

Metastatic Cholangiocarcinoma

Julia M Chernis

Dr. Allen Wolfe (MSK Fellow), Dr. Colleen Costelloe (Attending)

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RAD 4001

56 yo F with known history of cholangiocarcinoma presents to ED on 1/28/2020 with chest pain, SOB, and abdominal distention.

Presented June 2019 with N/V and RUQ abdominal pain. CT scan showed liver lesion and satellite lesions. Mixed cholangiocarcinoma and hepatocellular carcinoma diagnosed by liver biopsy.

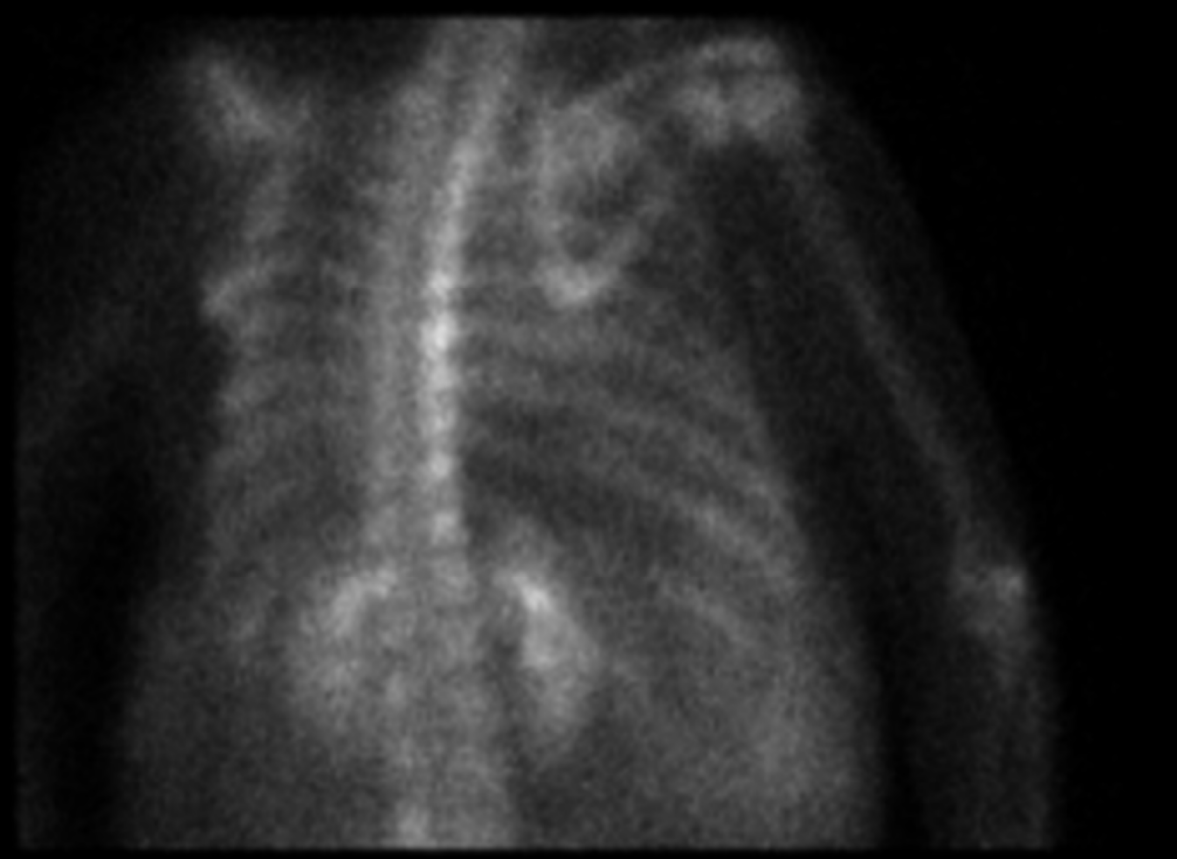
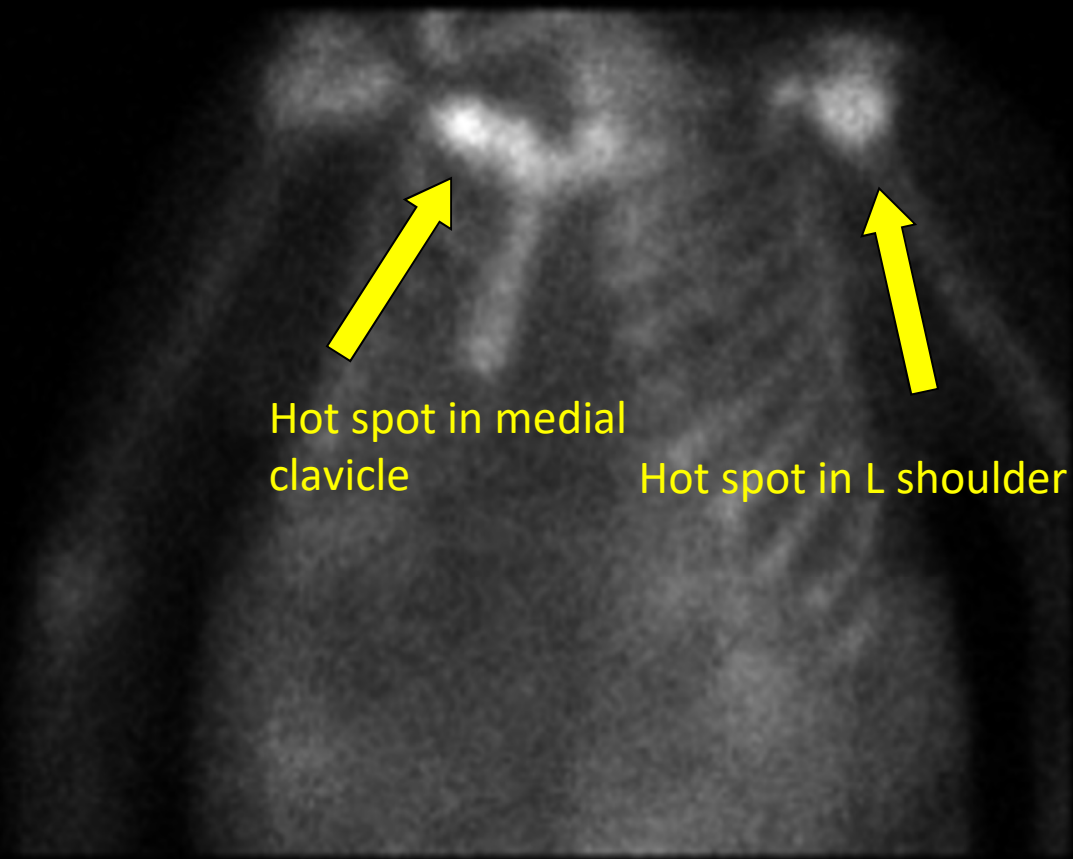
FOLFOX (leucovorin, fluorouracil, oxaliplatin) 8/2019 - 9/2019

