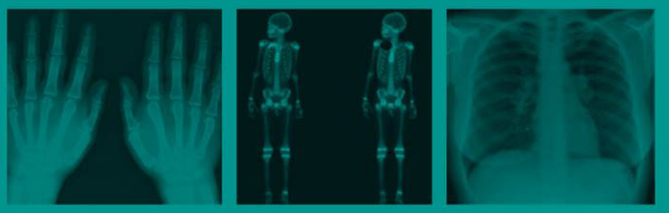
OXFORD CASE HISTORIES IN RHEUMATOLOGY



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OXFORD

Oxford Case Histories in Rheumatology

Oxford Case Histories

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A note from the series editors

Case histories have always had an important role in medical education, but most published material has been directed at undergraduates or residents. The Oxford Case Histories series aims to provide more complex case-based learning for clinicians in specialist training and consultants, with a view to aiding preparation for entry- and exit-level specialty examinations or revalidation.

Each case book follows the same format with approximately 50 cases, each comprising a brief clinical history and investigations, followed by questions on differential diagnosis and management, and detailed answers with discussion.

All cases are peer-reviewed by Oxford consultants in the relevant specialty. At the end of each book, cases are listed by mode of presentation, aetiology, and diagnosis. We are grateful to our colleagues in the various medical specialties for their enthusiasm and hard work in making the series possible.

Sarah Pendlebury and Peter Rothwell

From reviews of other books in the series:

Neurological Case Histories

'…contains 51 cases that cover the spectrum of acute neurology and the neurology of general medicine—this breadth makes the volume unique and provides a formidable challenge… it is a heavy-duty diagnostic series of cases, and readers have to work hard, to recognise the diagnosis and answer the questions that are posed for each case… I recommend this excellent volume highly…'

Lancet Neurology

'This short and well-written text is…designed to enhance the reader's diagnostic ability and clinical understanding…A well-documented and practical book.'

European Journal of Neurology

Oxford Case Histories in Gastroenterology and Hepatology

'…a fascinating insight in to clinical gastroenterology, an excellent and enjoyable read and an education for all levels of gastroenterologist from ST1 to consultant.'

Gut

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Preface

This book contains a series of case histories that the authors have encountered in the Oxford region. The purpose of the cases is to provide trainees, and indeed all practitioners in rheumatology, with clinical scenarios and an evidenced approach to answering questions raised by the cases. It is hoped that the book will be useful for training as well as in preparation for exit examinations. The book may also be helpful for rheumatologists in their re-validation. General medical trainees might find it useful in preparation for MRCP and PACES.

Many of the cases require clinical judgement in the approach to the management decisions and questions. The authors have expressed their views and hope that you generally agree! The cases cover inflammatory joint and connective tissue disease, paediatric rheumatology, sports and exercise medicine, and metabolic bone disease. Some of the cases include acute presentations and others are more chronic musculoskeletal and mechanical problems where there are dilemmas in clinical practice.

The authors have used the format of case reports, with detailed discussions of differential diagnosis and management, for three reasons. First, one of the best ways to learn advanced clinical medicine is through the analysis of individual cases. In almost all areas of medicine it is extremely difficult to illustrate the practical process of diagnosis within the format of a traditional textbook. Secondly, it is simply more interesting to consider real cases than to read a text. This allows a clinician to reflect on their own differential diagnosis and treatment. Finally, there is a lack of case series that stretch the abilities of experienced clinicians and specialists: most are aimed at medical students or young doctors doing early postgraduate exams. It is for this reason that the cases and questions are sometimes challenging, although many are simple since the aim is to educate. Wherever possible radiology and clinical pictures have been included.

The authors would like to thank their colleagues, including those allied to medicine, for contributing cases and providing illustrations or administrative support. The clinicians who contributed cases are listed in the Acknowledgements.

We hope you enjoy the book!

