Acromegaly

Dr Nasser Aghamohammadzadeh

Professor of Endocrinology

Tabriz University of Medical Sciences

Case study

History

- Male, 40 years old, Farmer, 3 children.

Symptoms

- Headache, vomiting, increased shoes size and rings. After 3 years- polyphagia, polyuria, polydypsia, diabetes and joint pain.

Past history and family history.

- No drugs, operation. No family history.

Diagnosis-General exam

Vital signs

- 37°c, BP- 160/90, regular pulse, fully conscious.

Head

- Elongated head, prominent supra-orbital ridges, enlarged nose, lips, ear, prognathism, separated teeth. Husky voice.

Neck

- By inspection, palpation

Diagnosis- Systemic examination

Skin

- Thickened, folds, sweaty, greasy skin.

Neuromuscular

- Myopathy and neuropathy.

Bone

- Crepitus in knee joint.

Investigation

- X-ray skull, heel, hand, joint.

Treatment

- Somatotatin analogue, GH antagonist, surgical removal of adenoma.

Diagnosis

- Acromegaly

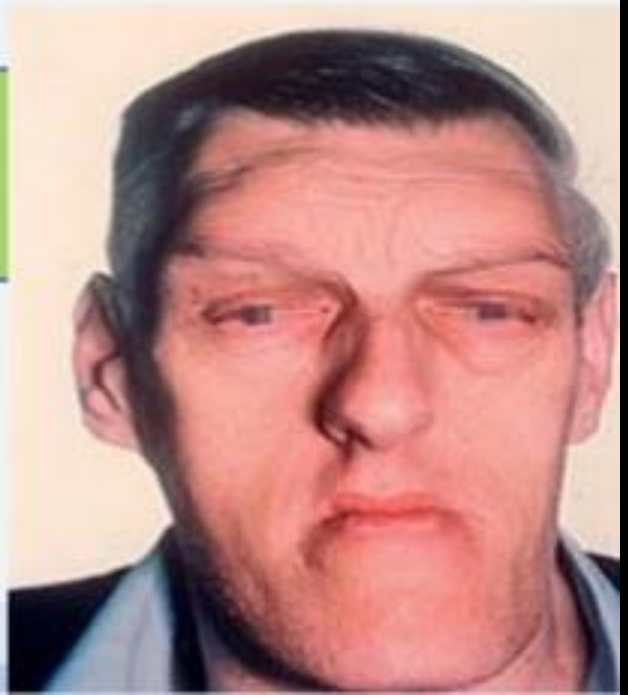


TABLE 373-1 Features of Sellar Mass Lesions[a]

IMPACTED STRUCTURE	CLINICAL IMPACT
Pituitary	Hypogonadism Hypothyroidism Growth failure and adult hyposomatotropism Hypoadrenalism
Optic chiasm	Loss of red perception Bitemporal hemianopia Superior or bitemporal field defect Scotoma Blindness
Hypothalamus	Temperature dysregulation Appetite and thirst disorders Obesity Diabetes insipidus Sleep disorders Behavioral dysfunction Autonomic dysfunction
Cavernous sinus	Ophthalmoplegia with or without ptosis or diplopia Facial numbness
Frontal lobe	Personality disorder Anosmia
Brain	Headache Hydrocephalus Psychosis Dementia Laughing seizures

[a]As the intrasellar mass expands, it first compresses intrasellar pituitary tissue, then usually invades dorsally through the dura to lift the optic chiasm or laterally to the cavernous sinuses. Bony erosion is rare, as is direct brain compression. Microadenomas may present with headache.

TABLE 373-2 Screening Tests for Functional Pituitary Adenomas

	TEST	COMMENTS
Acromegaly	Serum IGF-I	Interpret IGF-I relative to age- and sex-matched controls
	Oral glucose tolerance test with GH obtained at 0, 30, and 60 min	Normal subjects should suppress growth hormone to <1 μ/L
Prolactinoma	Serum PRL	Exclude medications
		MRI of the sella should be ordered if PRL is elevated
Cushing's disease	24-h urinary free cortisol	Ensure urine collection is total and accurate
	Dexamethasone (1 mg) at 11 P.M. and fasting plasma cortisol measured at 8 A.M.	Normal subjects suppress to <5 μ/dL
	ACTH assay	Distinguishes adrenal adenoma (ACTH suppressed) from ectopic ACTH or Cushing's disease (ACTH normal or elevated)

Abbreviations: ACTH, adrenocorticotropin hormone; GH, growth hormone; IGF-I, insulin-like growth factor I; MRI, magnetic resonance imaging; PRL, prolactin.