GEM/CIS (gemcitabine and cisplatin) 10/7/19 - 12/19

9/2019 CT Scan - Heavy tumor burden with left adrenal metastasis. Increasing ascites. Tumor thrombus right portal vein. Displaced fracture of the right medial clavicle.

9/2019 Bone Scan - increased tracer involving medial aspect of right clavicle suggesting previous trauma. No evidence of metastasis.

Bone Scan 9/2019



Initial Workup in ED

Physical Exam

VS: HR 121, RR 20 BP 104/71, T 97.3, Sat 96% on RA

CV: RRR, no murmurs, no gallops

Resp: CTAB, no wheezes, no rales

Abd: distention, generalized tenderness, fluid wave, no rebound or guarding, no deformity

MSK: no chest wall deformity or tenderness

CBC:

Hgb: 8.8

WBC: 9.2

Abs. Neut: 7.27

Platelet: 302

CMP:

Normal electrolytes

Albumin: 2.9

AST: 56

ALT: 15

Bili Total: 0.2

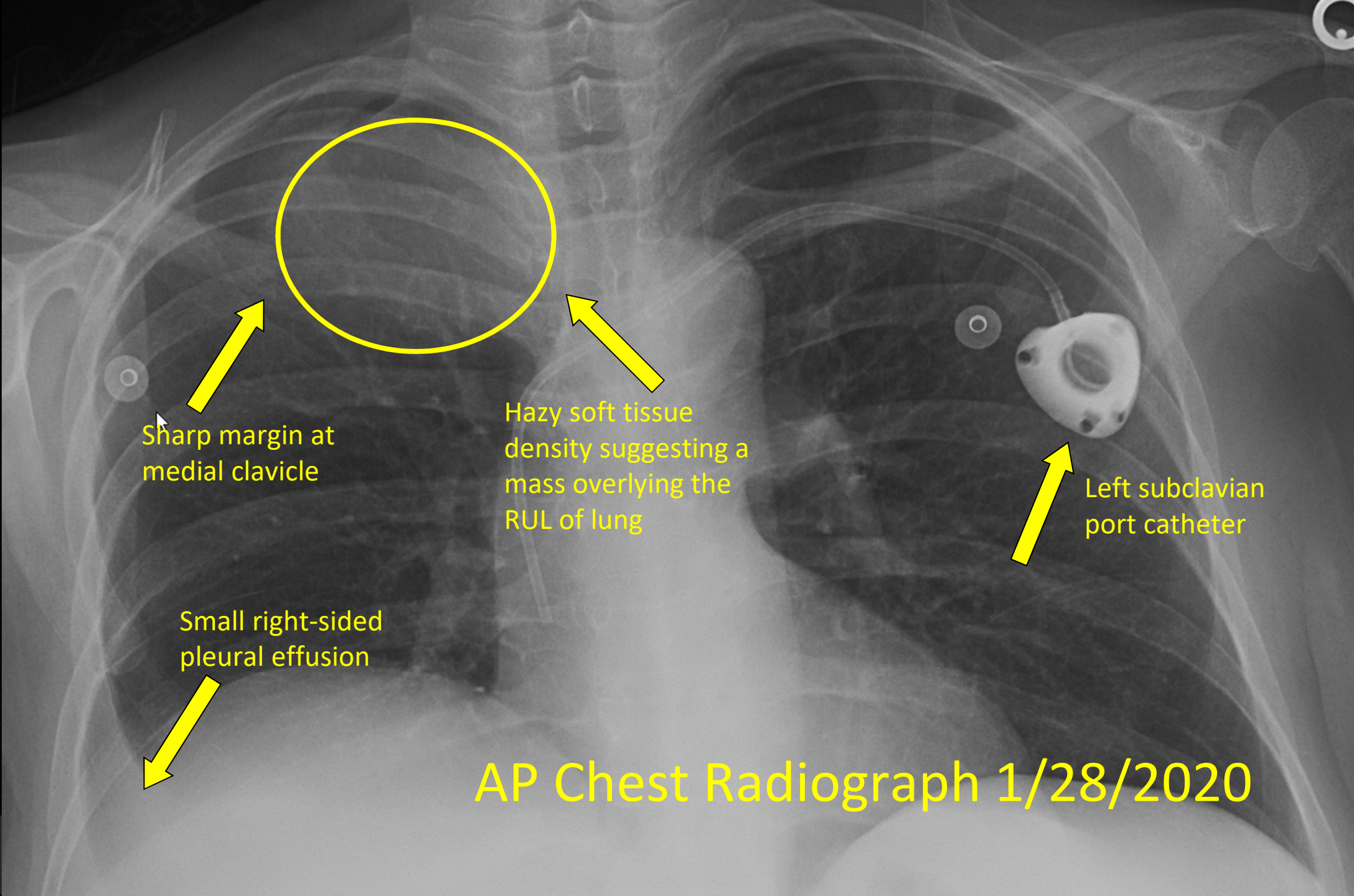
Bili Direct: <0.1

Coagulation:

