AMU Clinical Reasoning (CR) Session 29.8.26

Case 1 Summary

72-year-old lady with frailty (CFS 6-7) with significant vascular co-morbidities (vascular dementia, HF, CKD4, HTN, T2DM, AF on DOAC) presented with sepsis & AKI from presumed catheter associated UTI. She was treated with IV antibiotics & IV fluids whilst septic screen was sent.

The resident doctors were repeatedly asked to review the patient due to runs of AF with fast VR for which she was given bisoprolol and loading doses of digoxin. She also became fluid overloaded for which IV diuresis was commenced.

Few days later (around 1/52 into admission), she developed features of acute liver failure with thrombocytopenia, high INR & bilirubin, markedly raised ALT and was increasingly drowsy. Due to her unfortunate guarded prognosis, she passed away soon after.

Application of CR Frameworks

1. **Understanding the Problem**

   Problem Representation

   WWW:

   Who *– age, functional status, relevant co-morbidities (RFs)*
   When *– primary complaint/s: duration & tempo*
   What *– positive (+ relevant negative) findings*

   72-year-old lady with frailty (CFS 6-7) with significant vascular co-morbidities (vascular dementia, HF, CKD4, HTN, T2DM, AF on DOAC) initially presented with sepsis likely due to catheter associated UTI. Despite ward-based treatment, she developed multi-organ failure – decompensated HF (driven by AF with fast VR)

with subsequent hepatic hypoperfusion from ischaemic hepatitis resulting in acute liver failure. Due to her guarded prognosis, she passed away thereafter.

Root Cause Thinking

The sequence of events makes the case appear complex (busy with lots going on). However, taking a step back and looking at the root cause from the problem representation – we can see it all stems from ***her poor physiological reserve from her frailty & vascular end organ co-morbidities.***

We discussed how this is difficult to ascertain when resident doctors are on-call & busy and presented with only a piece of the patient's problems – i.e. decompensated HF with fast VR at the time. The advice would be two-fold - firstly practice applying the problem representation with ***a focus on RR – Risk factors and Root cause.*** *Secondly, search for* ***consultant and / or registrar entries*** *which may provide a helpful overview including trajectory & ceiling of care.*

2. Generating Hypotheses

Acute vs Chronic Pathology

This is perhaps the most important CR framework in this case. Understanding that the patient's acute presentation is not due to new pathology but representative of progression & decompensation of her frailty & multi-morbidity.

It is easy to get ***cognitively trapped in the cycle of thinking*** *- sepsis source (was it actually from the liver all along?) and list all the differentials for acute liver failure & deranged LFTs. This is important to do only when* ***we do not know the root cause and there is a new acute pathology rather than chronic frailty.***

A pragmatic approach in which we focus on updating the patient / NOK of their guarded prognosis with compassion with a holistic management approach is far more important!

For & Against Approach

This case demonstrates how in ***elderly frail patients – every management / medication has risks*** *('catch 22 medicine'). Digoxin for AF has risk of toxicity in AKI, IV diuresis for fluid overload but ongoing sepsis related hypotension with risk*

of cardio-renal syndrome and did the ischaemic liver failure result from hypotension from the sepsis or the diuretics?

The point is not to debate what is right or wrong – this goes against the very principle of pragmatism. List the pros and cons of any intervention and if you make a balanced decision in the patient's best interests then you have probably done the right thing. Remember ***– we can only make decisions with the available information at the time and hindsight bias should never be used to reprimand our actions!***

3. **Decision Making**

Trajectory thinking > diagnostic hunting

Closely tied to the acute vs chronic pathology framework – this is especially important in this case where the patient's overall declining trajectory with guarded prognosis should prompt a pragmatic approach rather than diagnostically hunting all the causes of liver failure & deranged LFTs etc.

Structured Teaching from this case

5 types of Cardio-renal syndrome

Type	Primary insult	Secondary effect	Typical example
T1	**Acute heart**	→ AKI	Acute HF → AKI
T2	**Chronic heart**	→ CKD	Chronic HF → progressive CKD
T3	**Acute kidney**	→ Acute cardiac failure	AKI → pulmonary oedema
T4	**Chronic kidney**	→ Chronic cardiac failure	CKD → LVH / IHD / HF
T5	**Systemic disease**	→ Heart & kidney	Sepsis → cardiac & renal failure

Important tips for Ischaemic hepatitis

- Look for period of hypotension prior to the markedly raised ALT
- ALT:LDH ratio <1.5 can be supportive of the diagnosis
- ALT tends to peak in a few days then downtrends in the following week
- Supportive inc. IV fluids whilst monitoring for any organ dysfunction / failure

Case 2 Summary

60-year-old Indian gentleman usually fit & well returned from travel to India 6/52 ago. He initially presented to another UK hospital with fever & fatigue but denied any other specific symptoms and had no significant abnormalities on his blood tests & blood cultures. He received multiple courses of antibiotics given persistent pyrexia albeit with nil signs of sepsis or focal source.