Joel David
Anne Miller
Anushka Soni
Lyn Williamson

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Abbreviations

AAS	atlanto-axial subluxation
ABPI	ankle–brachial pressure index
ACCP	anticitrullinated C-peptide (also referred to as ACPA)
ACE	angiotensin-converting enzyme
aCL	anticardiolipin antibody
ALP	alkaline phosphatase
ANA	antinuclear antibody
ANCA	antineutrophil cytoplasmic antibody
AND	adverse neural dynamics
APS	antiphospholipid syndrome
APTT	activated partial thromboplastin time
AS	ankylosing spondylitis
ASOT	antistreptolysin-O titre
AST	aspartate transaminase
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BD	Behçet's disease
BMD	bone mineral density
BMI	body mass index
BSR	British Society for Rheumatology
CK	creatine kinase
CMV	cytomegalovirus
CNSV	central nervous system vasculitic
COX-2	cyclo-oxgenase-2
CPK	creatine phosphokinase
CREST	calcinosis, Raynaud's, (o)esphageal involvement, sclerodactyly, telangiectasia
CRMO	chronic relapsing multifocal osteomyelitis
CRP	C-reactive protein
CRPS	complex regional pain syndrome
CSF	cerebrospinal fluid
CSS	Churg–Strauss syndrome
CT	computed tomography
CTX	carboxy-terminal collagen crosslinks
CXR	chest X-ray
DAS	Disease Activity Score
DEXA	dual-energy X-ray absorptiometry
DILS	diffuse infiltrative lymphocytosis syndrome
DISH	diffuse idiopathic skeletal hyperostosis
DMARD	disease-modifying anti-rheumatic drug
EBV	Epstein–Barr virus
ECG	electrocardiogram
EF	eosinophilic fasciitis
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assay
EMG	electromyography
ENA	extractable nuclear antigen
ESR	erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FBC	full blood count
FMF	familial Mediterranean fever
FSH	follicle-stimulating hormone
GACNS	granulomatous angiitis of the central nervous system
GCA	giant cell arteritis
GFR	glomerular filtration rate
GGT	gamma glutamyl transferase
GH	growth hormone
GPA	granulomatosis with polyangiitis (also known as Wegener's granulomatosis (WG))
HA	haemophiliac arthropathy
Hb	haemoglobin
HLA	human leucocyte antigen
hpf	high-power field

IBD	inflammatory bowel disease
IGF-1	insulin-like growth factor 1
INR	international normalized ratio
IP	interphalangeal
IRIS	immune reconstitution inflammatory syndrome
JIA	juvenile idiopathic arthritis
LA	lupus anticoagulant
LDH	lactate dehydrogenase
LFT	liver function test
LH	luteinizing hormone
MAGIC	mouth and genital ulcers with inflamed cartilage
MAS	macrophage activation syndrome
MCP	metacarpophalangeal
MCV	mean cell volume
MEN-I	multiple endocrine neoplasia I
MHC	major histocompatibility complex
MPA	microscopic polyangiitis
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MSCRAMM	microbial surface components recognizing adhesive matrix molecules
MTSS	medial tibial stress syndrome
NICE	National Institute of Clinical Excellence
NOF	neck of the femur
NSAID	non-steroidal anti-inflammatory drug
NSIP	non-specific interstitial pneumonia
NTX	cross-linked N-telopeptides of type 1 collagen
NYHA	New York Heart Association
OA	osteoarthritis
OI	osteogenesis imperfecta
PACNS	primary angiitis of the central nervous system
PAN	polyarteritis nodosa
PAS	periodic acid–Schiff
PCR	polymerase chain reaction
PET	positron emission tomography
PFJ	patello-femoral joint
PFPS	patello-femoral pain syndrome
PMR	polymyalgia rheumatica
PT	prothrombin time
PTH	parathyroid hormone
PTT	partial thromboplastin time
PUK	peripheral ulcerative keratitis
PUO	pyrexia of unknown origin
RA	rheumatoid arthritis
RBC	red blood cell
RCVS	reversible cerebral vasoconstrictive syndrome
RF	rheumatoid factor
RP	relapsing polychondritis
SAP	serum amyloid protein
SAPHO	synovitis, acne, pustulosis, hyperostosis, and osteitis
SD	standard deviation
SHBG	sex-hormone-binding globulin
SLE	systemic lupus erythematosus
SOJIA	systemic-onset juvenile idiopathic arthritis
STIR	short T_1 inversion recovery
TakA	Takayasu's arteritis
TENS	transcutaneous electrical nerve stimulation
TFT	thyroid function test
TGF-β	transforming growth factor-β
TNF	tumour necrosis factor
TPHA	*Treponema pallidum* haemagglutination test
TSH	thyroid-stimulating hormone
U&E	urea and electrolytes
VAS	Visual Analogue Score
VDRL	Venereal Disease Research Laboratory
VMO	vastus medialis obliterans
VS	ventral subluxation
VTE	venous thromboembolism
VZV	varicella zoster virus
WBC	white blood cell
WCC	white cell count
WG	Wegener's granulomatosis (also known as granulomatosis with polyangiitis (GPA))