PT: 13.5

PTT: 29.2

D-dimer: 5.25



Sharp margin at
medial clavicle

Hazy soft tissue
density suggesting a
mass overlying the
RUL of lung

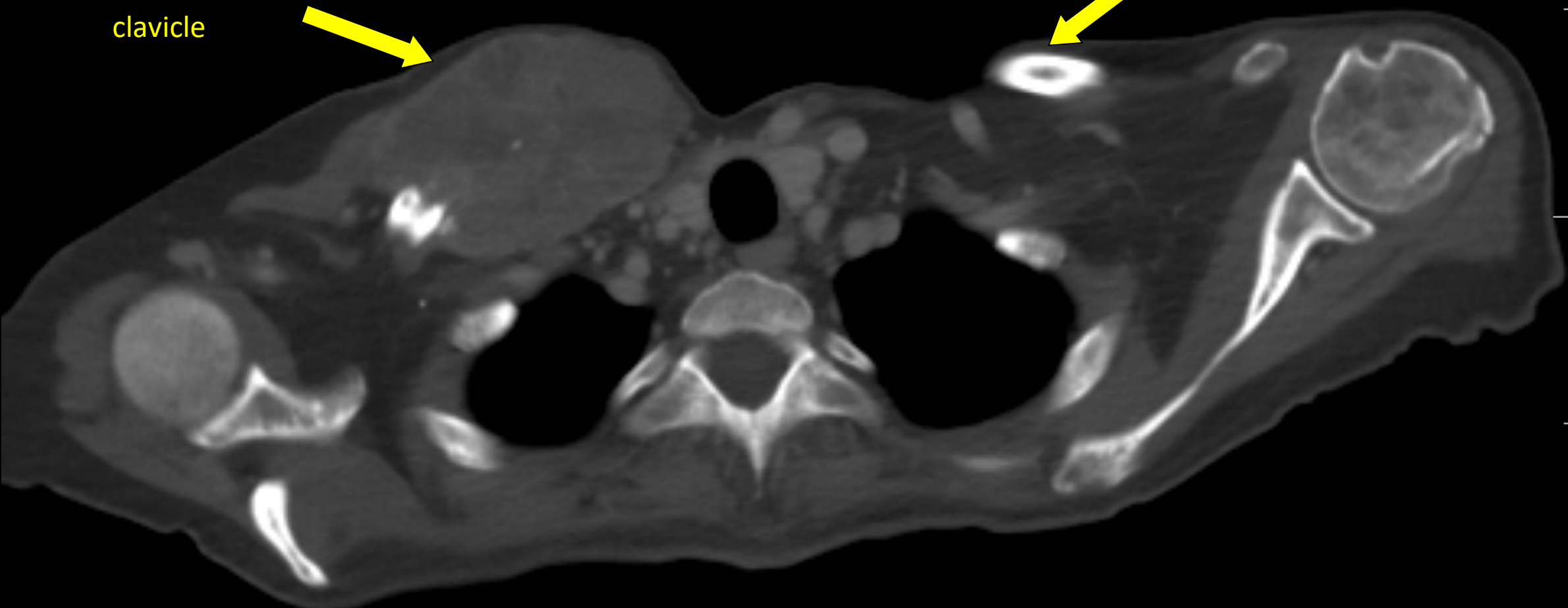
Left subclavian
port catheter

Small right-sided
