An Unusual Cause of Abdominal Pain in an HIV-positive Patient

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Background

- 68-year-old Caucasian heterosexual man
- Worked in Zambia for 14 years
- HIV diagnosed in 2004
- ART started in 2004
- Routine blood result (March 2010)
  - CD4 = 239 (20%)
  - HIV VL = Undetectable

Background

- PMH
  - Shingles (2004)
  - Recurrent pneumonia
  - Genital herpes

- Drugs
  - Truvada 1 tablet od
  - Efavirenz 600 mg od
  - Pravastatin 40 mg nocte
  - Adcal D3 1 bd
Hospital Admission (Surgical)  
(15/7/2010)

Flew back to Swansea from Zambia  
• Progressively worsening right-sided abdominal pain for 2 weeks  
• Dark stool for 1 week

• No nausea/vomiting/fever/jaundice/change in bowel habit/loss of appetite/abdominal mass  
• Admitted under surgeons

Admission findings

• Apyrexic  
• BP = 115/65, HR = 90 bpm, SaO2 = 98% (RA)  
• Abdomen  
  – Soft, tenderness on right lower quadrant  
  – No obvious mass  
  – BS (+)  
• PR  
  – NAD
Initial Impression

- ?Appendicitis
- ?Diverticulitis
- ?Biliary colic
- ?Malignancy

Admission Blood Results

<p>| | | | | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Hb</td>
<td>12.3 g/dl</td>
<td>Na⁺</td>
<td>137 mmol/L</td>
<td>Total protein</td>
<td>77 g/L</td>
</tr>
<tr>
<td>WBC</td>
<td>16 x 10^9/L</td>
<td>K⁺</td>
<td>3.4 mmol/L</td>
<td>Albumin</td>
<td>37 g/L</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>13.7 x 10^9/L</td>
<td>Urea</td>
<td>12.1 mmol/L</td>
<td>Bilirubin</td>
<td>20 umol/L</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>1.2 x 10^9/L</td>
<td>Creatinine</td>
<td>99 umol/L</td>
<td>ALP</td>
<td>124 IU/L</td>
</tr>
<tr>
<td>Monocyte</td>
<td>1.1 x 10^9/L</td>
<td>CRP</td>
<td>44 mg/L</td>
<td>ALT</td>
<td>42 IU/L</td>
</tr>
<tr>
<td>Platelet</td>
<td>223 x 10^9/L</td>
<td></td>
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</table>
CXR
(7/7/2010)

Supine Abdomen X-ray
(15/7/2010)
Where is the main abnormality in CT abdomen just shown? (please choose one answer)

- (A) Pancreas
- (B) Bowel
- (C) Blood vessel
- (D) Hepato-biliary tree
Based on the clinical and CT findings, which further investigation(s) would you request? (please choose one answer)

- (A) Porphyrin level
- (B) ERCP/MRCP
- (C) Thrombophilia screen
- (D) Mesenteric arteriography

CT abdomen
(16/7/2010)

- Dilatation of stomach
- Small bowel dilatation with highly abnormal loop in RIF
- Non-occlusive thrombus extending from Superior Mesenteric Vein into portal vein
- Features of portal hypertension
- No biliary dilatation, GB stones (+)
- Conclusion: Superior mesenteric vein thrombosis ± venous infarction of small bowel
CT abdomen (16/7/2010)

CT abdomen
(16/7/2010)
CT abdomen (16/7/2010)

Emergency Laparotomy (16/7/2010)

- Inflammatory mass in RIF (3 loops of small bowel, caecal mesentery and omentum)
- Perforation in the ileum, 60-70 cm from ileo-caecal valve
- Gangrenous patch – anti-mesenteric border, stuck to omentum and small bowel loop
- Resection of 40 cm segment of perforated small bowel performed
Small Bowel Biopsy

- Complete necrosis of the wall in perforated area
- Chronic ulceration with lining of the mucosal surface by granulation tissue
- Submucosal fibrosis and atrophy of muscularis propria
- Thrombosis in arterial and venous vessels in surrounding fat
- **Conclusion:** Acute on chronic mesenteric ischaemia and infarction
Normal Immunostain for smooth muscle actin: normal thickness left: chronic atrophy right

Vascular proliferation in sub-mucosa

ulceration

Immunostain for smooth muscle actin: normal thickness left: chronic atrophy right
# Thrombophilia Screen
*(16/7/2010)*

