Osteoporosis in young male secondary to cancer treatment – Case report

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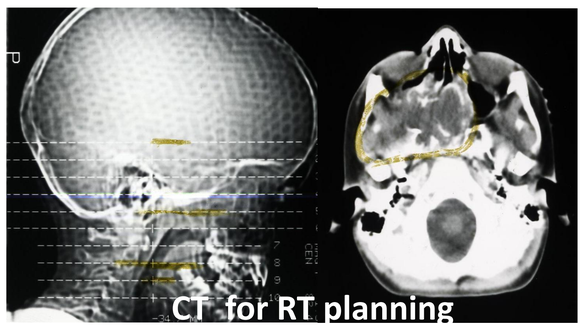
INTRODUÇÃO

Children undergoing treatment for cancer – chemotherapy (CT) and/or radiotherapy (RT) – are prone to several long-term endocrine complications, which can permanently affect bone tissue, leading to a serious decrease of **bone mineral density (BMD).**

CASE REPORT

5 years-old

- Male child with irrelevant past history.
- ***Right maxillary sinus rhabdomyosarcoma***
- **RT** – cervical + submaxillary (60 Gy)
- **CT** – intrathecal: Metothrexate + Prednisolone intravenous: Ifosfamide + Actinomicyn + Vincristine



12 years-old

Referenced to Endocrine Rehabilitation Clinics of our centre

- **Auxology:**
  Height 139 cm (p10)
  Predicted Adult Stature (PAS) 170 cm
  Growth velocity (GV) p90;
- **Tanner** P2, G2
  Testicular volume (TV) 5 mL
- **Bone age (BA)** 9 years.
- **Initial evaluation:**
  TSH 7.4 mUI/ml (0.3-4.2);
  T3 120 ng/dl (80-200)
  FT4 0.8 ng/dl (0.9-1.7)
  IGF-1 102 ng/ml (<p3)

Levothyroxine 50 µg/day

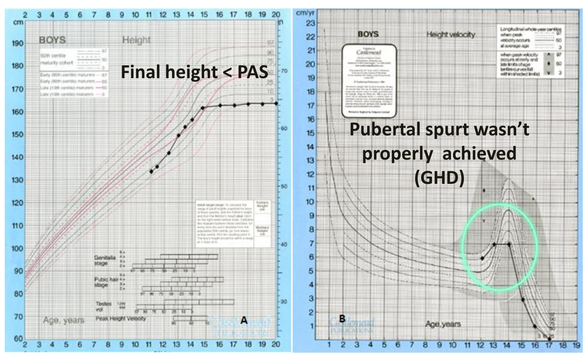
Gonadal and adrenal axes were normal.

Insulinic Tolerance Test			
	Glycemia (mg/dl)	**Cortisol** (µg/dl)	**GH** (ng/ml)
-15'	87	17.2	<0.2
0'	87	19.7	<0.2
15'	44	18.0	0.2
30'	33	21.1	0.6
45'	42	36.3	3.3
60'	36	43.9	3.5
75'	41	43.5	1.7
90'	44	45.6	2.2
120'	43	41.8	6.6

Growth Hormone Deficiency (GHD)
According to national criteria back then, he wasn't eligible for somatropin treatment.

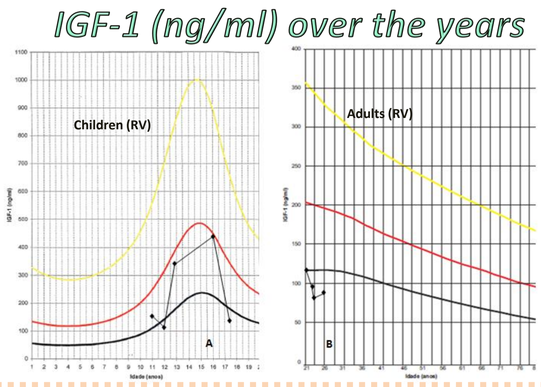
13 – 17 years-old

Growth Charts



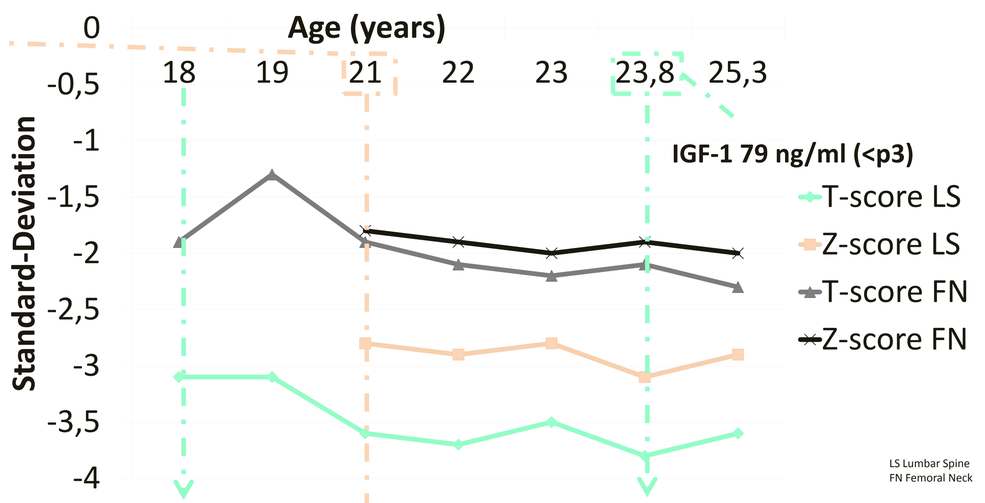
13 years-old – P3, G3, TV 15 mL; **BA** = 11 years.
17 years-old – P5, G5 e VT 25 mL; **BA** = 17 years.
Normal thyroid ultrasounds.

