

# CASE 1

# Case 1

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- Case description:
    - Ethnicity, gender, age: Caucasian, female, 37 years
    - Comorbid conditions: none, history of gestational diabetes and cholestasis of pregnancy
    - Alcohol consumption: occasionally
    - Suspected medication(s)/start and stop dates:  
azithromycin 500 mg/day (25/11/2013-28/11/2013)  
and amoxicillin-clavulanate 875-125 mg/8 hrs  
(27/11/2013-03/12/2013)
    - Concomitant medications (start and stop dates): none
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# Case 1

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- When did symptoms suggestive of DILI appear?  
pruritus (29/11/2013)
  - Liver parameters at DILI recognition:  
ALT 8.8x ULN, TBL 2x ULN (01/12/2013)
  - Baseline values prior to DILI episode: not available
  - Time to onset: 4 days (azithromycin), 2 days (amoxicillin-clavulanate)
  - Did the patient experience hypotension, bradycardia, sepsis, etc suggestive of ischemic hepatitis? No
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# Case 1

Anti-HAV IgM  
Anti-HCV  
RNA-HCV  
AgHBs  
Anti-HBc  
DNA-HBV  
EBV IgM  
CMV IgM  
HSV1 IgM  
HSV2 IgM

**Negative**

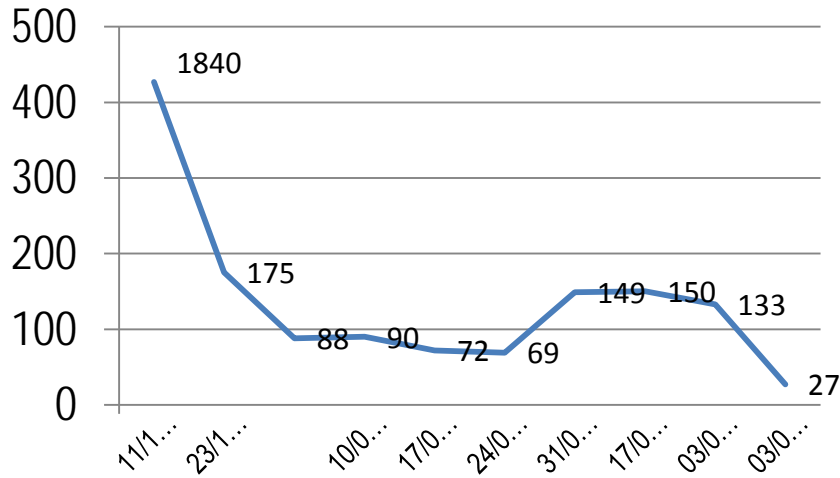
**Ultrasound:** Normal  
(30/12/2013)

**Autoantibodies:** ANA, ASMA,  
AMA, anti-LKM were negative  
(10/12/2013)

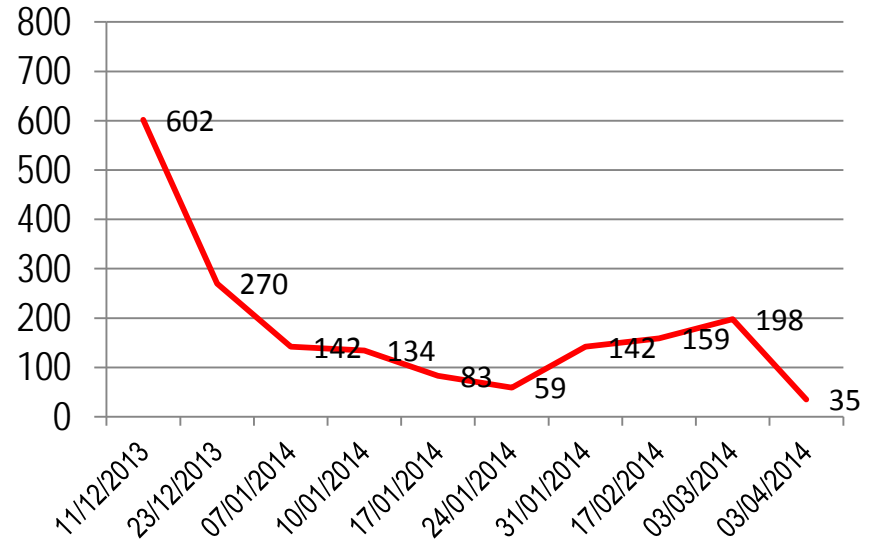
**Biopsy:** No information (not  
likely to have been performed)