Normal ranges

Haematology	
haemoglobin	
males	g/L (130–180)
females	g/L (115–165)
MCV	fL (80–96)
white cell count	$\times 10^9$/L (4.0–11.0)
neutrophil count	$\times 10^9$/L (1.5–7.0)
lymphocyte count	$\times 10^9$/L (1.5–4.0)
monocyte count	$\times 10^9$/L (<0.8)
eosinophil count	$\times 10^9$/L (0.04–0.40)
platelet count	$\times 10^9$/L (150–400)
CD4 count	$\times 10^6$/L (430–1690)
erythrocyte sedimentation rate	
under 50 years:	
males	mm/ h (<15)
females	mm/ h (<20)
over 50 years:	
males	mm/ h (<20)
females	mm/ h (<30)
Haematinics	
serum iron	µmol/L (12–30)
serum iron-binding capacity	µmol/L (45–75)
serum ferritin	µg/L (15–300)
serum transferrin	g/L (2.0–4.0)
Chemistry	
Blood	
serum sodium	mmol/L (137–144)
serum potassium	mmol/L (3.5–4.9)
serum creatinine	µmol/L (60–110)
estimated glomerular filtration rate	mL/min (>60)
serum corrected calcium	mmol/L (2.20–2.60)

serum total protein	g/L (61–76)
serum albumin	g/L (37–49)
serum globulin	g/L (24–27)
serum alanine aminotransferase	U/L (5–35)
serum alkaline phosphatase	U/L (45–105)
serum gamma glutamyl transferase	
males	U/L (<50)
females	U/L (4–35)
serum lactate dehydrogenase	U/L (10–250)
serum creatine kinase (CPK)	
males	U/L (24–195)
females	U/L (24–170)
fasting plasma glucose	mmol/L (3.0–6.0)
serum urate	
males	mmol/L (0.23–0.46)
females	mmol/L (0.19–0.36)
serum angiotensin-converting enzyme	U/L (25–82)

Urine

glomerular filtration rate	mL/min (70–140)
24-h urinary total protein	g (<0.2)

Lipids and lipoproteins

serum cholesterol	mmol/L (<5.2)
serum LDL cholesterol	mmol/L (<3.36)
serum HDL cholesterol	mmol/L (>1.55)
fasting serum triglycerides	mmol/L (0.45–1.69)

Thyroid hormones

plasma thyroid-binding globulin	mg/L (13–28)
plasma T4	nmol/L (58–174)
plasma parathyroid hormone	pmol/L (0.9–5.4)
serum cholecalciferol (vitamin D_3)	nmol/L (60–105)
serum 25-OH-cholecalciferol	nmol/L (45–90)
serum 1,25-$(OH)_2$-cholecalciferol	pmol/L (43–149)

Immunology

serum complement C3	mg/dL (65–190)
serum complement C4	mg/dL (15–50)

C-reactive protein (CRP)	mg/L (<8)
serum immunoglobulin G	g/L (6.0–13.0)
serum immunoglobulin A	g/L (0.8–3.0)
serum immunoglobulin M	g/L (0.4–2.5)

Autoantibodies

anticentromere antibodies	(negative at 1:40 dilution)
anticardiolipin antibodies:	
immunoglobulin G	U/mL (<23)
immunoglobulin M	U/mL (<11)
anti-cyclic citrullinated peptide antibodies (ACPA)	
anti-double-stranded DNA antibodies (ELISA)	U/mL (<73)
anti-neutrophil cytoplasmic antibodies:	
c-ANCA	
p-ANCA	
PR3-ANCA	U/mL (<10)
MPO-ANCA	U/mL (<10)
antinuclear antibodies	(negative at 1:20 dilution)
extractable nuclear antigen	
anti-Jo-1 antibodies	
anti-La antibodies	
antimitochondrial antibodies	(negative at 1:20 dilution)
anti-RNP antibodies	
anti-Scl-70 antibodies	
anti-Ro antibodies	
anti-Sm antibodies	
anti-smooth muscle antibodies	(negative at 1:20 dilution)
anti-thyroid colloid and microsomal antibodies	(negative at 1:10 dilution)
rheumatoid factor	kIU/L (<30)

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Case 1

A 76-year-old widow presented to the Emergency Department with a mid-shaft right femoral fracture after a low-impact fall outside a supermarket. She had a past history of ischaemic heart disease, peripheral vascular disease, intermittent claudication, and mechanical right knee pain. She had been reviewed in rheumatology outpatients 3 months prior to admission for investigation of a painful swollen right elbow. She lived alone and had moved from County Durham where her husband had been a coal miner. Her usual medication included aspirin, bendroflumethiazide, and simvastatin.

