A 16-year-old male with abdominal fullness and decreased appetite for 7 days

報告者：住院醫師賴以修
指導者：小兒腸胃科主任陳安琪
報告日期：2012/06/09

Basic Data

Chart No:0014681179

Date of admission : 101.04.04

Name: 江O助

Birth day:84/08/14

Age/Sex: 16y8m/o,male

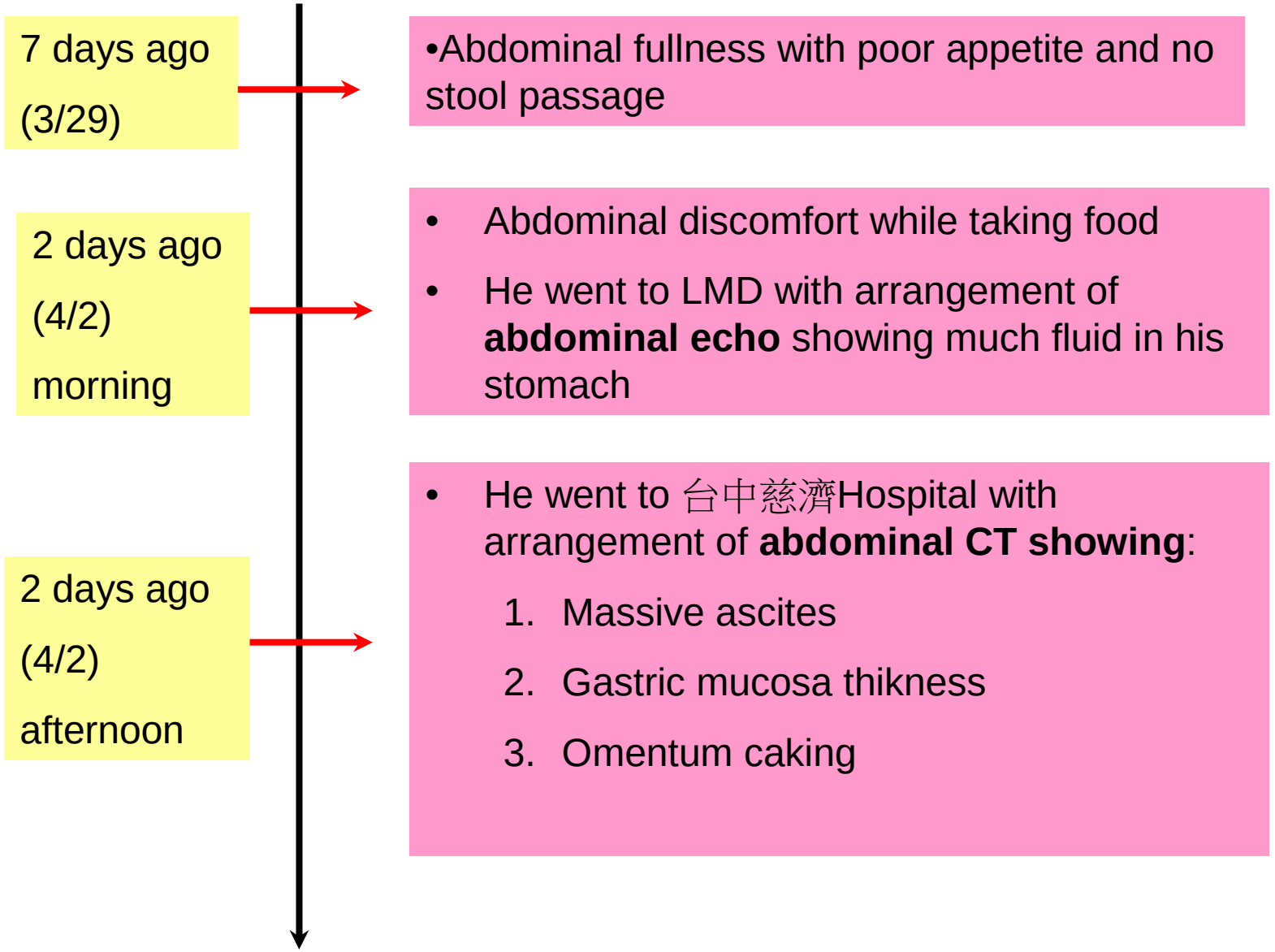
Place of residence :台中市潭子區

Past history: nil

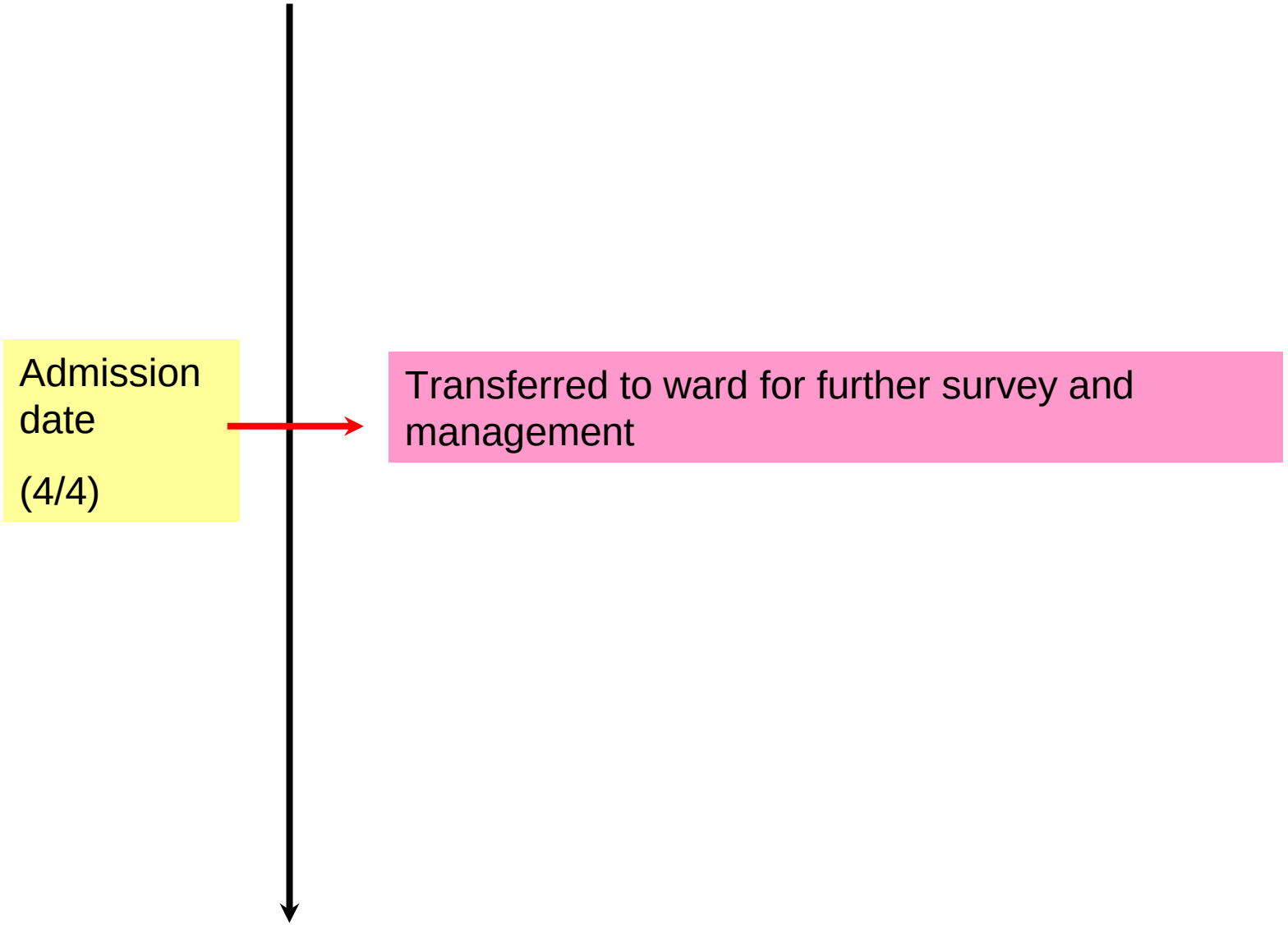
Chief complaint

Abdominal fullness and decreased appetite for 7 days

Present illness



Present illness



Review of Systems

- General: **fatigue; weakness**; no insomnia; no fever; **mild anorexia**;
- Integument: no hair loss; no rash; no pruritus; no change in color;
- HEENT:
- Head: no headache; no dizziness; no vertigo;
- Eyes: normal visual acuity; normal color vision; no corrective lenses; no photophobia; no diplopia; no pain;
- Ears: no pain; no discharge; no hearing loss; no tinnitus;
- Nose: no epistaxis; no discharge; no stuffiness; normal sense of smell;
- Throat: normal status of teeth; normal gums; no dentures; normal taste; no soreness; no hoarseness; no lump;
- Respiatory: no wheezing; no hemoptysis; no sputum; no cough;
- CV: no palpitation; no chest distress/pain; no edema; no dyspnea; no intermittent claudication; no cold limbs; no paroxysmal nocturnal dyspnea; no orthopnea;

Review of Systems

- GI: **nausea; change in bowel habit; no stool passage, abdominal fulliness**; no abdominal distress pain; no vomiting; no hematemesis; no melena; no blood in stools; no dysphagia;
- Metabolic and endocrine: no nervousness; no heat/cold intolerance; no weight change; no growth and development; no sweating; no polydipsia;
- GU: no dribbling; no urgency; no hesitancy; no incontinence; no dysuria; no hematuria; no nocturia; no polyuria; no urinary frequency;
- Hematotologic: no lymphadenopathy; no easy brusity or bleeding; no anemia;
- Neuropsychiatry: no speech disturbance; no seizures; no syncope; no dizziness; no loss of sensation; no paresthesia; no ataxia; no weakness or paralysis; no tremor; no anxiety; no depression; no irritablility;
- Musculoskeletal: no muscular weakness; no limitation of motion; no stiffness; no Joint pain; no wasting;

Past Medical History

- Birth History:

  G5P5 A0 , NSD, BBW: 2900gm
- Development History: as milestone
- Feeding History: as adult
- Previous Illnesses/Hospitalizations/Surgeries:nil
- Allergies: No known allergy
- Immunizations: as scheduled
- Medication:nil

Social and Personal History

- 1.**Smoking** with 1 pack of cigarette Q3D **for about 1 year**
- 2.Denied alcohol drinking, beetle nut chewing, drug abuse

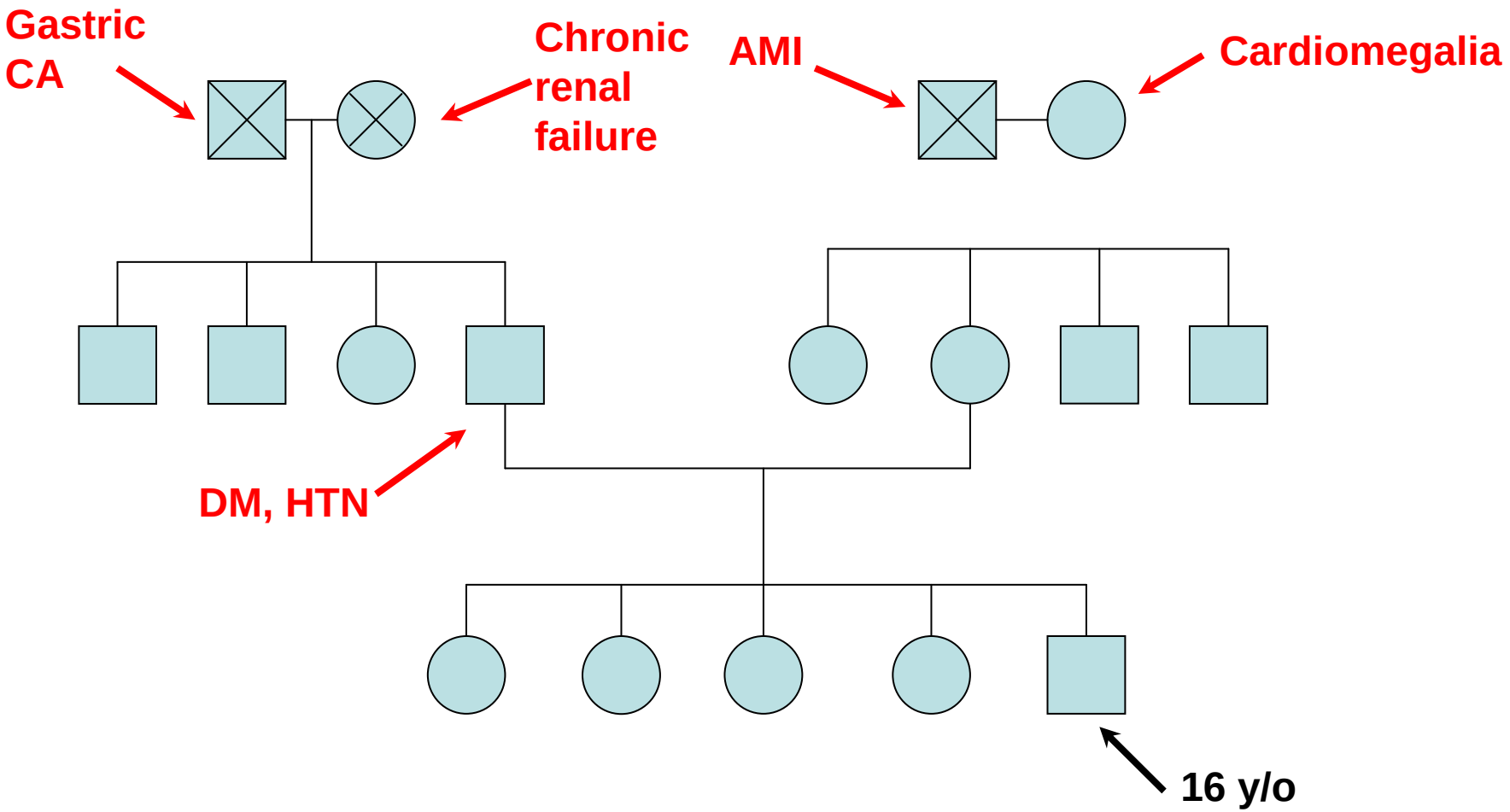
Allergic History

- Skin rash and mouth swelling to seafood

Family social history

- **Father** has **smoking, beetle chewing,** and **alcohol drinking habits**

Family History



Social History

- Live with parents and 4 older sisters
- Attending senior high school

Physical Examination

- Vital Signs: BT: 36.3 ℃, HR: 110 /min, RR: 21 /min,
  BP:142 / 87 mmHg
- Measurement: Height: 169 cm(75-90 th percentile);
- BW: 69 kg(50-75 th percentile)
- General: fair, well activity
- Skin: no rash, no vesicles, no petechiae, no jaundice, well-turgored
- HEENT: no rhinorrhea, no injected tonsil,
- no injected conjunctiva,
- no ear discharge, no headache
- Neck: **LAP over level V**, no tender lymph nodes,
- no swelling, no erythematous change
- Chest: symmetric expansion, no chest wall retraction.
- Breath sound: bil. clear breath sounds
- Heart: RHB, no murmur

