S-O-S

Chemotherapy-induced sinusoidal obstruction syndrome in colorectal cancer

Dr Catherine Payne, ST5 Radiology Registrar, NHS Lothian
Dr Thomas Eriksen, Consultant Radiologist, NHS Forth Valley

Learning Objectives

1

Recognise the common association between chemotherapy agents used for colorectal cancer and hepatic sinusoidal injury

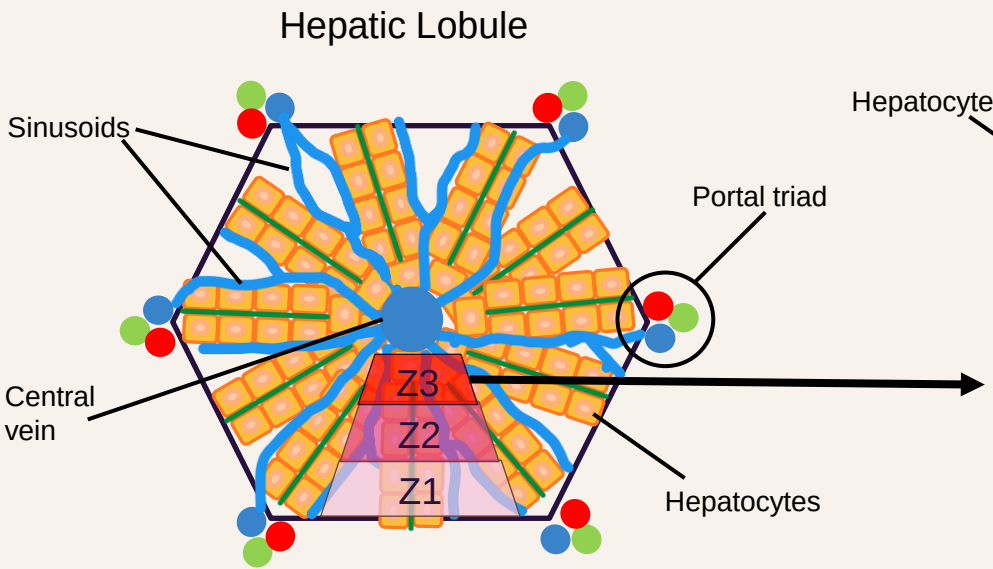
2

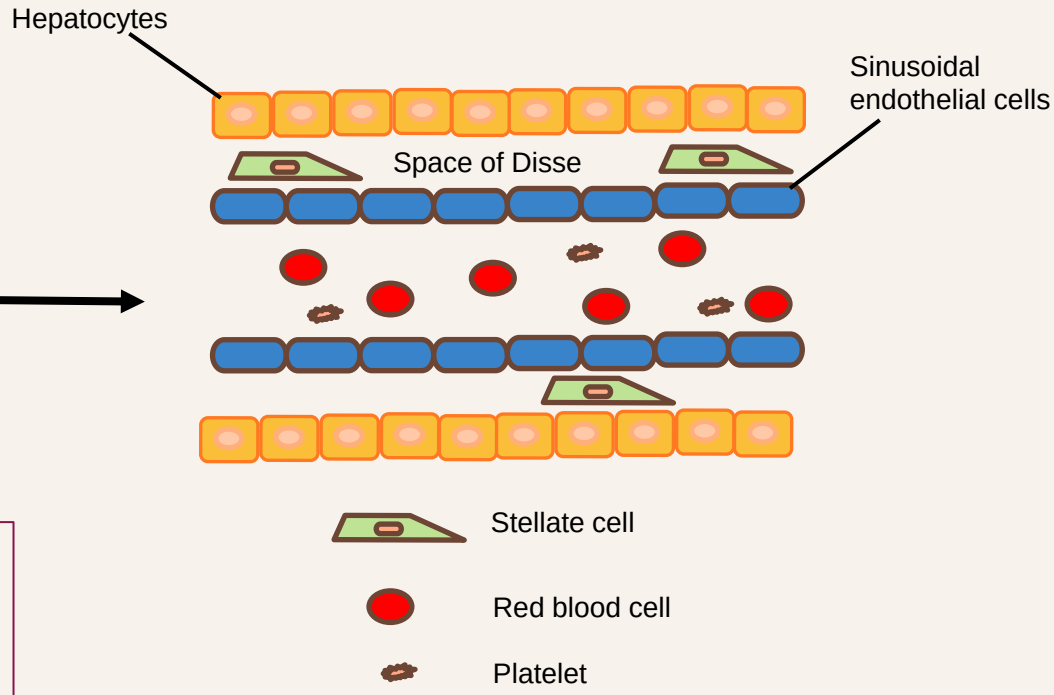
Identify the characteristic imaging features of sinusoidal obstruction syndrome (SOS)

