European Reference Network
for rare or low prevalence complex diseases

Network Paediatric Cancer (ERN PaedCan)

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SUCCESSFUL TREATMENT OF INOPERABLE RECURRENT CERVICAL SPINE OSTEOBLASTOMA WITH DENOSUMAB IN A 15-YEAR-OLD PATIENT

Moderation: Raheel Altaf Raja

Funded by the European Union's EU4Health Programme

SIOPE YOUNG

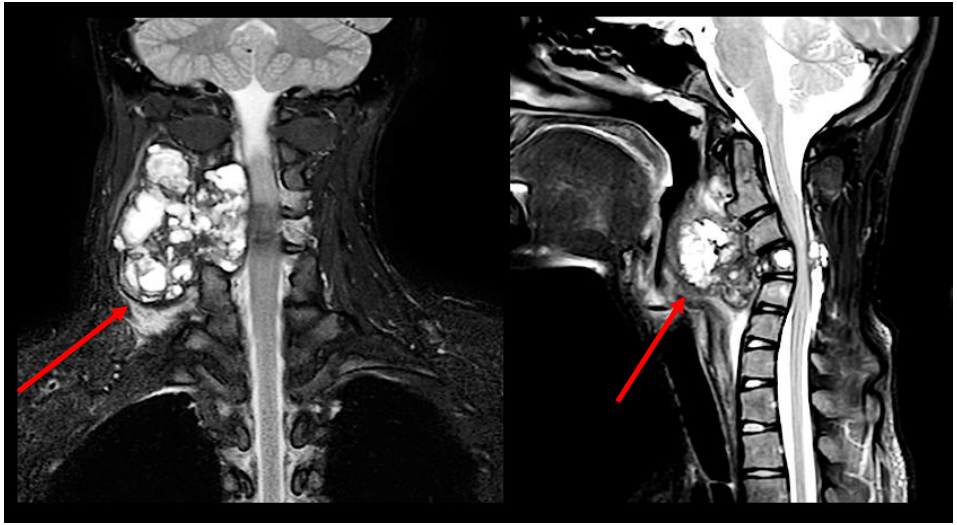
St. Anna Kinderkrebs Forschung

COI declaration

- the speakers declare no conflict of interest

Patient’s history

- 13-years-old male
- 6 months of **progressive neck deformity (torticollis) and pain**
- MRI (T2 seq): an extensive, hyperintense mass with nodular calcifications, infiltrating C3-C5 intervertebral foramina, **compressing the spinal cord and the larynx**



In this patient, which of the following would be the **least likely differential diagnosis**?

A) Aneurysmal bone cyst
B) Osteosarcoma
C) Osteoid osteoma
D) Ewing sarcoma
E) Chondroblastoma

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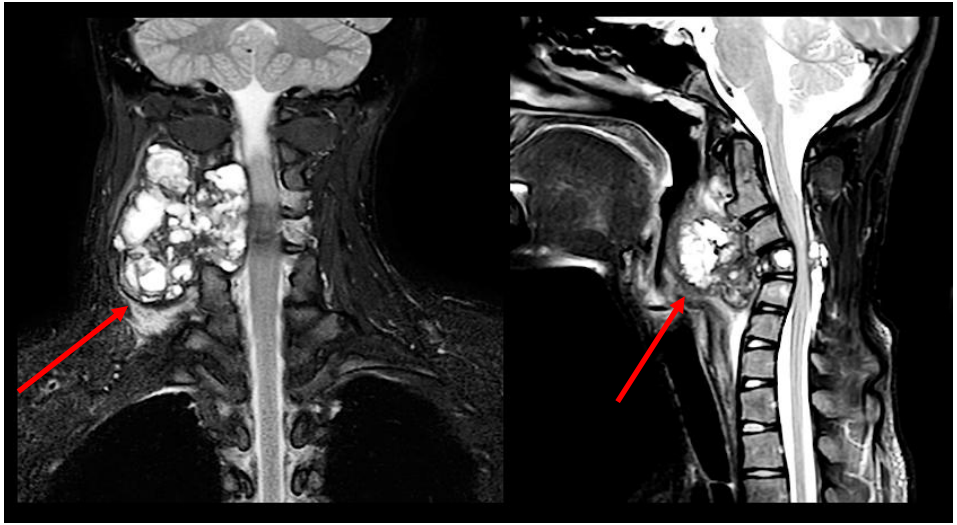

tumor biopsy ⇒ **osteoblastoma**

Which statement about osteoblastoma is **true**?