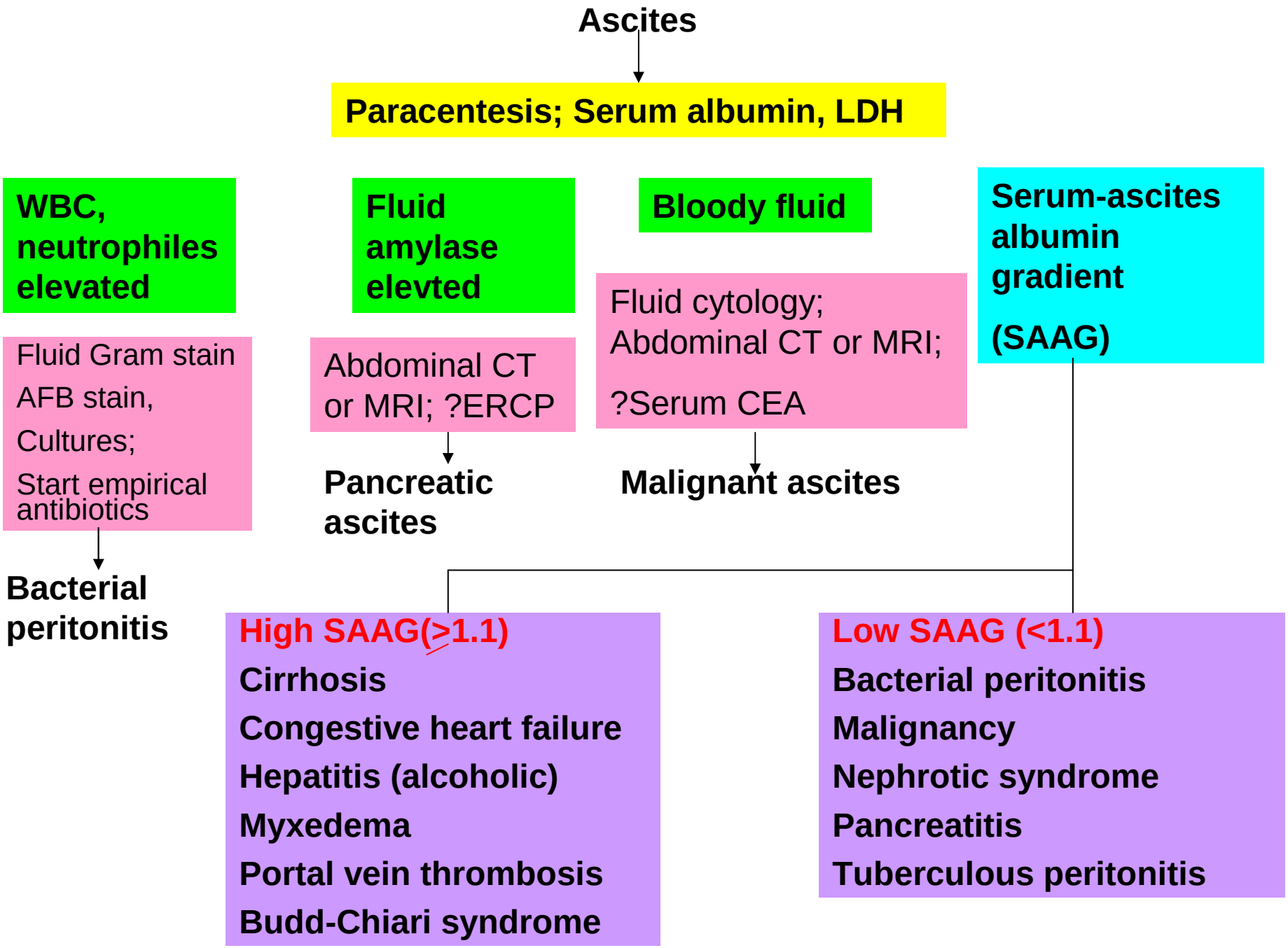
Physical Examination

- **Abdomen: tenderness over the epigastric area**
- **marked distension, shifting dullness**
- normal bowel sound, no mass palpable,
- no hepatomegaly, no splenomegaly.
- Extremities: freely movable.
- Neurological examination: grossly intact
- II, III: pupils: light reflex: +/+, pupil:3mm/3mm
- III, IV, VI: eye movement: full
- VII: facial expression: symmetric
- VIII: hearing: response to sound
- VII, IX, X, XII: dysphagia(-), tongue deviation(-)
- DTR:2+ , Muscle power: full
- Barbinski's sign(-/-), Brudzinski's sign(-)

Problems

- 1.Abdominal pain and epigastric tenderness
- 2.Massive ascites

- D/D Abdominal pain (請敘述)
- D/D Massive ascites


Ascites
Paracentesis; Serum albumin, LDH
WBC, neutrophiles elevated
Fluid amylase elevted
Bloody fluid
Serum-ascites albumin gradient (SAAG)
Fluid Gram stain
AFB stain,
Cultures;
Start empirical antibiotics
Abdominal CT or MRI; ?ERCP
Fluid cytology;
Abdominal CT or MRI;
?Serum CEA
Bacterial peritonitis
Pancreatic ascites
Malignant ascites
High SAAG(>1.1)
Cirrhosis
Congestive heart failure
Hepatitis (alcoholic)
Myxedema
Portal vein thrombosis
Budd-Chiari syndrome
Low SAAG (<1.1)
Bacterial peritonitis
Malignancy
Nephrotic syndrome
Pancreatitis
Tuberculous peritonitis

- Next steps?

Lab Data in our ER on 4/3

WBC	**11.19x1000/ul**	(3.99-10.39)
RBC	5.32x1000000/ul	(4.5-5.5)
Hb	15.9mg/dL	(14.0-18.0)
Hct	45.8%	(39-52)
Platelet	253x1000/ul	(130-400)
RDW	12.4%	(11.5-14.5)
MCV	86.1fl	(80-99)
MCH	29.9pg	(27-31)
MCHC	34.7g/dL	(33-37)

Hemogram on 4/03

Neutrophilic Segment	**80.4 * %**	(40-74)
Lymphocytes	9.9* %	(19-48)
Monocytes	9.2 %	(3.4-9)
Eosinophils	%	(0-7)
Basophils	%	(0-1.5)
N. Bands	%	
Metamyelocytes	%	
Myelocytes	%	
Promyelocytes	%	
Blasts	%	
Others	%	
Atypical Lymphocytes	%	
Normoblast	/100WBC	

Biochemistry in our ER on 4/3

- BUN:11 mg/dL (5-26)
- Creatinine:0.83 mg/dL (0.5-1.3)
- Glucose AC:105 mg/dL (70-110)
- Sodium(Na):137 mmol/L (135-147)
- Potassium(K):3.5 mmol/L (3.5-4.9)
- SGPT(ALT):29 IU/L (5-40)
- SGOT(AST):23 IU/L (5-34)
- Alk P-tase:44 IU/L (男/女:38-126 小孩:58-252)
- LDH:90 * U/L (98-192)
- Albumin(BCG):4.2 g/dL (3.8-5.3)

Blood smear interpretation on 4/3

- 一、WBC
- Neutrophilic Segment: 81 %
- Lymphocyte: 5 %
- Monocyte: 13 %
- Eosinophil: 1 %
- Basophil: 0 %
- N.Band: 0 %
- N.Metamyelocyte:0 %
- N.Myelocyte:0 %
- Promyelocyte:0 %
- Blast:0 %
- Remark:
- Other:0

二、RBC

- Microcytosis:-
- Macrocytosis:-
- Hypochromia:-
- Hyperchromia:-
- Anisocytosis:-
- Poikilocytosis:-
- Polychromatophia:-
- Target cell:-
- Spherocyte:-
- Elliptocyte: -
- Remark:
- Other: -

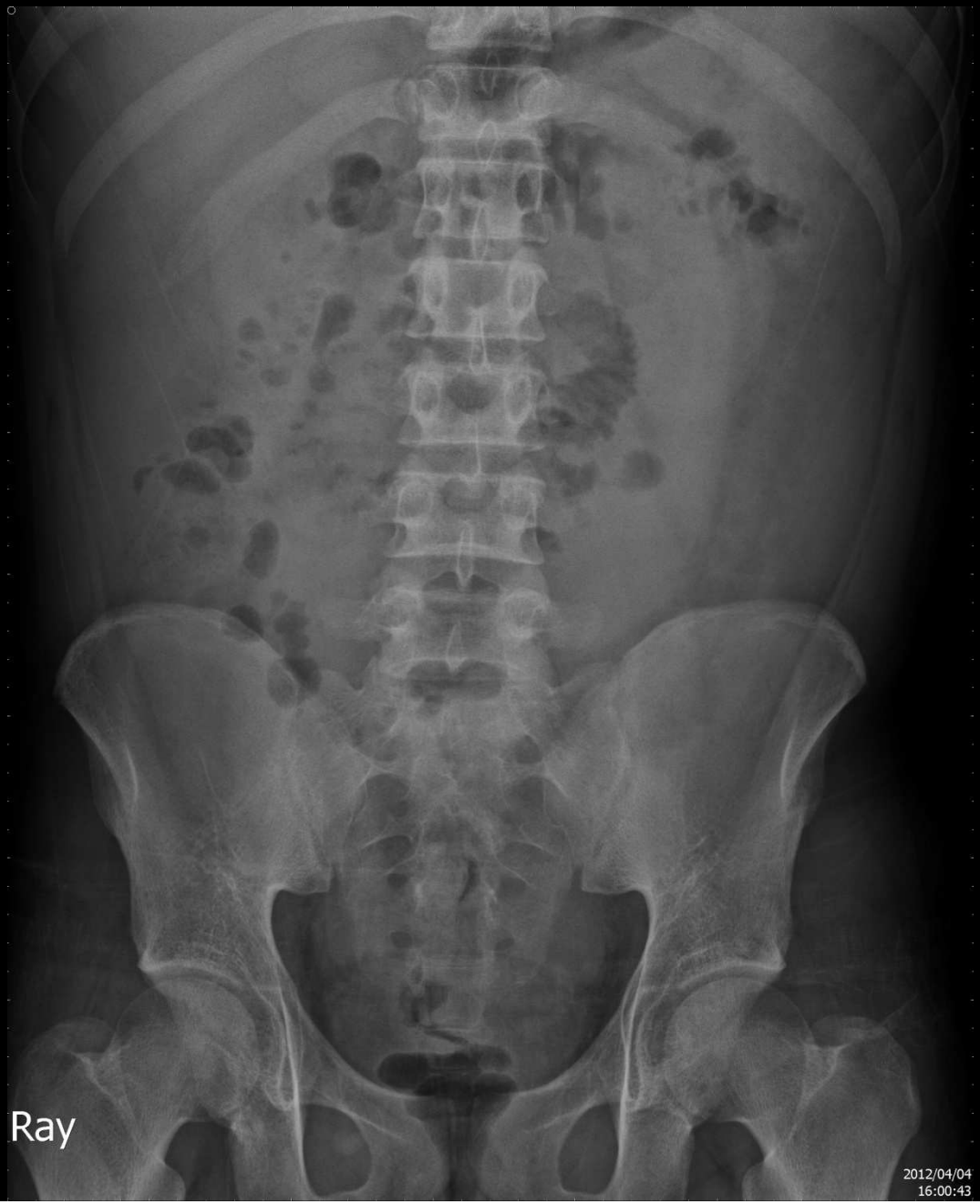
Urine routine in our ER on 4/3

- **Biochemistry EXAM**
- Sugar: Negative g/dL (Negative)
- Bilirubin: Negative (Negative)
- Ketone: 2+ (Negative)
- Specific Gravity:>=1.030 (1.005-1.030)
- Occult Blood:Negative (Negative)
- PH: 6.0 (5.0-8.0)
- Protein: 30 mg/dL (Negative)
- Urobilinogen:0.1 EU/dL (0.1-1.0)
- Nitrite: Negative
- Leukocyte esterase:Negative (Negative)