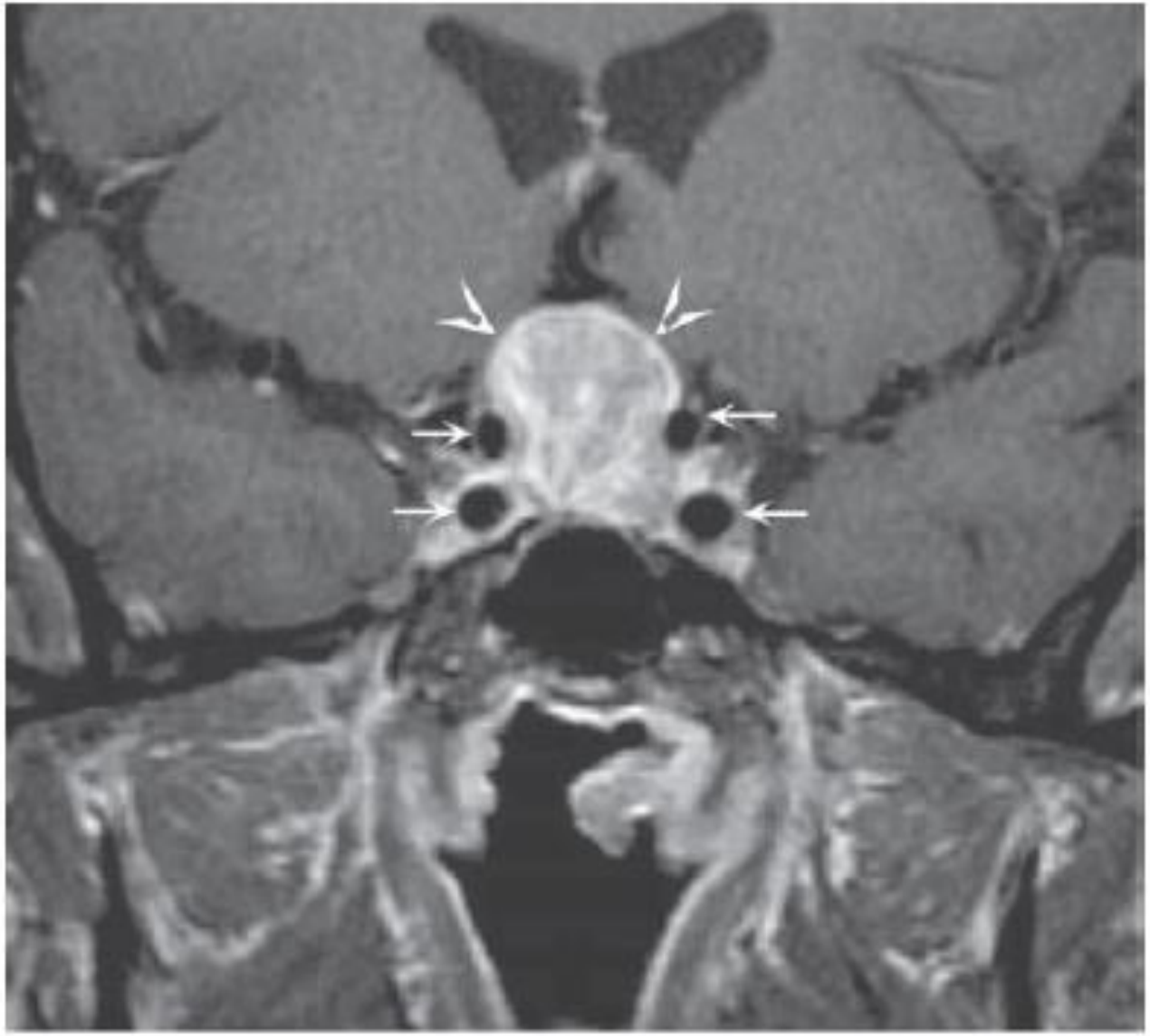


FIGURE 373-1 Pituitary adenoma. Coronal T1-weighted postcontrast magnetic resonance image shows a homogeneously enhancing mass (*arrowheads*) in the sella turcica and suprasellar region compatible with a pituitary adenoma; the *small arrows* outline the carotid arteries.