# Liver parameter progression

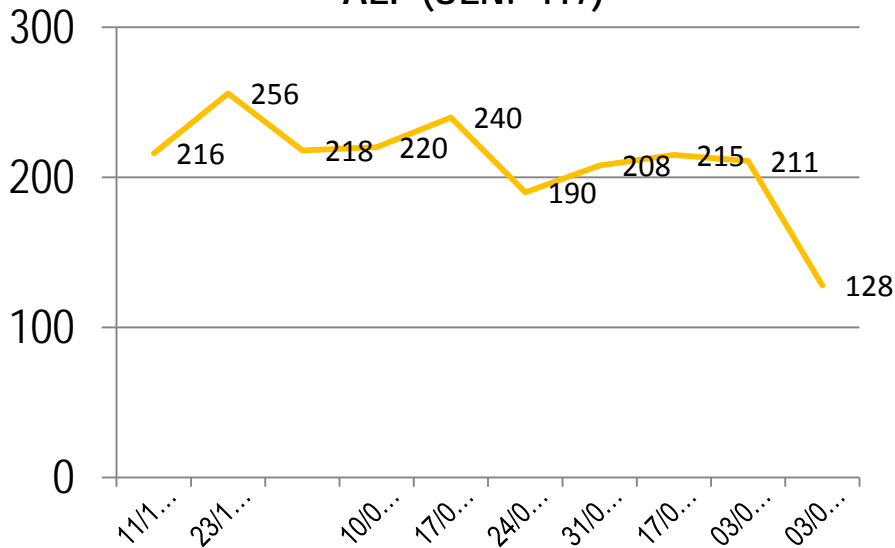
**AST (ULN: 40)**



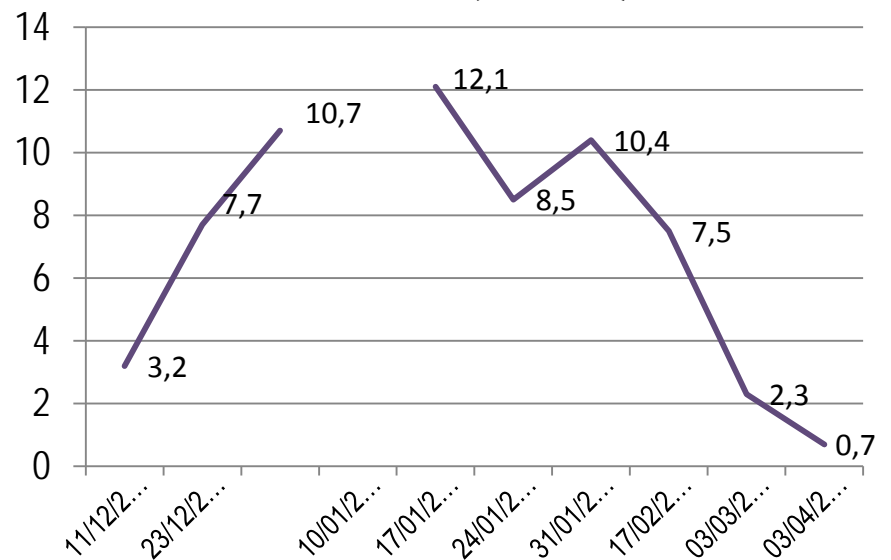
**ALT (ULN: 42)**



**ALP (ULN: 117)**



**TBL (ULN: 1.1)**



# Outcome

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- Outcome: Patient was treated with dexchlorpheniramine and cholestyramine for pruritus. Complete recovery.
  - Time to recovery: 124 days
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# CASE 2

# Case 2

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- Case description:
    - Ethnicity, gender, age: Caucasian, female, 85 years
    - Comorbid conditions: Hypertension, dyslipidaemia
    - Alcohol consumption: Denied
    - Suspected medication(s)/start and stop dates:  
**Amoxicillin-clavulanate: 1g/8h for 8 days (8-16 March 2008)**
    - Concomitant medications (start and stop dates)
    - Amiloride (longterm, specific dates unknown)
    - Lovastatin (longterm, specific dates unknown)
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# Case 2

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- When did symptoms suggestive of DILI appear?  
Pruritus, dark urine and scleral icterus (07/04/2008)
  - Liver parameters at DILI recognition:  
AST: 238 IU/L ALT: 495 IU/L ALP: 396 IU/L TBL: 6.4 mg/dL
  - Baseline values prior to DILI episode: unknown
  - Time to onset: 1 month
  - Did the patient experience hypotension, bradycardia, sepsis, etc. suggestive of ischemic hepatitis? No, but complete information on pneumonia outcome unavailable.
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# Case 2