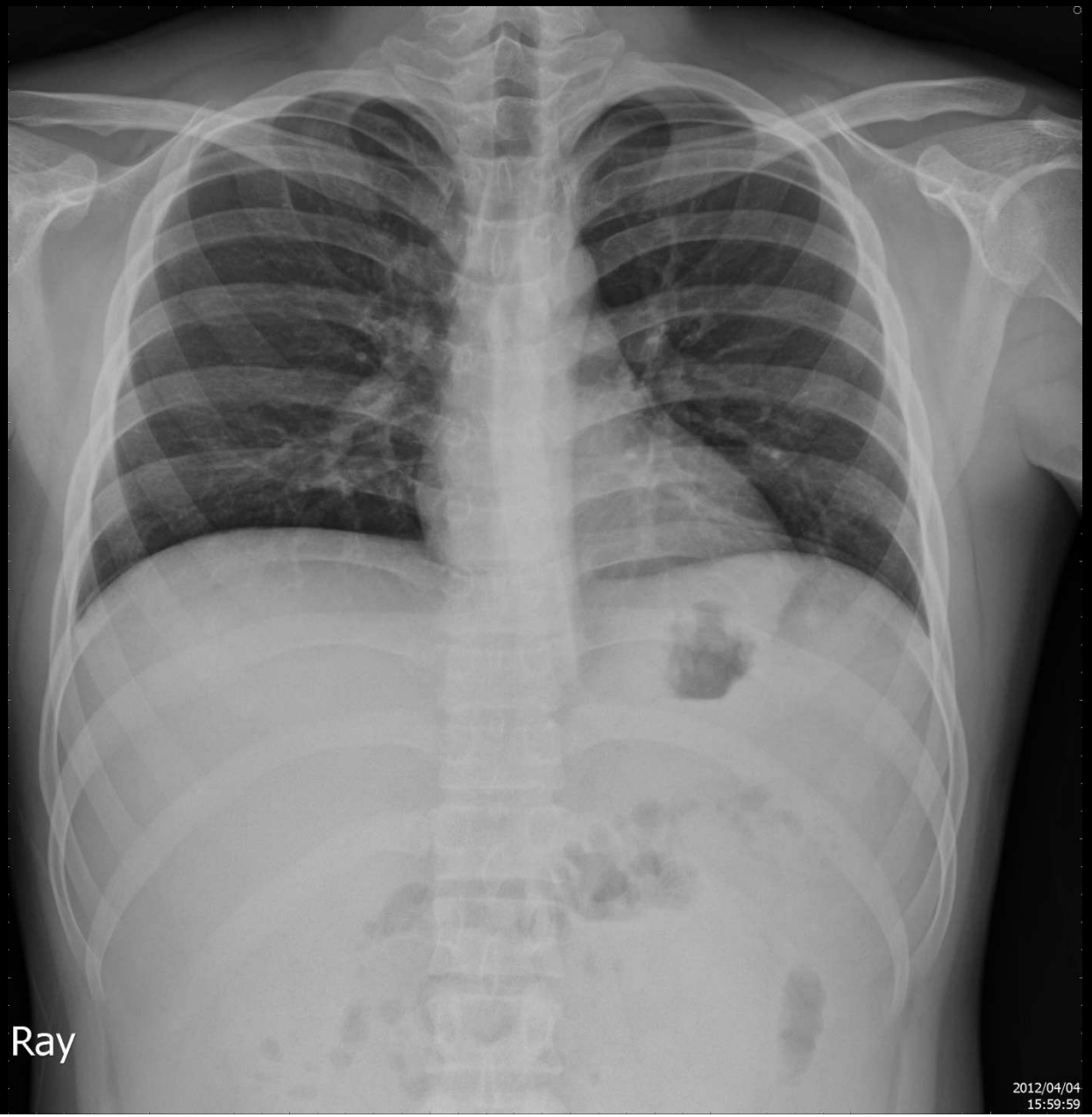
Microscopic EXAM:

RBC: 1 /uL (<17)
WBC: 1 /uL (<28)
Epith.Cell: 1 /uL (<28)
Cast: - /LPF
Crystal: - /HPF
Bacteria:- /HPF
Creatinine: >=300 mg/dL
P:C : 150 mg/g
Appearance:
Clear
Color:DK YELLOW