A) frequently metastasizes to the lungs
B) commonly transforms into osteosarcoma
C) is defined as a locally aggressive tumor
D) is highly radiosensitive
E) often regresses spontaneously without treatment

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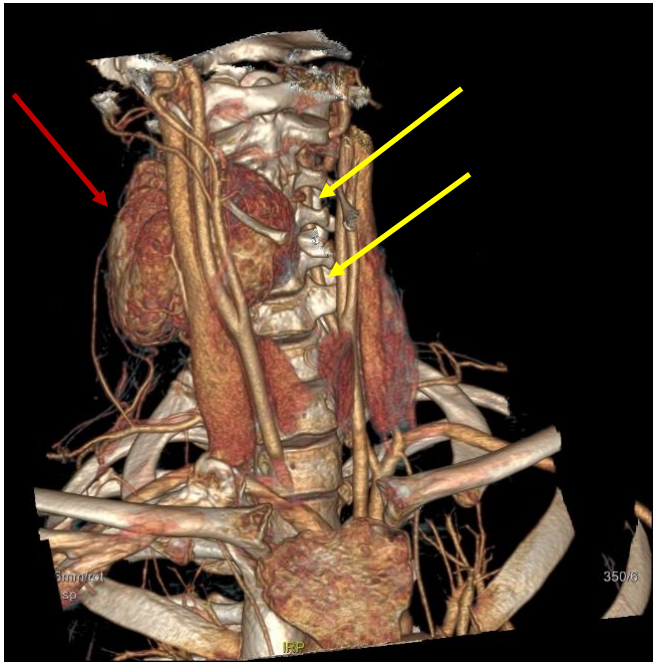
First-line treatment

- treatment provided in an outside institution
- tumor initially assessed as **inoperable**
  (highly vascularized; right vertebral artery encased by the tumor on C3 -C5 levels)
- neoadjuvant MAP chemotherapy (EURAMOS-1)

  ⇒ **tumor progression**



images: Copernicus Hospital in Gdansk, surgical team

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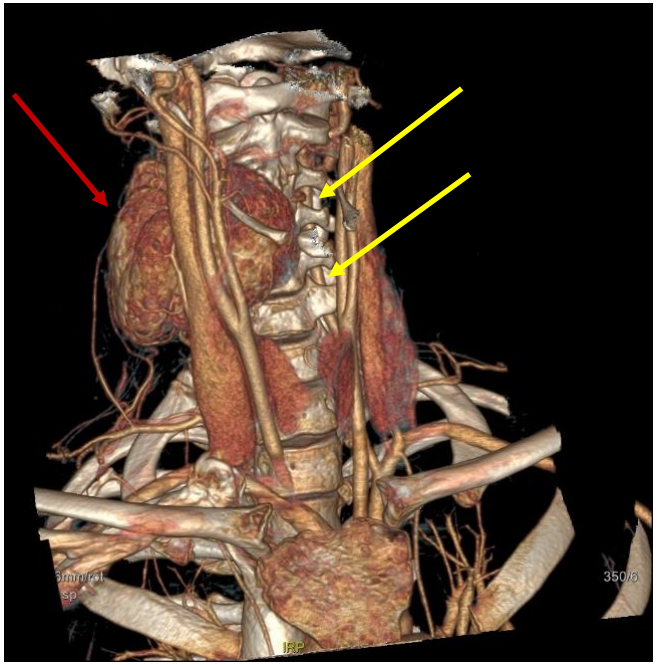
  ⇒ **tumor progression**

- 4 doses of **denosumab** (120mg s. c. weekly)

  ⇒ **tumor stabilization**, qualification for surgery (another center)