Background

- Sinusoidal obstruction syndrome (SOS), formerly known as veno-occlusive disease, is a condition caused by toxic injury to hepatic sinusoids.
- SOS was first recognised as a complication of haematopoietic stem cell transplantation (HSCT) in 1979. In this setting SOS is often severe with high mortality rates.
- SOS in colorectal cancer (CRC) has only been discovered in the last couple of decades following the introduction of newer chemotherapy agents in both adjuvant and neo-adjuvant settings.
- Oxaliplatin is the most frequently implicated drug with pathological evidence of sinusoidal injury in up to 78% of patients.
- In patients undergoing resection of liver metastases SOS has been linked to decreased tumour response, increased intra-operative blood transfusion requirements, prolonged postoperative hospital stays, liver failure and reduced overall survival.

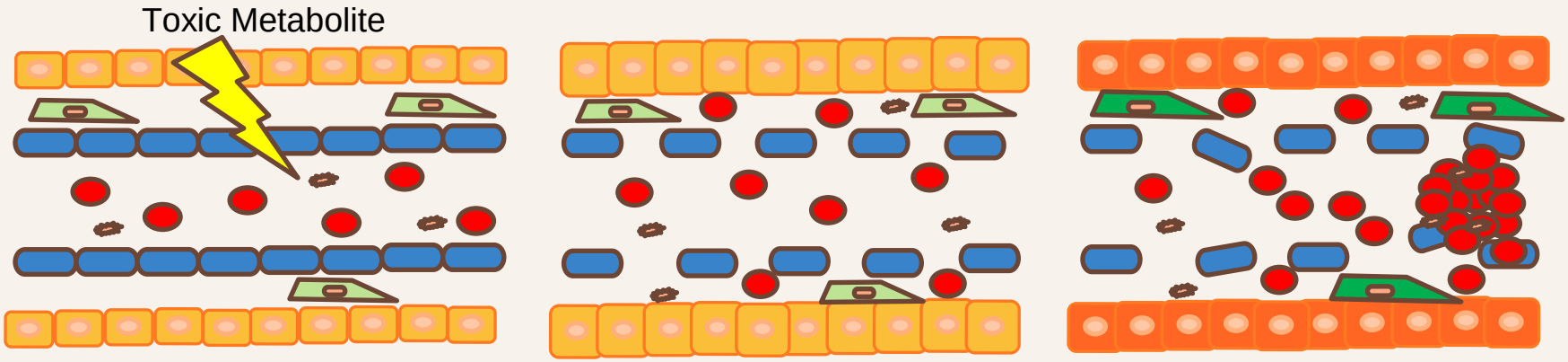
Pathophysiology





Hepatocytes in zone 3 are vulnerable to toxic insult as they are closest to the central vein and receive the least oxygen

Pathophysiology



Toxin

Damage to vulnerable sinusoidal endothelial cells (Zone 3)

Loss of fenestration

Swelling of cells

Dissection of endothelial lining

Sloughed cells embolise

Obstruction of sinusoidal blood flow

Hepatocyte damage

Clinical Presentation

Majority of cases are mild and most patients are **asymptomatic**

By contrast, in HSCT >60% of cases are moderate/severe with mortality rate of severe SOS as high as 80%