anti-HAV IgM  
HBsAg  
Anti-HBc  
Anti-HCV  
CMV IgM  
EBV IgM  
Anti-HBc

**Negative**

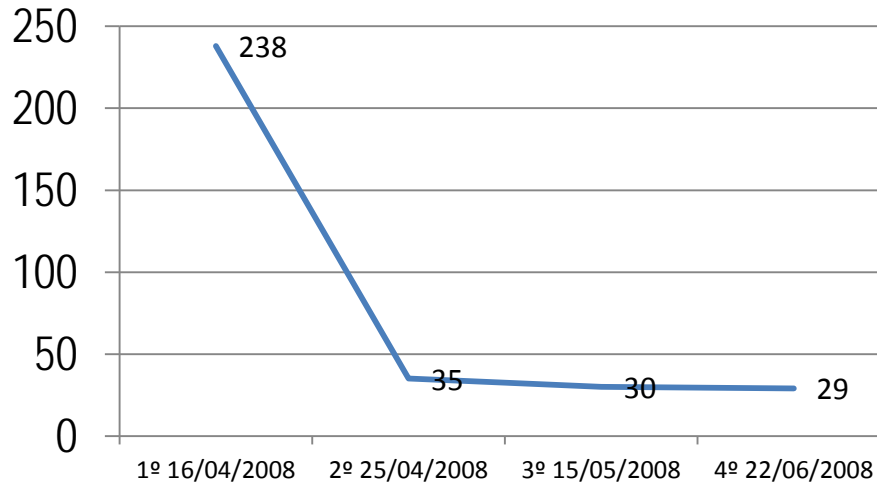
**Ultrasound:** Normal  
(15/04/2008)

**Autoantibodies:** ANA, ASMA,  
AMA, anti-LKM were negative  
(16/04/2008)

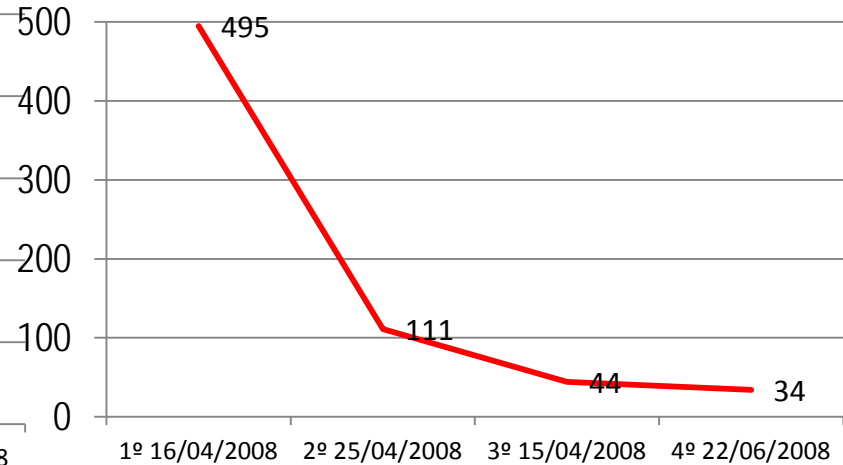
**Biopsy:** No information (most  
likely not performed)

# Liver parameter progression

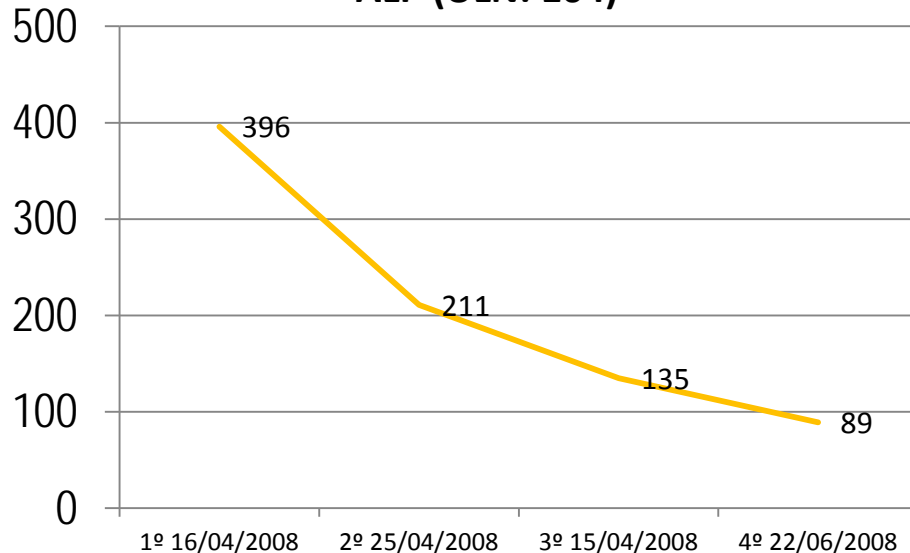
### AST (ULN: 40)



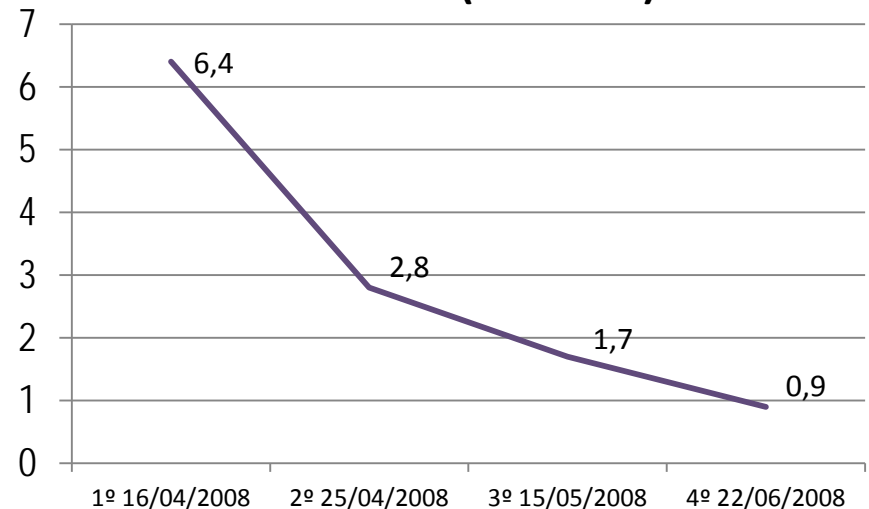
### ALT (ULN: 40)



