

Cushing's Syndrome and Broken Bones

INTRODUCTION

A 55 year old male presented to his GP with low backache and pain radiating down his left lower limb for 12 months. He had gained 10 kilograms in weight in 2 years and had noted that his blood pressure had been labile for 18 months requiring frequent changes of his antihypertensive medications. He was treated as sciatica and referred to orthopaedics for further investigations.

Past Medical History : Hypertension (5yrs); On Ramipril , Amlodipine and Indapamide

INVESTIGATIONS

X-ray Thoraco-lumbar spine: multiple wedge fractures T7,T9,T10 and L1,L2

MRI Thoracolumbar spine: collapse of T7,T9 vertebrae involving pedicle and extending to T9 rib with no evidence of cord compression, wedge fractures L1,L2

Isotope bone scan: multiple areas of increased activity in the ribs, thoraco-lumbar spine, sacrum, right iliac crest and right pubic ring

Imaging raised a diagnosis of malignancy which led to a CT scan of thorax, abdomen and pelvis which showed a 45 mm heterogeneously enhancing left adrenal adenoma.

He was reviewed in the endocrine clinic after 3 weeks. He had classical clinical features of Cushing's syndrome with cushingoid facies, central obesity, purple striae, proximal myopathy and extensive bruising on his arms and thighs.

BIOCHEMISTRY

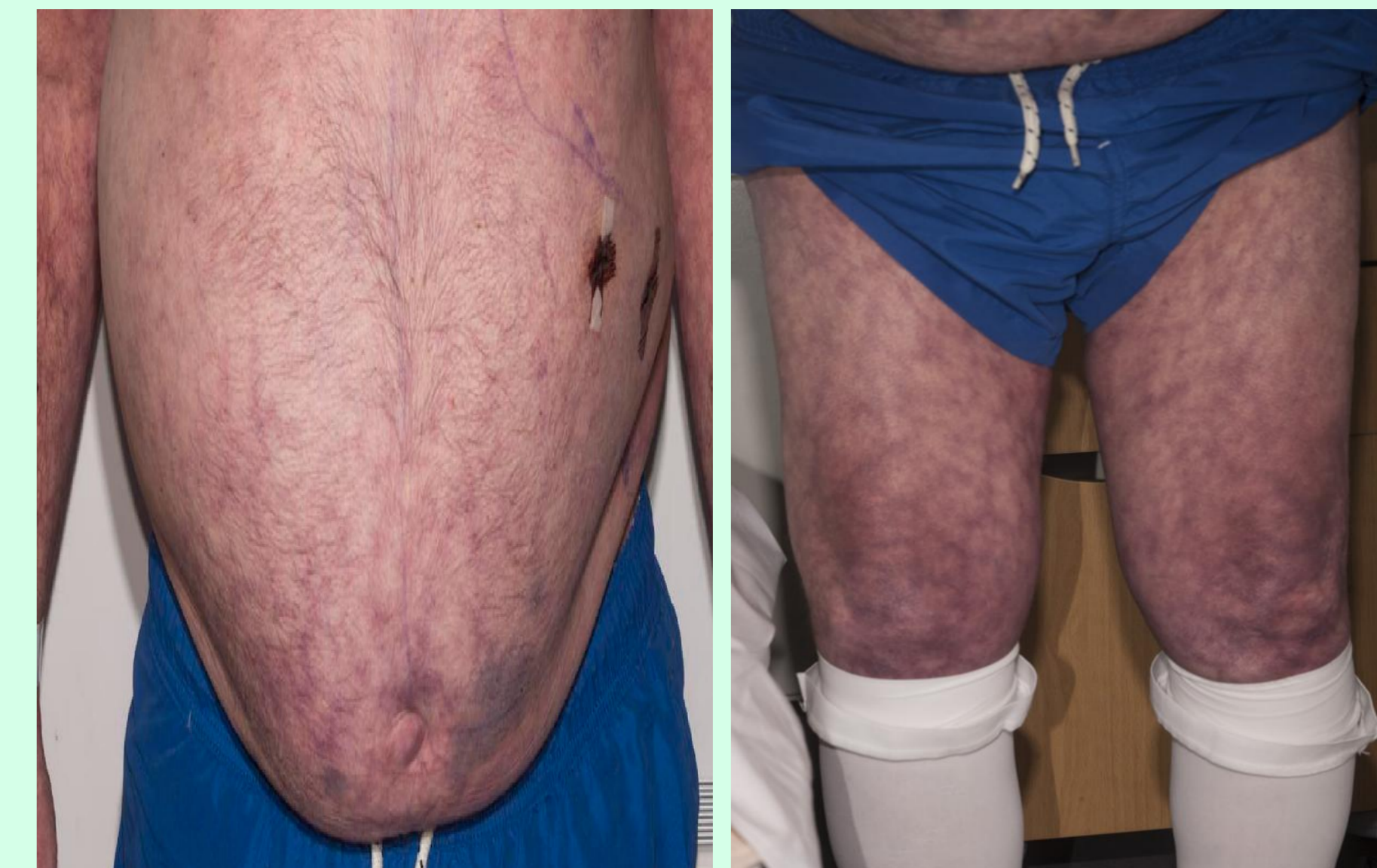
Cortisol (ODST)	741 nmol/l (normal <50 nmol/l)
ACTH	<1ng/l
24 hour UFC	625nmol/24 hr (normal <146 nmol/24hr) 639nmol/24 hr
24 hour Normetadrenaline	2.57µmol/24 hr (normal: 0-4.4 µmol/24hr)
24 hour Metadrenaline	0.56µmol/24 hr (normal:0-1.8 µmol/24hr)
TSH / T4	1.4mu/l (normal 0.27-4.2) / 14.4 pmol/l (12-22)
Testosterone (9 am)	3.2 nmol/l (normal 7.6-31.4)
Prolactin	435 mu/l (normal 86-324)
S Immunoelectrophoresis	IgG 5.3 g/l (normal 6-16 g/l) IgA 1.68g/l (normal 0.8-4g/l) IgM 0.33g/l (normal 0.5-2g/l) No paraprotein detected
Urine Bence Jones Protein	Negative