pleural effusion

AP Chest Radiograph 1/28/2020

7.4 x 4.9 cm destructive
soft tissue mass in R
clavicle

Normal Left clavicle



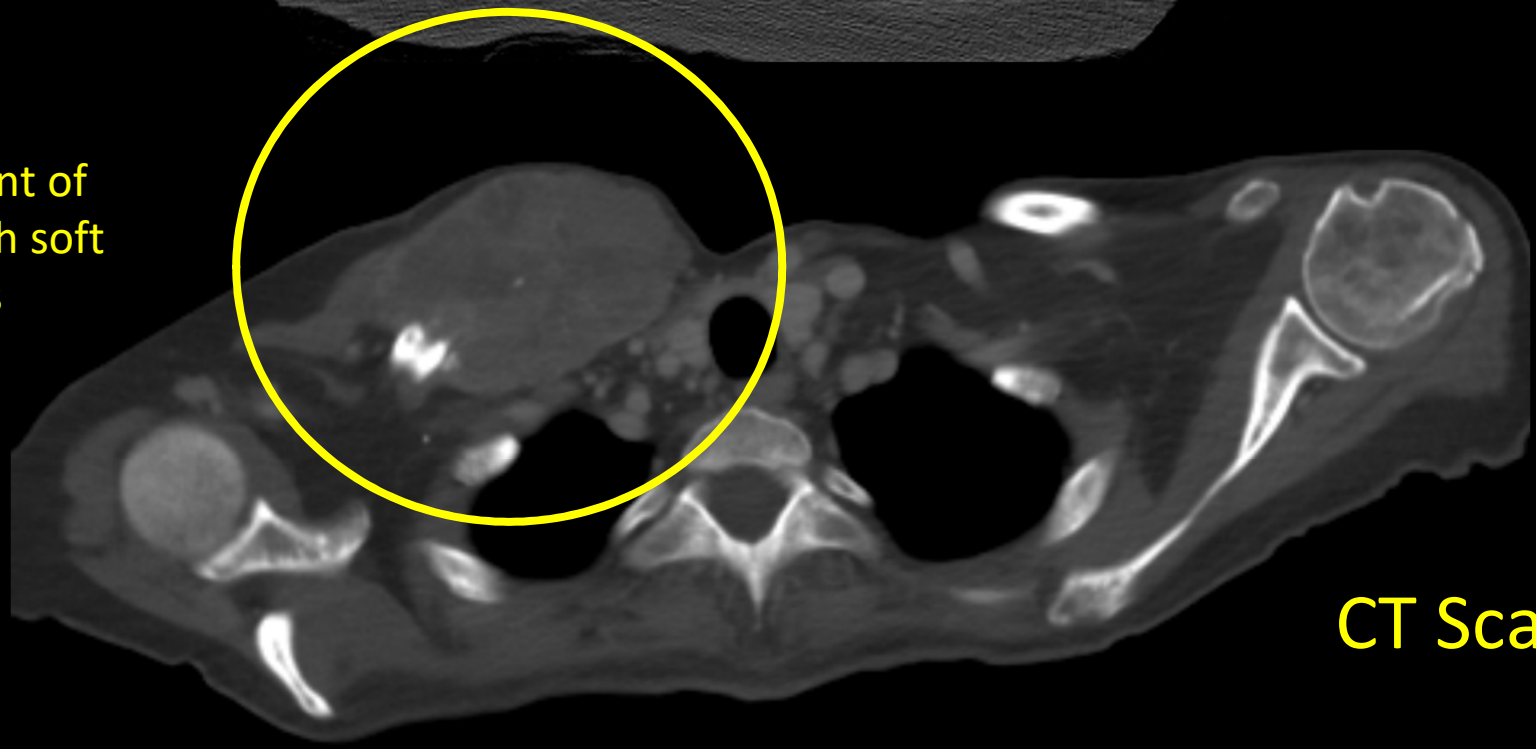
Transverse CT CAP Without Contrast 1/28/2020