When **symptomatic** patients may present with:

- Right upper quadrant pain
- Hepatosplenomegaly
- Ascites
- Jaundice
- Abnormal liver function tests

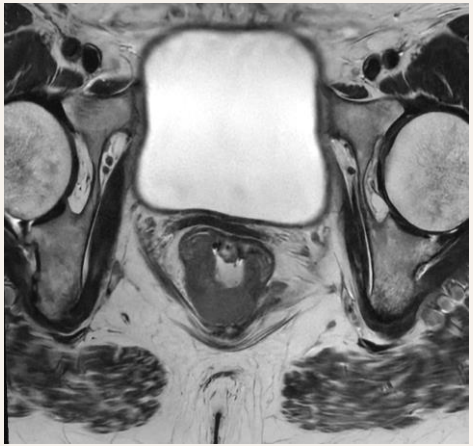
Imaging findings

Specific:
Diffuse reticular hypointensity on hepatobiliary phase MRI (specificity >95%).

Non-specific:
Heterogenous appearance of liver parenchyma on CT/MRI. Features of hepatic congestion and portal hypertension including; hepatosplenomegaly, ascites, recanalisation of the umbilical vein, paraoesophageal varices, gallbladder wall and periportal oedema.

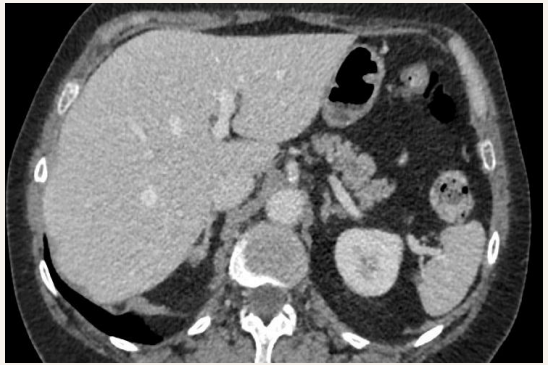
Case 1

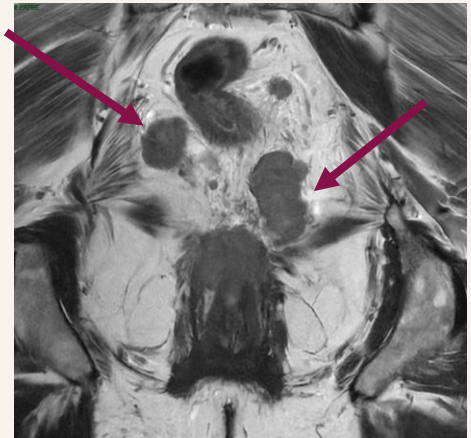
Clinical history: 56Y female with low rectal cancer and bulky pathological mesorectal lymph nodes. Treated with neoadjuvant chemoradiotherapy regimen including platinum-based chemotherapy (Oxaliplatin).



Axial T2 MRI shows mass in low rectum.

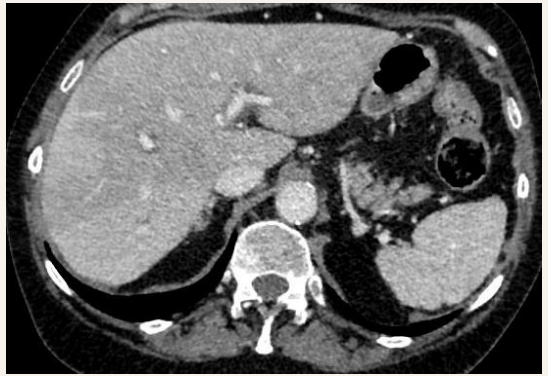
CT at diagnosis demonstrates normal liver parenchyma.





Coronal T2 MRI shows large abnormal mesorectal lymph nodes (arrowed) and rectal mass.