### ALP (ULN: 104)



### TBL (ULN: 1.1)



# Outcome

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- Outcome: Complete recovery
  - Time to recovery: 77 days
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# CASE 3

# Case 3

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- Case description:
    - Ethnicity, gender, age: Caucasian, male, 35 years
    - Comorbid conditions: none
    - Alcohol consumption: no
    - Suspected medication(s)/start and stop dates:  
**terbinafine: 500 g/12 hrs (17/03/2018-14/04/2018)**
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# Case 3

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- Case description:
    - Concomitant medications (start and stop dates):  
Amoxicillin-clavulanate (12/02/2018 - 22/02/2018)
    - Fusidic acid (topic) 12/02/2018 - 26/02/2018 and  
17/03/2018 - 27/03/2018)
    - Betamethasone clotrimazol (topic) 17/03/2018 –  
17/04/2018
    - Clobetasol propionate (topic) 17/03/2018 – ongoing  
during hospitalization
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# Case 3

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- **When did symptoms suggestive of DILI appear?**  
Jaundice, choluria, acholic stools, discomfort in upper right quadrant  
and pruritus (23/04/2018)
  - **Liver parameters at DILI recognition:**  
AST 4.6x ULN and TBL 4.3x ULN
  - **Baseline values prior to DILI episode:** Not available
  - **Time to onset:** 37 days
  - **Did the patient experience hypotension, bradycardia, sepsis, etc suggestive of ischemic hepatitis?** No
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# Case 3

Anti-HAV IgM  
HBsAg  
Anti-HBc  
Anti-HCV  
HCV-RNA  
Anti-HEV IgM  
Anti-EBV IgM  
Anti-CMV IgM  
Anti-HSV1 IgM  
Anti-HSV2 IgM

**Negative**

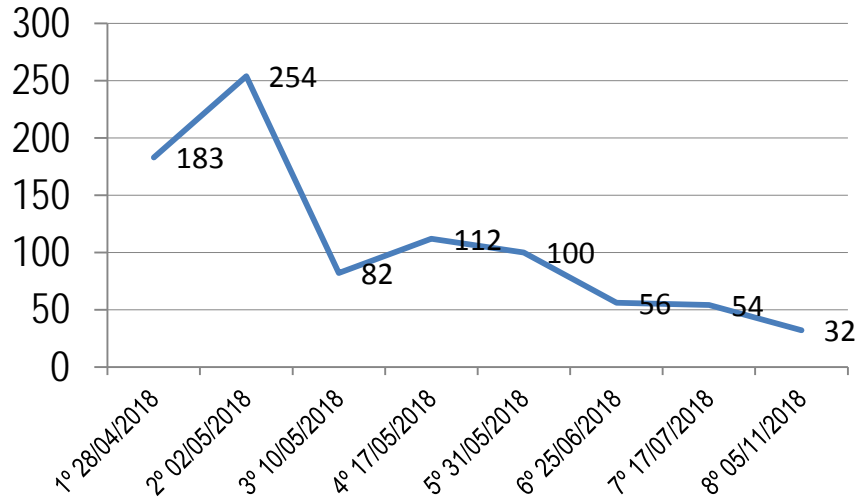
**Ultrasound:** Normal (28/04/2018)  
**MRCP:** Normal (28/04/2018)