He underwent a left unilateral adrenalectomy and was commenced on Hydrocortisone replacement, calcium supplements and bisphosphonates.

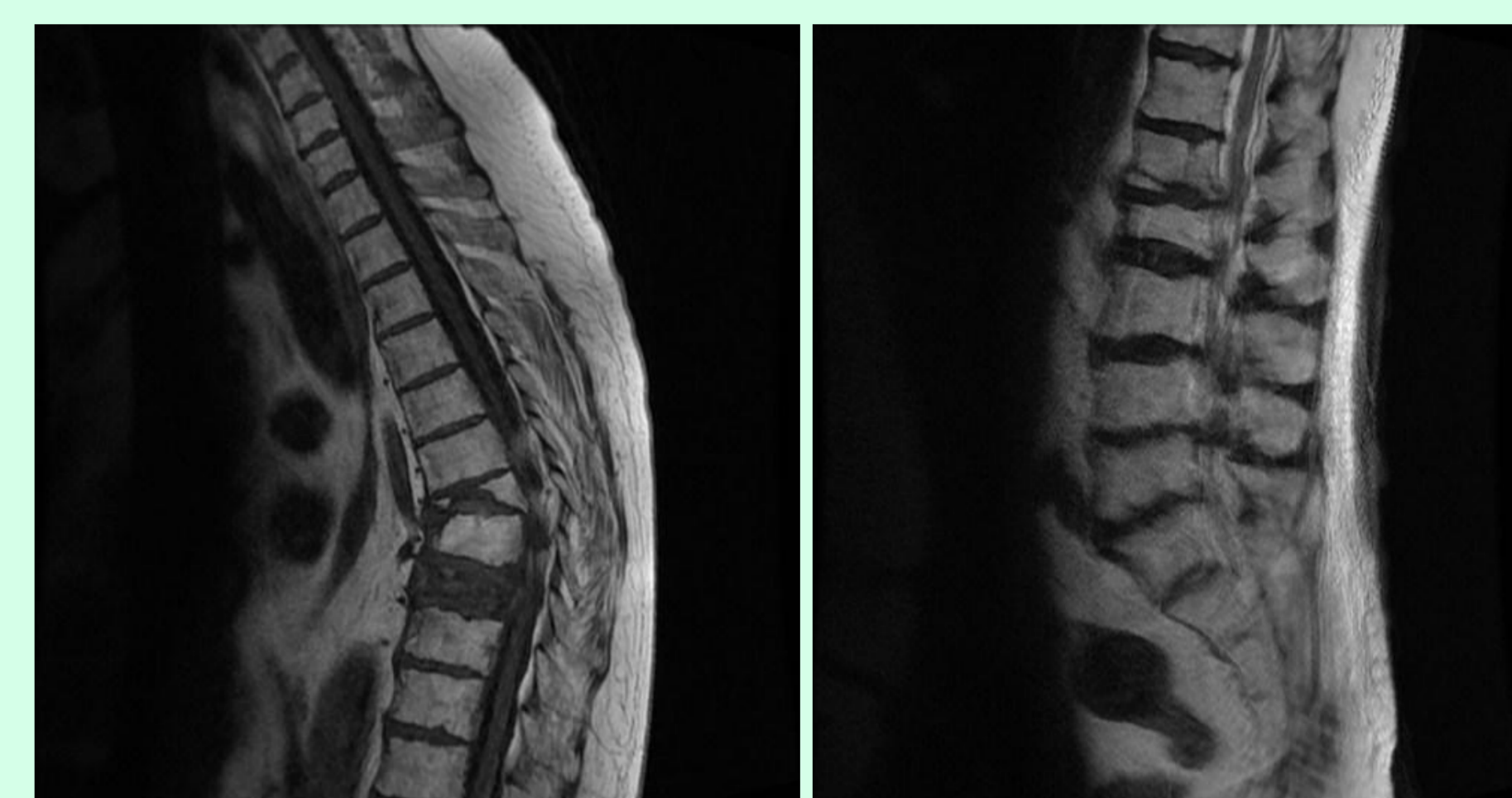
short synacthen test ([2 months post op)	0min 38 nmol/l; 30 min 123 nmol/l
24 hr urine free cortisol	<10 nmol/l
Serum ACTH	5.2 ng/l

CONCLUSION

- Cushing's syndrome is an important yet rare cause of secondary osteoporosis.
- 30-50% of patients with Cushing's syndrome experience fractures particularly in the vertebral body although reports of multiple pathological fractures are rare.
- Osteoporosis from hypercortisolism involves multiple mechanisms including increased apoptosis of osteocytes & osteoblasts, stimulation of RANKL & osteoclasts and suppression of gonadotropins and impaired calcium absorption.
- Bone loss affects trabecular bone rather than cortical bone and is more frequent in adrenal mediated Cushing's syndrome.
- Increased fracture risk will decrease to normal within 1-2 years following definitive cure.
- Adequate calcium and Vitamin D intake should be maintained in these patients.
- We recommend bone density scan in all cases of Cushing's syndrome