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein C</td>
<td>60.8% (75-160)</td>
<td>PT 14.6 secs (9-12.5)</td>
</tr>
<tr>
<td>Free protein S</td>
<td>44% (73-163)</td>
<td>APTT 23.6 secs (22.1-30.9)</td>
</tr>
<tr>
<td>Activated protein C ratio</td>
<td>2.56 (2-4)</td>
<td>Fibrinogen 3.5 g/L (1.5-4.2)</td>
</tr>
<tr>
<td>Anti-thrombin</td>
<td>100.6% (86-128)</td>
<td>FSL APTT 28.7 secs (26-35)</td>
</tr>
<tr>
<td>IgG cardiolipin Ab</td>
<td>3.6 GPLU/ml(0-10)</td>
<td>Thrombin clotting time 16 secs (12.5-17.4</td>
</tr>
<tr>
<td>IgM cardiolipin Ab</td>
<td>5 MPLU/ml(0-7)</td>
<td>KCT test ratio 0.69 (0-1.2)</td>
</tr>
<tr>
<td>Prothrombin mutation</td>
<td>heterozygous</td>
<td>DRVVT ratio 1.12 (0.8-1.2)</td>
</tr>
</tbody>
</table>

## Further Progress
- Uneventful post-operative recovery
- Ready to be discharged on 26/7/2010
What will you do next? (please choose one answer)

- (A) Change his current anti-retroviral regimen
- (B) Protein C and S replacement therapy
- (C) Low-molecular weight heparin and repeat thrombophilia screen
- (D) Immediate initiation of warfarin with close INR monitoring

Repeat Thrombophilia Screen

<table>
<thead>
<tr>
<th>Protein C</th>
<th>64.5% (75-160)</th>
<th>PT</th>
<th>11.3 secs (9-12.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free protein S</td>
<td>82.3% (63-132)</td>
<td>APTT</td>
<td>26.3 secs (22.1-30.9)</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>204.8% (48-204)</td>
<td>Fibrinogen</td>
<td>2.5 g/L (1.5-4.2)</td>
</tr>
<tr>
<td>IgG cardiolipin Ab</td>
<td>4.4 GPLU/ml(0-10)</td>
<td>FSL APTT</td>
<td>30.7 secs (26-35)</td>
</tr>
<tr>
<td>IgM cardiolipin Ab</td>
<td>3.6 MPLU/ml(0-7)</td>
<td>KCT test ratio</td>
<td>0.71 (0-1.2)</td>
</tr>
<tr>
<td>JAK mutation</td>
<td>negative</td>
<td>DRVVT ratio</td>
<td>1 (0.8-1.2)</td>
</tr>
</tbody>
</table>
Further Progress

- Uneventful post-operative recovery
- Haematology review
- LMW Heparin followed by life-long warfarinization after repeat thrombophilia screen

Classification of the causes of mesenteric venous thrombosis

<table>
<thead>
<tr>
<th>Primary (30%)</th>
<th>Secondary (60%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin III deficiency</td>
<td>Intra-abdominal sepsis</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>Umbilical sepsis following piercing</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Platelet disorders</td>
<td>Inflammatory intestinal disease</td>
</tr>
<tr>
<td>Myeloproliferative disorders</td>
<td>Trauma</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>Polycythaemia rubra vera</td>
<td>Sclerotherapy of varices</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Puerperium</td>
<td></td>
</tr>
<tr>
<td>Contraceptive pills</td>
<td></td>
</tr>
<tr>
<td>Idiopathic (10%)</td>
<td></td>
</tr>
</tbody>
</table>
Coagulation abnormalities in HIV infection\textsuperscript{2}

- Protein S deficiency
- Protein C deficiency
  - Increased level of complement binding protein 4
  - Acquired activated protein C resistance
  - Anti-cardiolipin/anti-phospholipid antibodies
  - Antithrombin III deficiency
  - Heparin cofactor II deficiency
  - Elevated factor VIII
  - Increased plasminogen activator inhibitor
  - Increased platelet activation
  - Activation of arterial smooth muscle cells by gp120

Protein C and S deficiency and thrombosis in HIV infection

- Incidence of thrombotic events in HIV patients requiring hospital admission: 0.26\% - 7.6\%\textsuperscript{5,6}
- Protein S deficiency incidence: 54\% - 67\%\textsuperscript{4}
- Protein C deficiency incidence: 8\% - 25\%\textsuperscript{4}
- Inflammatory state, endothelial injury, autoimmune mechanisms associated with HIV infection are implicated
- More prevalent in sick HIV patients with low CD4 count and those admitted for opportunistic infections or malignancies
Management strategies

- Treatment/removal of precipitating factors (e.g. opportunistic infections)
- Modification of ART (?protease inhibitors)
- Antiplatelet
- Anticoagulants
- Specific management of individual thrombotic complications

Specific Learning Points

- HIV-infected patients are at increased risk of venous and arterial thrombosis.
- Protein C and S deficiency have been well documented in patients with HIV infection presenting with thrombotic episodes.
- Systemic inflammation, endothelial injury, autoimmune mechanism and platelet activation associated with HIV infection are implicated in the development of thrombophilic abnormalities.
- Thrombophilia screen is mandatory in HIV patients presenting with thrombo-embolism who have no known risk factors for thrombosis.
- Effective management of precipitating factors (e.g. opportunistic infection) and, if indicated, life-long anticoagulation are proven to prevent recurrence of thrombotic complications in sick HIV patients.
References