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Musculoskeletal manifestations of endocrine disorders ☆,☆☆,★

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ABSTRACT

Endocrine disorders can lead to disturbances in numerous systems within the body, including the musculoskeletal system. Radiological evaluation of these conditions can demonstrate typical appearances of the bones and soft tissues. Knowledge of these patterns can allow the radiologist to suggest a diagnosis that may not be clinically apparent. This review will highlight the typical musculoskeletal findings of acromegaly, hypercortisolism, hyperthyroidism, hypothyroidism, hyperparathyroidism, pseudo- and pseudopseudohypoparathyroidism, and diabetes mellitus. The radiological manifestations of each of these endocrine disorders, along with a brief discussion of the pathophysiology and clinical implications, will be discussed.

1. Introduction

Endocrine disorders are a heterogeneous group of disorders that result in hormonal disturbances. Hormones are a vital part of homeostasis in the body. Thus, hormonal dysregulation affects nearly every body system, including the cardiovascular, pulmonary, gastrointestinal, genitourinary, dermatologic, neurologic, and musculoskeletal systems. Each disorder has a characteristic pattern of manifestations involving some or all of these body systems.

This review will focus on those endocrine disorders which may present with imaging findings involving the musculoskeletal system. The pathophysiology and common findings on radiography, ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear imaging will be reviewed, focusing on acromegaly, hypercortisolism, hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoparathyroidism, and diabetes mellitus (DM). In addition, the clinical implications of these musculoskeletal manifestations will be discussed.

The selected references for this review were gleaned from a literature search of the PubMed database, using various combinations of the search terms "musculoskeletal," "skeletal," "bone," "muscle," "joint," "radiology," "radiographic," and "imaging" with "endocrine," "acromegaly," "hypercortisolism," "hyperthyroidism," "hypothyroidism," "hyperparathyroidism," "pseudo- and pseudopseudo- and hypoparathyroidism," and "diabetes."

1.1. Gigantism and acromegaly

Growth hormone (GH), also known as somatotropin, is produced by the somatotropic cells of the pituitary gland [1]. It is regulated by the hypothalamic hormones growth-hormone-releasing hormone (GHRH), which induces secretion, and somatostatin, which inhibits its release [1]. Uncontrolled secretion of GH can lead to two separate but similar conditions. If the hormonal hypersecretion is present prior to physeal fusion, then gigantism results. Alternatively, if the increased levels of GH are present after skeletal maturity, then acromegaly is the resultant condition [2].

Greater than 90% of cases of GH hypersecretion are caused by benign pituitary adenomas. GH-secreting adenocarcinomas are exceedingly rare [1]. The remainder of cases are due to hypothalamic adenomas resulting in excess GHRH with secondary increase in GH or extrapituitary hypersecretion of either GH (i.e., pancreatic islet cell tumors and carcinoid tumors) [3] or GHRH [4].

Prior to skeletal maturity, endochondral bone formation is still occurring at the physeal growth plates. Thus, excess GH at this stage results in exaggeration of this normal process, resulting in increased

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longitudinal bone growth [2]. The resultant clinical syndrome is termed gigantism, as those affected develop excessive height. In contrast, after physeal fusion, normal endochondral bone formation has ceased. Thus, excess GH at this stage results in stimulation of cartilaginous growth factors, reactivation of endochondral bone formation primarily at the chondroosseous junctions, and new bone deposition [2,5]. This results in the clinical syndrome known as acromegaly.

Table 1
Summary of key musculoskeletal imaging findings associated with endocrine disorders

