinal tract complications

Acute GVHD
Pseudomembranous colitis
Neutropenic colitis or typhlitis
Infectious enterocolitis
Benign pneumatosis
Thrombotic microangiopathy
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Gastrointestinal tract complications

GVHD

Pathology: damage of the recipient’s epithelium produced by the donor’s lymphocytes

Incidence: among the second and tenth week after allogenic transplant (30-50%) depending on the grade of histocompatibility

Clinical: organs most likely to be affected are: skin, gastrointestinal tract and liver. It courses with diarrhea, abdominal pain, fever, nausea, vomit
CT

- Without oral contrast and with i.v contrast
- Any segment of the digestive tube could be affected
- Thickening of the intestine wall, water halo sign, mucosal enhancement, serosa enhancement
- Bowell dilatation
- Mesenteric fat stranding
- Ingurgited vessels
- Ascites

Axial contrast enhanced CT without oral contrast in a 65 year-old patient with AML, 35 days after allogenic HSCT. Skin and gastrointestinal GVHD. Diffuse bowel folds thickening with mucosal hyperemia and “halo sign” and ascites. Stomach, small bowel and colon affected.
Axial contrast enhanced CT without oral contrast in a 22 year-old patient with NHL, 45 days after allogenic HSCT. Folds thickening and “halo sign” in small bowel and mesenteric stranding. Intestinal GVHD
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Gastrointestinal tract complications

Pseudomembranous colitis

Pathology: acute infection colitis caused by toxins produced by an unopposed overgrowth of Clostridium difficile after broad spectrum antibiotic

Incidence: pre-engraftment phase

Clinical: acute diarrhea, abdominal pain and fever
Gastrointestinal tract complications

Pseudomembranous colitis

CT:
  - With i.v contrast and without oral contrast
  - Pancolitis; the most damaged segment is descendent colon and rectum
  - Thickening of the colon’s wall, secondary to intense edema
  - Mucosal enhancement: the most typical is “accordion sign”
  - Mesenteric fat stranding (lower grade than in other colitis)
Axial contrast enhanced CT in a 54 year-old patient with AML, pre-engraftment phase. Diffuse circumferential rectal and colonic wall thickening, “accordion sign”, pericolonic fat stranding and ascites. Psudomembranous colitis
Gastrointestinal tract complications

Neutropenic colitis (typhlitis)

**Pathology:** rare complication in adults (more frequent in children). Consists of a mucositis *with* damaged mucosal barrier

**Incidence:** among 0-30 days after transplant

**Clinical:** fever, vomit, right lower quadrant pain and bloody diarrhea
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Gastrointestinal tract complications

Neutropenic colitis (typhlitis)

CT:

- Most likely to be affected: cecum, right’s colon and terminal ileum’s wall
- Thickening of the cecum and terminal ileum’s wall
- Mucosal enhancement
- Pericolonic fat stranding
- It is possible to observe necrosis signs secondary to intestinal ischemia
Axial contrast enhanced CT in a 34 year-old patient with nodular sclerosis HL, 6 days after allogenic HSCT. Cecal wall thickening, pericolonic stranding and terminal ileum involvement (arrow). Neutropenic colitis (Typhlitis).
Axial contrast unenhanced CT in a 26 year-old patient with AML, 10 days after allogenic HSCT. Pneumatosis (arrows) appearing after typhlitis.
Gastrointestinal tract complications

Infectious enterocolitis

Pathology: bacterial (*Pseudomonas, Klebsiella*) fungal (*Aspergillus, Candida*) virus (*Cytomegalovirus, Rotavirus, Adenovirus*) and parasites

Incidence: among 0-100 days after transplantation

Clinical: main symptom is diarrhea with fever
CT:

- The most significant finding with high positive predictive value is a marked thickening wall and nodularity of a long segment of the bowel.

- It is possible to observe intestinal ischemia with pneumatosis in the intestinal wall.
Axial contrast enhanced CT without oral contrast in a 67 year-old patient with AML, 60 days after allogenic HSCT. Small bowel, ascending and transverse colon wall thickening, hepatosplenomegaly and ascites. Cytomegalovirus infection.
Axial contrast enhanced CT in a 52 year-old patient with NHL, 22 days after allogenic HSCT. Localized small bowel wall thickening with pneumatosis and mesenteric stranding. Pseudomonas aeruginosa bacteremia
PATOLGOY: It is thought to be caused by steroid therapy which induces hypertrophy of Peyer patches that results in mucosal defects through which gas can track.

INCIDENCE: Among 30-100 days.