**Autoantibodies:** ASMA: 1/320,  
actine-F positive, while ASMA, AMA  
and anti-LKM were negative  
(30/04/2018)

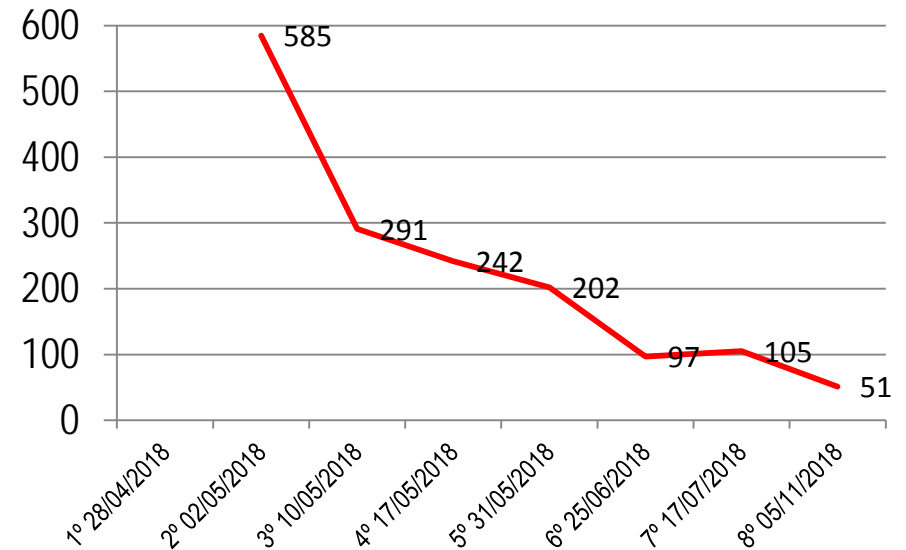
**Biopsy** (11/05/2018): Eosinophils,  
signs of cholestasis signs.  
Histological data not concordant with  
AIH, suggestive of mild stage drug-  
induced hepatitis

# Liver parameter progression

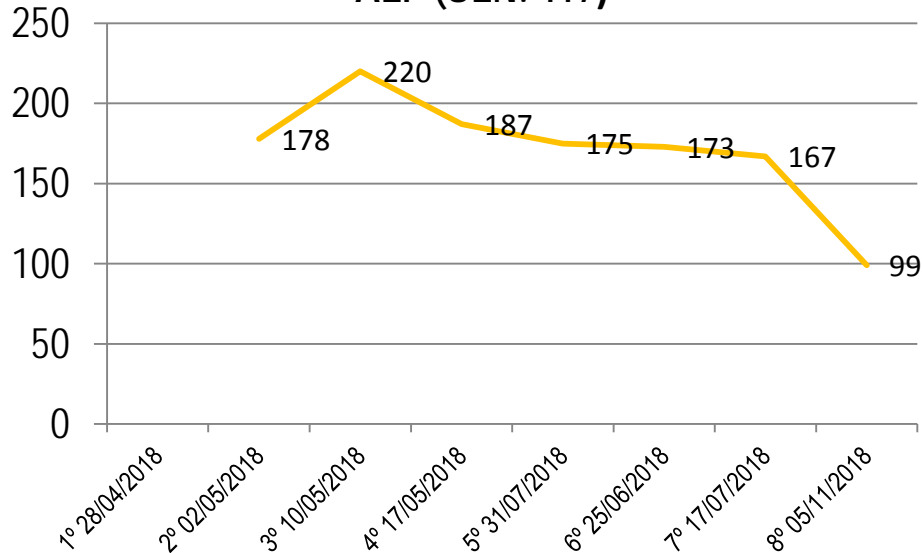
### AST (ULN: 40)



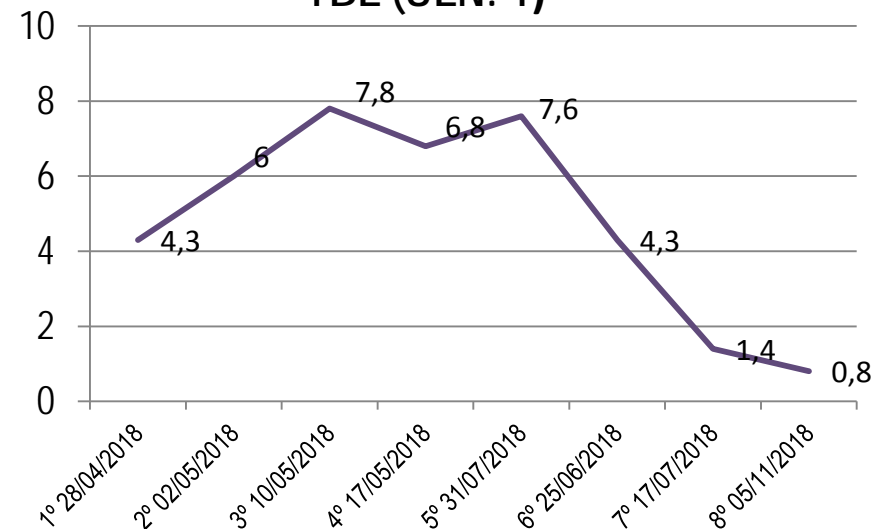
### ALT (ULN: 40)



### ALP (ULN: 117)



### TBL (ULN: 1)



# Outcome

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- Outcome: Complete recovery
  - Time to recovery: >180 days
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# CASE 4

# Case 4

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- Case description:
    - Ethnicity, gender, age: Caucasian, female, 49 years
    - Comorbid conditions: hypertension, history of knee surgery and miscarriages (4)
    - Alcohol consumption: no
    - Suspected medication(s)/start and stop dates:  
**paracetamol: ~ 7 g (12 February 2015)**
    - Concomitant medications (start and stop dates):  
unknown
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# Case 4