Disorder	Findings
Gigantism	Increased longitudinal bone growth leading to excessive height
Acromegaly	Coarsened facial features with frontal bossing and mandibular prognathism Spade-like terminal tufts and widened phalanges Joint space widening early but premature osteoarthritis Soft tissue hypertrophy, ncluding heel pad thickening, median neuropathy, and trigger finger
Hypercortisolism	Osteopenia and osteoporosis with insufficiency fractures Osteonecrosis Muscle wasting and increased fat deposition
Hyperthyroidism	Osteopenia and osteoporosis with insufficiency fractures Myopathy with atrophy and fatty infiltration Acropachy, pretibial myxedema, and ophthalmopathy Adhesive capsulitis
Hypothyroidism	Delayed skeletal maturation and fontanelle closure Irregular or stippled epiphyses Proximal muscle myopathy Dupuytren contracture Carpal tunnel syndrome
Hyperparathyroidism	Bone resorption (subperiosteal, endosteal, subchondral, intracortical, subtendinous, or subligamentous), including acroosteolysis, "salt and pepper" skull, and "pseudowidening" of sacroiliac or other fibrocartilaginous joints Brown tumors Tendon rupture Soft tissue calcifications, including chondrocalcinosis
Renal osteodystrophy	Findings of hyperparathyroidism plus: Osteosclerosis, including "rugger-jersey" spine Osteomalacia with Looser zones Osteoporosis "Tumoral" calcinosis
Pseudo- and pseduopseudohypoparathyrodism	Albright hereditary osteodystrophy: Metacarpal and/or metatarsal shortening (usually 4th/5th) Short middle and distal phalanges with coned epiphyses Short stature, rounded facies, central obesity Subcutaneous calcifications
DM	Neuropathic arthropathy Osteomyelitis and septic arthritis Insufficiency fractures (despite normal or increased bone density) Myonecrosis (muscle infarction) Adhesive capsulitis Dupuytren contracture

The clinical changes of acromegaly are insidious, with slow progression of coarsening of the facial features, growth of the hands and feet, and soft tissue hypertrophy [6]. Musculoskeletal manifestations of acromegaly are usually apparent approximately 10 years after the estimated onset of GH hypersecretion in the majority of patients. There is no clear relationship between the duration of GH hypersecretion and presence or severity of arthropathy [5].

Joint findings are seen in up to 70% of patients, resulting in a spectrum of findings termed acromegalic arthropathy [7]. Typical locations for these findings include the metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal and distal interphalangeal joints of the hands and feet (Fig. 1). The initial radiographic finding is joint space widening due to activation of cartilaginous growth factors by GH. However, prolongation of the hormonal dysregulation ultimately results in cartilage degeneration, with radiological findings simulating osteoarthritis, including joint space narrowing and osteophytosis [5,8]. This process also occurs in the vertebral bodies, which results in the typical appearance of increased intervertebral disc height with scalloping of the posterior margin of the vertebra [7].

Excess GH also results in periosteal new bone formation, often noted at several common sites. Subperiosteal new bone formation along the mental eminence and mandibular rami results in enlargement and forward protrusion of the mandible, termed mandibular prognathism [6]. New bone formation along the supraorbital ridges, facial bones, and calvarium leads to hypertrophy of the paranasal sinuses and frontal bossing (Fig. 2) [6]. These findings result in the typical lateral skull radiograph findings and characteristic facial features. New bone formation within the long bones results in both cortical thickening and irregularity, which often manifests as osseous widening. In the phalanges, this results in spade-like terminal tufts (Fig. 1) [6].

If the pituitary is enlarged by a GH-secreting adenoma, expansion of the sella turcica can also be seen on a lateral radiograph of the skull [6]. Clinically, patients can present with headaches or visual disturbances, prompting imaging to determine if there is a functional cause [1].

In addition to bone and joint findings, acromegaly also affects the soft tissues. Hypersecretion of GH results in connective tissue hyperplasia [9]. A common location that can be evaluated on radiographs is that of increased heel-pad thickness (Fig. 3). Measurements greater than 23 mm in males and more than 21.5mm in females are suggestive of acromegaly after other causes of heel pad/skin thickening are excluded [9]. However, this measurement is controversial [10]. Hypertrophy of the annular pulley of the fingers can also occur, resulting clinically in a trigger finger [7].

Soft tissue hypertrophy also results in enlargement of peripheral nerves by edema. Clinically, this can result in peripheral neuropathies such as median neuropathy or carpal tunnel syndrome (which is seen in up to 64% of patients at the time of presentation) and ulnar neuropathy or cubital tunnel syndrome, with tingling, numbness, or dysesthesias [5,7]. Ultrasound will demonstrate increased nerve size with preservation of the normal fascicular architecture; however, at sites of entrapment, there will be decreased echogenicity with loss of the normal fascicular pattern. On MR, peripheral nerves in acromegaly demonstrate increased size and signal intensity on the T2-weighted sequences due to intrinsic edema [7].

1.2. Hypercortisolism

Cortisol is a glucocorticoid produced by the zona fasciculata of the adrenal gland. Cortisol regulation is a complex process primarily mediated by the hypothalamic–pituitary axis [11]. The hypothalamus secretes corticotropin-releasing hormone (CRH), which acts on the corticotroph cells of the anterior pituitary to release adrenocorticotropic hormone (ACTH), which then stimulates the adrenal cortex to