

Osteoblastic and hyperostotic craniofacial lesion detected by ^{99m}Tc -labeled methylene diphosphonate bone scintigraphy and single-photon emission computed tomography/computed tomography: a pictorial essay

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^{99m}Tc -bisphosphonates bone scan, planar and single-photon emission computed tomography/computed tomography (SPECT/CT) modalities, is a commonly used technique that provides high sensitivity and specificity for detection of osseous metastases. However, besides bone metastases, SPECT/CT provides an accurate evaluation of the localization of the lesions and supplies anatomic information that can be valuable for diagnosis of nonmalignant bone diseases, occasionally disclosed in the skull. Reporting of craniofacial lesions detected by ^{99m}Tc -MDP (^{99m}Tc -labeled methylene diphosphonate) bone scintigraphy and SPECT/CT in the literature is limited. The aim of this pictorial review is to present the findings detected by ^{99m}Tc -MDP bone scintigraphy and SPECT/CT including cases under two broad categories: osteoblastic

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Introduction

Craniofacial uptake is occasionally seen in the ^{99m}Tc -MDP (^{99m}Tc -labeled methylene diphosphonate) whole-body bone scans (WBS). Single-photon emission computed tomography/computed tomography (SPECT/CT) offers the opportunity to obtain diagnostic quality in patients with craniofacial lesions [1]. Although some are diagnosable histologically, most require a combined assessment of clinical, microscopic and radiologic features [2]. ^{99m}Tc -MDP WBS has been widely used for detection of metastasis for various malignant diseases. However, some benign diseases also showed significantly increased ^{99m}Tc -MDP uptake, which may mimic bone metastasis [3,4]. Therefore, active diagnosis and radiological familiarity of craniofacial bone lesions are thought to be essential for distinguishing different bone diseases and preventing unnecessary examinations or therapy. At our institution, we encountered ^{99m}Tc -MDP bone scan that demonstrated a variety of craniofacial bone lesions with uptake. The purpose of this atlas article is to demonstrate a spectrum of osteoblastic and hyperostotic craniofacial lesions, both benign and malignant, which can show increased uptake on SPECT/CT imaging (Table 1). In

addition, available radiological images are presented in this article because familiarity with the imaging features of different imaging modalities is helpful for making differential diagnosis.

Osteoblastic and hyperostotic craniofacial lesions

Hyperostosis frontalis interna

Hyperostosis frontalis interna (HFI) is benign thickening of the inner table of frontal bones in the pattern of bilateral deposition. It is commonly observed incidentally due to its lack of direct clinical significance. The incidence of HFI is high in postmenopausal elderly women [5] (Fig. 1). It has been inferred that the etiology is linked to sex hormones levels and their regulation. Recent research has demonstrated that higher expression of fibroblast growth factor ligands in the frontal bone leads to a specific increased capacity for the frontal bone to regenerate [6]. SPECT/CT is needed for evaluation of bone lesions to differentiate metastatic disease in cancer patients [7].

Fibrous dysplasia

Fibrous dysplasia is a rare nonhereditary constitutional osteopathy triggered by mutations in the *GNAS* gene, which cause normal bone to be replaced with fibrous tissue and abnormal bone [8,9]. It is a benign disease with exceptional potential for malignant transformation [10]. Fibrous dysplasia lesions manifest commonly

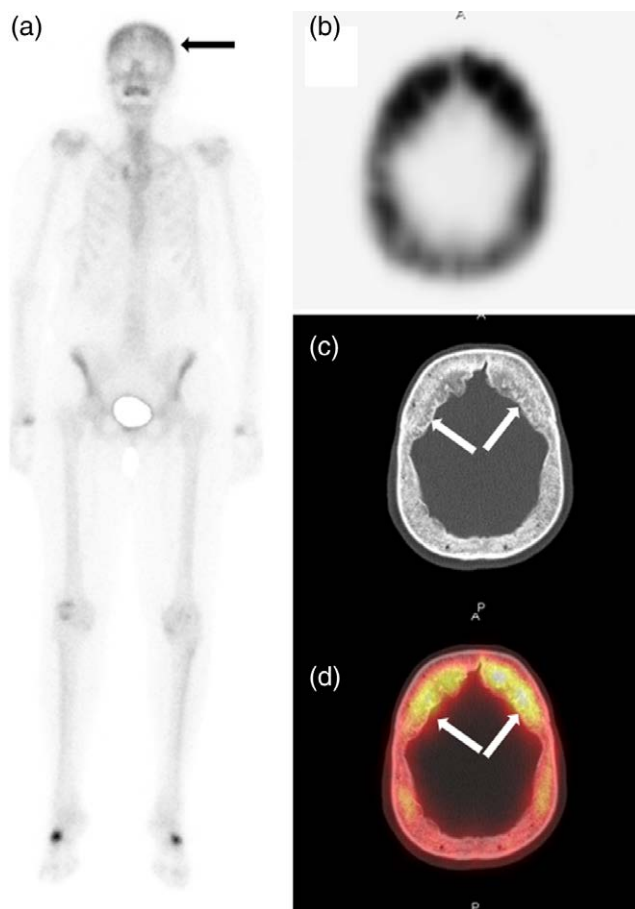
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Table 1 Imaging features of different sclerotic (osteoblastic) and hyperostotic craniofacial lesions

	HFI	FD	EPM	Osteoma	PDB	Melorheostosis	Osteopetrosis
Craniofacial location	Frontal bones	Frontal bones ethmoid	Sphenoid	Paranasal sinuses	Cranial vault	Rare	Skull base (type 2)
Symmetry	+	-	-	-	±	-	±
Respect outer table	+	+	-	-	±	-	-
Respect inner table	-	+	-	±	±	+	-
SPECT/CT	To evaluate bone lesions and to differentiate metastatic disease in cancer patients	To determine sites of skeletal involvement and bone turn-over	To determine sites of skeletal involvement and bone uptake	Useful in to diagnosing Gardner's syndrome	Assess the extent of the disease	To distinguish from other sclerosing bone dysplasias	To assess the extent of the disease