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- **When did symptoms suggestive of DILI appear?**  
abdominal pain, nausea, anorexia, dark urine (13/02/2015)
  - **Liver parameters at DILI recognition:**  
AST 26 xULN, ALT 40xULN, ALP 3xULN and TBL 3xULN
  - **Baseline values prior to DILI episode:**  
ALT and TBL: normal (21/05/2013)
  - **Time to onset: 1 day**
  - **Did the patient experience hypotension, bradycardia, sepsis, etc suggestive of ischemic hepatitis?** No, but received hyaluronic acid injections, which may have resulted in infection
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# Case 4

Anti-HAV IgM

Anti-HCV

RNA-HCV

AgHBs

DNA-HBV

EBV IgM

CMV IgM

HSV1 IgM

HSV2 IgM

**Negative**

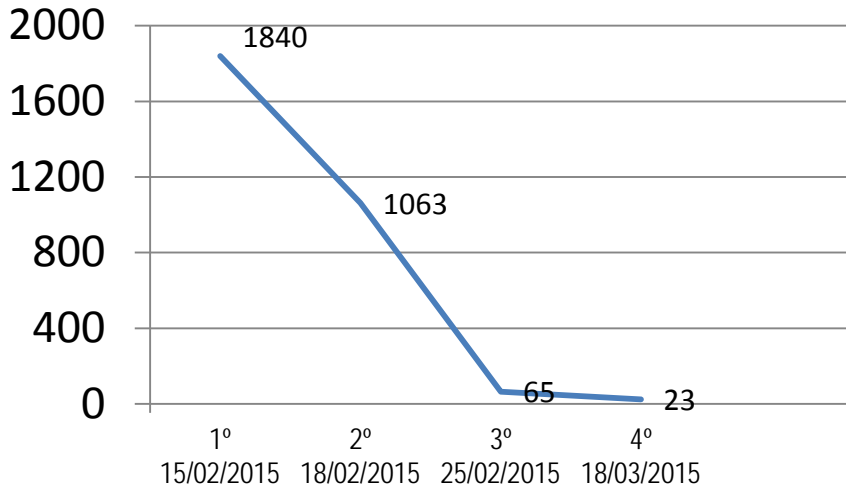
**Ultrasound:** Normal  
(14/02/2014, no ultrasound made more recently)

**Autoantibodies:** ANA, ASMA, AMA, anti-LKM were negative  
(18/02/2015)

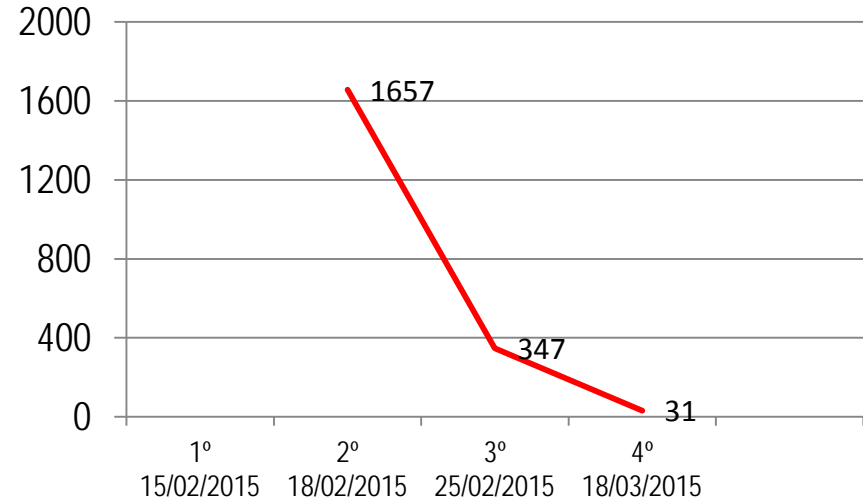
**Biopsy:** Not performed

# Liver parameter progression

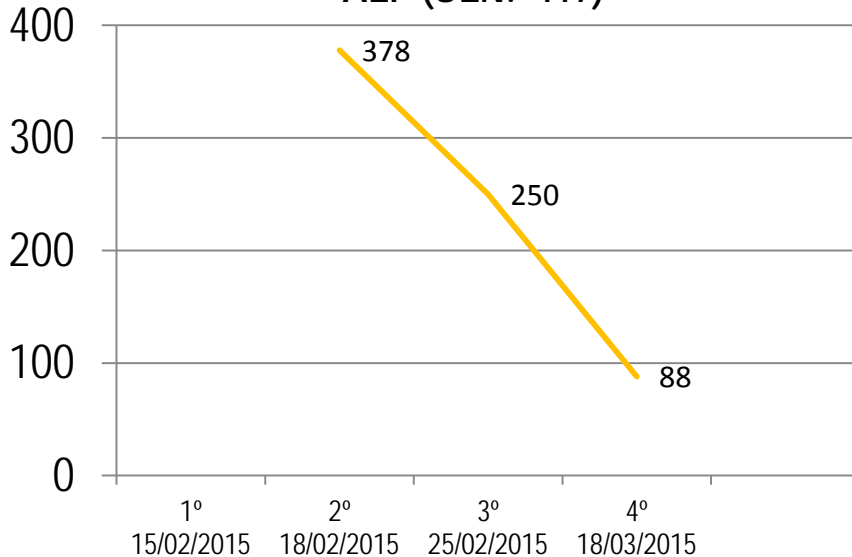
### AST (ULN: 40)



