Complex clinical case session

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Case 1: Alessandro VOLPE
Clinical Case
M.R.F., female, 69 y.o.

- Overweight
- High blood pressure
- IDDM
- Dyslipidemia
- Bilateral glaucoma
- Acute bleeding from gastric ulcer (2010)
• Macroscopic hematuria
• Abdominal US
  • 12 cm right renal mass
  • 15 mm left renal stone
• Total body CT scan  
  • Brain/neck/chest negative
Clinical Case
M.R.F., female, 69 y.o.

- Large renal mass replacing the upper and mid third of the right kidney and infiltrating the renal pelvis
- Renal vein thrombus extending in the IVC (level 2)
- No retroperitoneal lymphadenopathy
- sCr 1.1 mg/dL, eGFR 63 mL/min
Management options

1. Renal tumor biopsy and systemic treatment
2. Cytoreductive radical nephrectomy and tumor thrombectomy
3. Cytoreductive radical nephrectomy and tumor thrombectomy + lymph node dissection
4. Cytoreductive radical nephrectomy and tumor thrombectomy with previous angioembolization of the renal artery
Open right radical nephrectomy +
tumor thrombectomy +
paracaval/interaortocaval LND

Pathology
Clear cell RCC - Fuhrman IV
renal sinus fat invasion – venous thrombus
pT3b N0
Management options

1. Adjuvant treatment with Sunitinib
2. Adjuvant treatment with Pazopanib
3. Surveillance and treatment of left renal stone
4. Surveillance
No evidence of disease

Left RIRS with lithotripsy of the renal stone + JJ ureteral stenting
Total body CT scan

Brain and neck negative
No local recurrence
No mediastinal and retroperitoneal lymphadenopathy

MAR 2013 — JAN 2014 — JUN 2014
Clinical Case
M.R.F., female, 70 y.o.

- Metastatic RCC (multiple lung mets)
- ECOG 0
- sCr 1.5 mg/dL, eGFR 46 mL/min
- Hb, WBC and PLTs normal
- Corrected calcium 10.42 mg/dL
- Albumin, ALP, LDH normal
- High blood pressure
Management options

1. Wait and see
2. Multiple metastasectomy
3. Start Sunitinib
4. Start Pazopanib
5. Start Bevacizumab + IFN
Starts wait and see
Total body CT scan
Brain and neck negative
No local recurrence
No mediastinal and retroperitoneal lymphadenopathy

MAR 2013  →  JAN 2014  →  JUN 2014  →  DEC 2014
Clinical Case
M.R.F., female, 70 y.o.

• Metastatic RCC (PD lungs)
• ECOG 0
• sCr 1.5 mg/dL
• Hb, WBC and PLTs normal
• Calcium, Albumin, ALP, LDH normal
• Well controlled blood pressure
Management options

1. Continue wait and see
2. Multiple metastasectomy
3. Start Sunitinib
4. Start Pazopanib
5. Start Bevacizumab + IFN
Starts

Sunitinib 50 mg weeks
4 weeks on / 2 weeks off
Total body CT scan

Brain and neck negative

No local recurrence

No mediastinal and retroperitoneal lymphadenopathy

MAR 2013
JAN 2014
JUN 2014
DEC 2014
MAR 2015
Total body CT scan

Brain and neck negative
No local recurrence
No mediastinal and retroperitoneal lymphadenopathy

Total body CT scan

Brain and neck negative

No local recurrence

No mediastinal and retroperitoneal lymphadenopathy

JAN 2014
JUN 2014
DEC 2014
MAR 2015
JUN 2015
DEC 2015
Total body CT scan
Brain and neck negative
No local recurrence
No mediastinal and retroperitoneal lymphadenopathy

Management options

1. Continue Sunitinib
2. Switch to second line therapy
3. Lung metastasectomy + Sunitinib
4. Lung metastasectomy + wait and see
Right lung VATS metastasectomy

Pathology
Metastasis of clear cell carcinoma
Negative surgical margins
No evidence of disease

Total body CT scan

Brain and neck negative
No lung and abdominal recurrence
No mediastinal /retroperitoneal lymphadenopathy
Case 2: Tobias KLATTE
Patient

- 65 yr old male patient
- 40 py, BMI 35, ECOG PS 0
- Vascular surgery
  - 6.5 cm inflammatory AAA
  - 1.9 cm right renal tumour
Management option