KUB on 4/4

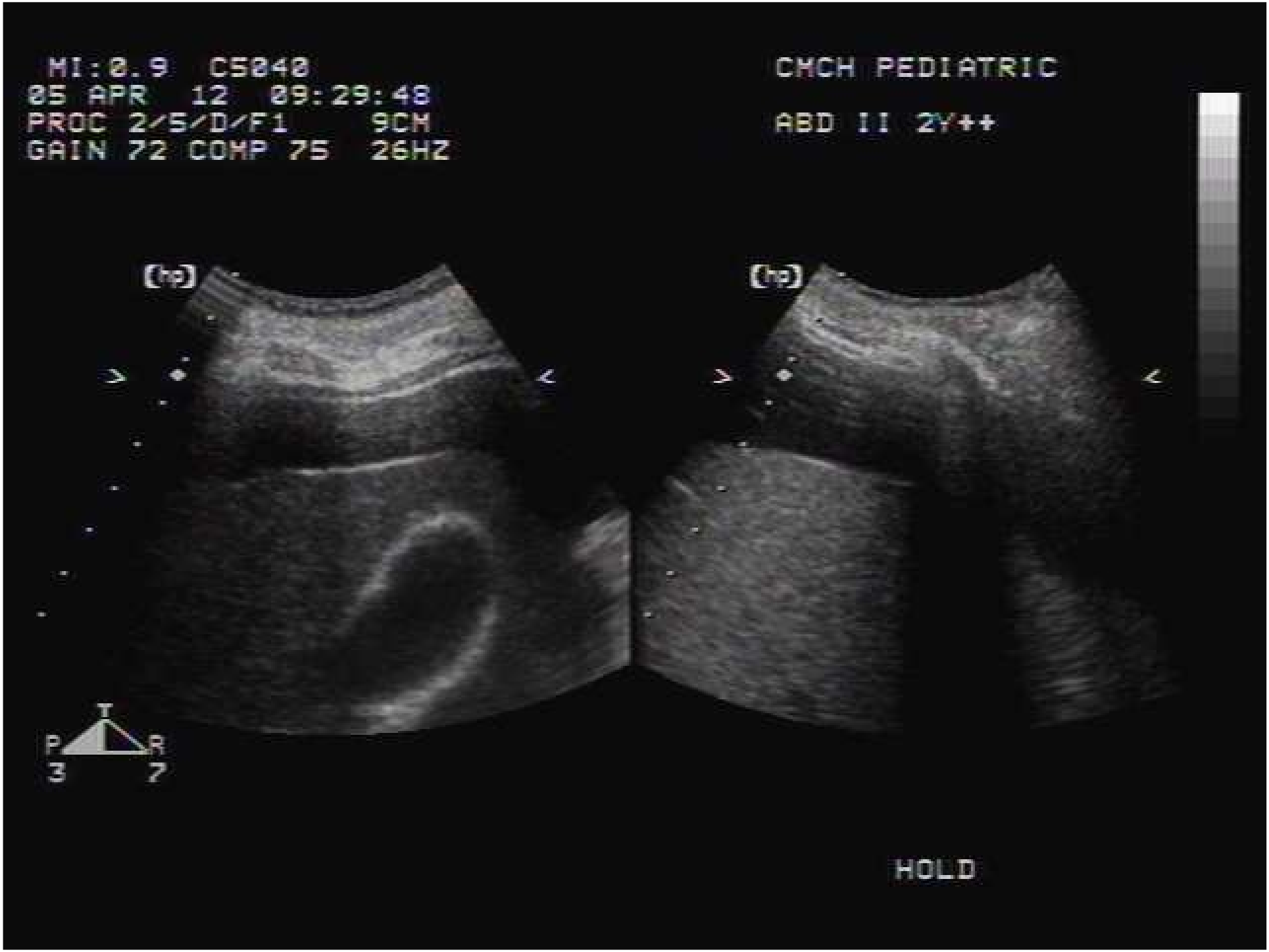


CXR on 4/4



Echo for Abdomen on 4/5

- Finding :
- Liver : normal echogenicity, no focal lesion,
- size :9cm over RMCL (range 9.5-14.5cm)
- IHD size : normal
- CBD size : normal
- GB :normal, not visible, due to not enough NPO time
- Biliary tract:normal
- Hepatic and portal vein: negative
- Pancreas : obliterated by stomach air
- Spleen : normal, length9.12 cm (range 8.5-12.0cm)
- Hepatic and portal vein:np
- No focal lesion , massive ascites
- **Diagnosis:1.Massive ascites**
  2.mild smal liver
- A-C Chen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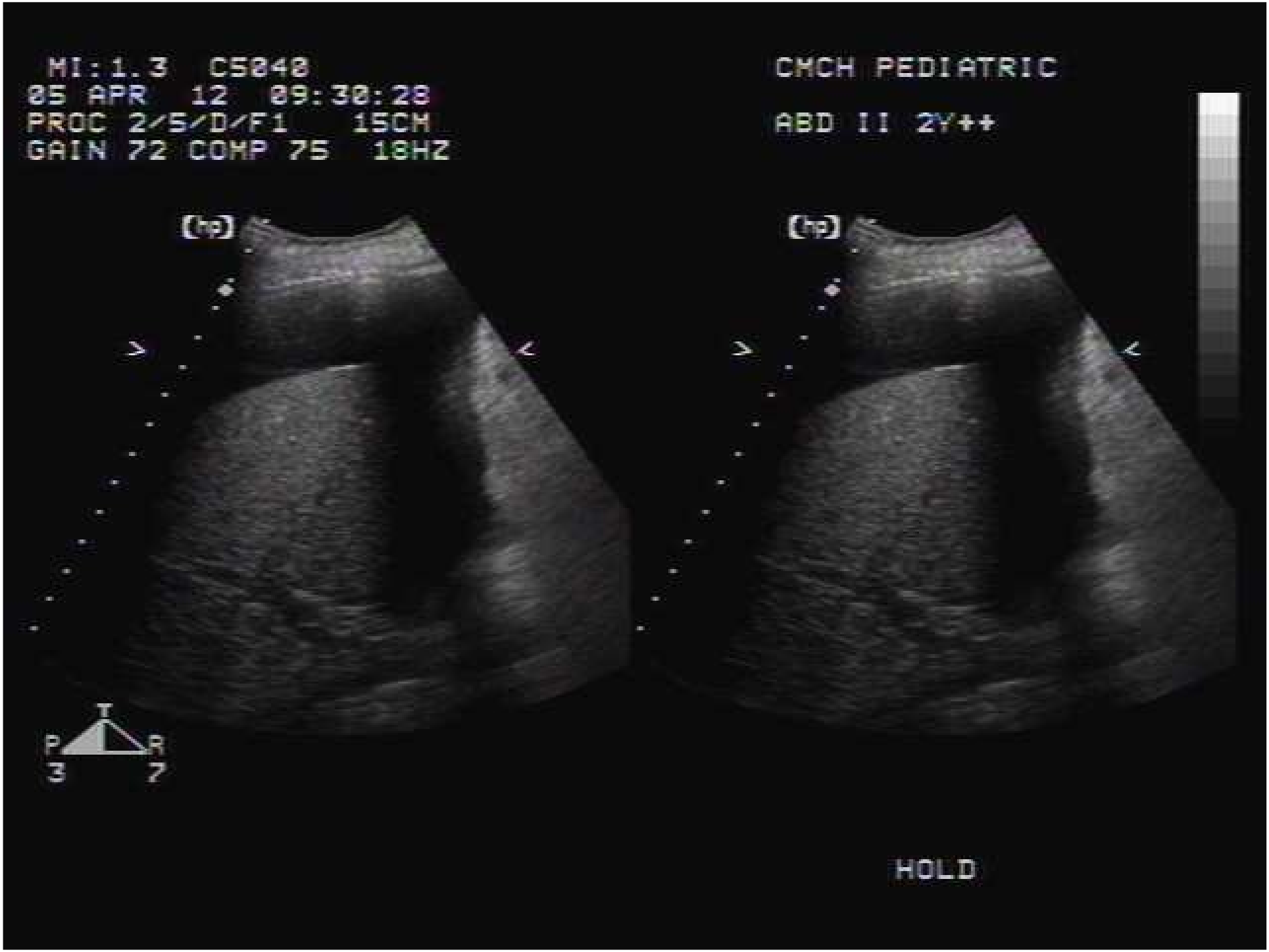
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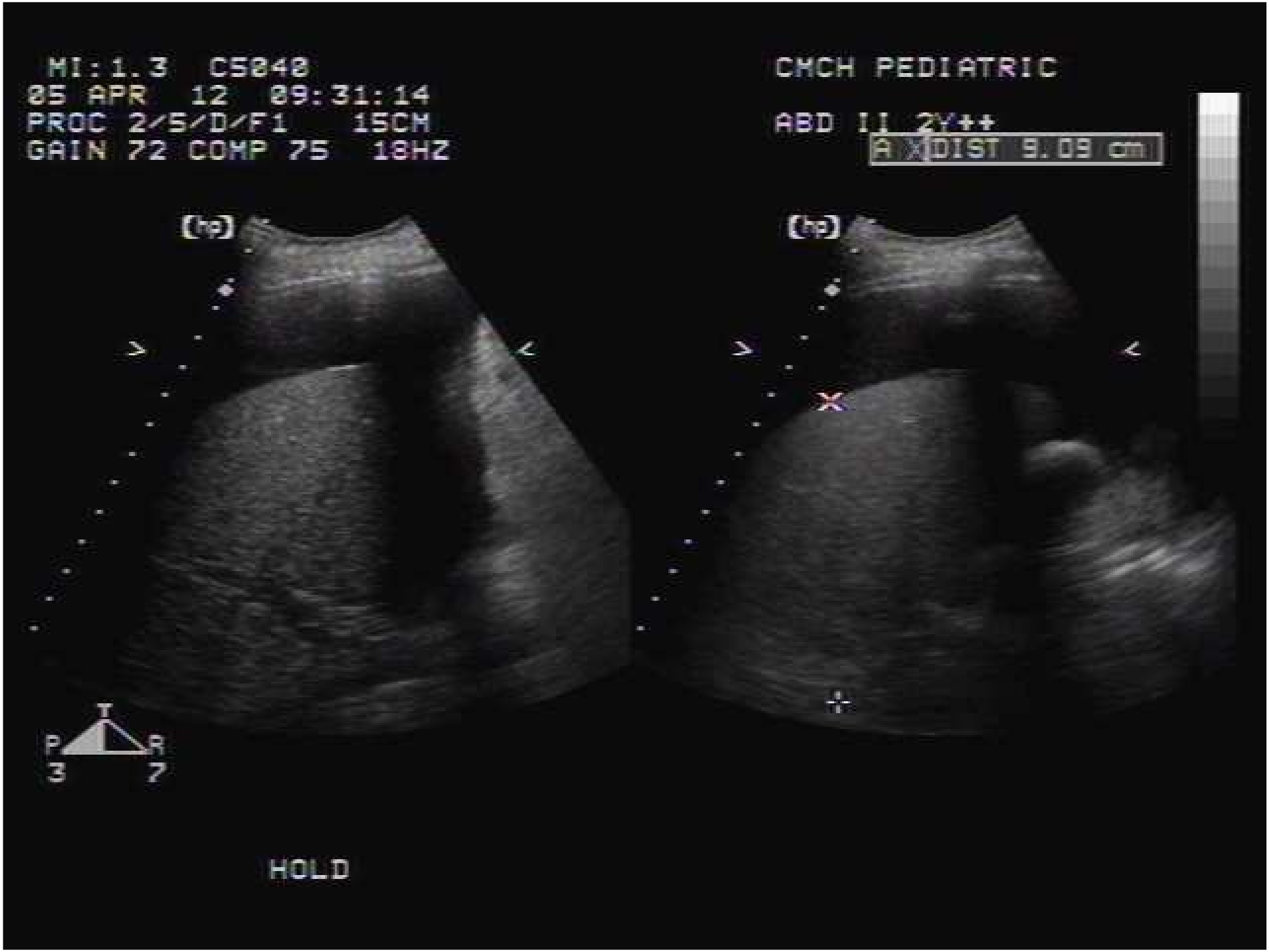
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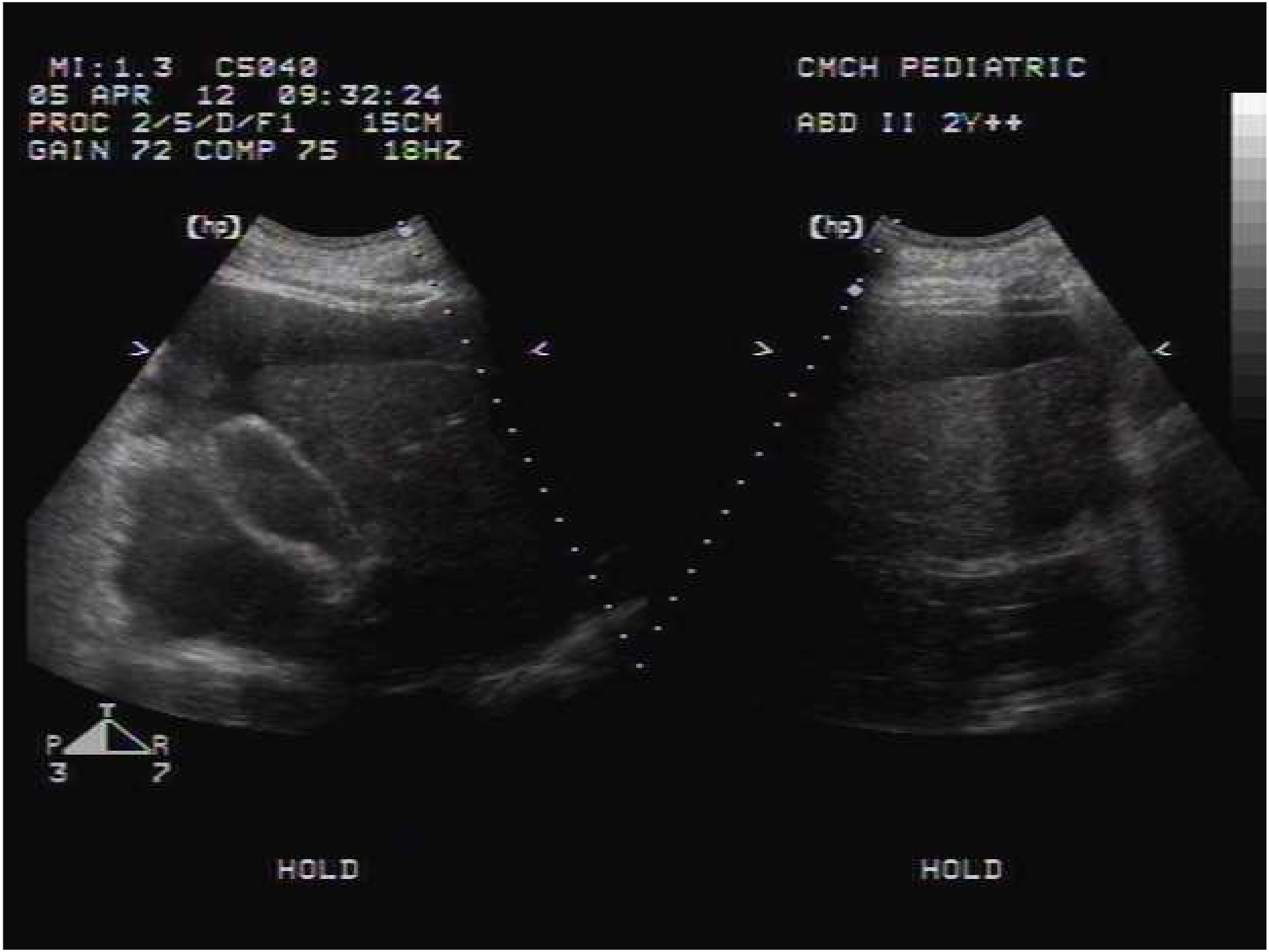
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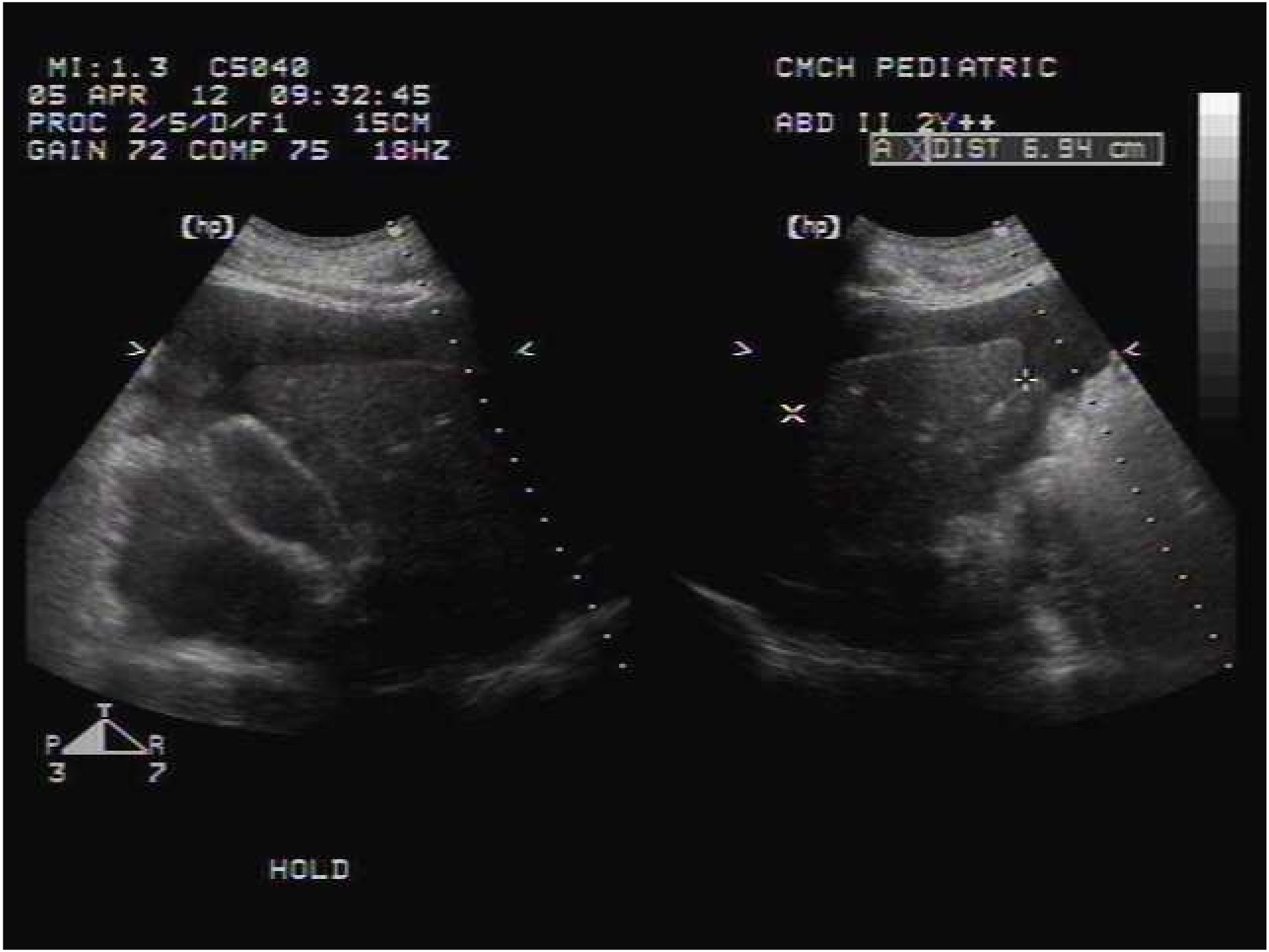
HOLD
HOLD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A X DIST 6.94 cm
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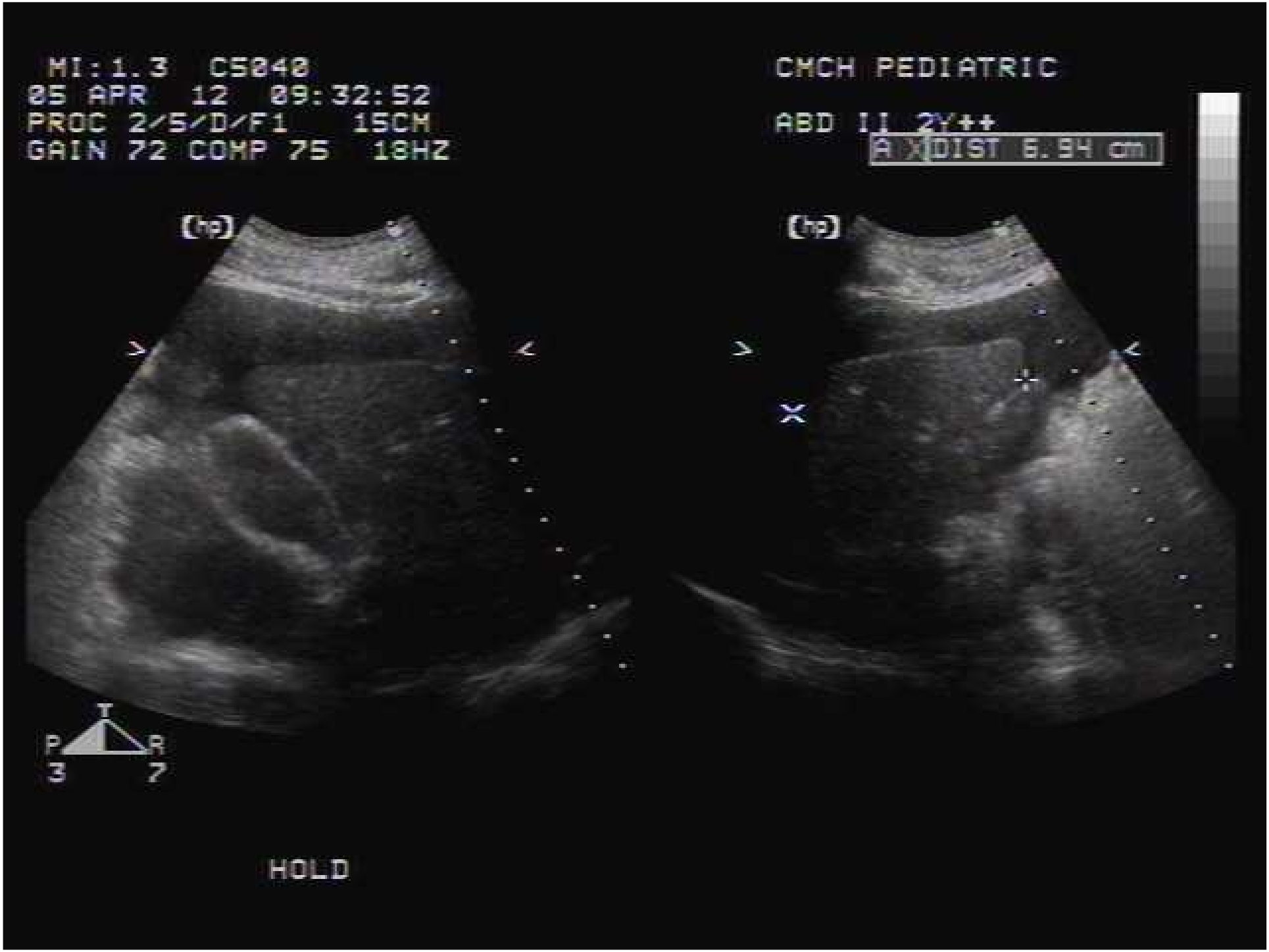
P
R
3
7
HOLD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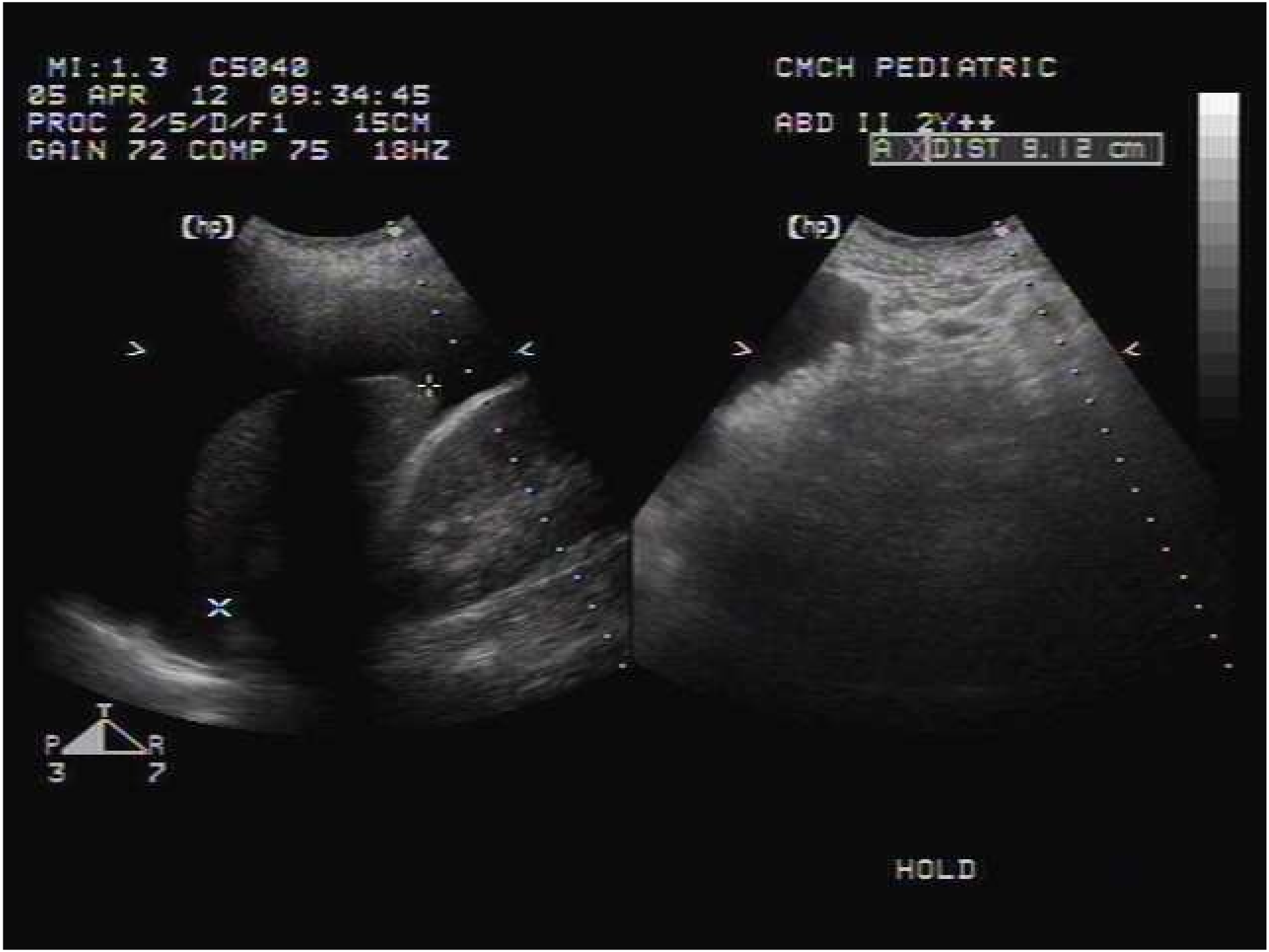
A DIST 6.94 cm
HOLD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A X DIST 9.12 cm
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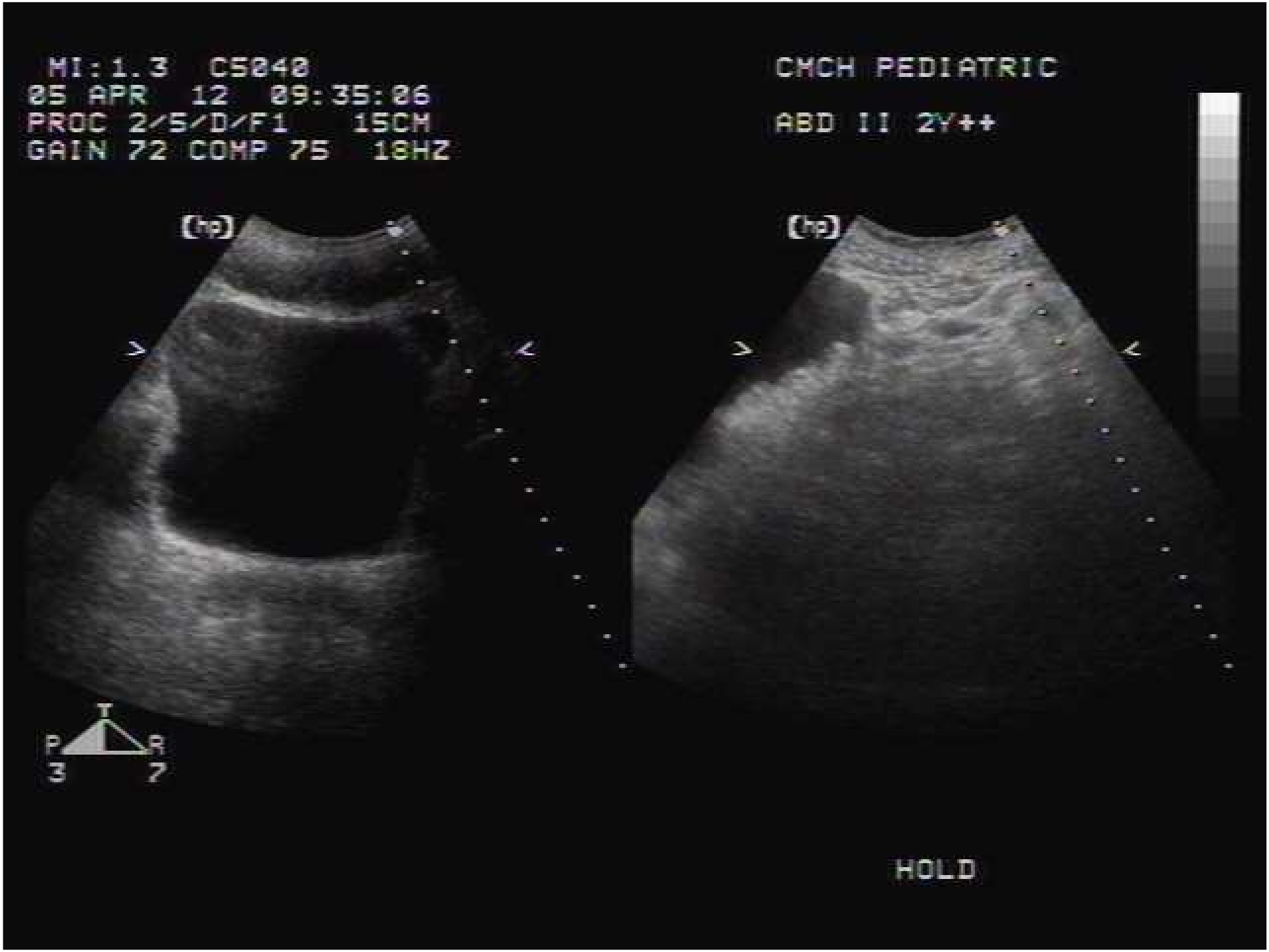
HOLD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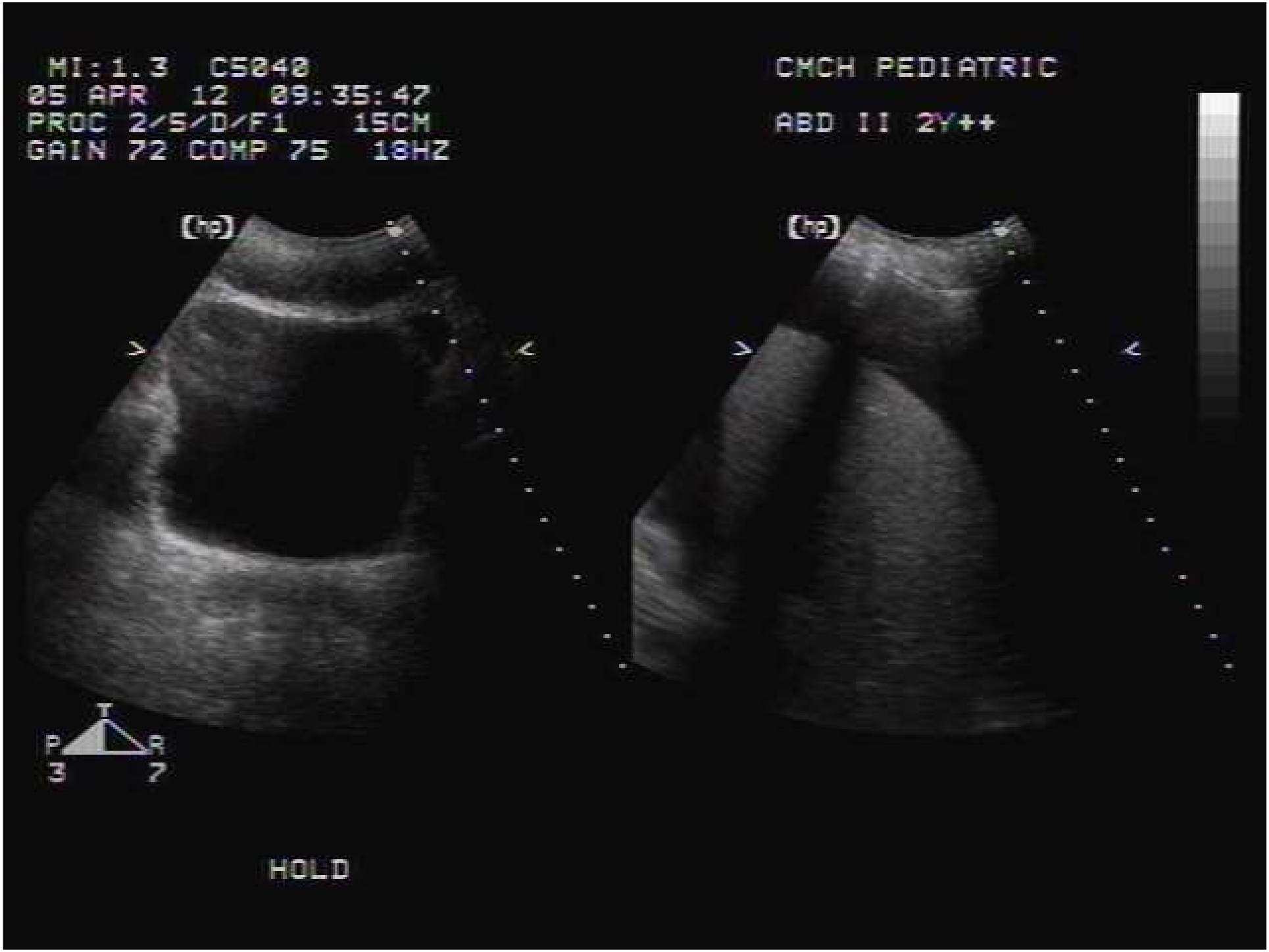
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CMCH PEDIATRIC
ABD II 2Y++
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HOLD