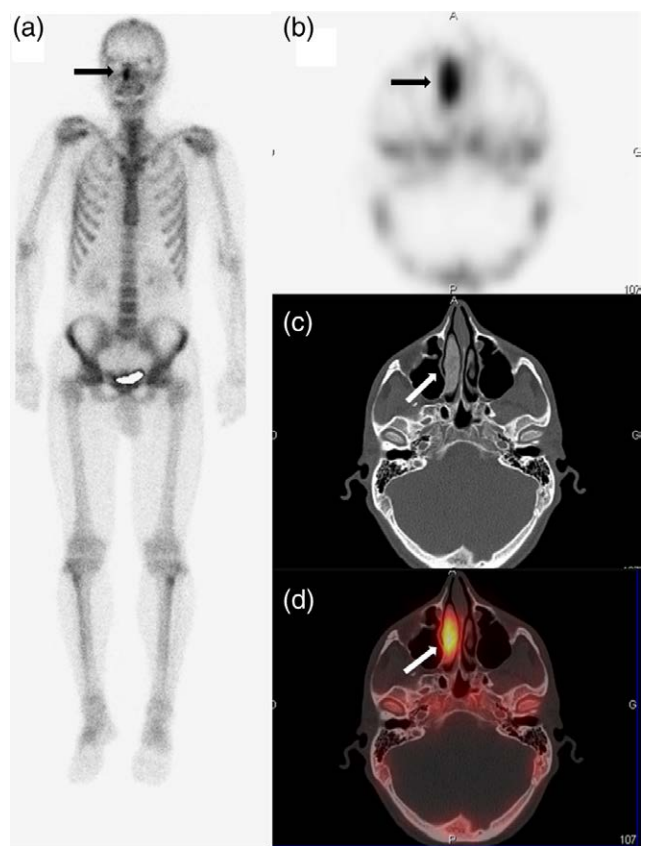
EPM, En plaque meningioma; FD, fibrous dysplasia; HFI, hyperostosis frontalis interna; PDB, Paget's disease of bone.

Fig. 1



A 70-year-old woman presented with atypical temporo-frontal headaches for 1 month. Bone scintigraphy (a and b) reveals a moderate symmetric frontal bone increased uptake (black arrow). Axial (c) CT confirms the radial and symmetrical thickening with papillary edges of the inner table of the frontal bone (white arrows). SPECT/CT (d) confirms frontal bone increased uptake of the lesion.

Fig. 2

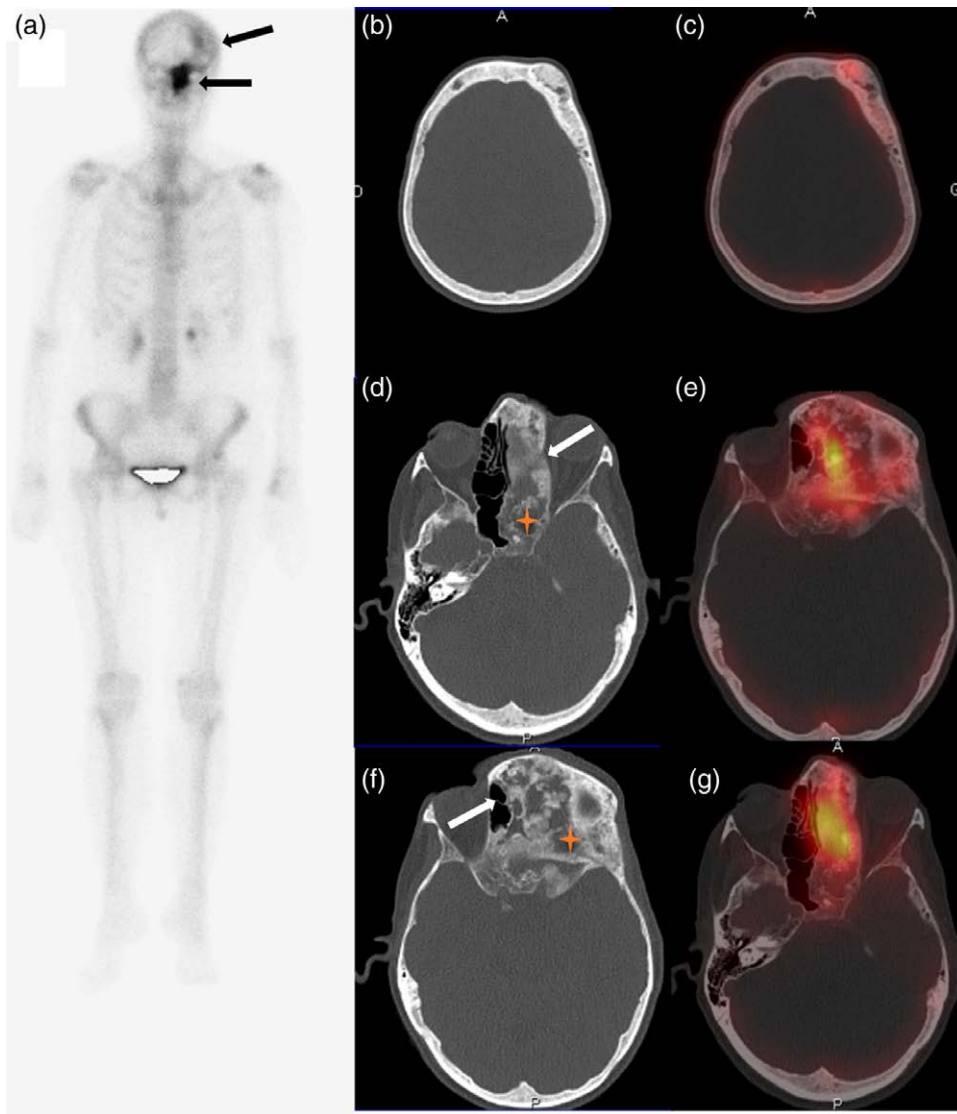


A 29-year-old man presented with fibrous dysplasia incidentally discovered by CT. Bone scintigraphy was ordered for assessment of extension and progression. Bone scintigraphy (a) reveals an intense uptake in the right nasal cavity (black arrow); absence of significant uptake on the remainder of the skeleton. Axial CT (c) shows typical ground-glass appearance of the middle and lower turbinate (white arrows); this is a result of woven bone superimposed on a fibrous tissue matrix. SPECT/CT (d) confirms the uptake of the lesion (white arrows). This patient was diagnosed as fibrous dysplasia of middle and lower turbinate (monostotic).

in the craniofacial skeleton, with reports ranging from 10 to 25% in monostotic disease (Fig. 2) and as high as 90% in polyostotic disease [11] (Fig. 3). In fibrous dysplasia, the bone disease may occur in combination with hyperfunctioning endocrinopathies and hyperpigmented skin lesions (McCune-Albright syndrome). Craniofacial

lesions in older individuals typically become less homogeneous on CT, developing discrete radiolucent, 'cystic' appearing areas (Fig. 3, asterisk). Technetium-99 m bisphosphonates scintigraphy is useful for determining sites of skeletal involvement and bone turn-over [12].