Displaced fracture of the right medial clavicle



CT Scan 9/2019

Replacement of clavicle with soft tissue mass



CT Scan 1/28/2020

Coronal CT CAP without contrast 1/28/2020

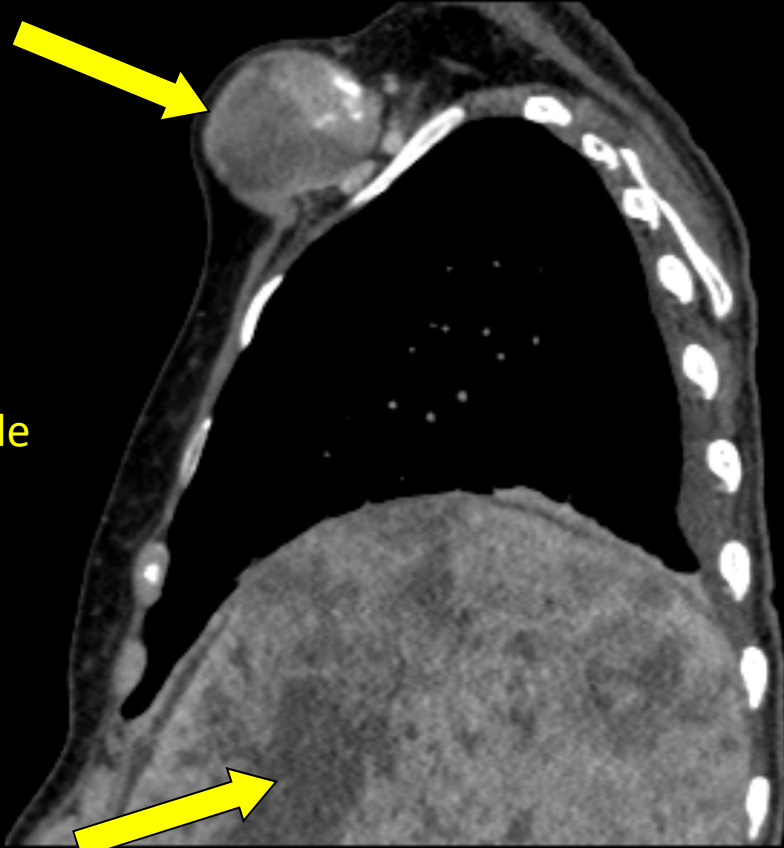


Obliteration of medial right clavicle and replacement with heterogeneous soft tissue

Normal Left Clavicle

Scattered hypoattenuated lesions in right liver consistent with advanced cholangiocarcinoma

Sagittal CT CAP without contrast 1/28/2020



Key Findings

- 56 yo F with known history of cholangiocarcinoma found to have clavicular mass at site of previous fracture