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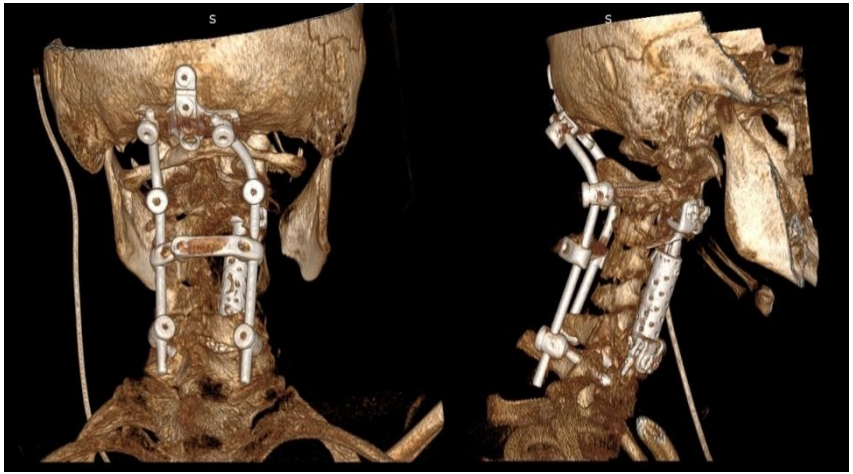
Surgery

- **multidisciplinary team**: neurosurgeons, cardiothoracic surgeons, interventional radiologists, otolaryngologists…
- **single-stage tumor resection** preceded by embolization of the right vertebral artery and right thyrocervical trunk
- **complicated** with cerebellar infarction, mild motor paresis of right upper limb, raise in ICP requiring V-P shunt
- ultimately – **very good functional outcome**



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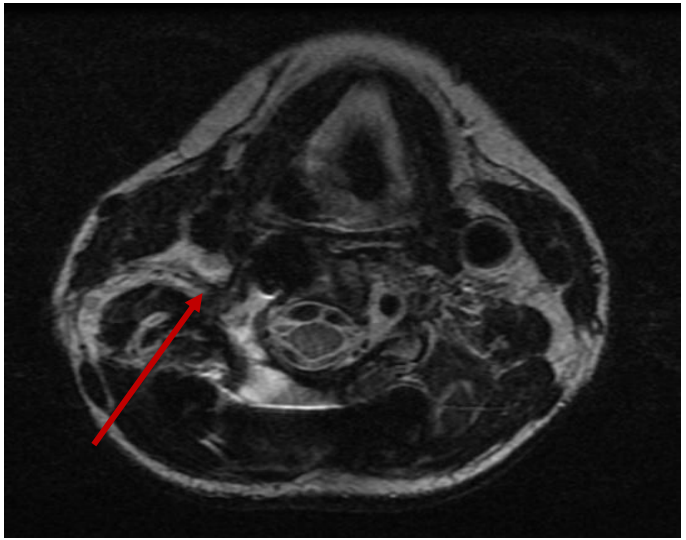
Recurrence

- 15 months after surgery – a nodule in the surgical scar on the neck
- imaging – suspicion of **multifocal local/locoregional relapse** (2nd lesion near the right cervical vessels)
- biopsy – confirmed **recurrent osteoblastoma**
- **the patient referred to our institution**