Fig. 3



A 70-year-old woman presented with pain of fronto-orbito-sinus of skull in recent appearance. The pain is in fact in recurring after the first episode 50 years ago. Bone scintigraphy (a) reveals an intense uptake in the left nasal cavity and a moderate uptake of the left frontal bone (black arrow). Axial CT (b, d and f) shows typical features of cortical thinning without breaching the bony cortices and endosteal scalloping (white arrows), and the periosteal surface is smooth and nonreactive with no visible trabecular pattern of the left frontal bone, left hemi-ethmoid, middle turbinate and the left part of the sphenoid. SPECT/CT (c, e and g) confirm the uptake of the lesions. This patient was diagnosed as craniofacial polyostotic fibrous dysplasia.

En plaque meningioma

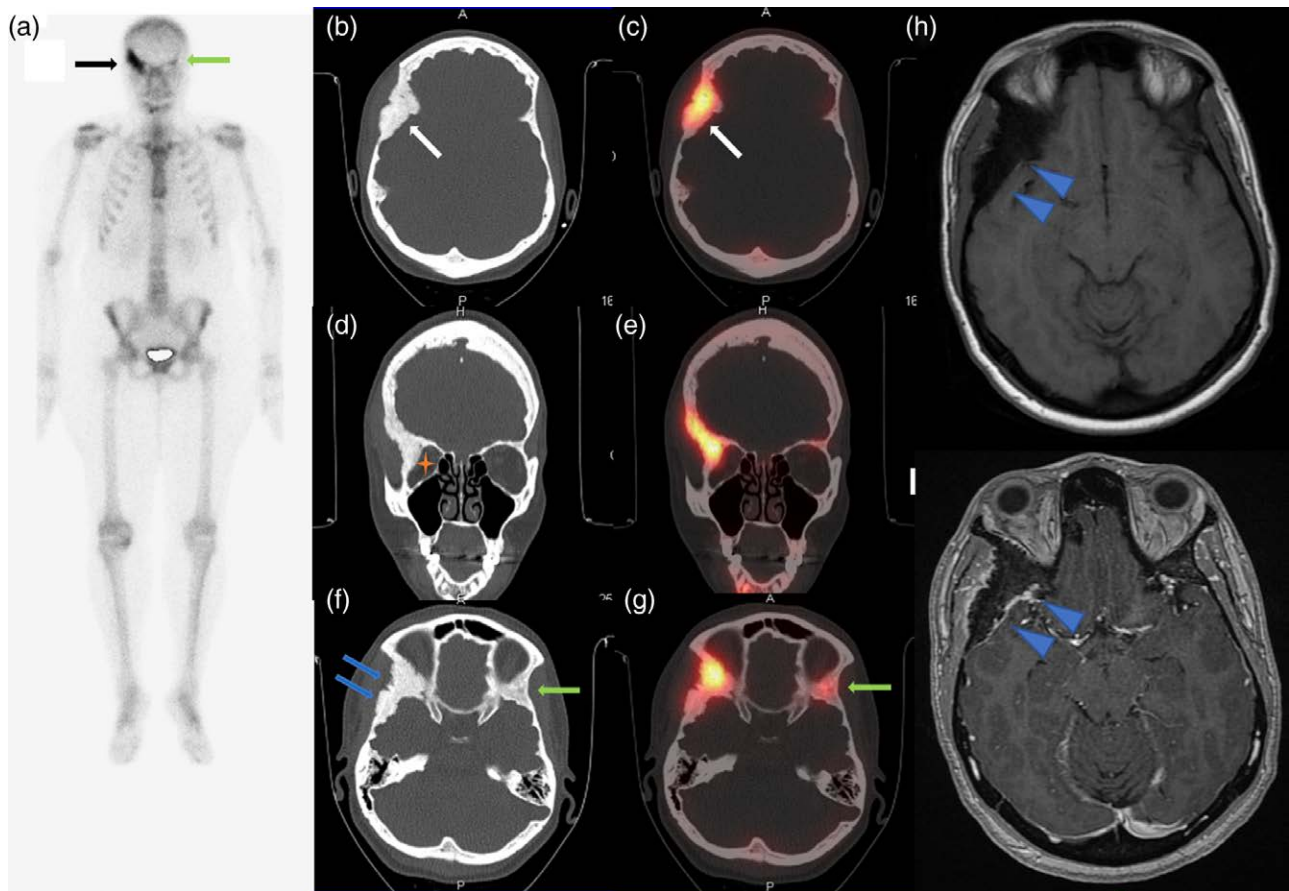
Meningiomas are common, primary intracranial tumors that arise from the meninges. An en plaque meningioma is a distinct subtype of meningioma characterized by 'sheet-like' patterns of growth than the more common globular form [13] (Figs. 4 and 5). For reasons unclear, they are more likely to provoke adjacent bony hyperostosis with the sphenoid ridge or sphenoid convexity being the most commonly affected site [14–16]. It is more common in women and proptosis is the most common presentation [17]. The differential diagnosis based on the CT

imaging includes fibrous dysplasia [18], osteoma, Paget disease of the bone and metastases to the skull base.