Differential Diagnosis

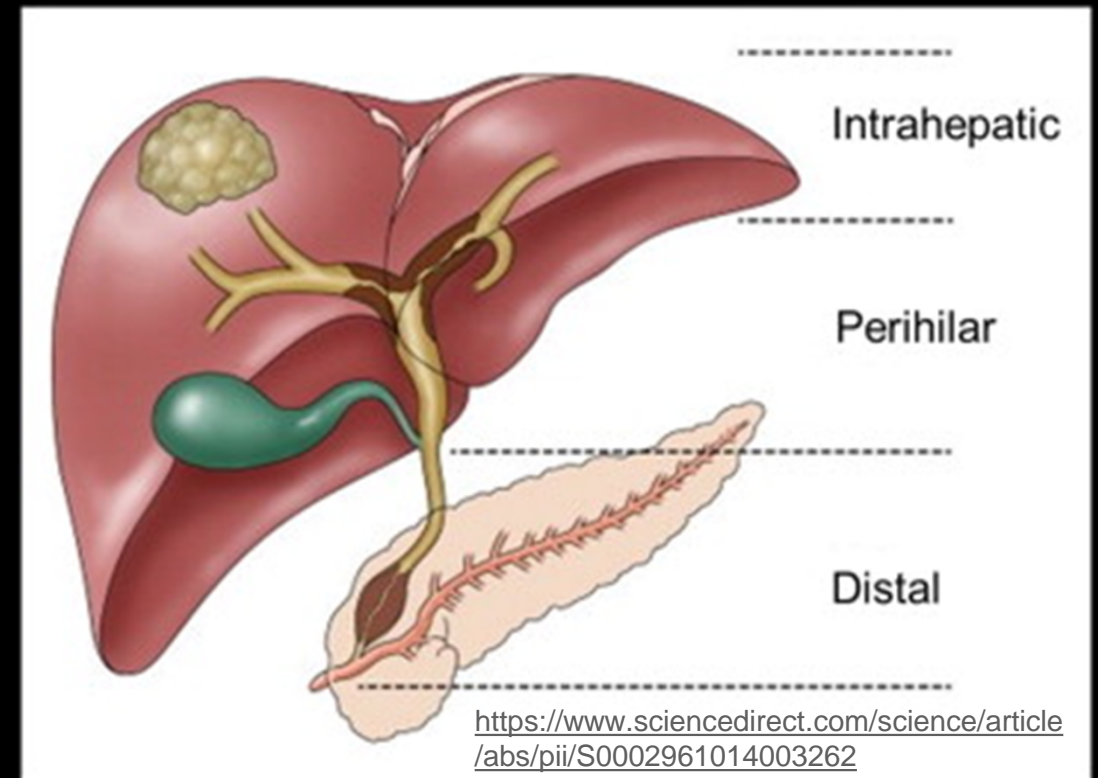
- Metastatic cholangiocarcinoma¹
 - Most likely, due to presence of primary tumor
 - Unusual site for metastasis
- Osteosarcoma²
 - Most commonly presents with bone pain in the metaphyseal region of long bones
 - Generally arise as consequence of Paget disease or bone infarcts in older adults +65
- Aneurysmal bone cyst³
 - Benign tumor-like lesion associated with deformity and pathological fracture of any bone in the body. Expanding osteolytic lesions containing blood-filled spaces of variable size.
 - Soap-bubble appearance on Xray with well-defined sclerotic bone margins

Final Diagnosis

- Stage IV mixed hepatocellular and cholangiocarcinoma with bone metastasis to the clavicle originally presenting as pathologic fracture.
- In ED: 1750 cc of ascitic fluid drained and patient discharged for f/u with her outpatient provider