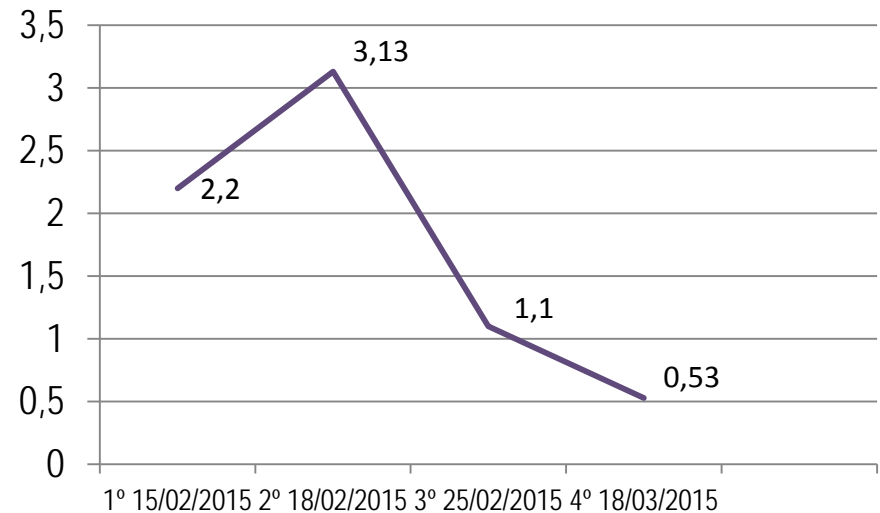
### ALT (ULN: 42)



### ALP (ULN: 117)



### TBL (ULN: 1.1)





# Outcome

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- Outcome: Complete recovery
  - Time to recovery: 35 days
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# CASE 5

# Case 5

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- Case description:
    - Ethnicity, gender, age: Caucasian, male, 20 years
    - Comorbid conditions: Thalassemia minor
    - Alcohol consumption: Occasionally
    - Suspected medication(s)/start and stop dates:  
**Anabolic steroids (epithiostanol) : (26/09/2016-31/10/2016)**
    - Concomitant medications (start and stop dates): None
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# Case 5

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- When did symptoms suggestive of DILI appear?  
Pruritus, jaundice, asthenia (31/10/2016)
  - Liver parameters at DILI recognition:  
ALT: 344 IU/L ALP: 190 IU/L TBL: 13 mg/dL (creatinine: 1.4 mg/dL)
  - Baseline values prior to DILI episode: unknown
  - Time to onset: 1 month
  - Did the patient experience hypotension, bradycardia, sepsis, etc. suggestive of ischemic hepatitis? No.
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# Case 5

anti-HAV IgM  
HBsAg  
Anti-HBc  
Anti-HCV  
CMV IgM  
EBV IgM  
Anti-HBc

**Negative**

**Ultrasound:** Normal (07/11/2016)  
**MRI:** Normal (08/11/2016)

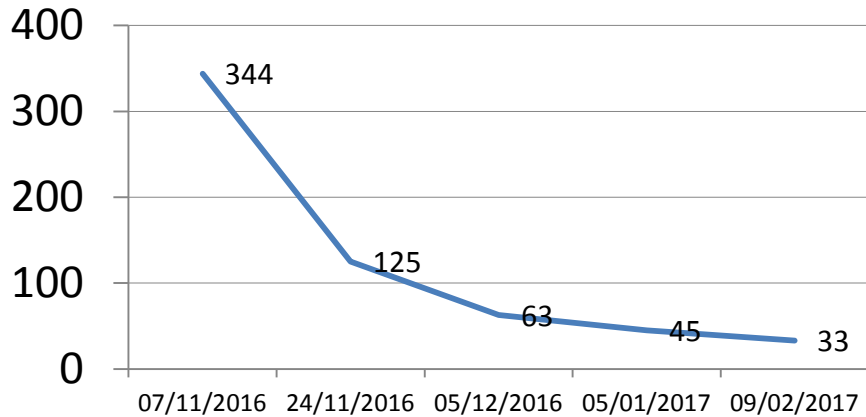
**Autoantibodies:** ANA, ASMA, AMA, anti-LKM were negative (10/11/2016)

**Biopsy (27/11/2016):** Accumulation of biliary pigment inside hepatocytes together with necrosis and a small number of neutrophil and eosinophil aggregates mostly in central areas.