Osteoma

Osteomas are benign neoplasms characterized by the proliferation of compact or cancellous bone [19]. The nose and paranasal sinuses are most commonly affected [20]. Most of these patients are in the fifth to sixth decades, and there is a male preponderance. Paranasal sinus osteomas (PSO) have a potential to grow; however, there was no increase in the size of osteomas in almost half

Fig. 4



A 45-year-old woman suffers right frontal pain for 2 months with exophthalmia. Bone scintigraphy (a) reveals an intense uptake of the right sphenoid region (black arrow). There is a moderate increased uptake of the left sphenoid (green arrow). Axial CT (b and f) demonstrates significant diffuse hyperostosis along inner and orbital surfaces of greater sphenoidal wing and calvaria (white and blue arrows). The outer table of bone was spiculated, while the inner table had a more lobular pattern. Coronal CT (d) shows right calvarial thickening and orbital oppression (asterisk). SPECT/CT (c, e and g) confirms the increased uptake of the lesions. There is a moderate uptake of the post-lateral portion of the left orbit (green arrow). Axial T1 MRI (h) demonstrates hyperostosis (blue arrow heads). Axial T1 post-gadolinium fat suppression MRI (i) demonstrates meningeal enhancement (blue arrow heads) and hyperostosis. This patient was diagnosed as en plaque meningioma (EPM) of right orbital-sphenoid.

of the patients [19] just like our case (Fig. 6). Multiple osteomas are frequently associated with Gardner's syndrome, which is an autosomal dominant hereditary disorder characterized by intestinal polyposis, osteomas, and cutaneous and soft tissue tumors [21]. Bone scintigraphy and SPECT/CT could be helpful to diagnose Gardner's syndrome [22].

Paget disease

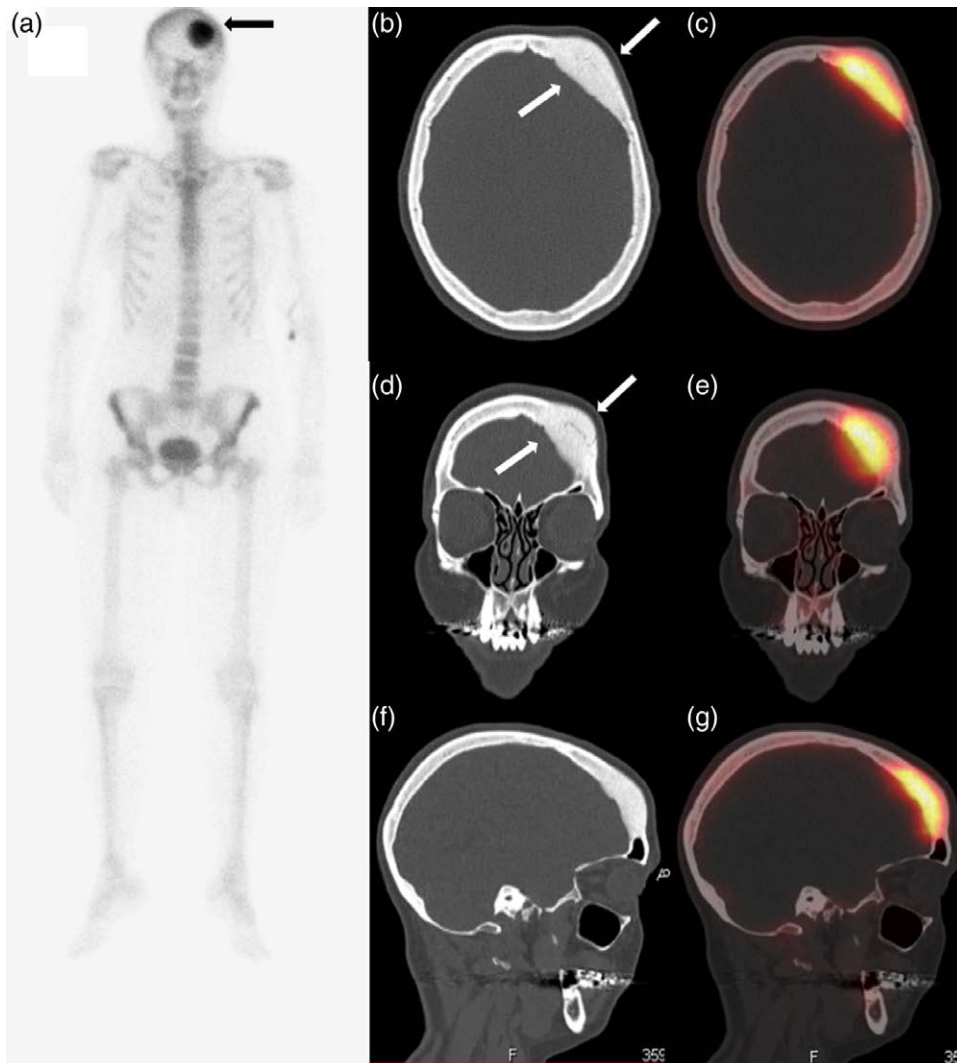
Paget's disease of bone (PDB) is a common disorder characterized by focal areas of increased and disorganized bone remodeling affecting one or more bones throughout the skeleton due to an increase in the number and size of osteoclasts in affected sites while the rest of the skeleton remains normal. PDB most frequently affects the pelvis (70%), femur (55%), lumbar spine (53%), skull (42%) and tibia (32%) (Fig. 7). Paget's disease is rare

before the age of 55 years and affects slightly more men than women [23]. Although some patients are asymptomatic others develop complications such as bone pain, deformity, secondary osteoarthritis, nerve compression syndromes and fragility fractures [24]. The diagnosis can usually be made on the basis of a radiograph showing the typical features of focal osteolysis with coarsening of the trabecular pattern, bone expansion and cortical thickening. Bone scintigraphy is used to assess the extent of the disease and can be helpful if new symptoms develop at sites distant from those identified on radiographs [23–25].

Melorheostosis

Melorheostosis is a rare benign disease of irregular cortical thickening with a characteristic 'melting wax' appearance on conventional radiographs or CT (Fig. 8). The

Fig. 5



A 46-year-old woman complains a painless tumor of left frontal bone. Bone scintigraphy (a) reveals an intense uptake of the left frontal bone (black arrow). CT (b, d and f) shows hyperostosis in left frontal bone in vicinity of coronal suture. Hyperostosis is of homogeneous density with inner, middle, and external tables not distinguishable as separate structures (white arrows). The hyperostotic bone shows a biconvex appearance. SPECT/CT (c, e and g) confirm the hyper-uptake of the lesion. This patient was diagnosed as en plaque meningioma (EPM).