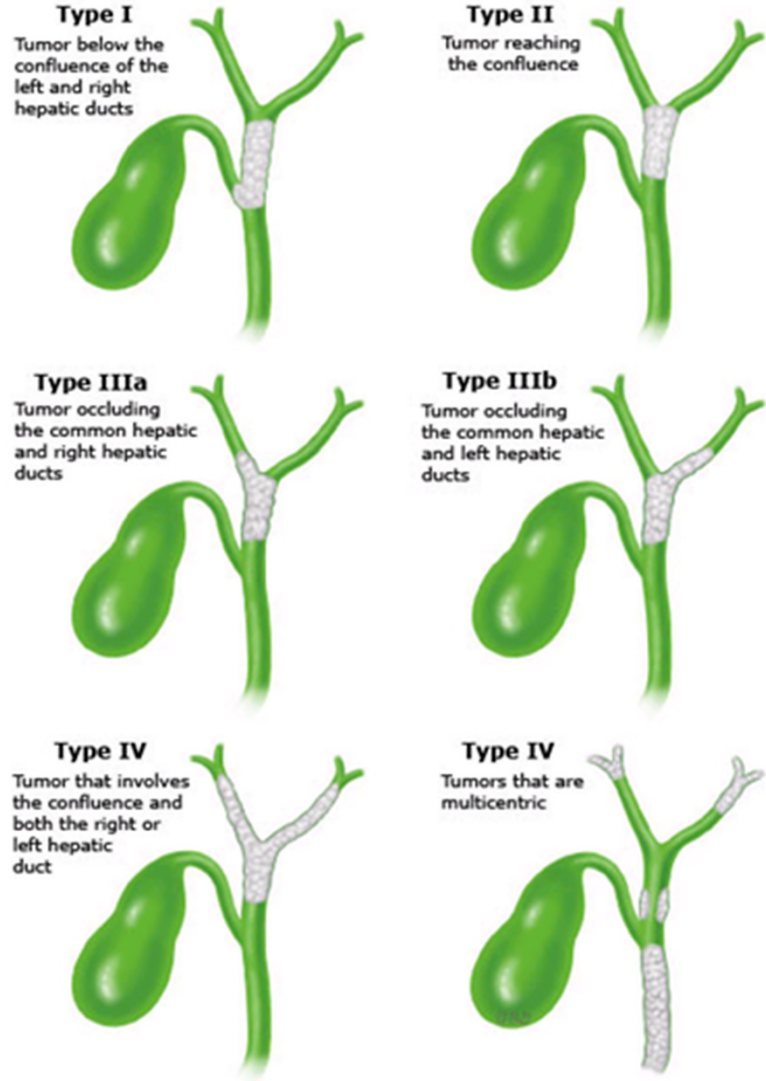
Discussion

- Cholangiocarcinoma
 - Bile duct cancer
 - Highly lethal because often advanced at presentation¹
 - Epidemiology: Rare in the US. 1-2 per 100,000
 - Risk factors: primary sclerosing cholangitis, chronic liver disease (cirrhosis, viral infection), chronic hepatolithiasis, Lynch syndrome, Schistosoma



- Liver and surrounding lymph nodes are most common sites of metastasis
- Distant metastases to peritoneum and lung are uncommon but can occur in advanced disease. Brain and bone mets are even less common.⁴

Bismuth-Corlette classification of biliary tract cancers

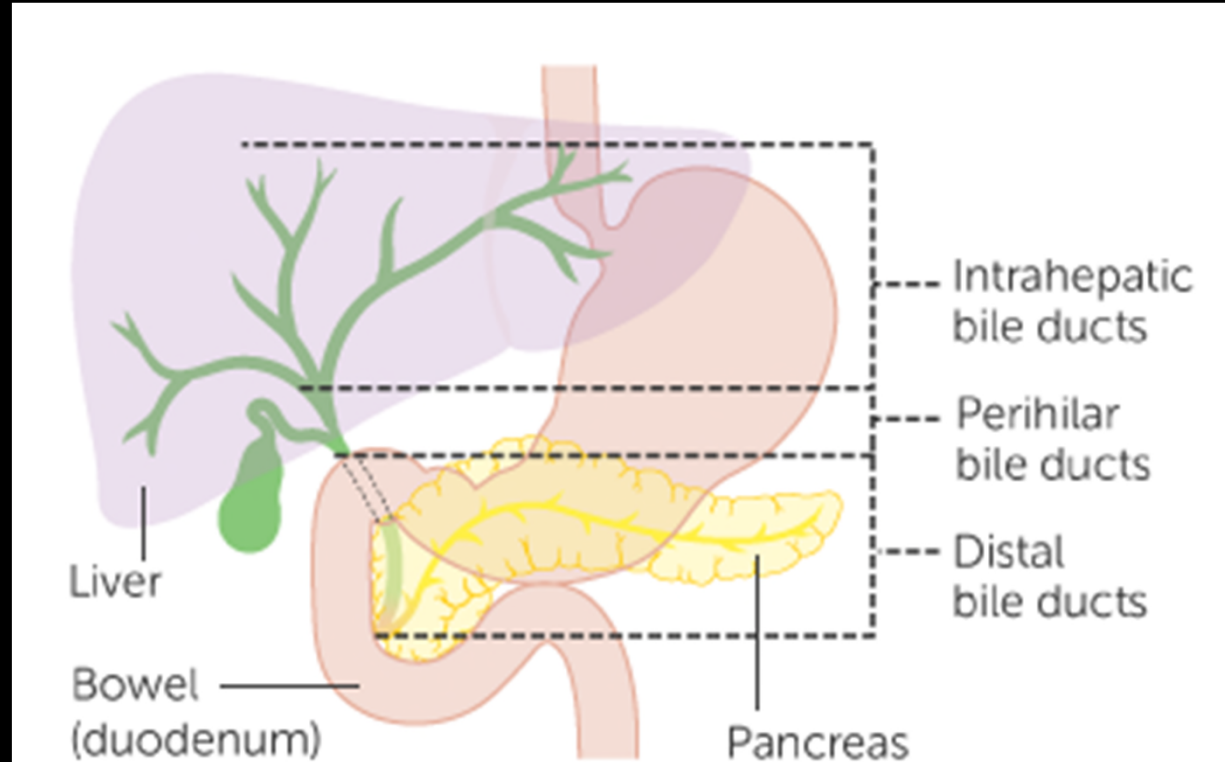


The Bismuth-Corlette classification of biliary tract. White areas represent tumor and green areas normal bile duct.
Modified from de Groen PC, Gores GJ, LaRusso NF, et al. *N Engl J Med* 1999; 341:1368.