On examination, in addition to the fractured femur she had a warm swollen R distal upper arm. She was haemodynamically stable, normotensive, and in sinus rhythm. Her distal pedal pulses were all impalpable.

Her initial blood results showed the following:

- Hb 10.5 g/dL (MCV 88 fL); WCC 6.8×10^9/L; platelets 468×10^9/L
- Creatinine 138 μmol/L; asparatate transaminase (AST) 48 IU/L; gamma glutamyl transferase (GGT) 52 IU/L; ALP 785 IU/L
- Corrected calcium 2.23 mmol/L; phosphate 1.2 mmol/L
- C-reactive protein (CRP) 8 mg/L.

Her femoral fracture was successfully pinned and plated, and she made a good post-operative recovery. Prior to discharge she was given an intravenous infusion. One week after discharge she was re-admitted profoundly unwell with nausea, vomiting, and tingling in her hands and feet.

Second admission bloods were as follows.

- Hb 11.5 g/dL (MCV 88 fL); WCC 7.9×10^9/L; platelets 488×10^9/L
- Creatinine 144 μmol/L; asparatate transaminase (AST) 55 IU/L; gamma glutamyl transferase (GGT) 30 IU/L; ALP189 IU/L
- CRP 10 mg/L
- Corrected calcium 1.87 mmol/L; phosphate 0.8 mmol/L
- Vitamin D level 7 nmol/L (threshold 20).

Radiographic findings are shown in Figs 1.1, 1.2, 1.3 and 1.4

Questions

1. What is the underlying bony diagnosis? What is the differential diagnosis? Describe the radiographic features in Figs 1.1–1.4.
2. Describe the clinical features, natural history, and potential complications of this condition.
3. What is the likely infusion she was given?
4. What complication of treatment did she develop and why?
5. Her daughter accompanies her to appointments and asks if she is likely to have this condition?

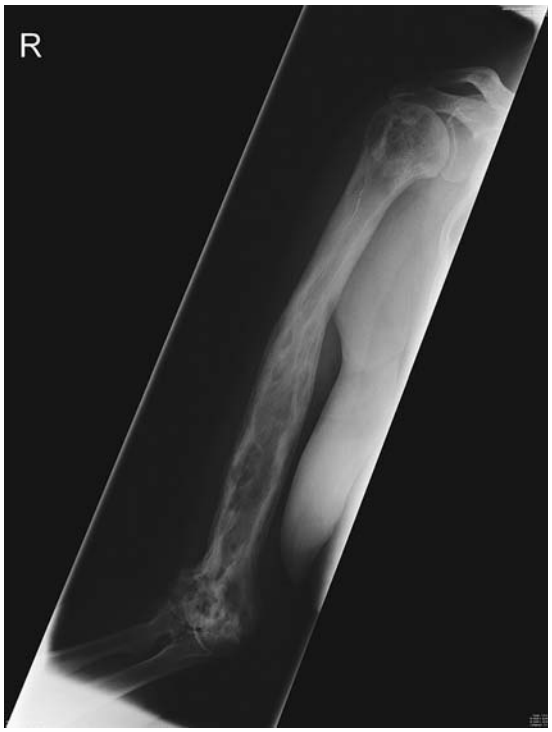

Fig. 1.1 Right humerus.