Ascites survey on 4/5

- **Glucose: 97 mg/dL (<60?)**
- **LDH: 288 U/L**

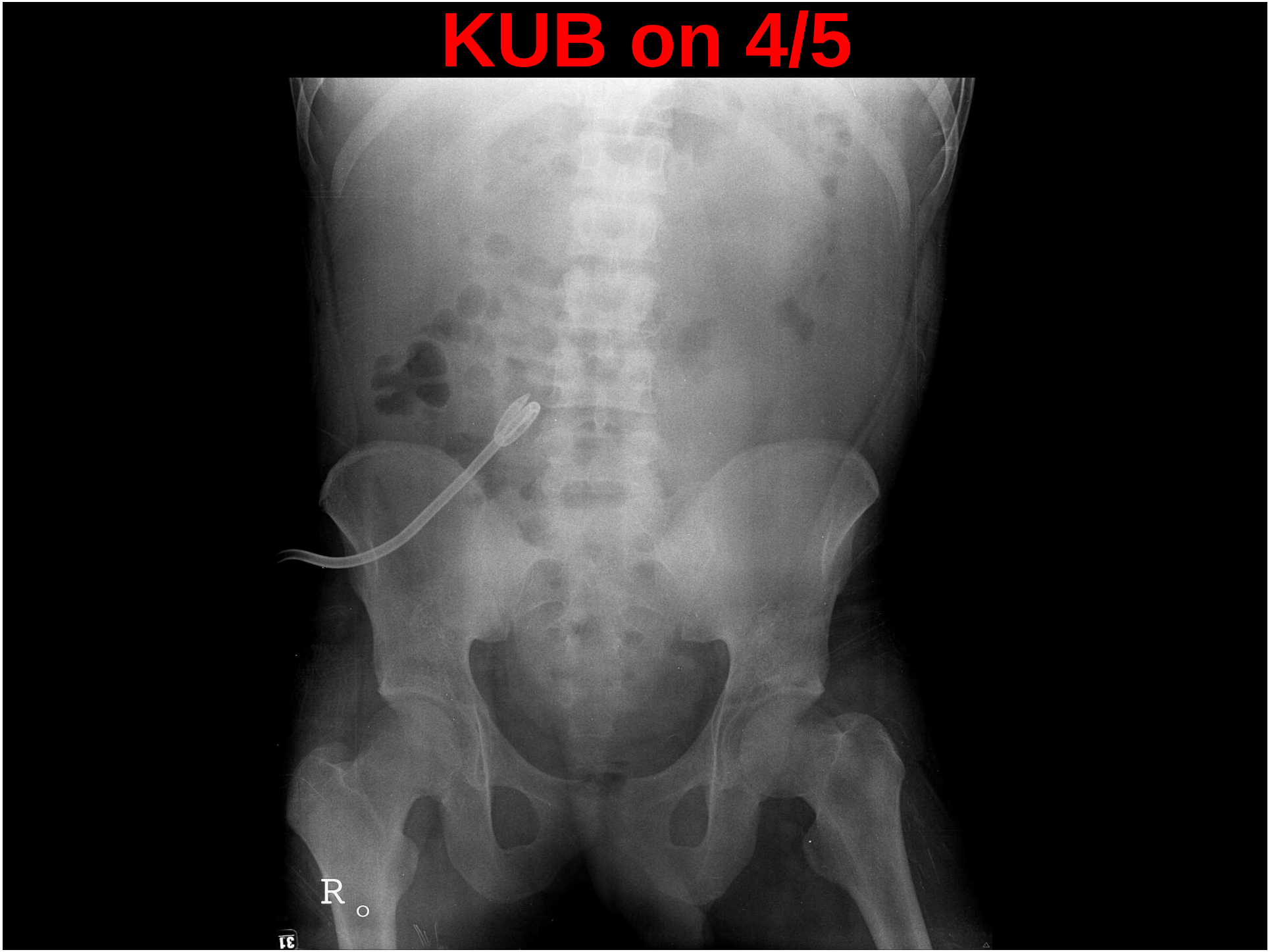
  (Fluid LDH:288 /Serum LDH:90 ratio >0.6)
- **Total Protein: 4.2 g/dL(>3)**
- Amylase: 37 U/L(<1000U/L)
- Lipase: 19 U/L
- **Albumin(BCG): 2.9 g/dL (3.8-5.3)**

(Serum-Ascites Albumin Gradient:4.2/2.9 <1.1?)