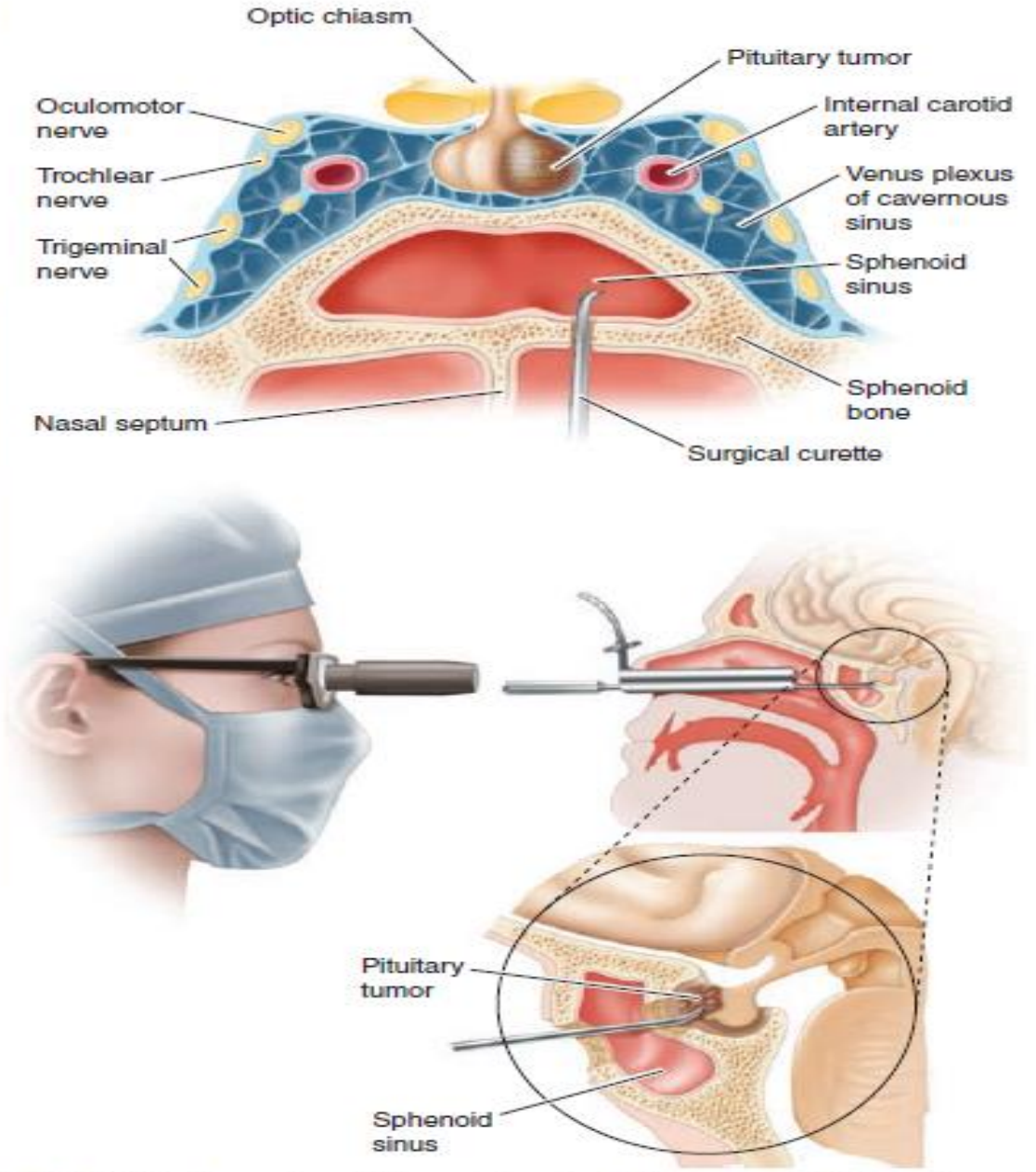


FIGURE 373-2 Transsphenoidal resection of pituitary mass via the endonasal approach. *(Adapted from R Fahlbusch: Endocrinol Metab Clin 21:669, 1992.)*

TABLE 373-3 Classification of Pituitary Adenomas[a]

ADENOMA CELL ORIGIN	HORMONE PRODUCT	CLINICAL SYNDROME
Lactotrope	PRL	Hypogonadism, galactorrhea
Gonadotrope	FSH, LH, subunits	Silent or hypogonadism
Somatotrope	GH	Acromegaly/gigantism
Corticotrope	ACTH/none	Cushing's disease or silent
Mixed growth hormone and prolactin cell	GH, PRL	Acromegaly, hypogonadism, galactorrhea
Other plurihormonal cell	Any	Mixed
Acidophil stem cell	PRL, GH	Hypogonadism, galactorrhea, acromegaly
Mammosomatotrope	PRL, GH	Hypogonadism, galactorrhea, acromegaly
Thyrotrope	TSH	Thyrotoxicosis
Null cell	None	Pituitary failure/none
Oncocytoma	None	Pituitary failure/none

[a]Hormone-secreting tumors are listed in decreasing order of frequency. All tumors may cause local pressure effects, including visual disturbances, cranial nerve palsy, and headache.

Note: For abbreviations, see text.

Source: Adapted from S Melmed: Nat Rev Endocrinol 7:257, 2011.