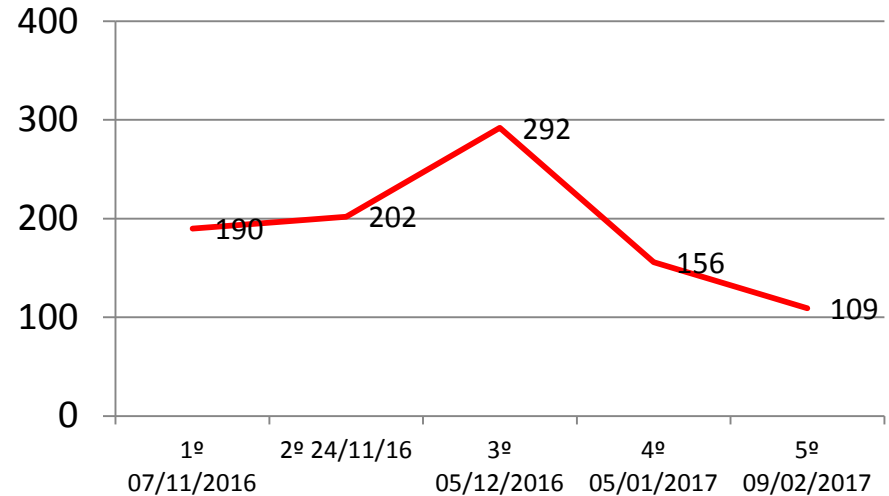
**Renal biopsy (25/11/2016):** Acute tubular necrosis with tubular deposits of biliary pigment

# Liver parameter progression

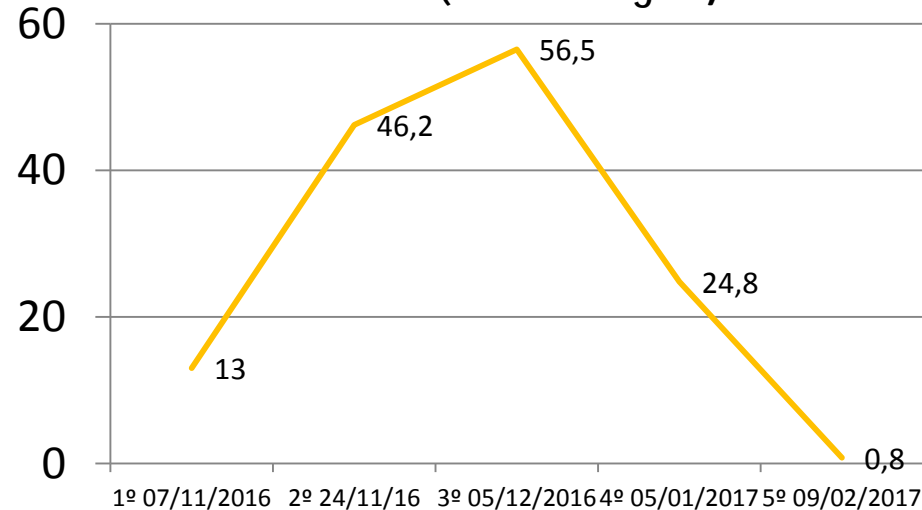
### ALT (ULN: 40 IU/L)



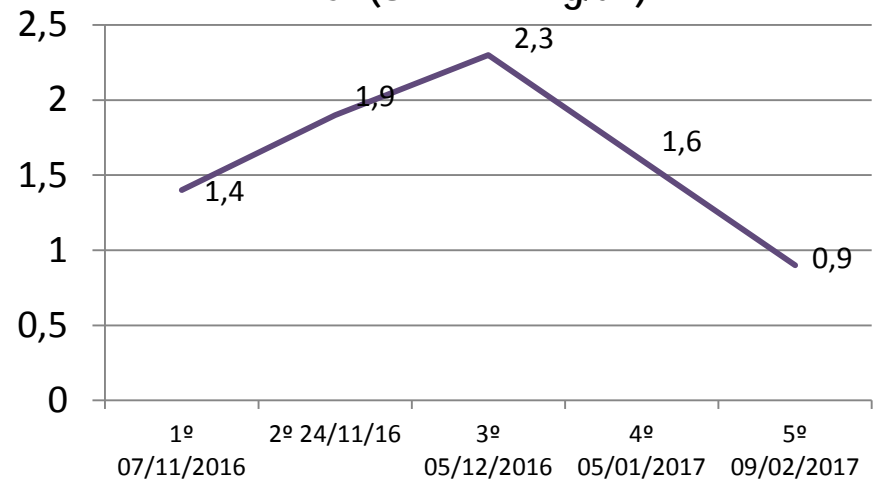
### ALP (ULN: 117 IU/L)



### TBL (ULN: 1.1 mg/dL)



### Cr (ULN: 1.1 mg/dL)



# Outcome

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- Outcome: Required extracorporeal albumin dialysis (MARS). Complete recovery
  - Time to recovery: 101 days
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