Purple striae on abdomen with central adiposity and proximal myopathy



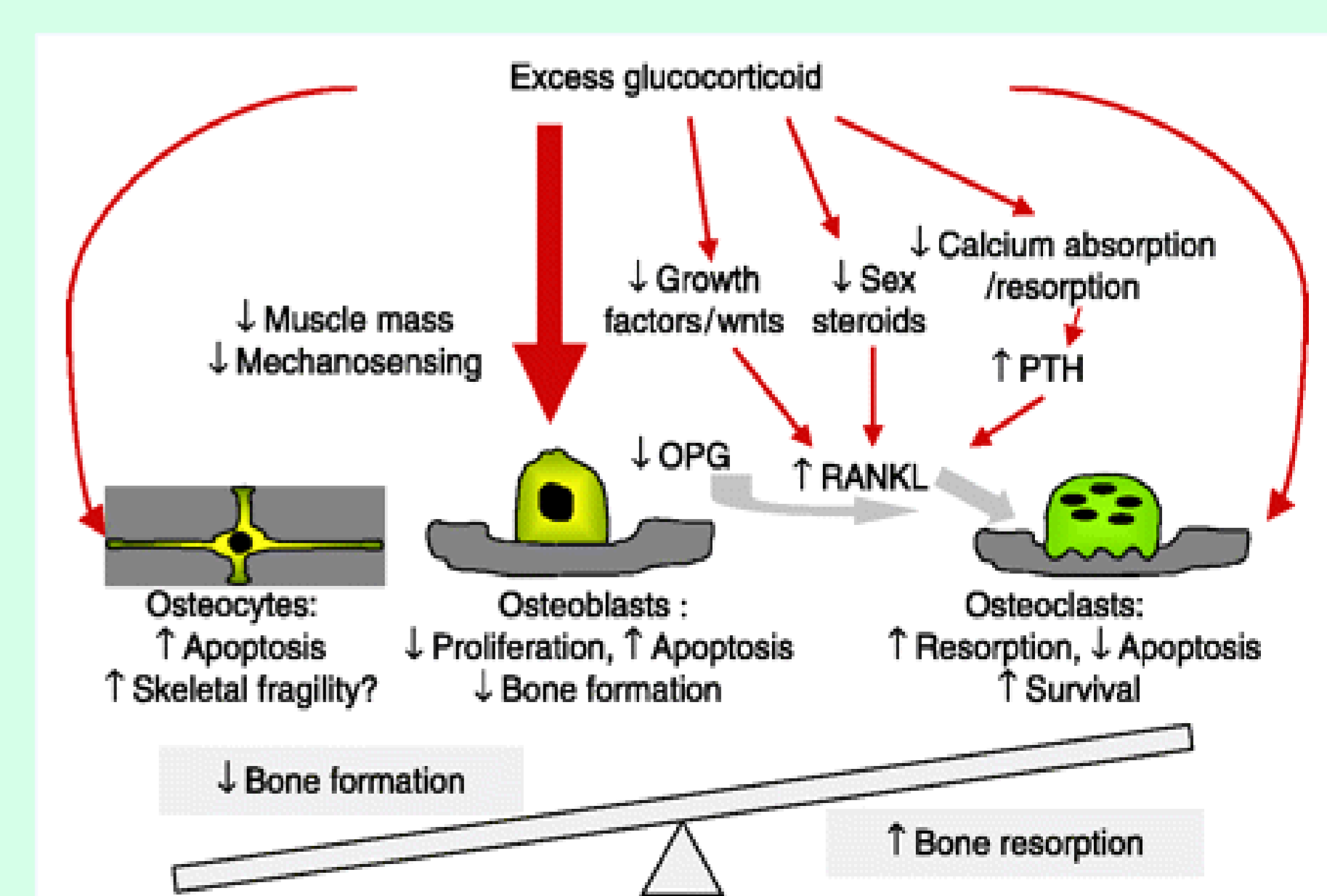
MRI thoraco-lumbar spine showing multiple fractures of T7,T9,L1 and L2 vertebrae



CT abdomen showing a heterogeneously enhancing left adrenal adenoma measuring 45mm (arrowheads).



Isotope bone scan showing increased uptake in the ribs, lower thoracic spine, lumbar spine, sacrum, right iliac crest and right pubis



Effects of glucocorticoid excess on bone cells