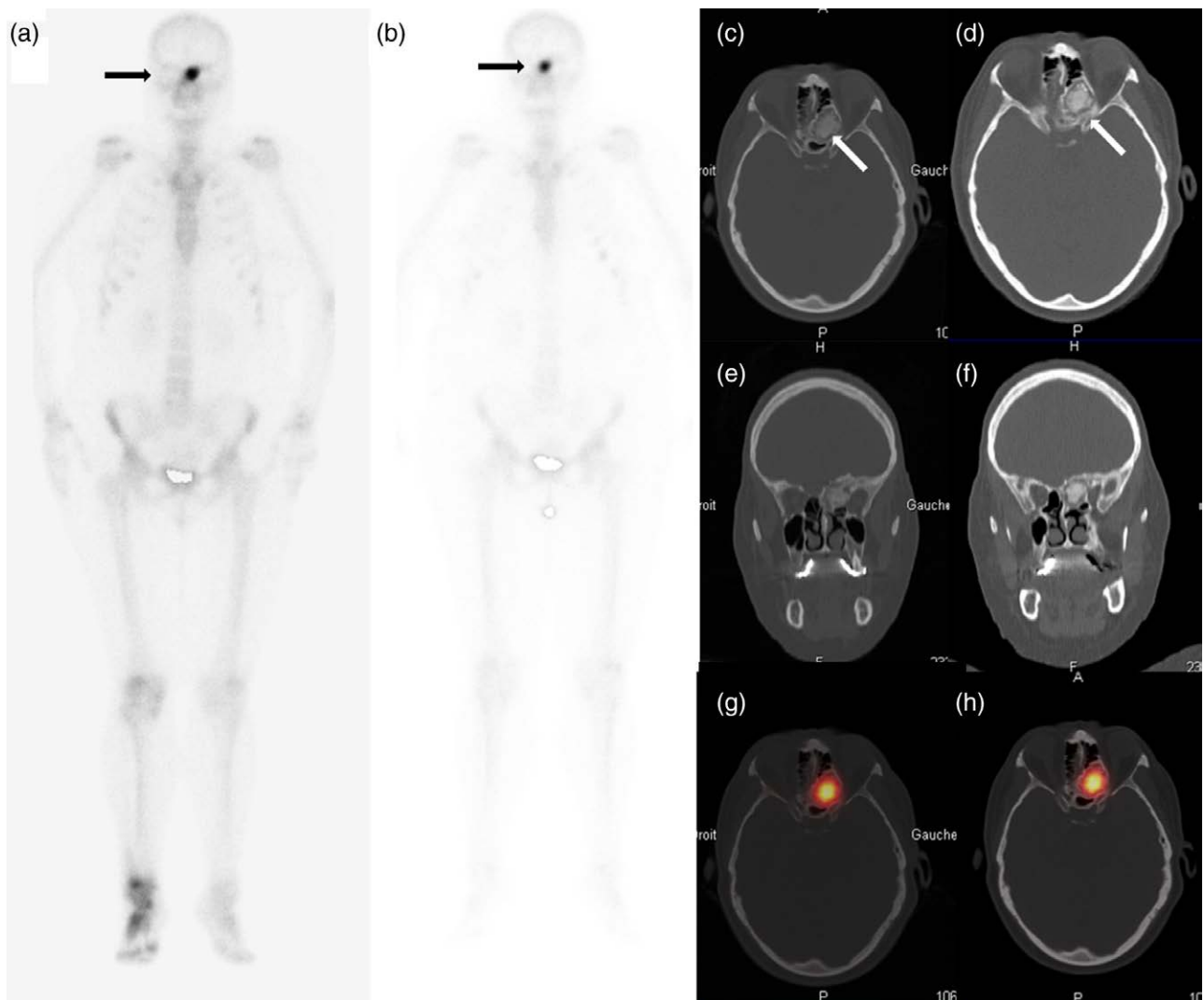
disease most frequently affects the appendicular skeleton and more than one-half of patients had lower limb involvement but is rarely seen in the craniofacial bones [26–29]. It is a disease mainly in the young adult population in the second or the third decade of life. Some recent studies have pointed toward the loss of functional mutations in the *LEMD3* gene as a potential cause of melorheostosis [30]. The clinical features of melorheostosis most often include varying degrees of bone pain associated with the progressively enlarging mass [28]. Diagnosis is based on a combination of clinical and radiological features that help differentiate this condition from other sclerosing bone dysplasias [31]. Bone scans show increased uptake in the involved bones due to increased

blood flow and osteoblast activity in the affected bones [32]. The increased uptake noted on bone scans helps distinguish melorheostosis from other sclerosing bone dysplasias, such as osteopoikilosis and osteopathia striata, which do not show scintigraphic abnormalities.

Osteopetrosis

Osteopetrosis is a group of rare bone disorders characterized by reduced osteoclastic bone resorption that results in a high bone mass. There are three different subtypes classified on the basis of the pattern of inheritance, severity, age of onset and clinical features: autosomal recessive (or infantile malignant type), mild autosomal recessive (or intermediate type)

Fig. 6



A 52-year-old man suffers right ankle pain for 2 months. Planar image of year 2013 (a) accidentally revealed an increased uptake in the nose root (black arrow) besides uptake of the right ankle. Image b was a follow-up image in 2016, the uptake in the nose root was almost the same. The CT images of 2013 (c and e) and 2016 (d and f) revealed an oval-shaped, dense, homogeneous, well-circumscribed masses (white arrows) in the left ethmoid sinus. There was intensively elevated BP uptake on the corresponding SPECT/CT fusion (g for 2013 and h for 2016) images. Osteoma in the left ethmoid sinus was considered.

and autosomal dominant (or adult benign type) [33]. The autosomal-dominant forms of osteopetrosis have a delayed-onset phenotype and usually are associated with mild symptoms and a benign prognosis. The diagnosis frequently is made coincidentally on radiographic examination, because patients often are asymptomatic. Symptoms are progressive with age and correlated with osteosclerosis. The autosomal dominant osteopetrosis type I is the most frequent form. The hallmark of the disease is a generalized osteosclerosis, more pronounced in the cranial vault (Fig. 9). Classic radiographic features of osteopetrosis is the minimum needed to make the diagnosis [34,35].