• Active surveillance without biopsy
• Biopsy
• Partial nephrectomy
• Other?
Follow-up

• CT @6 months: not done
• CT @12 months: 2.1 cm, but retroperitoneal lymph nodes from the diaphragm to the bifurcation, hernia
• CT chest: normal
• MDT meeting
• Probably unrelated
Questions

• Nephrectomy?
• Lymphadenectomy?
• Medical therapy?
• What is the most likely histology for this tumor?
Open PN + Herniotomy

• Surgery: uneventful, „complete“ resection
• Histology:
  • Papillary type 2
  • Extensive tumour necrosis
  • ISUP Grade 3
  • T3a (perirenal fat)
  • Margins positive
  • Excision of retrocaval lymph node: pap RCC
6 months later

- Nodal recurrence:
  - Paraortic (1.2 cm)
  - Pelvic (0.8 cm)
- No organ metastases
Questions

• Observation?
• Lymph node dissection?
• Medical therapy?
Case continued

• Sunitinib for 9 months
• Last follow-up 4/2017: SD
Case 3: Lisa PICKERING
61 year old man. ECOG PS 0  
**August 2010**: 11cm G2pT3bN0M?  
Clear cell RCC. Nephrectomy.  
Lung nodules up to 5mm, suspicious.  
**Oct 2010**: Multiple small pulmonary metastases up to 18mm. Nil else.  
Hb 115g/L; CCa 2.35mMol/L (9.4mg/dL)  
Nphil 3.5 x 10⁹/L; Plt:= 280 x 10⁹/L  
**Intermediate risk**

**Options?**

1. Anti-VEGF therapy  
2. mTOR inhibitor  
3. High dose interleukin-2  
4. Clinical trial  
5. Surveillance  
6. Other
Sunitinib 50mg 4/2

**January 2011, 12 weeks later**
CT partial response eg lung nodule decreased 17 to 12mm
G2 toxicities; fatigue / diarrhoea
Supportive measures then dose reduction to 37.5mg 4/2

**April 2011, Another 12 weeks**
Further response in marker lung lesion to 9mm. Ongoing G2 toxicities.

**Options?**

1. Further dose reduction in sunitinib
2. Schedule alteration sunitinib
3. Pazopanib
4. Treatment interruption / surveillance
5. Axitinib
6. Everolimus
Treatment interruption.
Three monthly CTs. Stable until:

January 2013, almost two years later:
Disease progression
New lung, mediastinal LN, pancreatic and bone metastases (up to 2.5 cm diameter)

Options?
1. Axitinib
2. Everolimus
3. Sunitinib rechallenge
4. Pazopanib
5. Nivolumab
6. Cabozantinib
We chose: Pazopanib (Still first line but prior sunitinib toxicity)

Responded: pancreatic met necrotic; reduced 24 to 20 mm. Lung and LN mets reduced in size.

Whilst on pazopanib April 2013:
G3 transaminitis: treatment interruption and dose reduction but didn’t resolve

Other G2 toxicities esp diarrhoea despite supportive measures

What now?
April 2013: restarted sunitinib
Dose reduction: 37.5 mg

Should I have used schedule modification?

Further response to sunitinib at 37.5mg:

Pancreatic met reduced from 20 to 13 mm (overall 24 to 13mm with necrosis)
Lung & LN metastases reduced further
February 2014, one year later:
Disease progression in L4/5 spine
Large lytic met with soft tissue in spinal canal.
Other sites stable

Options?
1. Restart sunitinib
2. Axitinib
3. Everolimus
4. Bone directed therapy
5. Radiotherapy
6. Surgical stabilisation
7. Other
Spinal surgery + RT

March 2014
Three weeks after discharge from spinal surgery, due to restart sunitinib

Fell downstairs. Opened spinal wound.

Help! What to do now?
Spinal surgery + RT

March 2014
Three weeks after discharge from spinal surgery, due to restart sunitinib

Fell downstairs. Opened spinal wound.

Help! What to do now?