TABLE 373-4 Familial Pituitary Tumor Syndromes

	GENE MUTATED	CLINICAL FEATURES
Multiple endocrine neoplasia 1 (MEN 1)	*MEN1* (11q13)	Hyperparathyroidism Pancreatic neuroendocrine tumors Foregut carcinoids Adrenal adenomas Skin lesions Pituitary adenomas (40%)
Multiple endocrine neoplasia 4 (MEN 4)	*CDKNIB* (12p13)	Hyperparathyroidism Pituitary adenomas Other tumors
Carney complex	*PRKAR1A* (17q23-24)	Pituitary hyperplasia and adenomas (10%) Atrial myxomas Schwannomas Adrenal hyperplasia Lentigines
Familial pituitary adenomas	*AIP* (11q.13.2)	Acromegaly/gigantism (~15% of afflicted families)

TABLE 373-6 Causes of Acromegaly

	PREVALENCE, %
Excess Growth Hormone Secretion	
Pituitary	98
Densely or sparsely granulated GH cell adenoma	60
Mixed GH cell and PRL cell adenoma	25
Mammosomatotrope cell adenoma	10
Plurihormonal adenoma	
GH cell carcinoma or metastases	
Multiple endocrine neoplasia 1 (GH cell adenoma)	
McCune-Albright syndrome	
Ectopic sphenoid or parapharyngeal sinus pituitary adenoma	
Extrapituitary tumor	<1
Pancreatic islet cell tumor	
Lymphoma	
Excess Growth Hormone–Releasing Hormone Secretion	
Central	<1
Hypothalamic hamartoma, choristoma, ganglioneuroma	
Peripheral	<1
Bronchial carcinoid, pancreatic islet cell tumor, small cell lung cancer, adrenal adenoma, medullary thyroid carcinoma, pheochromocytoma	

Abbreviations: GH, growth hormone; PRL, prolactin.

Source: Adapted from S Melmed: N Engl J Med 355:2558, 2006.

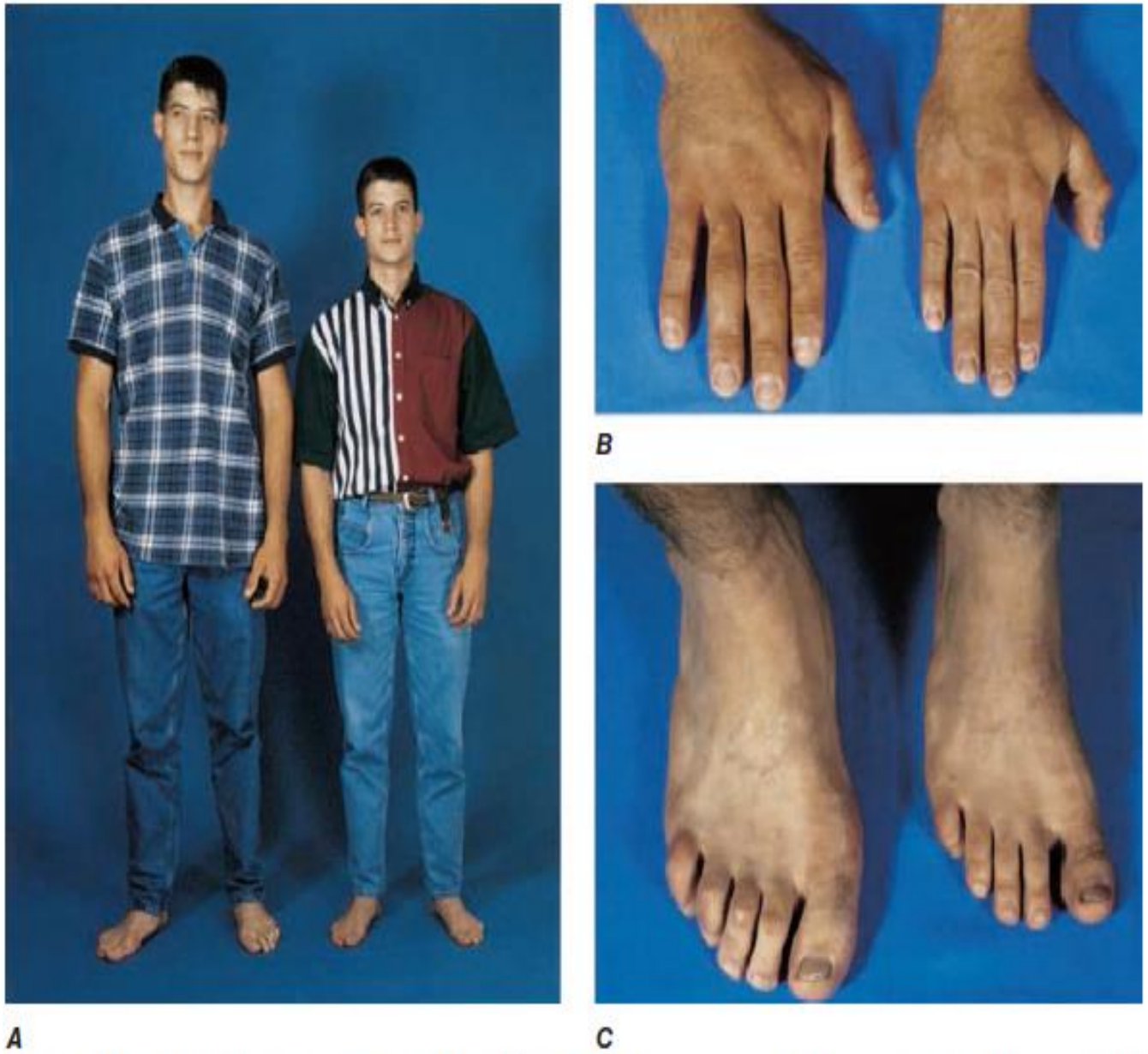


FIGURE 373-4 Features of acromegaly/gigantism. A 22-year-old man with gigantism due to excess growth hormone is shown to the left of his identical twin. The increased height and prognathism (***A***) and enlarged hand (***B***) and foot (***C***) of the affected twin are apparent. Their clinical features began to diverge at the age of ~13 years. *(Reproduced from R Gagel, IE McCutcheon: N Engl J Med 324:524, 1999; with permission.)*