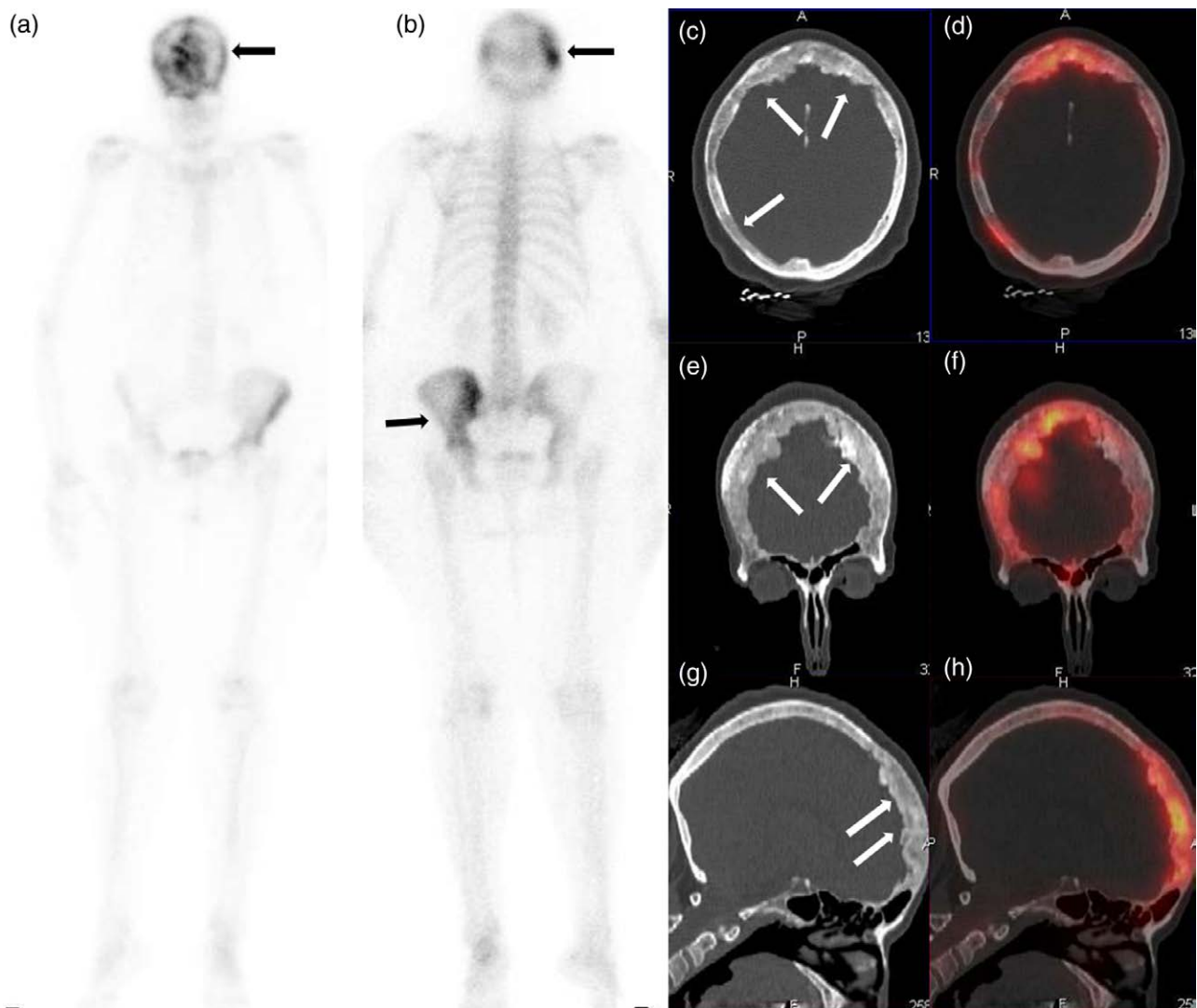
Osteoblastic bone metastases

Prostate cancer (PCa) is the commonest type of malignancy in the males in western countries [36]. It has a propensity to metastasize to bone, and the bone metastases represent the initial and the main metastatic site in about 80% of PCa patients [37,38] (Fig. 10). Although multiple new tracers have been developed [39], ^{99m}Tc -bisphosphonates bone scintigraphy and SPECT/CT is still widely used in PCa.

Conclusion

Craniofacial lesions are occasionally detected in bone scan. It is difficult to distinguish different lesions in the

Fig. 7



A 58-year-old man suffers frontal pain and left hip pain for several months. Bone scintigraphy (a and b) reveals an intense uptake of the frontal and parietal skull as well as the left ilium (black arrow). CT (c, e and g) shows both frontal-parietal bones appears as lytic lesions with coarsening trabeculae, bony expansion, widening of the diploe, with more inner table expansion than outer (white arrow). The left occipital bone also appears as lytic lesions. SPECT/CT (d, f and h) confirms the increased uptake of the lesions. There is a heterogeneous and diffuse increased uptake of the left hip exhibiting the same CT features. This patient was diagnosed as Paget disease.

planar imaging for lack of anatomic information and morphological features. SPECT/CT provides necessary information for diagnosis and differential diagnosis. In this atlas article, we describe most prevalent lesions, which we have encountered, in an attempt to assist other interpreting physicians in expanding the differential diagnosis for the osteoblastic and hyperostotic craniofacial lesions on a bone scan.