UpToDate®

Bismuth-Corlette Classification

Based on patterns of involvement of hepatic ducts for perihilar tumors ⁴



<https://www.cancerresearchuk.org/about-cancer/bile-duct-cancer/stages-grades/stages>

Cancer Research UK

McGovern Medical School

Staging - TNM (Tumor, Nodes, Metastasis)

Staging by the American Joint Committee on Cancer (AJCC)/Union for International Cancer control gives separate staging systems based on location of bile ducts. ⁴

Mixed hepatocellular and cholangiocarcinoma type falls into intrahepatic bile duct category.

Any distal metastasis of this subtype is automatically classified as Type IV.

Intrahepatic bile duct cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)

T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma <i>in situ</i> (intraductal tumor)
T1	Solitary tumor without vascular invasion, ≤5 cm or >5 cm
T1a	Solitary tumor ≤5 cm without vascular invasion
T1b	Solitary tumor >5 cm without vascular invasion
T2	Solitary tumor with intrahepatic vascular invasion or multiple tumors, with or without vascular invasion
T3	Tumor perforating the visceral peritoneum
T4	Tumor involving local extrahepatic structures by direct invasion

Regional lymph nodes (N)

N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis present

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis
M1	Distant metastasis present

Prognostic stage groups

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1a	N0	M0	IA
T1b	N0	M0	IB
T2	N0	M0	II
T3	N0	M0	IIIA
T4	N0	M0	IIIB
Any T	N1	M0	IIIB
Any T	Any N	M1	IV

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.

Prognosis

- Defining tumors by their location in the bile ducts has helped improve the accuracy of prognostic predictions.⁴
- 5 year survival is < 16.2%

Stage-stratified comparison in 5-year survival outcomes between the 7th (2010) and 8th (2017) edition of the AJCC staging system, Kaplan-Meier analysis

	N (%)	5-year (%)	95% CI
AJCC 7th edition*			
I	93 (18.1)	58.8	44.9-70.3
II	110 (21.4)	38.8	26.5-51.0
III	70 (13.6)	39.7	24.1-54.9
IVa	242 (46.9)	18.4	11.9-6.1
AJCC 8th edition†			
Ia	15 (5.1)	90.0	47.3-98.5
Ib	18 (6.1)	50.6	19.9-75.0
II	37 (12.5)	55.1	34.5-71.7
IIIa	22 (7.4)	49.7	16.6-76.2
IIIb	204 (68.9)	16.2	9.5-24.5

AJCC: American Joint Committed on Cancer; N: number of patients.

* N = 515.

† N = 296.

Treatment

- Localized cholangiocarcinoma ⁵
 - Intrahepatic
 - <30% achieve curative resection
 - Perihilar
 - Hepatic and hepatic duct resection achieve <50% curative resection
 - Distal
 - Pancreaticoduodenectomy (Whipple Procedure)
- Advanced cholangiocarcinoma ⁶
 - Often heterogeneous
 - **No chemotherapy regimen consistently leads to tumor shrinkage, extends survival, or contributes to palliative intervention**
 - Good performance status and no hyperbilirubinemia:
Gemcitabine + Cisplatin (GEM/CIS)
 - Borderline performance or persistent biliary obstruction:
Leucovorin-modulated fluorouracil

Suggested Further Workup

- MRI of clavicular mass to confirm metastasis
- Bone scan to evaluate for other mets
- Palliative surgical intervention in case of symptomatic airway compression

ACR appropriateness Criteria: Acute nonlocalizing abdominal pain ⁷

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen and pelvis with IV contrast	Usually Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	Usually Appropriate	☼☼☼
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	○
US abdomen	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
CT abdomen and pelvis without and with IV contrast	May Be Appropriate	☼☼☼☼
Radiography abdomen	May Be Appropriate	☼☼
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼☼
WBC scan abdomen and pelvis	Usually Not Appropriate	☼☼☼☼
Nuclear medicine scan gallbladder	Usually Not Appropriate	☼☼
Fluoroscopy upper GI series with small bowel follow-through	Usually Not Appropriate	☼☼☼
Fluoroscopy contrast enema	Usually Not Appropriate	☼☼☼

Cost of Imaging at MH TMC ⁸

- Cost of CXR 2-views: \$762
- Cost of Bone scan: \$2892
- Cost of CT CAP: \$5873.25

Take Home Points

- Cholangiocarcinoma often presents at advanced stages
- Trauma and early bone metastasis can appear very similar on bone scans
- It's easy to find something you're looking for, but hard find something that's missing

References

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Questions?

Scattered hypoattenuated lesions in right liver consistent with advanced cholangiocarcinoma