Presentation and Diagnosis Protean manifestations of GH and IGF-I hypersecretion are indolent and often are not clinically diagnosed for 10 years or more. Acral bony overgrowth results in frontal bossing, increased hand and foot size, mandibular enlargement with prognathism, and widened space between the lower incisor teeth. In children and adolescents, initiation of GH hypersecretion before epiphyseal long bone closure is associated with development of pituitary gigantism (Fig. 373-4). Soft tissue swelling results in increased heel pad thickness, increased shoe or glove size, ring tightening, characteristic coarse facial features, and a large fleshy nose. Other commonly encountered clinical features include hyperhidrosis, a deep and hollow-sounding voice, oily skin, arthropathy, kyphosis, carpal tunnel syndrome, proximal muscle weakness and fatigue, acanthosis nigricans, and skin tags. Generalized visceromegaly occurs, including cardiomegaly, macroglossia, and thyroid gland enlargement.

The most significant clinical impact of GH excess occurs with respect to the cardiovascular system. Cardiomyopathy with arrhythmias, left ventricular hypertrophy, decreased diastolic function, and hypertension ultimately occur in most patients if untreated. Upper airway obstruction with sleep apnea occurs in >60% of patients and is associated with both soft tissue laryngeal airway obstruction and central sleep dysfunction. Diabetes mellitus develops in 25% of patients with acromegaly, and most patients are intolerant of a glucose load (as GH counteracts the action of insulin). Acromegaly is associated with an increased risk of colon polyps and mortality from colonic malignancy; polyps are diagnosed in up to one-third of patients. Overall mortality is increased about threefold and is due primarily to cardiovascular and cerebrovascular disorders and respiratory disease. Unless GH levels are controlled, survival is reduced by an average of 10 years compared with an age-matched control population.

Laboratory Investigation Age-matched serum IGF-I levels are elevated in acromegaly. Consequently, an IGF-I level provides a useful laboratory screening measure when clinical features raise the possibility of acromegaly. Owing to the pulsatility of GH secretion, measurement of a single random GH level is not useful for the diagnosis or exclusion of acromegaly and does not correlate with disease severity. The diagnosis of acromegaly is confirmed by demonstrating the failure of GH suppression to <0.4 μg/L within 1–2 h of an oral glucose load (75 g). When newer ultrasensitive GH assays are used, normal nadir GH levels are even lower (<0.05 μg/L). About 20% of patients exhibit a paradoxical GH rise after glucose. PRL should be measured, as it is elevated in ~25% of patients with acromegaly. Thyroid function, gonadotropins, and sex steroids may be attenuated because of tumor mass effects. Because most patients will undergo surgery with glucocorticoid coverage, tests of ACTH reserve in asymptomatic patients are more efficiently deferred until after surgery.