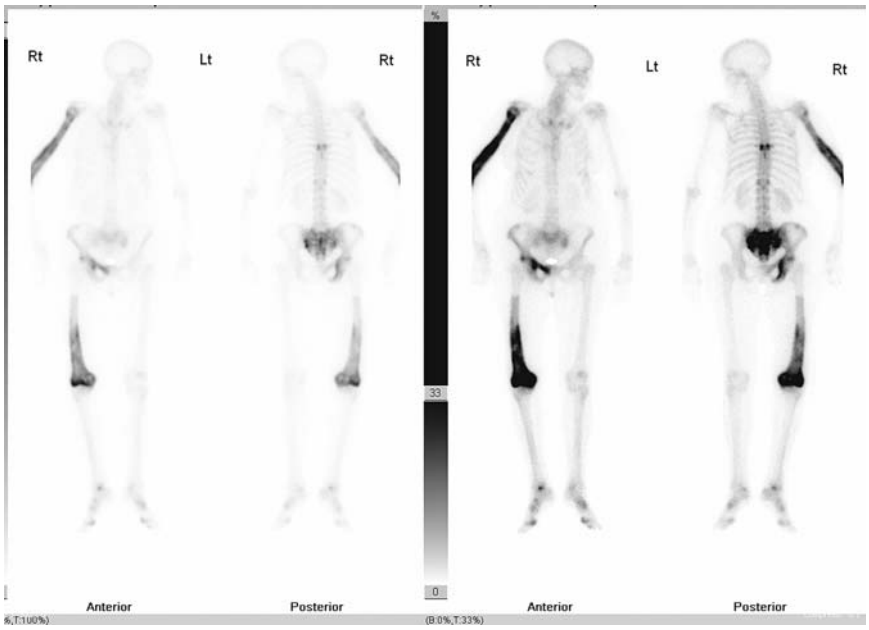

Fig. 1.2 Isotope bone scan.

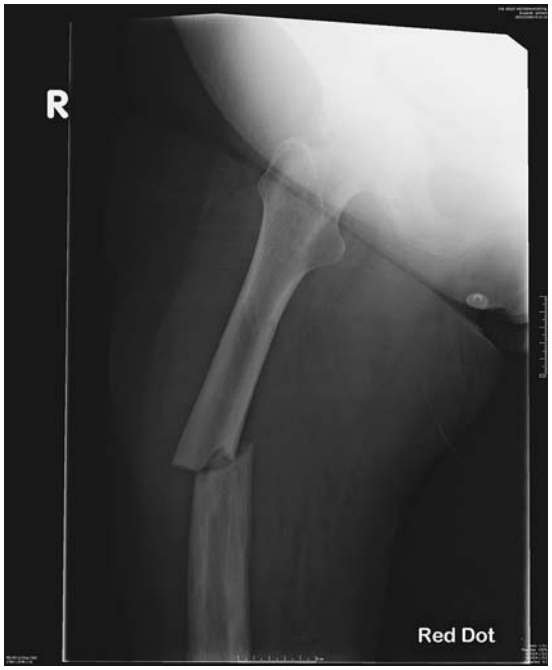

Fig. 1.3 Right femoral mid-shaft fracture.

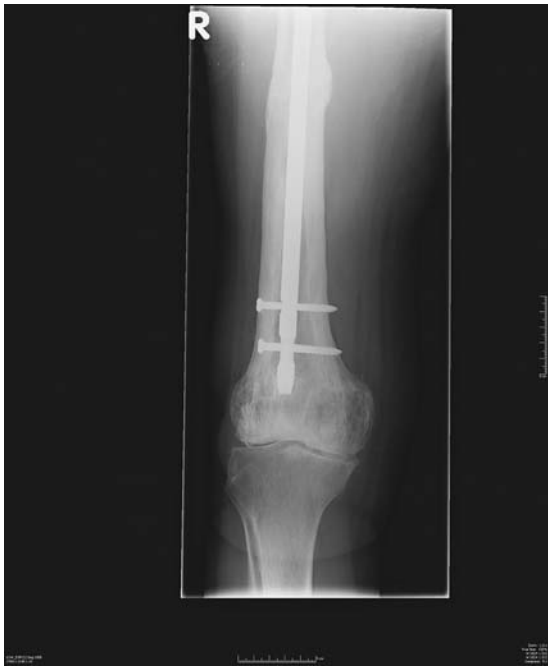

Fig. 1.4 Repaired right femoral mid-shaft fracture.

Answers

1. What is the underlying bony diagnosis? What is the differential diagnosis?

The diagnosis is Paget's disease of bone.

The differential diagnosis of a low-impact fracture in an elderly woman includes osteoporosis, osteomalacia, pathological fracture through a malignant focus, and Paget's disease. This patient's calcium was low normal on admission. Her phosphate was also low normal and her alkaline phosphate was very high. The rise in ALP could have been due to Paget's disease, osteomalacia, malignancy, or her recent fracture.