Recurrence – treatment

- safe resection of the lesion near cervical vessels considered **unfeasible**

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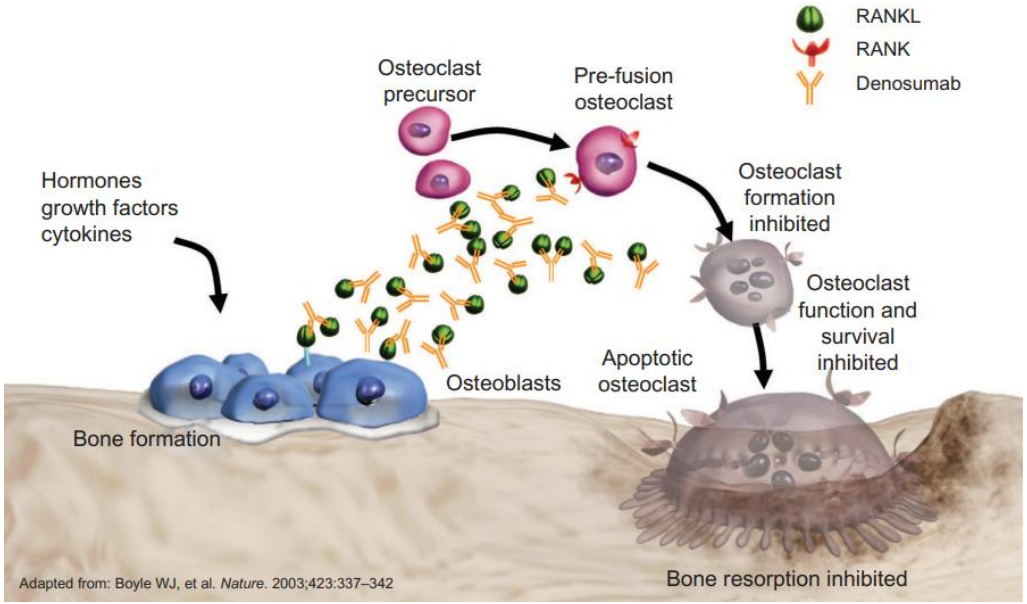
- **other options**
  - **radiotherapy** (poor radiosensitivity, risk of malignant transformation)
  - **embolization** (no evident feeding arteries, small lesion)
  - **observation** (high risk of further progression and neurological deterioration)
  - ……

  - **denosumab?**

Denosumab

- a fully human monoclonal antibody to RANKL ⇒ inhibitor of bone resorption
- originally used in the treatment of **osteoporosis** and **bone metastases of solid tumors**



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Denosumab and bone tumors

- **RANK/RANKL (over)activation has a role in the progression of primary bone tumors**

- denosumab effectiveness described in:
  - **giant cell tumor (GCT)** – several clinical trials; approval in 2011 (EMA), 2013 (FDA): adults and skeletally mature adolescents,
  - aneurysmal bone cyst (ABC) – *off label* use,
  - fibrous dysplasia – *off label* use,
  - chondroblastoma – *off label* use,
  - **osteoblastoma** – *off label* use.

Denosumab in osteoblastoma

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Author, year	Sex	Age	Tumor size (max diameter)	Tumor location	Denosumab role	Denosumab dose & treatment duration	Response to denosumab treatment
Naresh 2018	M	19	2.5 cm	sacrum	N/A	120mg, number of doses not provided	PR
Naresh 2018	F	29	4.1 cm	cervical spine	N/A	120mg, number of doses not provided	PR
Reynolds 2018	M	14	5.2 cm	sacrum	neoadjuvant	120mg x 4 doses	PR
Kooner 2019	M	18	3 cm	hand	only treatment	120mg x 6 doses (1st line treatment); 120mg x 6 doses (treatment of relapse)	PR (both in the 1st line treatment and in the treatment of relapse)
Hung 2022	M	32	8 cm	rib	neoadjuvant	120mg x 8 doses	SD (tumor mineralization and ossification)
Hung 2022	F	16	3.8 cm	cervical spine	neoadjuvant	120mg x 6 doses	SD (tumor mineralization and ossification)
Yamaga 2024	F	17	3 cm	cervical spine	only treatment	120mg x 14 doses	SD (tumor ossification)
Machak 2024	M	18	5.5 cm	cervical spine	only treatment	120mg x 7 doses	SD (tumor calcification)
Celayir 2025	F	21	4.3 cm	sacrum	adjuvant	120mg x 10 doses	N/A

Denosumab – practical aspects

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BENEFITS

- possible alternative to mutilating surgery
- analgesic effect
- improved mobility
- outpatient treatment
- (usually) good tolerance and **good QoL**

RISKS

- hypocalcemia, hypophosphatemia
- rebound hypercalcemia
- jaw osteonecrosis
- pathological fractures
- unknown treatment duration
- tumor progression upon treatment cessation
- malignant transformation (?)