Ascites routine on 4/5

- Ascites
- Appearance:cloudy
- Color:yellow
- **RBC count :4000 /ul**
- **WBC count :10707 /ul**
- Diff. Count
- **Neutrophil : 89 %**
- Lymphocyte : 9 %
- Monocyte : 2 %
- Eosinophil : 0 %
- Basophil : 0 %
- Remark
- Mesothelial cell: -
- Histiocyte : -
- Other :

KUB on 4/5



Ascites culture on 4/5

- **Gram stain: Not found**
- Neutrophil : 1+
- Specimen: ascites (x2)
- **Impression: Negative for malignancy**.
- Presence of numerous neutrophils mixed with mesothelial cells, lymphocytes and macrophages.

Stem cell study from ascites on 4/5

- **B-lineage markers**
- CD20(B1): 0.98 %
- CD19(B4): 0.64 %
- CD10(J5): 0.04 %
- κ : %
- λ : %
- T-Lineage markers
- CD5(Leu1): %
- CD7(Leu7): %
- CD2(T11): %
- CD3(T3): 3.93 %
- CD4(T4): 2.03 %
- CD8(T8): 1.64 %

Myeloid markers

CD13(My7): %
CD33(My9): 94.99 %
CD14(My4): 4.80 %
CD15(LeuM1): %

Lineage nonspecific markers:

CD34: 0.72 %
CD38: %
HLA-DR: 7.20 %
CD1a: %
CD68: %
CD16: %
CD56: %

Genetic study of cells from ascites on 4/5

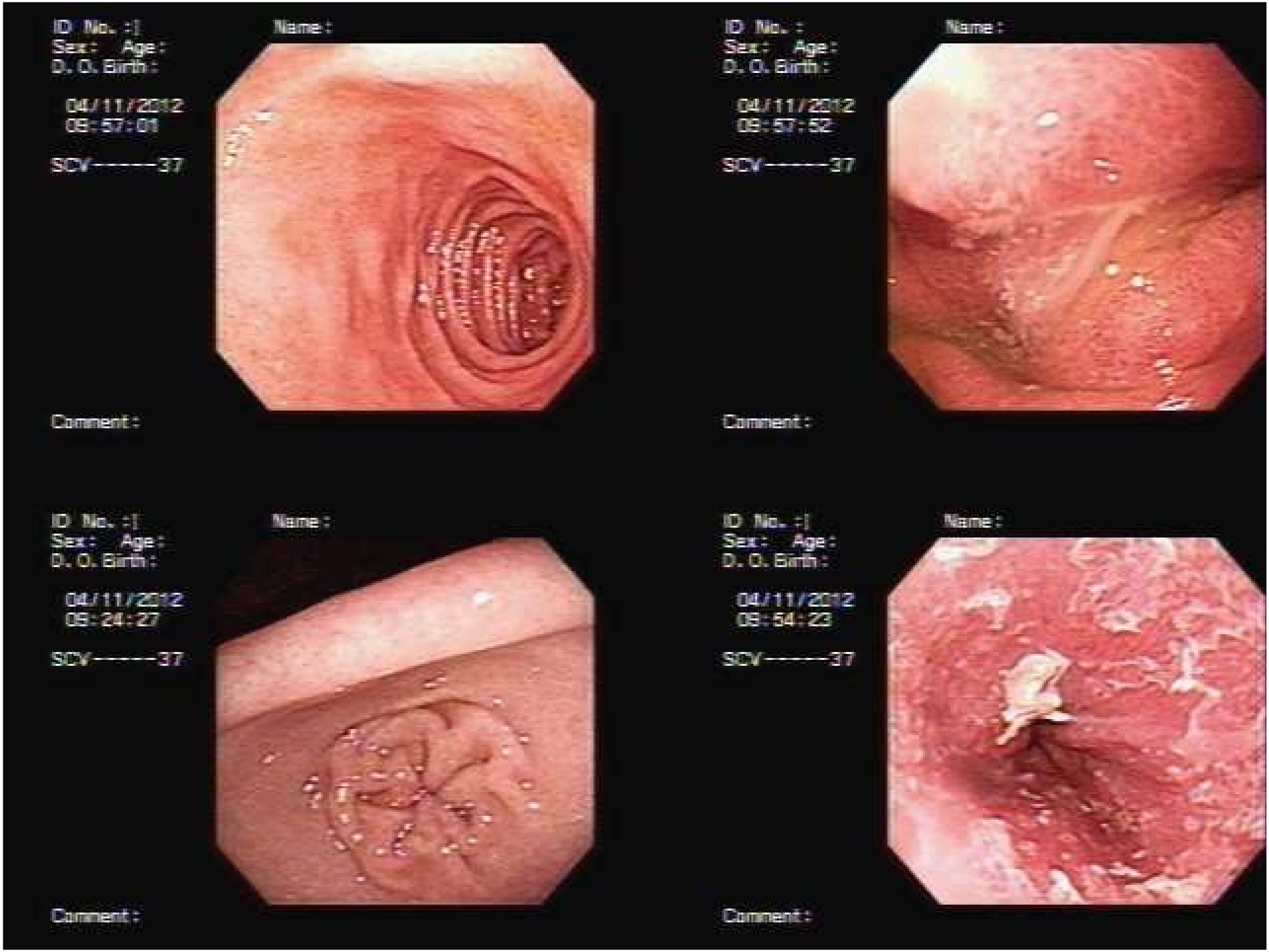
- Results:
- Chromosome counts: <45 45 46 47 >47 Total
- No. of cells:
- **Karyotype: no metaphase**
- Interpretation:
- Due to absence of mitotic activity , no metaphase was detected from the ascites specimen. Chromosome analysis was not possible.

Cell culture from ascites on 4/5

- No growth to date Gram's stain :
  Not found
- **Anaerobic culture no growth for 7 days**