The plain radiographic features in the humerus (Fig. 1.1), and below the femoral fracture site (Fig. 1.3) in this case are typical of Paget's disease (Fig. 1.5). The bones are expanded with coarse trabeculation, cortical thickening, a mixture of lytic and sclerotic areas with intra-cortical resorption, loss of cortico-medullary junction, and early secondary osteoarthritis changes in the knee. Radiographic features are pathognomonic in established disease, but early or isolated lesions might be confused with malignancy and severe osteomalacia.

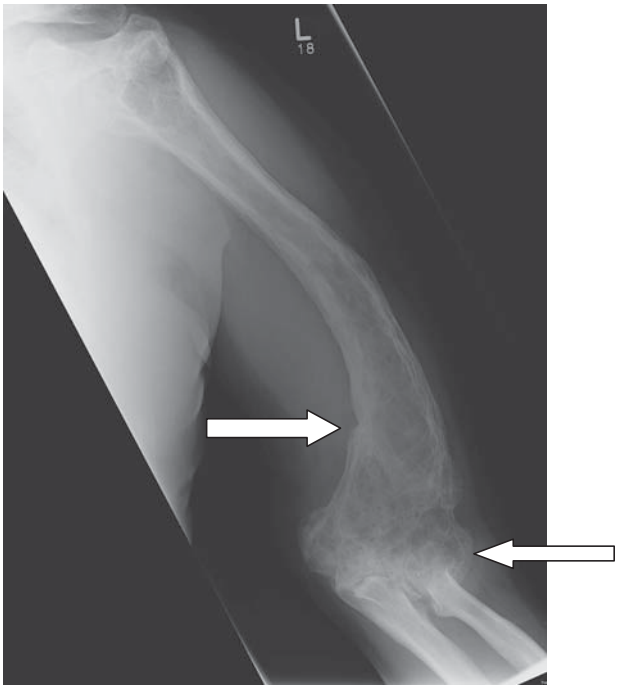

Fig. 1.5 Typical pagetic changes in a humerus with disorganized architecture, coarse trabeculation, cortical thickening, bowing and fractures in the cortex (arrow), and osteoarthritic changes in elbow (arrow) and shoulder.

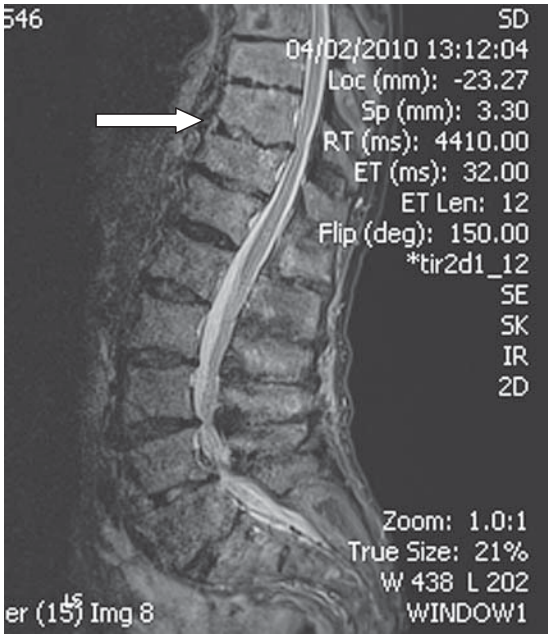

Fig. 1.6 MRI spine with spinal cord compression (arrow) and multi-level degeneration.

The technetium-99m isotope bone scan (Fig. 1.2) shows increased uptake in the right humerus right distal femur, right hemi-pelvis, and thoracic spine.

Isotope bone scans are the current standard method of establishing the pattern of skeletal site involvement. Typical abnormalities are easily recognized. However, if abnormalities are detected, further clinical and radiographic assessment is necessary. There is a move towards limited skeletal survey, imaging the clinically significant sites of skull, long bones, and spine as first-line investigation.

In this patient's technetium scan the characteristic V-shaped advancing front of Paget's disease is seen in the femur and humerus. This represents marked osteolysis without accompanying sclerosis. Other affected areas include the sacrum and the T9 vertebral body.

CT imaging may be useful to delineate difficult fractures and MRI should be used to characterize spinal Paget's disease which may cause nerve root compression and spinal canal stenosis (Fig. 1.6).

2. Describe the clinical features, natural history, and potential complications of this condition

Paget's disease of bone occurs in up to 10% of the population aged over 80 years and can affect any bone. The most common bones affected are pelvis (75%), lumbar spine (50%), femur (35%), sacrum (35%), skull (35%), tibia (30%) radius (15%). Patients often present with pain or deformity. The pain is of a deep bony, boring