Acknowledgements

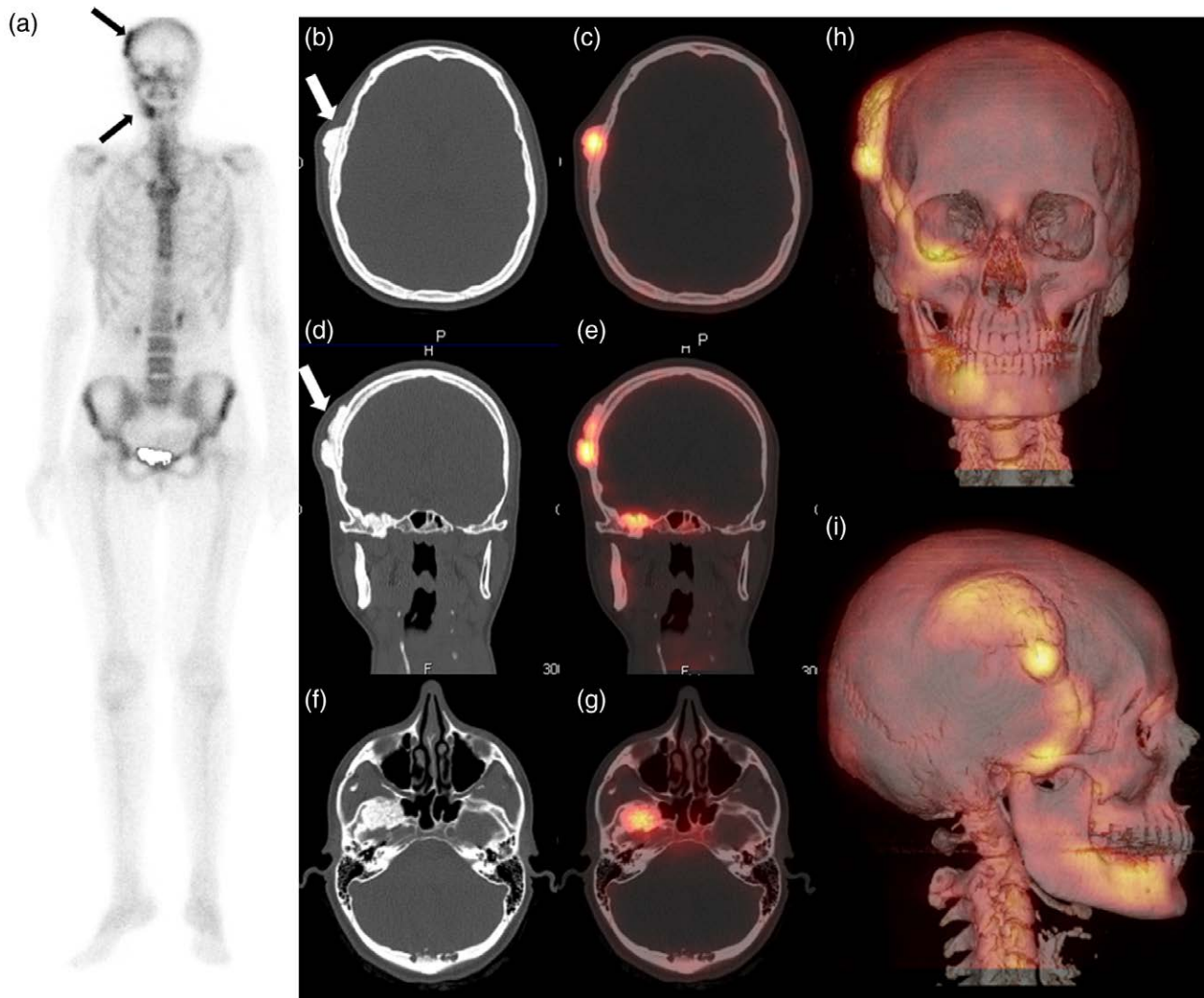
Conflicts of interest

There are no conflicts of interest.

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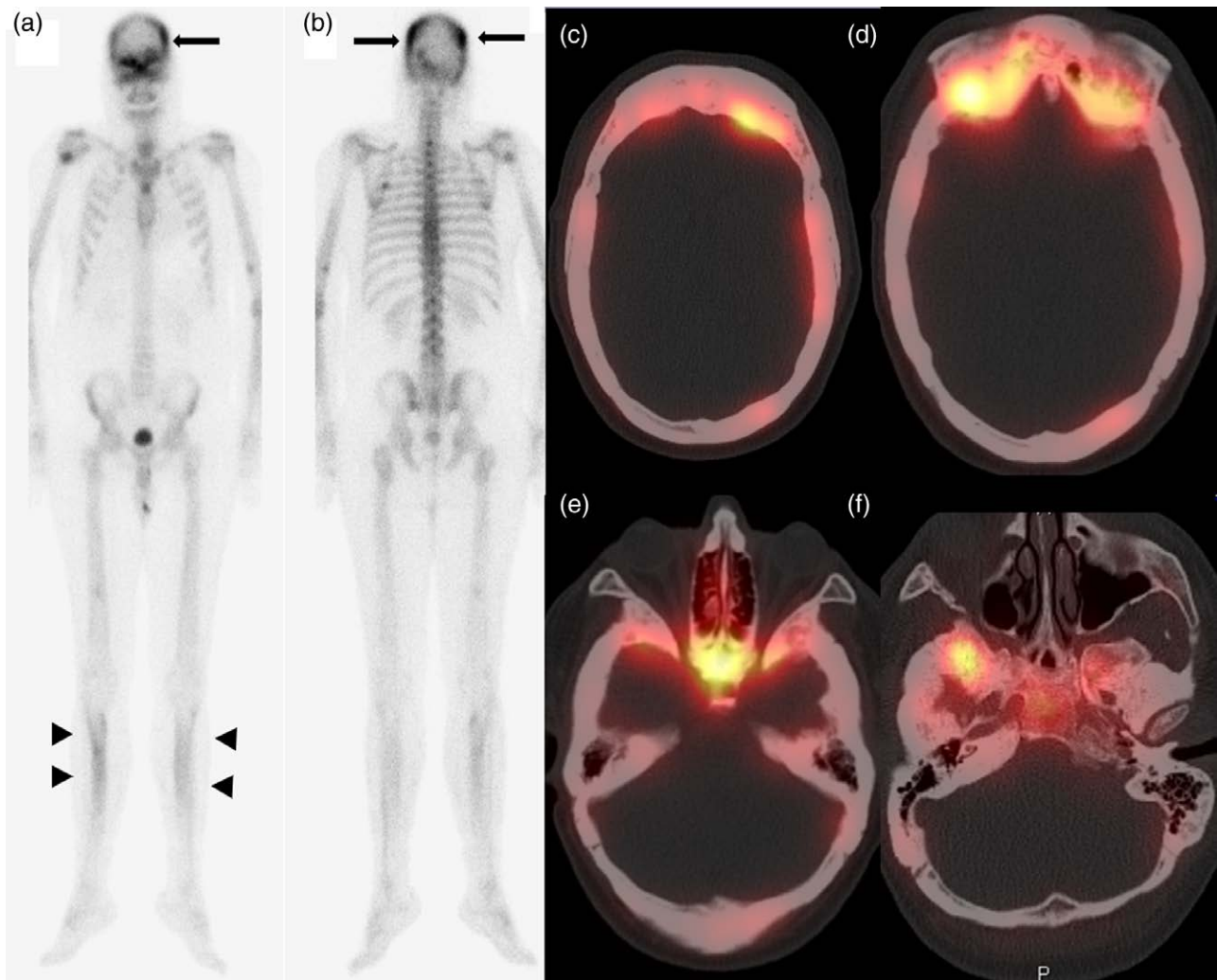
Fig. 8