IGF-1 (ng/ml) over the years



≥ 18 years-old

Partial mixed hypogonadism		
LH	1.7 mUI/ml	(>8)
FSH	2.0 mUI/ml	(>10)
Test T	324.8 ng/dl	(160-730)
Test.L	10.2 ng/dl	(9-27)
DHT	253 ng/dl	(300-850)



Calcium + cholecalciferol + Regular physical exercise

Somatropin 0.1mg/day

Testosterone enanthate 250 mg/mL monthly

DISCUSSION

Developed Endocrinopathies

GH Deficiency ← **RT**

Primary Hypothyroidism ← **RT**

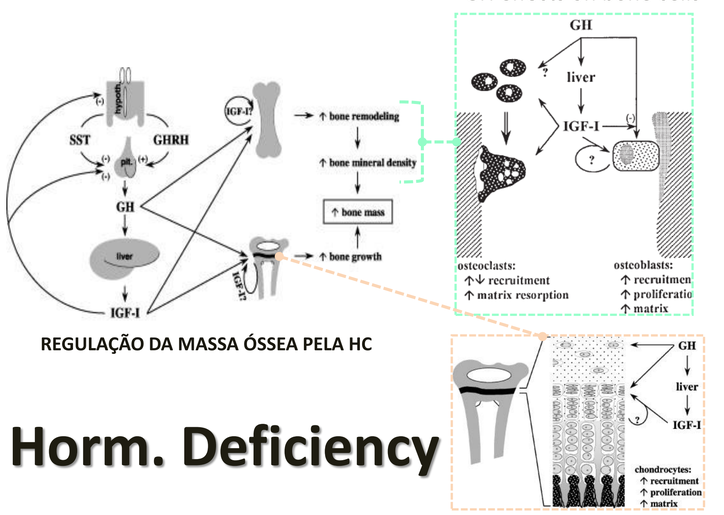
OSTEOPOROSIS

SECONDARY TO… ?

Primary and Central Hypogonadism ← **RT + QT**
(established at the age of 21)

- **METHOTREXATE** – direct bone toxicity; reversible after withdrawal.
- **IFOSFAMIDE** – Damage to proximal tubules of kidneys→ loss of renal phosphate; primary hypogonadism.
- **GLUCOCORTICOIDS** – ↑ resorption e↓ bone formation (direct effect on calcium metabolism; ↓ testosterone and E_2)
- **HYPOGONADISM** – alters linear growth; epiphyseal maturation; acquisition and maintenance of BMD.

GH effects on bone cells

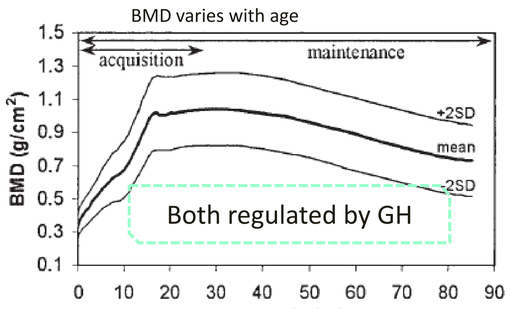


REGULAÇÃO DA MASSA ÓSSEA PELA HC

⇨Growth Horm. Deficiency

GH effects on growth plates

BMD varies with age



Acquisition

- Acceleration of BMD during puberty as a result of accelerated growth and bone remodeling.

Maintenance

- Bone remodeling regulated by hormonal factors.

DISCUSSION

Our patient developed GHD secondary to radiotherapy. This contributed to impaired bone mass acquisition. Methotrexate and glucocorticoids' adverse effects on bone are usually reversible. Peak bone mass should already been reached when partial gonadal axis insufficiency was established.
The benefits of somatropin therapy are evident in several studies. It's required a long period for them to be observed, because the activation of osteoclasts preceds osteoblasts .
It's important to identify the risk of endocrine complications in order to treat these patients properly.

R Olney. Regulation of bone mass by Growth Hormone. Med Pediatr Oncol 2003; 41:228-234
A Mukherjee, S Shalet. Growth Hormone Replacement Therapy (GHRT) in children and adolescents: skeletal impact. Med Pediatr Oncol 2003; 41:235-242.