Upper GI panendoscopy on 4/10

- Esophagus: negative finding, GE junction opening
- **Stomach**: **Large gastric ulcer(A2) was noted over lower part of body**
- **Its size is about 4*4cm.**
- **Bizzare ulcer appearance looks like snake skin with multi-nodule shape**
- Biopsy*9 was performed over low body(pathology A) for pathologic study.
- Biopsy*3 was done over pre-pyloric area(pathology B) for pathologic
- study and CLO test.
- Duodenum: No active bleeding
- negative finding till 2nd portion
- **Diagnosis: Large A2 stage of Gastric ulcer, highly suspect gastric cancer**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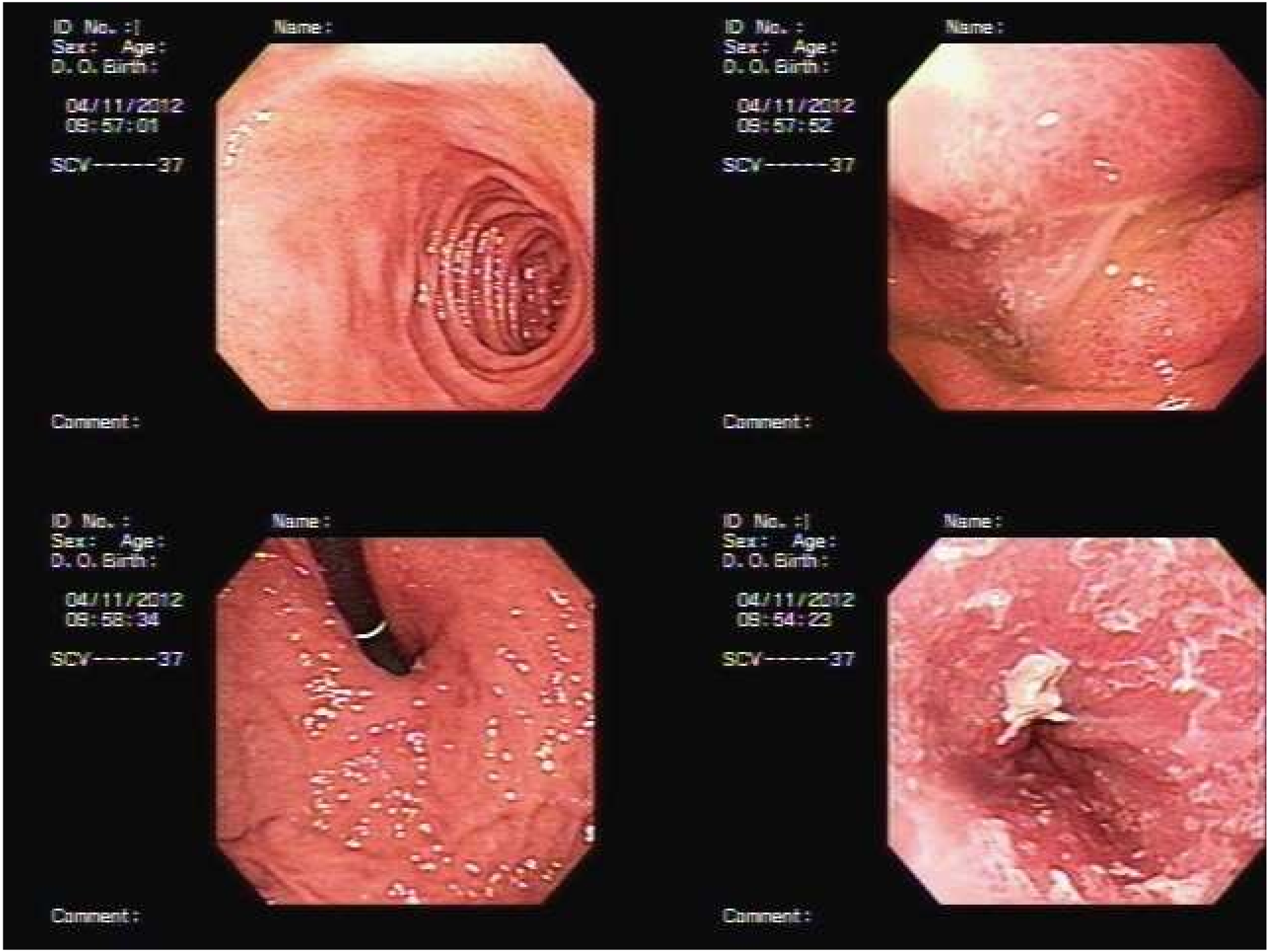
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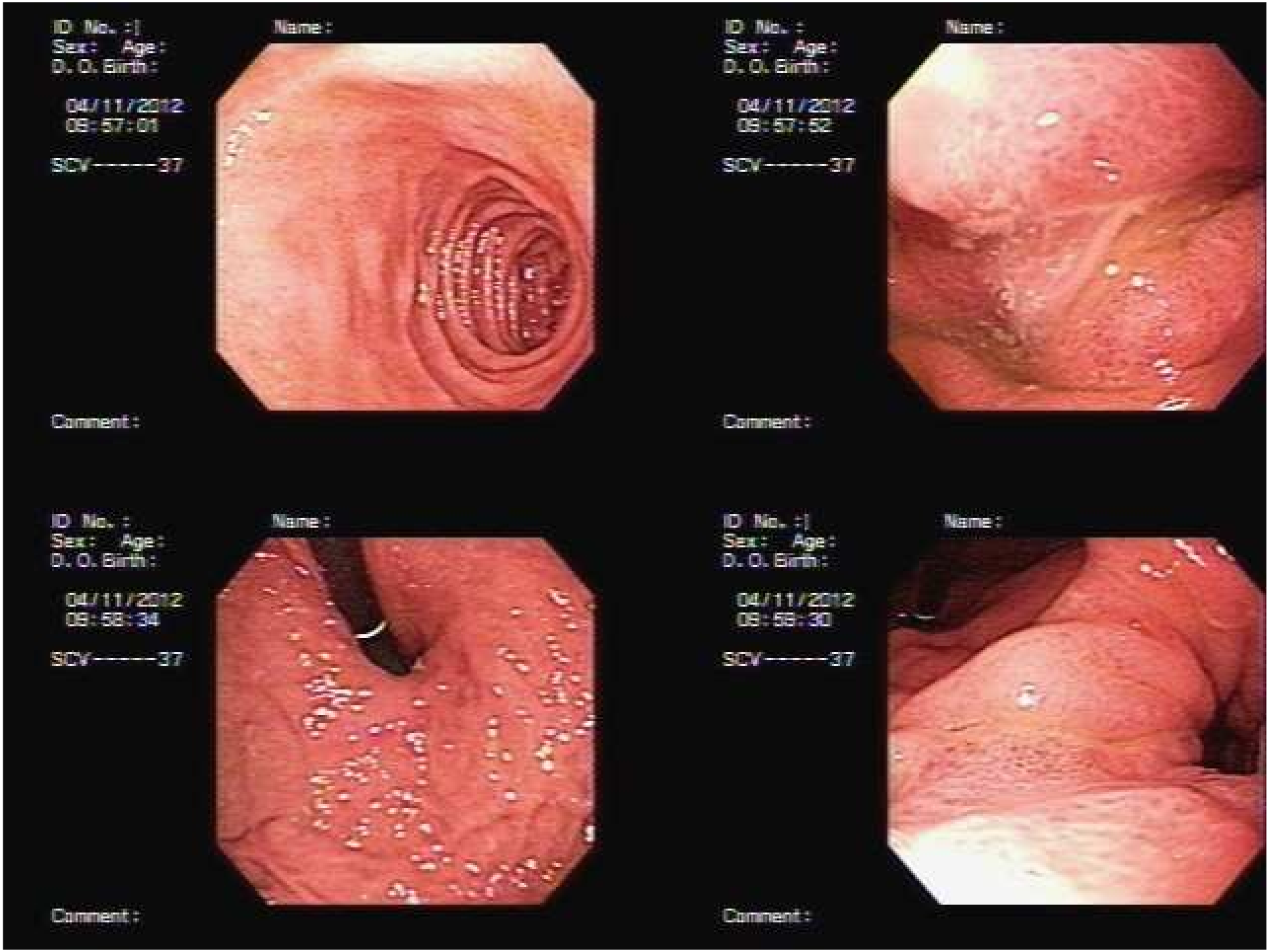
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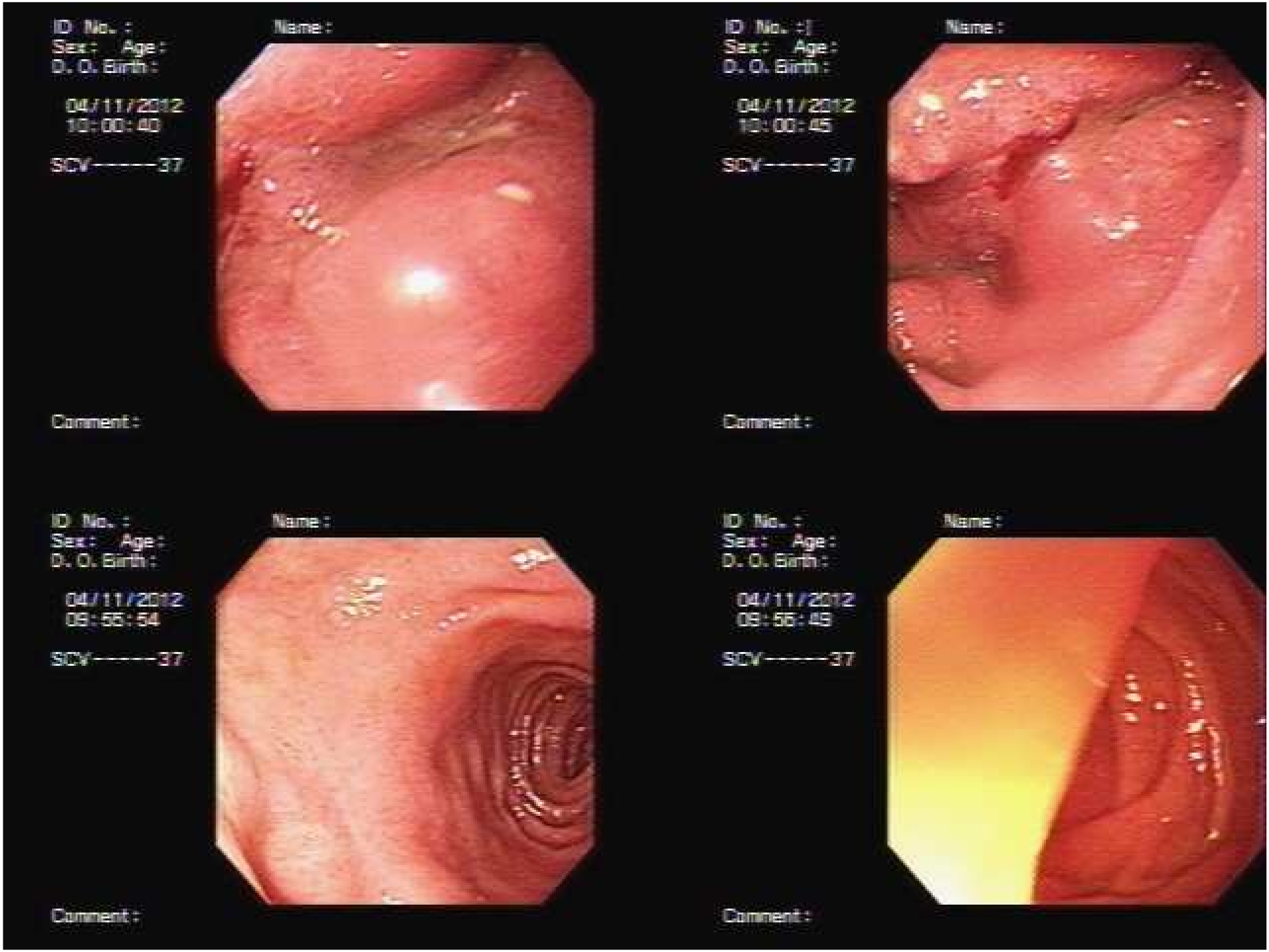
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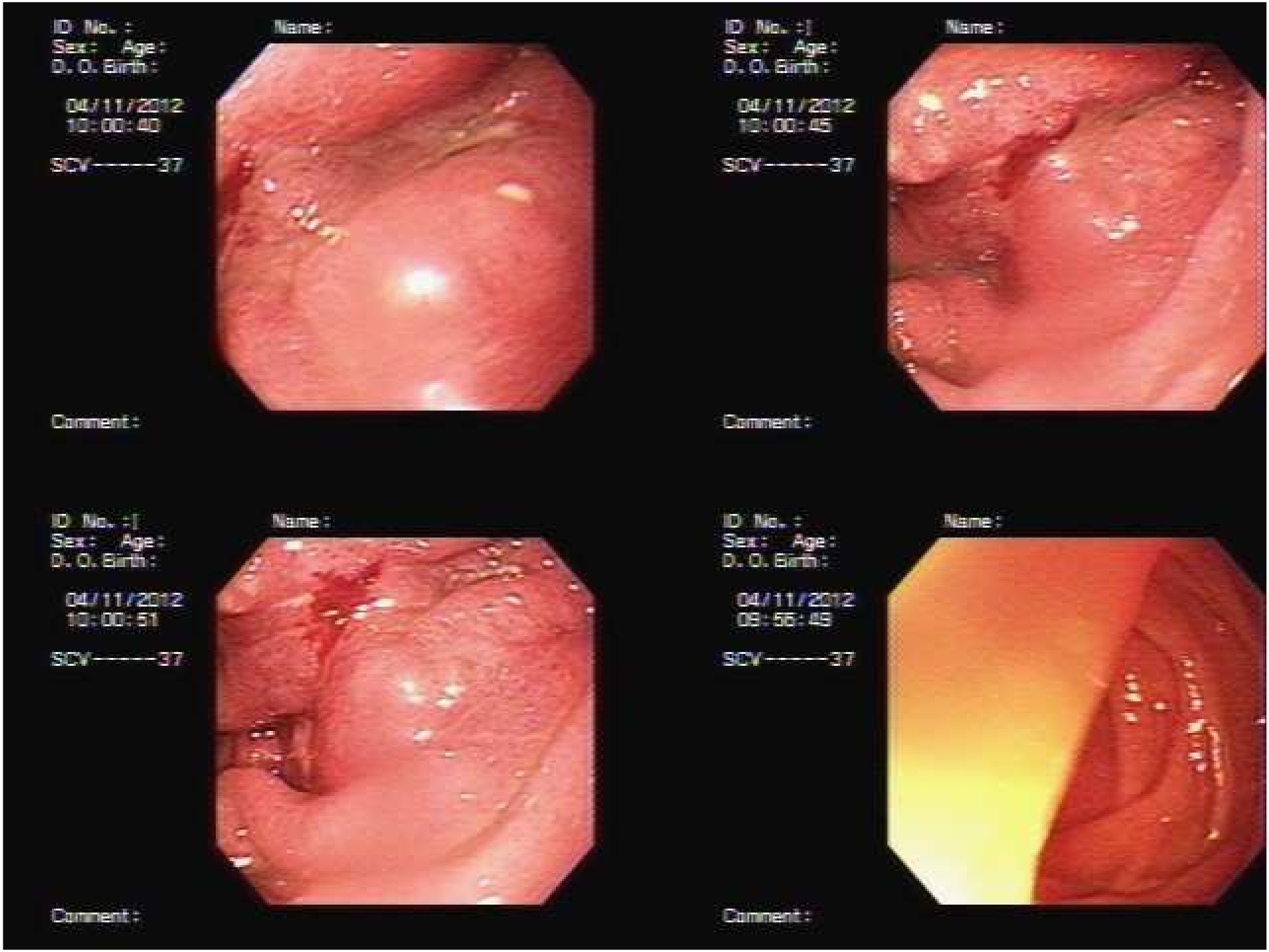
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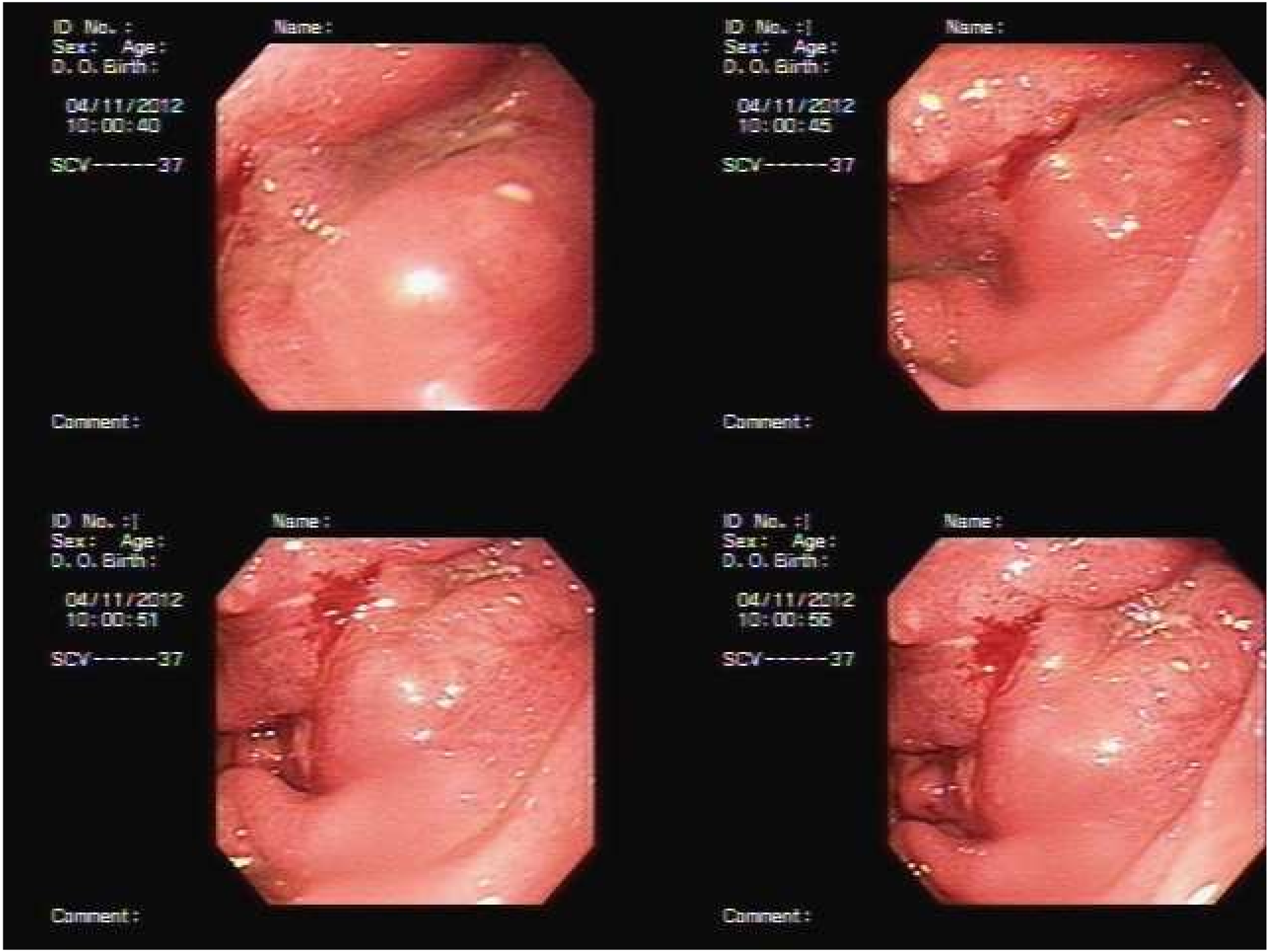
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10:00:51
SCV------37
Comment :
ID No. :
Name :
Sex : Age :
D. O. Birth :
04/11/2012
10:00:56
SCV------37
Comment :

Pathologic study on 4/11

- CLO test 幽門桿菌檢驗(-)
- Stomach, biopsy (A), adenocarcinoma, poorly differentiated.
- The specimen submitted consists of nine tissue fragments measuring up to 0.3x0.2x0.1 cm. in size fixed in formalin.
- Grossly, they are tan and elastic.All for section. Jar 0
- Microscopically, it shows **round-to-oval neoplastic cells** arranged in abortive glandular pattern or individually over the lamina propria.
- **Signet ring tumor cells** are focally identified.
- **Helicobacter bacilli and mucosal ulceration are evident.**

13C-Urea Breath Test on 4/13

- **13C-Urea Breath Test: Positive.**

Tumor marker on 4/13

- CEA(EIA):0.51ng/mL (<5:Negative)
  - Glycoprotein associated with certain malignancies, particularly epithelial tumors
- **CA-125(EIA):109.1 * U/mL(<35:Negative)**
- CA19-9(EIA): 6.8 U/mL (<35:Negative)

Operation on 4/14

- Port-A insertion

Hepatits virus study on 4/15

- HBsAg: Nonreactive(0.00) IU/mL (<0.05 IU/mL)
- HCV Ab: Nonreactive(0.07) S/CO (<1.0 S/CO)

EBV virus molecular medical study on 4/15

- EBV DNA 定量PCR ：<600　copies/mL

Treatment with intravenous chemotherapy

- 101/04/17
- **Dexamethasone phosphate** iv use
- **Oxaliplatin** iv use
  - (**Alkylating agent**: platinum coordination complex)
- **Capecitabine** oral use
  - (**Pyrimidine antagonist**; prodrug of 5-FU)
- Removal of pig-tail
- 101/4/18-discharge

Review

- BRIEF REPORT
- **Gastric Adenocarcinoma in Children and Adolescents**
- Vivek Subbiah, MD,1* Gauri Varadhachary, MD,2 Cynthia E. Herzog, MD,1 and Winston W. Huh, MD
- **From: Pediatr Blood Cancer**

  2011;57:524–527

Introduction

- **Median age at diagnosis** for **gastric adenocarcinoma (GAC)** is **50t years**,
- **Extremely rare** in **children**
- **Gastrointestinal malignancies in children** comprise just **5%** of all pediatric neoplasms
- **Primary GAC** represents **0.05%** of all childhood cancers
- **Adult population in the United States** there will be an estimated **21,000 new cases of gastric cancer** with **more than 10,000 deaths** in 2010 alone
- **Median survival time** of **7–10 months**, **metastatic GAC** is an **aggressive malignancy in adults**, and the **2-year survival is approximately 10–15%** with conventional chemotherapy..