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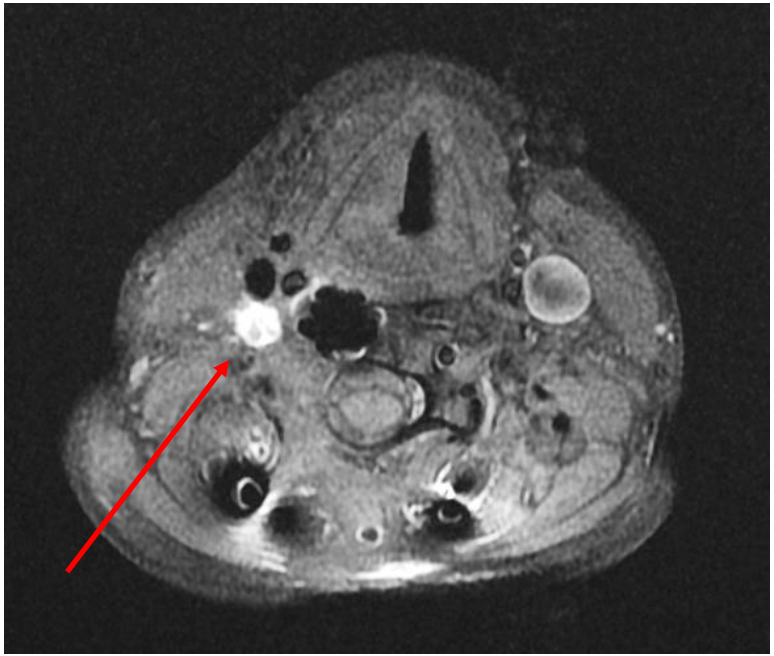
together with the patient and his parents,
we decided to start denosumab therapy (*off-label)*

Recurrence – treatment

- **denosumab s. c. treatment started**
  (*off-label,* as per GCT protocol)

- control imaging ⇒ gradual
  calcification/ossification
  of the recurrent tumor

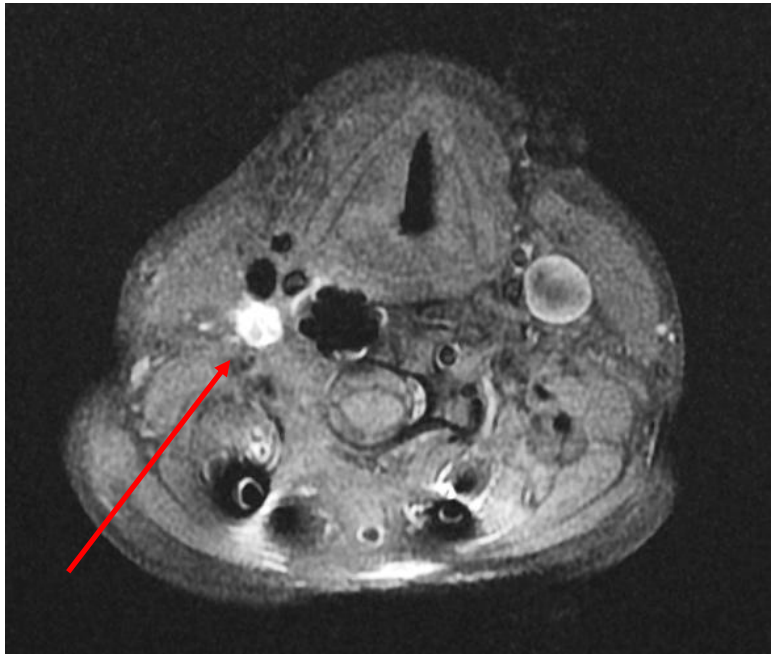


Recurrence – treatment

- **denosumab s. c. treatment started** (*off-label,* as per GCT protocol)

- control imaging ⇒ gradual **calcification/ossification** of the recurrent tumor

- **30 months follow-up** (26 doses)
- currently – 120mg every 2 months
- good tolerance of the treatment
- very good functional status



What to do next?

a) continue current treatment protocol (denosumab 120mg every 2 months)

b) gradually decrease the frequency of denosumab doses (e. g. 120mg every 3 months, then every 6 months…)

c) discontinue denosumab, start surveillance

d) re-qualify for the surgery

e) other possibilities?

+/- bisphosphonates?

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DISCUSSION

Funded by the European Union's Health Programme

Take home message

- in patients with extensive and/or inoperable osteoblastoma, treatment with denosumab may lead to long-lasting partial regression or stabilization of the tumor, allowing to avoid high risk of surgery and/or surgical complications