Waited for wound healing and improvement of performance status

April / May 2014: restarted sunitinib
**August 2014: Stable disease**

**December 2014, seven months after restarting sunitinib:**
Disease progression in L1 vertebra. Lytic lesion at risk of collapse. No soft tissue disease / cord compromise

Other sites stable

**Options?**

1. Axitinib
2. Everolimus
3. Zoledronic acid
4. Denosumab
5. Cement kyphoplasty
6. Radiotherapy
7. Other
October 2015: 17 months after restarting sunitinib; 5 years after first starting sunitinib:

Disease progression in lungs, adrenal and bone (multiple sites)

Options?

1. Axitinib
2. Everolimus
3. Denosumab
4. Nivolumab
5. Cabozantinib
6. Other
December 2015 (2-3 months after starting axitinib):
Clinical deterioration. G2-3
Nausea, vomiting, diarrhoea, weight loss
ECOG Performance Status 3
Axitinib suspended.
Hospice for symptom control.
CT: stable disease. ?toxicity

January 2016:
Clinically improved
Performance status: ECOG 2
Switch to everolimus approved (for toxicity)
February 2016:
New R frontal scalp metastasis

What to do now?
1. Continue everolimus
2. Radiotherapy to scalp metastasis
3. Palliative care
4. Switch to nivolumab
5. Switch to cabozantinib
6. Other
Tolerated everolimus well SD at all sites until:

**August 2016:**
Disease progression:
- L1 extra-osseous disease with spinal cord / cauda equina compression
- Progression in scalp metastasis
PS: ECOG 2

What to do now?
1. Continue everolimus
2. Redo spinal surgery
3. Retreat radiotherapy
4. Cabozantinib
5. Nivolumab
6. Palliative care
Retreat RT & Cabozantinib

**November 2016:**
Partial response in scalp and spine
Clinical improvement

**February 2017:**
Increasing pain++ in spinal lytic metastasis: No radiological progression
Only slight improvement from analgesia despite palliative care team
CT: Stable disease

Options?
November 2016:
Partial response in scalp and spine
Clinical improvement

PS: ECOG 2

G2 Hepatic impairment: cabozantinib interruption and dose modification

February 2017:
Stable disease
Increasing pain in spinal lytic metastasis: No radiological progression
Only slight improvement from analgesia despite palliative care team

Options?
February 2017: Options?
Further spinal surgery: debulking and kyphoplasty.
Cabozantinib interrupted for surgery.
4 weeks later: wound well healed, cabozantinib restarted.

March 2017, 3 weeks after cabozantinib restarted:
Wound dehiscence
Note: spinal surgery, radiotherapy, repeat surgery, retreat radiotherapy, several TKIs
What now??
April 2017:

Readmitted to spinal team
- 6 weeks iv antibiotics
- Off cabozanitinib
Progression in scalp metastasis

What to do about scalp?
Patient 4: Paul Nathan
Patient

• 65 y.o. male
• 2006 Left Radical Nephrectomy
• pT2, G2 clear cell RCC

• 6 years later:
• March 2012 presented with severe shoulder pain
What would you do?
What would you do now?

• Total Body CT scan
• Biopsy the lesion
• Initiate systemic therapy with a VEGF TKI
• Surgical intervention
• RT to the shoulder
Patient

- CT SCAN: Head, Chest, Abdomen & Pelvis – no other sites of disease
- 20Gy 5 fractions to the shoulder
- Bisphosphonates initiated
Patient

- August 2012 R leg pain
- Lytic lesion R femoral shaft
- Whole body MRI and CT chest abdomen pelvis showed no other sites of disease
Management

- Intramedullary nailing of Right femoral shaft
- 8Gy adjuvant radiotherapy
- 3/12ly clinical review and 6/12ly repeat imaging
Question?

• Should adjuvant therapy be initiated?
Patient

- No additional therapy initiated
Patient- 3 years later

- June 2015 c/o Right leg pain
- Solitary metastasis mid R femur
- WB MRI & TB CT Scan revealed solitary lytic lesion with no other emerging disease.
Questions?

• Surgery to single metastasis
• RT to single metastasis
• Systemic therapy with a TKI?
Patient

- Metastasis excised
- 4/12ly repeat imaging – WB MRI & TB CT Scans
Further management?

• RT to single metastasis after surgery?
• Systemic therapy with a TKI?
No further therapy - 1 year later

• May 2016
• Pathological fracture Left humerus
• MRI – extensive disease
Patient

- Limb salvage surgery not feasible
- Intractable pain. No function.
Management

• Amputation July 2016

• September 2016 start pazopanib
Feb 2017 – new lung disease