CLINICAL: Asymptomatic patients. Responds to conservative management.
CT:
- Pneumatosis in the intestinal wall
- Pneumoperitoneum
- Mesenteric or portal gas
- Differential diagnosis with infectious colitis or perforation
Axial contrast enhanced CT without oral contrast in a 33 year-old patient with AML, 80 days after allogenic HSCT. Benign pneumatosis intestinalis in the colon wall (ascending, tranverse and descending), dilated small bowel. GVHD on steroid therapy
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Complicaciones Intestinales

Thrombotic microangiopathy

Pathology: uncommon complication with high mortality rate. Damage to the microvasculature followed by microthrombo formation. Considered by many as grade IV GVHD

Incidence: among 0-100 days

Clinical: intense bloody diarrhea which does not respond to conservative management
Complicaciones Intestinales

Thrombotic microangiopaty

CT:
• Without oral contrast. Basal and with i.v contrast
• Slight thickening of the small intestine’s wall
• Intraluminal and intramucosal hemorrhages
• Mesenteric fat stranding
• Bowell dilatation
Axial contrast unenhanced CT (a,b) and contrast enhanced CT (c,d) in a 30 year-old patient with CML, 37 days after allogenic HSCT. Increased intraluminal and mucosal attenuation (bleeding), hypodense submucosal zone, distended small bowel loops, ascites and mesenteric stranding.
Renal and urinary tract complications

Hemorrhagic cystitis

Renal abscesses and pyelonephritis

Renal vein thrombosis

Renal lithiasis
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Renal and urinary tract complications

Hemorrhagic cystitis

Pathology: two forms differing in moment of appearance and severity

• Early: a few days after transplantation. Responds to conservative management

• Late: among eighty and one hundred days posttransplantation. Generally associated with GVHD. Surgical intervention

Clinical: hematuria and dysuria
ABDOMINAL COMPlications FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Renal and urinary tract complications

Hemorrhagic cystitis

US and CT

- Thickening of the bladder wall
- Intraluminal clot
- Mucosa sloughed
- In CT with i.v contrast intense mucosal enhancement
Transabdominal US of the bladder (a,b) and axial contrast enhanced CT (c,d) in a 26 year-old woman with ALL, 3 days after allogeneic HSCT. Diffuse thickening of the bladder wall and intraluminal clot (a,b). Diffuse contrast enhancement of the bladder wall, ascites and right anexial cyst (c,d)
Abdominal complications following hematopoietic stem cell transplantation

Renal and urinary tract complications

Renal abscesses and pyelonephritis

Pathology: bacterial and fungal

Incidence: in pre-engraftment phase

Clinical: fever, low urinary symptoms
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Renal and urinary tract complications

Renal abscesses and pyelonephritis

Ultrasound:
- Normal or with hypoechoic or hyperechoic lesions

CT:
- With i.v contrast
- One or more wedge shaped areas of lesser enhancement that extends from the papilla to the renal cortex
- Alternating bands of hypoattenuation and hyperattenuation
Axial contrast enhanced CT cortico medular (a, b) and nephrographic phase (c, d) in a 29 year-old patient with AML, 35 days after the second allogenic HSCT. Minimal perfusion defects in the kidney cortex (arrows). Systemic candidiasis.
Transabdominal and Doppler US (a,b) and axial contrast enhanced CT (c,d) in a 35 year-old patient with AML, 35 days after allogenic HSCT. Hyperechoic/hypodense mass effect in the left kidney (*). Focal bacterial nephritis.
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Late complications

Post-transplantation linfoproliferative syndrome

Chronic GVHD

Second tumors
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Late complications

Post-transplantation linfoproliferative syndrome

Pathology: uncontrolled overgrowth of virus Epstein Barr

Incidence: 1-1.5% allogenic transplants

Clinical: hepatosplenomegaly and lymphadenopathy
**Late complications**

**Chronic GVHD**

**Pathology:** the most common late complication. Patients who have acute GHVD generally develop the chronic form, although it is not an essential requirement.

**Incidence:** 60-80% allogenic transplant

**Imaging findings:** gastrointestinal GHVD often courses without imaging findings whereas hepatic chronic GHVD usually to have findings similar to primary sclerosing cholangitis

**Diagnostic:** must be performed through biopsy
MR enterography in a 34 year-old patient with CML, 100 days after allogenic HSCT. No abnormal findings in MR enterography with proven biopsy of chronic GVHD.
ABDOMINAL COMPLICATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Late complications

Second tumors and recurrence

**Incidence**: patients who have undergone HSTC are at higher risk (8.3) of developing second tumors in the future: dermatological, oropharyngeal, gynecological, thyroid

**Clinical**: the majority of the tumors are treatable and don’t course different from patients who haven’t undergone HSTC

Higher relapse rate of recurrence at two first years
Axial contrast enhanced CT in a 45 year-old patient with MM, one year after allogenic HSCT. Liver masses (*), solid lesions in the small bowell wall (arrows) and massive ascites. Aggressive recidiva of MM.
Axial contrast enhanced CT in a 45 year-old patient with NHL, 60 days after autologous HSCT. Bilateral pleural effusion, hypodense mass in the retrocrural, pleural and retroperitoneal spaces. Recidiva of lymphoma
Abdominal Complications Following Hematopoietic Stem Cell Transplantation

Conclusion
**Neutropenia**

- Pancytopenia
- Persistent cellular and humoral deficiency
- A progressive recovery of cellular and humoral immune function

- Bacterial and fungal infections
- CMV
- Neutropenic colitis
- VOD
- Early hemorrhagic cystitis
- Late hemorrhagic cystitis
- Acute GVHD
- Chronic GVHD

- Posttransplantation
- Lymphoproliferative syndrome
- Second tumors