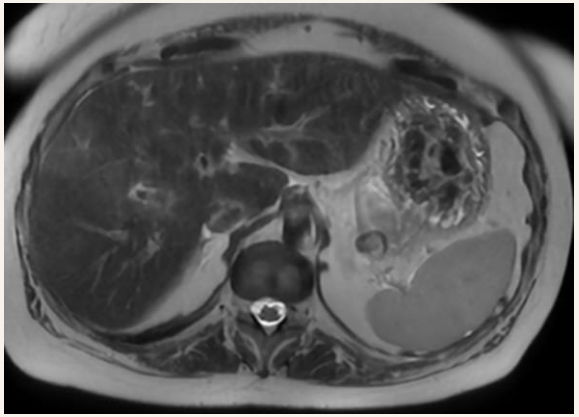
CT following neoadjuvant chemoradiotherapy identified new heterogeneity of liver parenchyma.

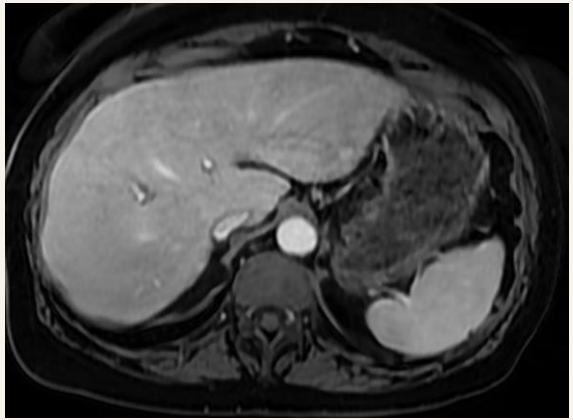


Case 1

The cause for the change in appearance of the liver on CT was uncertain and MRI with hepatocyte-specific contrast was arranged. This demonstrated classical appearances of sinusoidal obstruction syndrome.

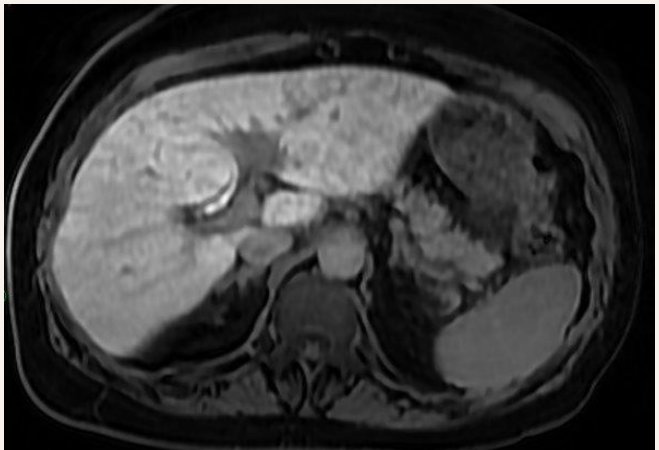
T2w MRI shows heterogenous liver with patchy increased signal.





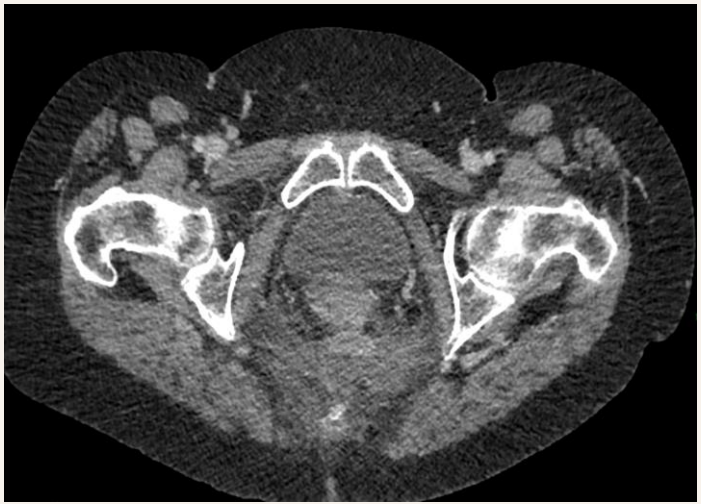
Portal venous phase is unremarkable. Note absence of reticular hypointensity.