He re-presented to his local hospital with ongoing pyrexia for which he received a 10-day course of tazocin – repeat blood cultures, blood tests and viral & autoimmune / vasculitis screen all returned negative. Again, he denied any focal symptoms and systemic examination was largely unremarkable. His culture showed Entamoeba. CT CAP reported bowel twisting and gastric wall thickening but nil lymphadenopathy or other pathology. ECG during admission showed new-onset AF.

Whilst deciding on the best course of action with regards to further imaging & biopsy with Gastroenterology and Surgery input – unfortunately the patient deteriorated with melaena and haematemesis with haemodynamic instability. As such, he was intubated and transferred to ITU where further invasive tests including endoscopy were conducted. Later biopsies revealed he had T cell lymphoma.

Application of CR Frameworks

1. Understanding the Problem

Problem Representation

60-year-old Indian gentleman usually fit & well who returned from travel to India 6/52 ago presented with pyrexia of unknown origin. Asides from fatigue, he denied any other symptoms with unremarkable systemic examination. His pyrexia did not settle despite multiple courses of antibiotics and all investigations inc. blood cultures, blood tests, extended viral & autoimmune screen all returned negative. CT CAP however did reveal gastric thickening and twisted bowels.

This is a difficult case as despite lots of relevant negatives – there are few positives to go on. It is therefore important in cases like this to group differentials into categories (i.e. infective, malignant, autoimmune, endocrine) rather than focus all efforts on one category such as infection.

Diagnostic Discrimination

- *Disproportionate sign/s – persistent pyrexia then GI findings on CT which proved to be the main red flag of the case.*

- *Red flag or red herring – difficult initially of whether the travel to India is a red flag or red herring but when all infective panels are negative; we must consider it as a red herring. Entamoeba also turned out to be a red herring.*

- *Hallmark features – importantly, the GI pathology seen on CT (gastric thickening & twisted bowels) does narrow the wide differentials to* ***either malignancy (e.g. lymphoma), vasculitis (e.g. Localized Vasculitis of the GI tract – LVGT) or infective (e.g. Whipple's disease).***

2. Generating Hypotheses

Hypothesis A vs B

In complex cases like this, instead of thinking of individual rare conditions, we must categorise differentials into groups and investigate broadly.

For example, in this case – we can group the hypotheses as follows:

- *?Malignant process (e.g. GI lymphoma – fever, fatigue, GI findings on CT)*
- *?Vasculitic process (e.g. LVGT – localised GI findings with pyrexia)*
- *?Infective process (e.g. Whipple's disease – fever & fatigue with GI findings)*

As you can see from the list – the GI findings on CT becomes the anchoring red flag but the lack of other hallmark signs means all must be investigated. Grouping differentials with their supportive signs in this way structures our thoughts and enables for a coherent management plan towards the diagnosis.

Pre-test Probability (Bayesian reasoning)

We know from the uncertainty of the case that this is an atypical presentation of an atypical condition (top of the pyramid of likelihood). Consider the groups of differentials above – lymphoma is far more statistically likely than Whipple's disease or LVGT (limited to case series). Hence, it is important to utilise pre-test probability even amongst relatively rare conditions!

3. Decision Making

Show Your Working (Metacognition)

Also important in rare cases is to always ask yourself the question ***– what is the next best management step/s which investigates for most / all the groups of differentials with the highest yield.***

In this case, the common denominator for all hypotheses is definitive imaging +/- biopsy. PET CT could be helpful as it could provide the aetiology of the GI findings on the CT and importantly – potential sites for biopsy. OGD could also be the next best step although this is more invasive and there is no guarantee that the gastric thickening is amendable to biopsy. Perhaps a GI radiologist or Gastroenterology opinion on the CT may be the best way forward (if they think the gastric thickening is amendable to biopsy then you could potentially have saved the additional step of PET CT).

As such, there is not always a definitively correct next best step hence highlighting the ***importance of an MDT approach and thinking about how you are thinking – metacognition!***

4. Avoiding Cognitive Error

Cognitive Biases

Anchoring & Framing – it is often tempting to accept the first or someone else's diagnosis without further thought - for example in this case – thinking it is infection as another hospital thought that way.

