DISCLOSURE

IPSEN: honoraria for advisory board
Clinical case

- May 2010
- 26 years old, female
- No medical history
- Soprano opera singer
- Complains of abdominal left pain and asthenia
- ECOG 1
- ALT 2 ULN, ALP 3ULN
Clinical case

A CT scan is performed (early liver i.v. contrast imaging):

Hypervascular pancreatic primary and secondary liver lesions:
→ neuroendocrine tumour suspicion

CT, computed tomography; i.v., intravenous
Q1. What is the baseline work-up for this putative pNET?

(one correct answer)

1. Biopsy of a liver metastasis
2. Somatostatin receptor imaging (68Ga-DOTA PET or somatostatin receptor scintigraphy SPECT/CT)
3. Serum chromogranin A measurement
4. Search for symptoms of functioning tumours
5. Search for MEN1-associated features
6. Liver MRI
7. All the above

CT, computed tomography; MEN1, multiple endocrine neoplasia type 1; MRI, magnetic resonance imaging; PET, positron emission tomography; pNET, primitive neuroendocrine tumour; SPECT, single-photon emission computed tomography
Pathology report:
Well-differentiated neuroendocrine tumour (NET)
Pan-cytokeratin +, CgA +, synaptophysin +
< 2 mitosis/10 HPF, Ki67 5%-8%: WHO grade 2

Scintigraphic/PET evaluation:
Somatostatin receptor scintigraphy:
Liver: grade 0-3
Pancreas: grade 4 periphery

FDG-PET:
Liver: SUVmax 4.5
Pancreas: SUVmax 7.6 (necrotic)

CgA, chromogranin A; FDG-PET, fluorodeoxyglucose positron emission tomography; HPF, high power field; MEN1, multiple endocrine neoplasia type 1; FDG-PET, fluorodeoxyglucose positron emission tomography; SUV, standardised uptake value; WHO, World Health Organization
Q2. All are suitable therapeutic options except which one?

(one wrong answer)

1. Watchful follow-up
2. Somatostatin analogues
3. Platinum-etoposide chemotherapy
4. Debulking surgery
5. Sunitinib
6. Everolimus
Clinical case

Lanreotide 120 mg every 28 days from May 2010 to September 2010

Stable disease
Q3. All are suitable therapeutic options except which one?

(one wrong answer)

1. Continue somatostatin analogues and imaging work-up 3 months later
2. Combine somatostatin analogues with locoregional treatment including surgery
3. Change for streptozotocin/TMZ-based chemotherapy
4. Change for everolimus or sunitinib
5. Change for Peptide Receptor Radionuclide Therapy with $^{177}$Lu-DOTATATE
Therapeutic goal: to obtain tumour shrinkage may improve prognosis.

Expert surgeons’ opinion:
Complete resection is not achievable. Peripancreatic and perigastric varices could become problematic. Bulky liver: safety concerns with TA(C)E

Systemic treatments
→ Lanreotide provides only stable disease
→ Everolimus provides 5% partial responses in the RADIANT-3 phase III trial
→ Sunitinib provides 9% partial responses in the sunitinib phase III trial
→ Chemotherapy can provide objective responses in an average of 35% of cases

TA(C)E, transarterial (chemo)embolisation; TMZ, temozolomide
• From October 2010 to April 2011:
  ✓ 5-FU/STZ
  ✓ Temozolomide /capecitabine → TMZ alone.

• Stable disease, stopped for grade 4 thrombocytopenia and

• Several haematemesis episodes:
  ✓ Oesophageal varices treated by several rounds of endoscopic ligation
  ✓ Portal vein hypertension without thrombosis, splenic vein thrombosis, ascitis
  ✓ Liver biopsy: no cirrhosis, sinusoidal obstruction syndrome related to chemotherapy and tumor infiltration

5-FU, 5-fluorouracil; SMS, somatostatin; STZ, streptozocin; TMZ, temozolomide
Clinical case

- **Everolimus**: 10 mg decreased to 5 mg/day because of grade 2 pneumonia.
Clinical case

Multidisciplinary neuroendocrine tumour board

April 2012

Goal = tumour volume reduction in this young patient (28 yo) with non progressive disease.
Q4. How would you achieve that goal (4th line)?

(one correct answer)

1. Continue everolimus
2. Resume somatostatin analogues
3. Change for sunitinib
4. Change for platinum-etoposide
5. Debulking surgery and/or transplantation
Surgery of the primary on May 2012: pancreatosplenectomy

Complication: retro-gastric haematoma and high-volume ascites

Pathology Report: 10 x 9 x 7cm tumour of the pancreas tail, spread into peri-pancreatic space, 15% of the tumour has been sterilised due to previous treatment, spleen involvement, no metastatic lymph node, Ki67 12%

TNM-ENETS Stage: T4N0M1
Clinical case

Multidisciplinary neuroendocrine tumour board April 2013:

Is patient eligible for liver transplant?
→ Liver surgeon: yes, provided disease remains stable

Maintenance capecitabine

Liver transplant performed in August 2015

Complete resolution of portal hypertension-related complications
August 2017:
2 years after liver transplant, 
7 years after initial diagnosis, 
no sign of liver metastasis

October 2018: the patient is back in France after a 1-year period abroad and several concerts

→ ultrasonography : 2 suspicious lesions near the gallbladder bed…
Combining systemic therapies and loco-regional treatments over a 8-year period

- Lanreotide 120 mg
- 5FU/STZ
- Cap Tem
- Everolimus
- Surgery of primary
- Capecitabine
- Liver transplant

- No objective response
- Haematemesis episodes
- Grade 4 thrombopaenia
- Grade 2 respiratory toxicities
- Retro-gastric haematoma
- Portal vein hypertension

Will one treatment-related toxicity impede further line(s)?

Back to normal life
Thank you for your attention

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