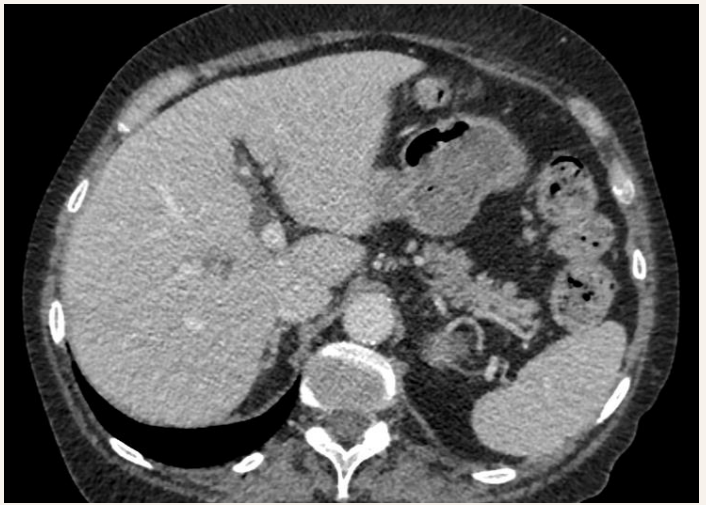
Hepatobiliary phase MRI demonstrates characteristic diffuse reticular hypointensity.



Case 1

The patient remained asymptomatic with normal LFTs and underwent abdominoperineal resection 3 months later.

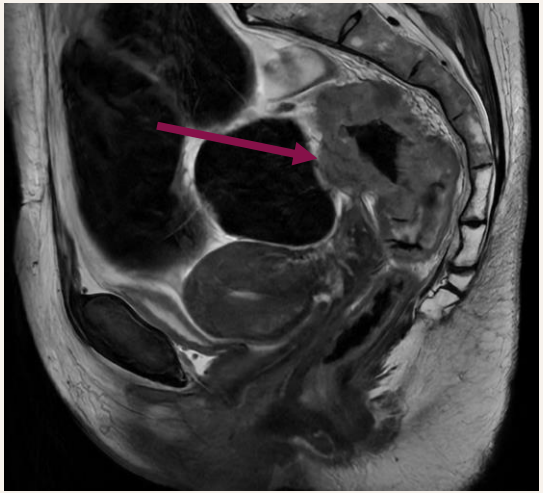




CT at time of resection demonstrates normal liver enhancement with some interval volume loss in the left lobe.

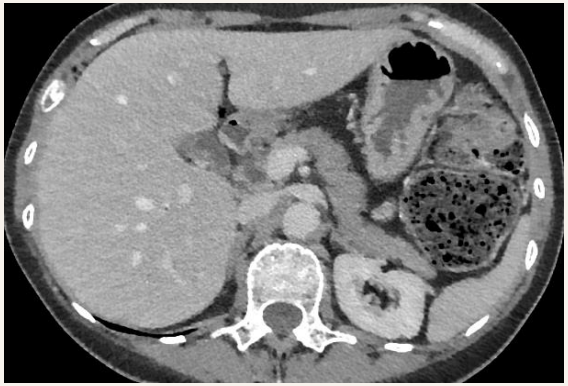
Case 2

Clinical history: 48Y female with locally advanced upper rectal cancer. Treated with neoadjuvant chemoradiotherapy with FOLFOX regimen (folinic acid, fluorouracil and oxaliplatin)