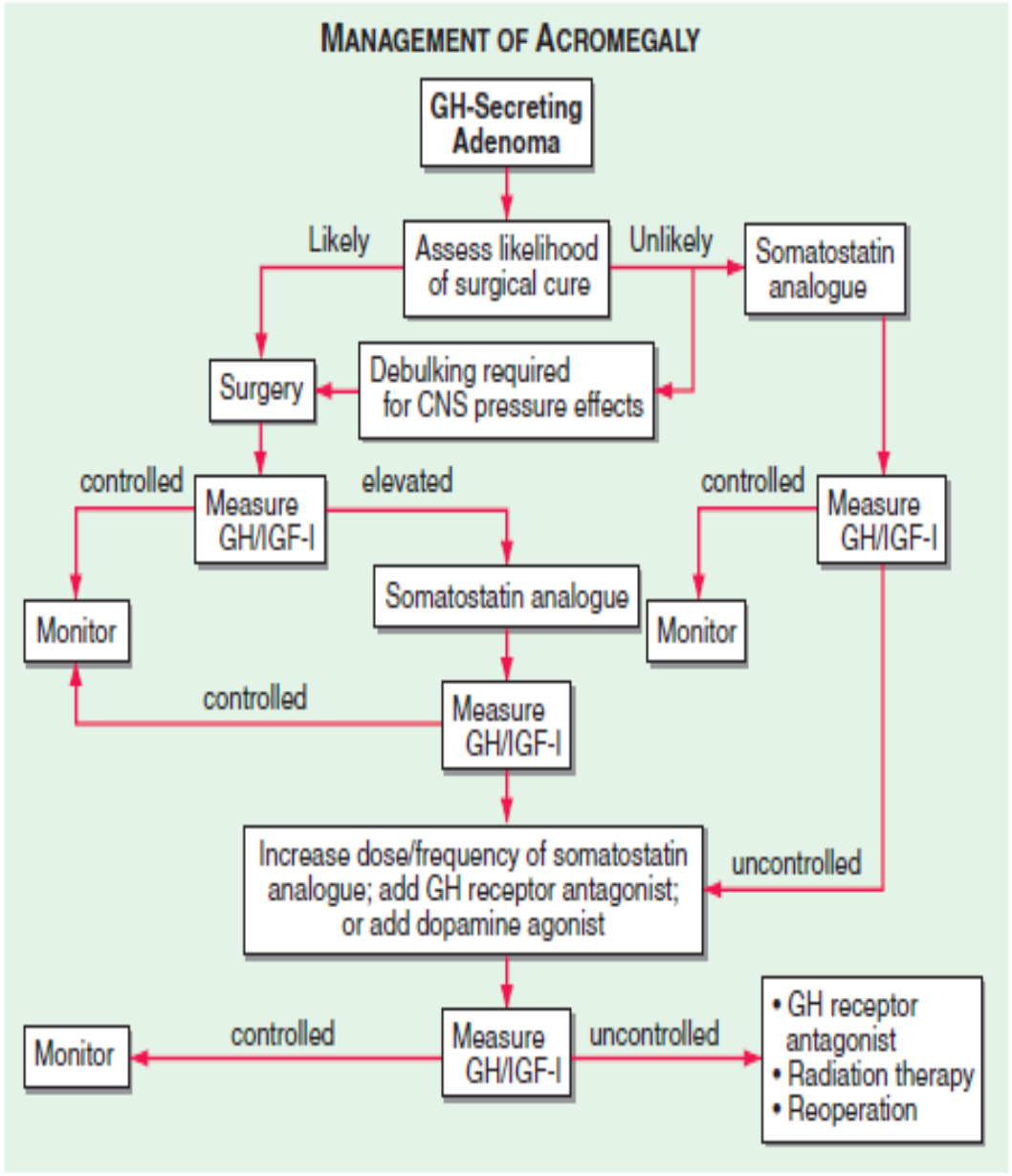
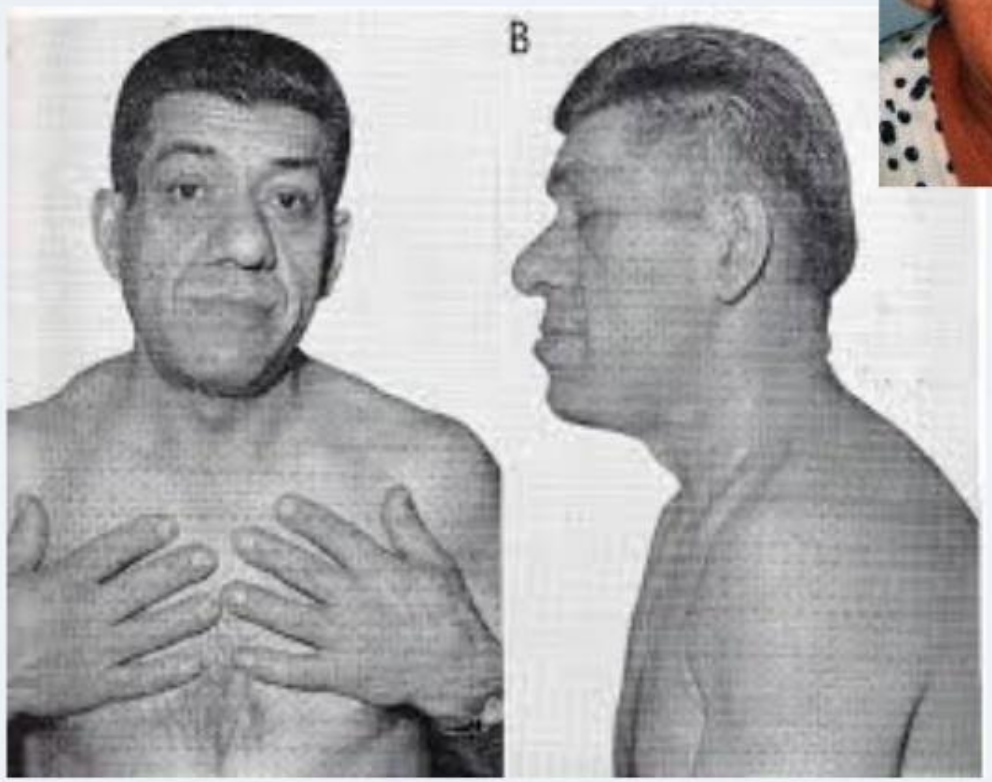