Confirmation bias & premature closure – it is important not to only look for evidence for one diagnosis and stopping the search after prematurely committing to a diagnosis too early – for example only looking for infection.

Availability bias – it is important not to over-apply rare diagnoses to future 'similar' cases. For example, future cases of pyrexia of unknown origin should not immediately prompt a diagnosis of T cell lymphoma because of this case. Each case is independent of each other and carries different clinical contexts.

Structured Teaching from this case

Pyrexia of Unknown Origin (PUO)

Persistent pyrexia with an unclear diagnosis – this requires a careful clinical assessment & approach which does not relapse into an indiscriminate shotgun battery of tests.

Structured Four Category Differentials:

1. **Infection** – esp. deep-seated, occult and indolent (look for RFs – travel abroad, features of immunosuppression, PMH, lifestyle, recent surgery / procedure etc).

2. **Malignancy** – predominantly haematological (e.g. lymphoma, leukaemia, MDS) or solid tumours. Blood film, LDH are esp. useful. Think PET CT if CT CAP & infective panel negative.

3. **Inflammatory / Immune-mediated** – very large group of vasculitis and connective tissue disorders. Look for systemic signs or organ involvement and consider checking autoimmune & vasculitis screen, ferritin, ESR, complements.

4. **Miscellaneous** – often forgotten or overlooked in PUO. Always check for drugs causing fever! Endocrine causes such as thyrotoxicosis & adrenal insufficiency and psychiatric causes such as catatonia, malignant neuroleptic syndrome etc.

Important tips for Clinical Approach:

- **History & exam approach:** PUO requires a careful assessment – repeating the history +/- collateral often provides the key disproportionate sign which leads the path to the diagnostic work-up. Repeated examination may reveal what was not present days earlier. Be vigilant!

- **Trajectory approach:** instead of looking at one isolated set of results – look at the trend & trajectory of the blood tests, observations, clinical features etc!

- **Targeted approach:** deliberate diagnostic strategy to avoid the 'do everything testing' where abnormal results (false positives or cross reactivity) generate more confusion than diagnostic clarity. Continuously update the problem representation with new findings which helps a targeted approach!

Instead of asking – 'what tests haven't we done yet?'

Ask – **'What diagnostic hypotheses do we have so far and what are the highest yield next management steps?'**

Case 3 Summary (Short)

62-year-old lady who works as a pharmacy technician was diagnosed with metastatic cholangiocarcinoma (liver & adrenal mets) 2/12 ago. She presented with significant ascites & bilateral pitting oedema with rising CRP, deranged LFTs, hypoalbuminemia with electrolyte disturbance (hyponatraemia & hyperkalaemia). Her main concern was severe pain for which she was given 10mg oral morphine despite her opiate naivety.

Overall, the medical team instigated a Best Supportive Care (BSC) approach for the patient with focus on symptom control & comfort care with the involvement of the Palliative Care team. Time was taken to compassionately explain the guarded prognosis and palliative approach to the patient who understood and was in agreement in her best interests.

Application of CR Frameworks

1. **Understanding the Problem**

   Problem Representation

   62-year-old lady who works as a pharmacy technician diagnosed with metastatic cholangiocarcinoma with liver & adrenal involvement 2/12 ago presented with disease progression causing significant frailty & predominantly pain. Clinical features included ascites & pitting oedema with biochemical markers of progression (inc. rising CRP, LFTs, hypoalbuminemia, hyponatraemia & hyperkalaemia). She was managed with BSC approach including involvement of the Palliative Care team to optimise symptom control & comfort care.

Root Cause Thinking

The root cause of the patient's features was all due to progression of her metastatic cholangiocarcinoma with an overall guarded prognosis. As such, if we do not link all of her problems into her root cause – we are in danger of spiralling into intangible tangents by investigating each abnormal finding in isolation.

2. Generating Hypotheses

Acute vs Chronic Pathology

This case also demonstrates that the patient did not present with an acutely new pathology but features all due to progression of her chronic pathology. As such, spending time to compassionately communicate the prognosis and explore the patient's needs & wishes holistically should be the clinical priority.

3. Decision Making

Trajectory thinking > diagnostic hunting

Indeed, even if some of the patient's abnormalities were due to another pathology – it does not change the overall trajectory of her guarded prognosis hence emphasizing the importance of thinking of trajectory over diagnosis.

XYZ Formula

This case also shows the importance of not investigating or managing if it will not change the patient's trajectory. Although Oncology review and CT CAP may be helpful in confirming a palliative approach and providing evidence for disease progression respectively; it is unlikely to change management hence focus & efforts should be directed towards a palliative approach.