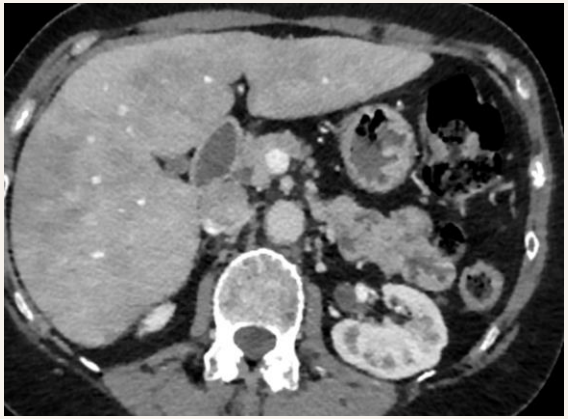


Sagittal T2w MRI demonstrates bulky tumour at rectosigmoid junction with invasion of the peritoneal lining (arrow)

CT at time of diagnosis demonstrates normal liver parenchyma

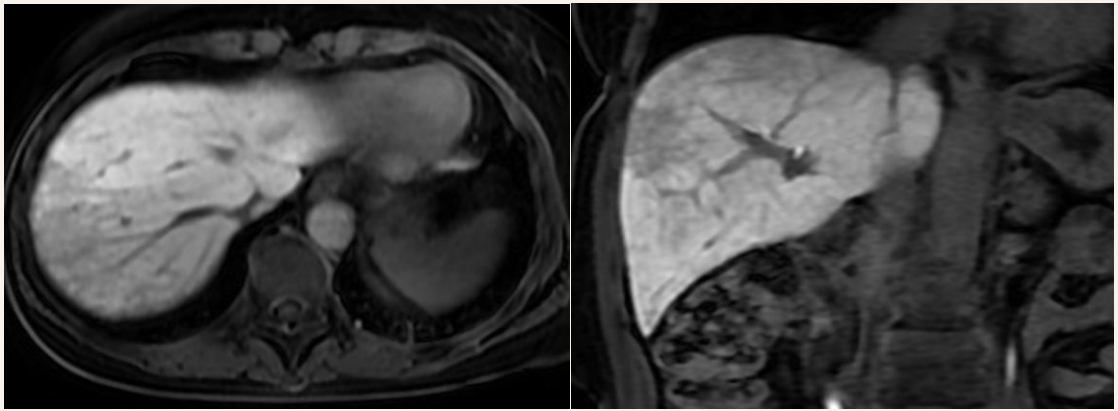


New patchy heterogeneity of the liver parenchyma identified on follow up CT to assess therapeutic response

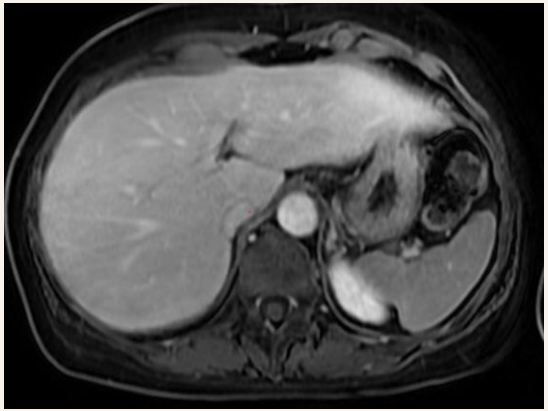


Case 2

MDT discussion raised possibility of liver metastases or sinusoidal obstruction syndrome. Subsequent MRI with hepatocyte-specific contrast demonstrated classical appearances of SOS. The patient remained asymptomatic with normal liver function and proceeded to pelvic exenteration.



Hepatobiliary phase axial and coronal images demonstrating diffuse reticular pattern of the liver parenchyma in keeping with sinusoidal obstruction syndrome.



Portal venous phase sequence from the same study is unremarkable.

Summary

- Sinusoidal obstruction syndrome is a common but under-recognised complication of chemotherapy for colorectal cancer.
- Diffuse reticular hypointensity during hepatobiliary phase MRI is a striking and highly specific feature.
- Chemotherapy-induced SOS appears to be less severe than in HSCT and is commonly asymptomatic. However, limited data is available, and further research is necessary to determine the full clinical impact in CRC patients.
- SOS is associated with increased peri-operative morbidity for resection of liver metastases and pre-operative diagnosis may help to improve outcomes.

References

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