FIGURE 373-5 Management of acromegaly. CNS, central nervous system; IGF, insulin-like growth factor; GH, growth hormone. *(Adapted from S Melmed et al: J Clin Endocrinol Metab 94:1509–1517, 2009; © The Endocrine Society.)*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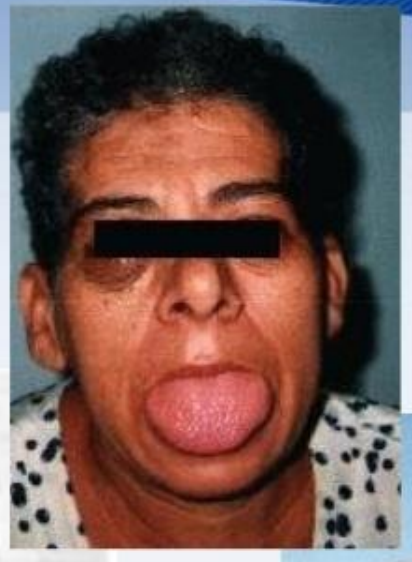
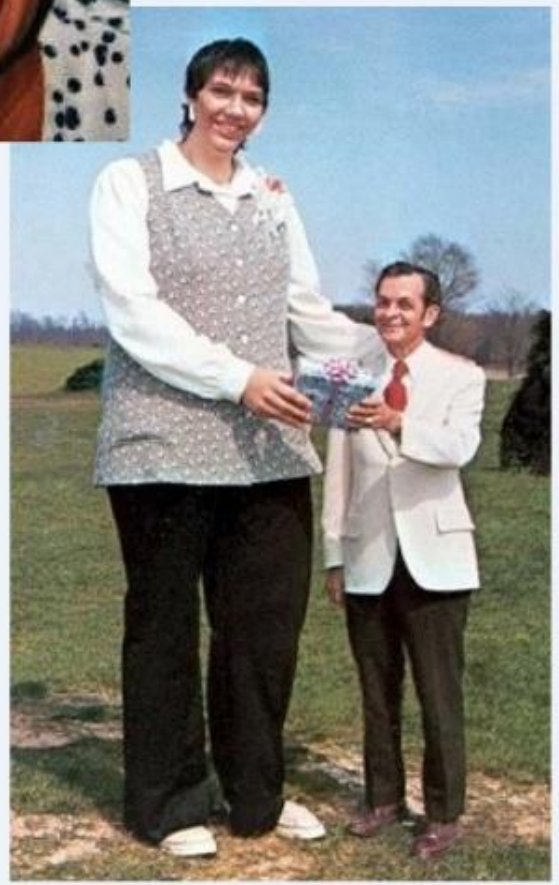
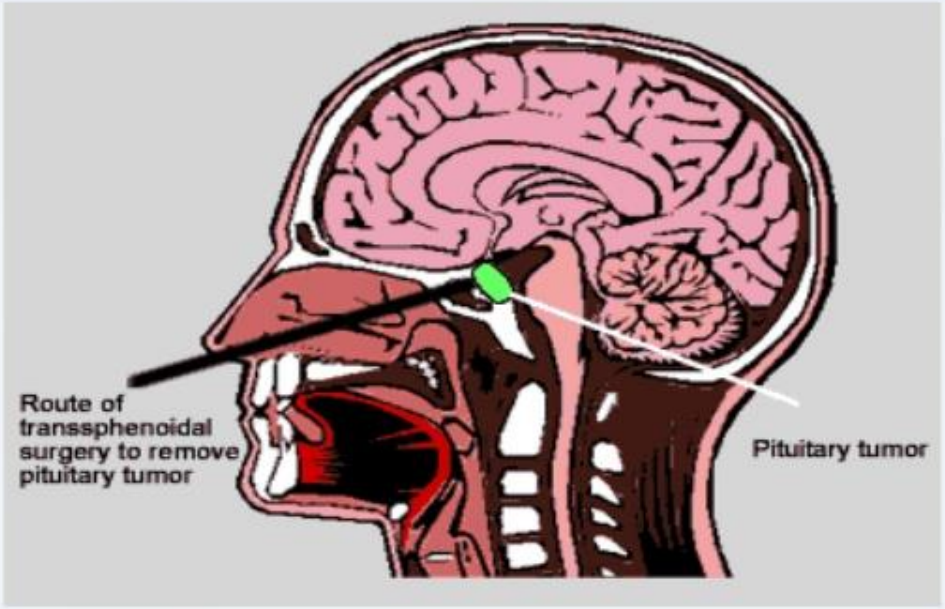




- Joint aches
- Thick, coarse and oily skin
- Deepening of voice due to enlarged sinuses and vocal cords
- Sleep apnea
- Excessive sweating and body odour
- Fatigue and weakness
- Headaches
- Impaired vision
- Abnormal menstruation
- Impotence
- Widely spaced teeth
- Carpal tunnel syndrome
- Heavy sweating