Introduction

- **Limited data** on the clinical presentation and outcomes **in pediatric GAC**.
- Staging and therapy in children **is based on the adult oncology experience**.
- Herein, we report **the clinical experience of GAC in children and adolescents** treated at **The University of Texas M. D. Anderson Cancer Center (MDACC).**

Patients and Methods

- Identified all **pediatric patients from the MDACC tumor registry (<18 years of age)** diagnosed and treated for **GAC at MDACC, January 1, 1990–December 31, 2008.**
- **Time to disease progression (TTP)** was defined as **duration of time** from **diagnosis date** (defined as date of **tissue biopsy**) to date of noted **radiographic disease progression**.
- **Duration of clinical follow-up** was defined as duration of time **from diagnosis date** to **last documented clinical follow-up** or **date of death**.

Results-Patient Characteristics

- Among **292,621 cancer patients** (**6,134 <18 years of age**) who presented to **MDACC (1990–2008), 4,204 patients** had **gastric cancer.**
- **Five patients** were identified **(3 females)** with gastric cancers who were **<18 years of age** which is
  - **0.0017%** of all patients **with cancer**,
  - **0.11%** of all patients **with gastric cancer**,
  - **0.08%** of all **cancer patients <18 years of** age treated in this time period.
- The **median age at diagnosis** was **17 years (range: 8–17 years).**
- **Three** patients were **Hispanic/Latino**, **1** was **African-American**, and **1** was of **Arabic** ethnicity.

Results-Patient Characteristics

- Initial **clinical presentations** were **mostly nonspecific**; the **most common symptoms** were
  - vomiting
  - hematemesis,
  - abdominal pain,
  - anemia, and
  - weight loss.
- **One patient** presented in **shock with pulmonary hypertension** and **hemolytic anemia.**
- **Median duration of symptoms prior to diagnosis was 3 months (range: 0.5–24 months).**
- One patient had a **family history** of **GAC** while another patient had family history of **colorectal carcinoma**.
- **Four patients** presented with **metastatic disease**.
- **Sites of involvement** included
  - 3 patients with peritoneal carcinomatosis,
  - 3 with liver metastases,
  - 1 with lung metastases (Table I).

Results-Patient Characteristics

- **Histology of tumor** was **poorly differentiated adenocarcinoma** for all patients, and **in 3** of the tumors **signet ring cells** were identified.
- **One of the 2 patients tested** for **Helicobacter pylori** was **positive**.
- **Immunohistochemical analysis** was performed in **2 patients**.
- One patient had tumor that was
  - **positive** for cyclo-oxygenase -2 **(COX-2)**
  - **negative** for epidermal growth factor receptor **(EGFR)**, human epidermal growth factor receptor 2**(HER-2/neu)**, and **c-kit**,
- Another patient had tumor
  - **positive** for **Her-2/neu** by immunohistochemistry
  - **negative** for estrogen receptor **(ER)** and progesterone receptor **(PR).**

Treatment

- Chemotherapy regimens were varied,
- **All** patients received
  - **platinum-based** chemotherapy (3 patients with **cisplatin** and 2 with **oxaliplatin**)
  - and **5-fluoro-uracil (5-FU)** with leucovorin rescue
- **2 patients** also had **surgical treatment**.
- In **1 patient bevacizumab** was added to cisplatin plus **irinotecan** after two cycles .
- **One patient** had definitive **preoperative radiation treatment** to a total of 45 Gy in 25 fractions.

Clinical Outcomes

- All patients experienced progression of disease,
- **Median TTP** was **4 months** (range: **2–7 months**).
- **Four** patients **died** of disease,
- **Mean time to death** from initial progression was **2.8 months** (range: **1–5 months**).

Clinical Outcomes

- The **one** patient who presented **without metastasis** remains **alive** at last clinical follow-up **8.5 years** after diagnosis and **7.5 years** since last evidence of disease.
- This patient underwent a **total gastrectomy** for initial local tumor control
- Her tumor tested **positive for**
  - **Helicobacter pylori**
  - **COX-2**.

TABLE I. Clinical Characteristics of Evaluated Pediatric Patients With Gastric Adenocarcinoma

Pt. no.	Age	Race	M/F	Location	Metastases	Duration of symptom (months)	Histology	Blood group	HP status	Genetics	Pregnancy
1	16.3	H	F	Stomach	Peritoneal carcinomatosis + right ovary + ascites	4	Diffuse adenoca + signet ring cell	A+	Unk	Unk	No
2	8.6	Arabic	F	Stomach	None	24	PDA + signet ring cells	O+	+	Pos COX 2, Neg EGFR, Neg HER2 neu, Neg C-kit	No
3	17.3	H	M	Stomach/gastro-esophagus junction	Liver	3	PDA	Unk	Unk	Unk	N/A
4	16.8	AA	M	Stomach	Liver + peritoneal carcinomatosis + rectum	1	PDA	O+	–	Unk	N/A
5	16.9	H	F	Stomach	Diffuse + liver + lung + intra-abd + vetebral	0.5	PDA + signet ring	A+	Unk	Her 2 neu Neg, ER, Neg PR	Yes

HP status, *Helicobacter pylori* status; H, Hispanic; AA, African-American; M, male; F, female; PDA, poorly differentiated adenocarcinoma; N/A, not applicable; Unk, unknown; ER, estrogen

TABLE II. Clinical Presentation, Treatment, and Outcome of Evaluated Pediatric Patients With Gastric Adenocarcinoma

Pt. no	Clinical presentation	Tumor markers	XRT (dose, Gy)	Surgery	Primary chemotherapy	Relapse regimen	SOP	TTP (months)	A/D	F/u duration (months)
1	Nausea + vomiting + weight loss	LDH 508, CEA <1, CA 125–305.3	None	No	Cisplatin + 5-FU	Irinotecan	Stomach	4.0	D	5.0
2	Anemia + abd pain + melena + hematemesis	Unk	Yes (45)	Yes—total gastrectomy, partial colectomy, partial pancreatectomy, and splenectomy	Irinotecan + taxotere + 5-FU × 4 cycles—followed by cisplatin + 5-FU adjuvant	Radiofrequency ablation	Liver	7.0	A	102
3	Dysphagia + dyspepsia + hemoptysis	LDH 587, CEA <1, CA 125–47.9, CA 19.9–724.4	None	Subtotal gastrectomy + distal esophagectomy	Epirubicin + oxaliplatin + 5-FU × 2 cycles	Irinotecan + cisplatin × 3 cycles	Stomach	4.0	D	9.0
4	Weight loss + pernicious anemia + iron deficiency anemia + diarrhea	Unk	None	No	Oxaliplatin + 5-FU + leucovorin + irinotecan	Gemcitabine + imatinib	Stomach	2.0	D	6.0
5	Epigastric pain + hemetamesis + Pul HTN + hemolytic anemia + coagulopathy + cholecystitis + pancreatitis	Unk	Yes (9)	No	Cisplatin + irinotecan + avastin × 5 cycles	None	Multiple	3.0	D	4.0

A, alive; D, dead; XRT, radiation treatment; SOP, site of progression; TTP, time to progression in months; Unk, unknown; 5-FU, 5-fluorouracil; A/D, alive/dead.

Discussion

- Our case series suggests that **pediatric GAC** patients clinically present with a pattern of disease **similar to adult GAC** patients indicating the **aggressive nature of the disease.**
- Our **lone long-term survivor** did **not** have **metastatic disease** at presentation and was able to **achieve complete local tumor therapy.**

Discussion

- The **etiology of GAC** in **adults** seems to stem from **multifactorial interaction**.
- **Lifestyle factors** such
  - **alcohol** consumption,
  - **smoking**,
  - **dietary factors**,
    - such as very **high salt** diet,
    - **low vegetable** diet,
    - **nitroso compound** content in food,
  - **infectious factors**, such as **Epstein–Barr virus** infection have been associated with GAC

Discussion

- **Helicobacter pylori infection**, especially with the positive **genotype**:
  - **vacAs1-,**
  - **vacAm1-,**
  - **cagA-**
- have also been linked toGAC.

Discussion

- The role of these factors appear to be **accentuated** in patients who already **possess** certain types of **genetic cytokine polymorphisms** like :
  - **IL-1B-511T/T**
  - **IL-1B-511T/C**
- Also individuals with **blood group A** have been known to have an **increased risk for gastric cancer** than other blood groups.

Discussion

- However, the role of these factors in the **pediatric population** is **unknown**.
- In **children GAC** develops either
  - as **de novo** occurrence,
  - as part of the **hereditary polyposis syndromes**,
  - or after treatment of **gastric lymphomas**

Discussion

- **In our case series**, none of the children had polyposis or a prior history of lymphoma, thus they are **likely de novo occurrences**.
- **One Arabic patient** tested **positive for Helicobacter pylori,** a known risk factor for GAC and commonly found in the Middle East.

Discussion

- The **differential diagnosis** of **pediatric gastric tumors** should include
  - **gastrointestinal stromal tumors**,
- and although **rare**, other tumors, such as
  - **hemangioma,**
  - **lymphoma,**
  - **squamous cell carcinoma,**
  - **carcinoids,**
  - **leiomyoma,**
  - **Peutz-Jeghers-type polyps of the stomach,**
  - **leiomyosarcoma,**
  - **lipoma,**
  - **teratoma**
- should be considered

Discussion

- Germ line **mutation** in **E-Cadherin (CDH-1)** has been reported in patients with **hereditary diffuse gastric cancer**.
- These patients were described as having a **highly penetrant susceptibility** to **diffuse gastric cancer** with an **autosomal dominant** pattern of inheritance.
- Unfortunately, none of our patients were tested for this mutation.

Discussion

- However, these **mutations** may need to **be tested** in

  young patients as these may have **major implications for survival.**
- Akin to **prophylactic mastectomy** in **BRCA1/2** patients, there are recommendations to consider **prophylactic gastrectomy** in **young**, **asymptomatic** carriers of germ-line truncating **CDH1 mutations in families with highly penetrant hereditary diffuse gastric cancer**.

Discussion

- **Clinical presentations** also varied with **mostly non-specific abdominal symptoms.**
- **One patient** had a history of **recent pregnancy** when she presented with
  - **epigastric pain,**
  - **hematamesis,**
  - **a septic shock-like syndrome**.
- On evaluation she had
  - **cholecystitis,**
  - **pancreatitis,**
  - **pulmonary hypertension,**
  - **hemolytic anemia,**
  - **coagulopathy,**
  - **diffuse metastatic signet ring carcinoma**.

Discussion

- Most of these **symptoms** and the **paraneoplastic syndromes** **resolved** after she received **two cycles of chemotherapy** consisting of **cisplatin with irinotecan (Topoisomerase inhibitor).**
- There are reports elucidating the potential role of **pregnancy** and **related hormonal stimuli** in the **progression of gastric cancer** especially in younger patients.

Discussion

- **Adult GAC** is a **very challenging cancer** and most patients present with **advanced disease at diagnosis.**
- Patients with **localized disease** are candidates for **multimodality approach** which clearly offers a **survival benefit** compared to surgery alone.
- **Complete surgical resection** offers a **potential cure** though **recurrences** within **2 years** are **still common**.

Discussion

- In the **United States**,
  - **preoperative chemoradiation** or
  - **post-operative adjuvant chemoradiation**
- is commonly practiced and has shown to **improve survival**.
- The **UK Medical Research Council (MRC) Adjuvant Gastric trial** showed survival benefit with **perioperative chemotherapy alone**, and this approach is common in **Europe**.

Discussion

- In the **metastatic setting**, **chemotherapy** can provide **palliation** and provide **some survival benefit**.
- The **5-FU(pyrimidine antagonist) with cisplatin** regimen has been the standard frontline regimen for many years.
- **Irinotecan (topomerase inhibitor)plus cisplatin** has also been studied as both a frontline and salvage regimen.
- Subsequent clinical trials have also demonstrated **docetaxel (mitotic inhibitor) and capecitabine (prodrug of 5-FU)** as being active agents.
- Another novel **fluoropyrimidine,S1**, has shown promise and is currently being evaluated in adult trials **paired with cisplatin.**

Discussion

- One prospective, randomized, multicenter phase III trial demonstrated that **trastuzumab (topoisomerase inhibitor) plus standard chemotherapy improved survival** compared to chemotherapy alone **in Her-2 positive** patients **with gastric cancer**.
- A recent randomized clinical trial did not demonstrate a survival benefit for bevacizumab added to standard chemotherapy.

Discussion

- Because of its **rarity**, the diagnosis and treatment of children and adolescents with GAC remains a **significant challenge**.
  - large multiinstitutional trials are not possible given that GAC is extremely rare in children.
  - establishing an **international tumor registry**
  - **additional molecular investigations** including **E-cadherin testing** of the tumor samples,
  - identification of **targeted genetic polymorphism**
  - **screening of families at risk**
- may offer more choices for these patients.