A 35-year-old woman complains of painless fronto-parietal swelling. Bone scintigraphy (a) reveals an intense uptake of the right parietal bone and right mandible (black arrow). CT (b, d and f) shows dense, irregular, and eccentric hyperostosis of the right temporal and parietal bone, the great wing of the sphenoid, the upright branch and body of the right hemi-mandible. SPECT/CT (c–f) confirms the uptake of the lesions. 3D images (h and i) shows irregular cortical thickening with a characteristic 'melting wax' appearance. Bone scintigraphy suggests in the first place melorheostosis.

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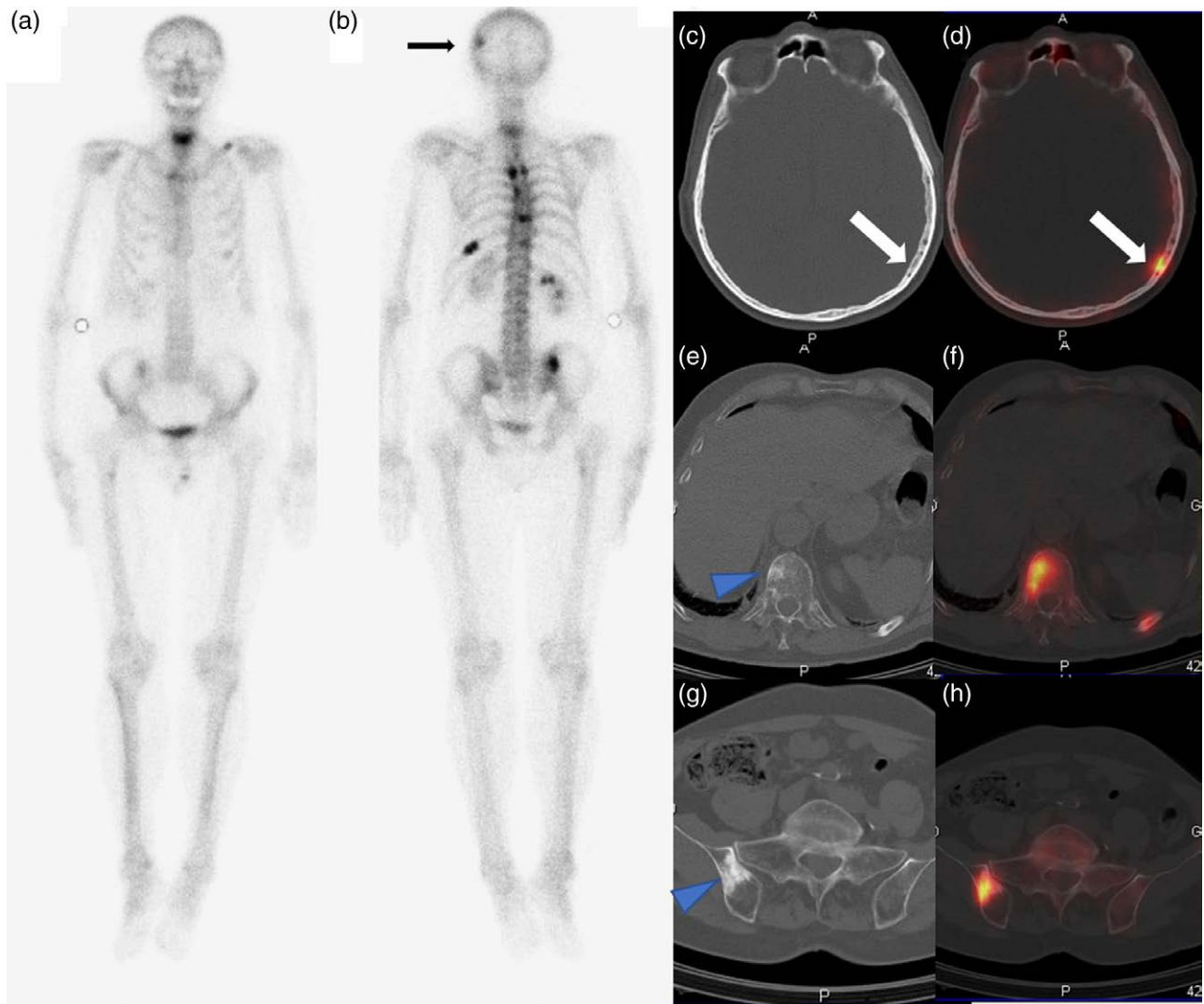
Fig. 9



A 48-year-old man with a pituitary prolactin adenoma accidentally discover asymptomatic bone thickening of the frontal bone; bone scintigraphy was performed for assessment of extension. Bone scintigraphy (a) reveals an intense uptake of the nose root and both parietal bone (black arrow). A moderate uptake was seen in both tibiae (arrow head). Axial view of SPECT/CT (c–f) shows a generalized thickening of the skull and confirms the uptake of the lesions. Bone scintigraphy suggests in the first place autosomal dominant osteopetrosis (ADO).

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Fig. 10



A 64-year-old man presented with prostate cancer; bone scintigraphy was performed for assessment of extension and progression. Bone scintigraphy (a and b) reveals an intense uptake of the left parietal bone (black arrow), left clavicle, multiple vertebrae, left 11th rib, right ilium and right femur. CT (c, e and g) shows multiple sclerotic lesions (white arrow). SPECT/CT (d, f and h) confirms increased uptake of the lesions. This patient was diagnosed as prostate cancer with multiple bone metastasis.

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