Treatments

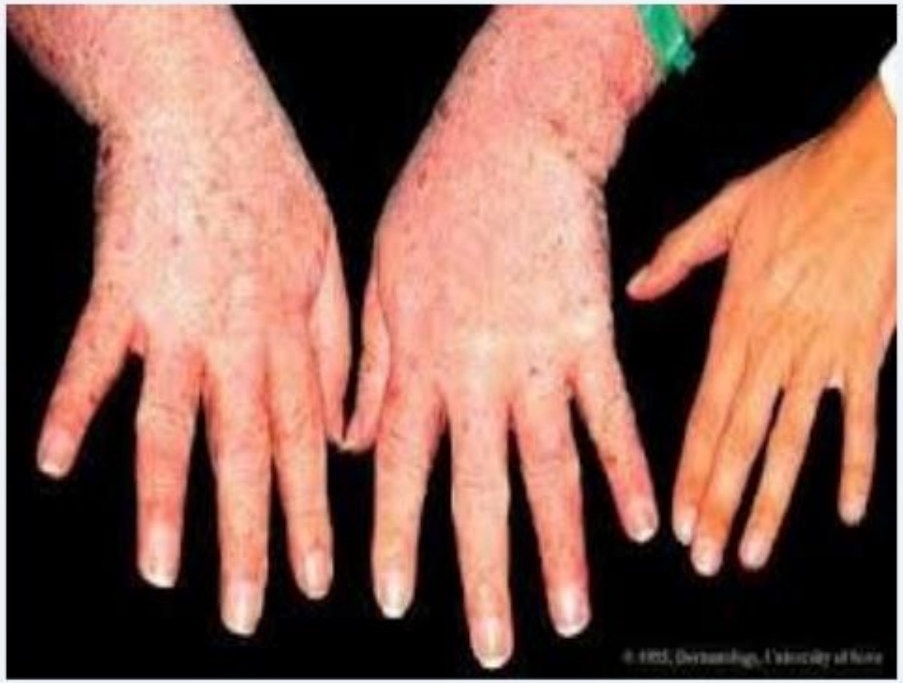
- Surgery :
  - Remove pituitary tumors - transsphenoidal surgery.



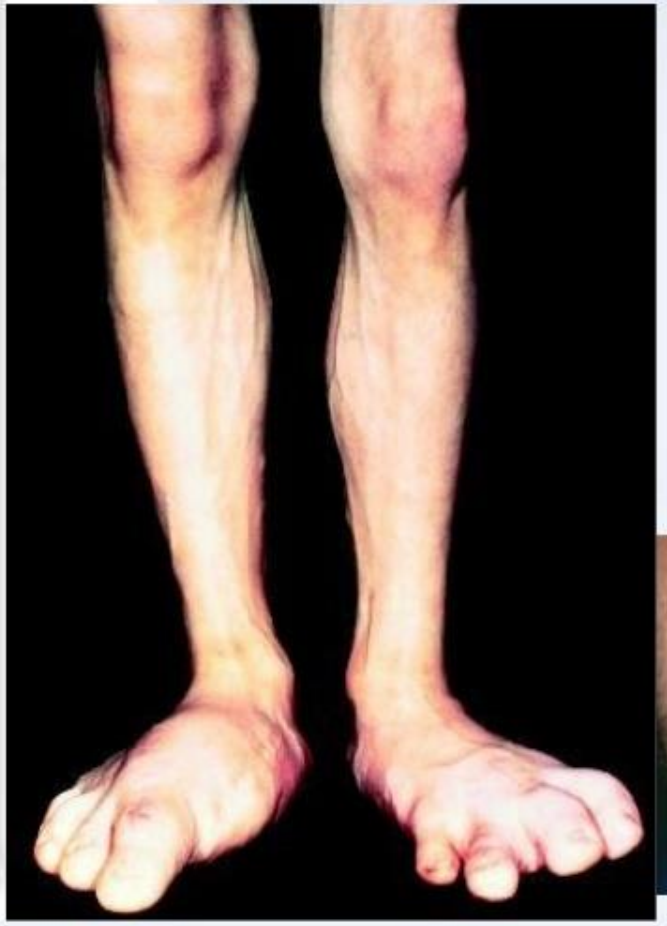
- Radiation :
  - When tumor cells remain after surgery.

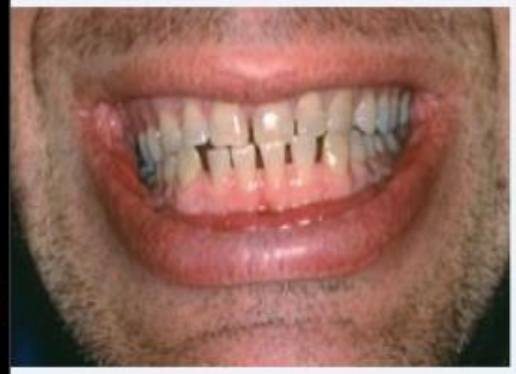
Prevention

- Early treatment may prevent complications.



Conclusion



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