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Role of MR imaging in the evaluation of pituitary lesions

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ABSTRACT

Pituitary gland plays a central role in body growth, metabolism, and reproductive function. Pituitary lesions, albeit relatively infrequent, can significantly alter the quality of life. The sellar and parasellar region is an anatomically complex area where a number of neoplastic, infectious, inflammatory, developmental and vascular pathologies can occur. Differentiation among various etiologies may not always be easy, since many of these lesions may mimic the clinical, endocrinologic and radiologic presentations of pituitary adenomas. The diagnosis of sellar lesions involves a multidisciplinary effort, and detailed endocrinologic, ophthalmologic and neurologic testing are essential. CT and, mainly, MRI are the imaging modalities to study and characterise normal anatomy and the majority of pathologic processes in this region. Recent advances in neuroimaging helps the radiologists and endocrinologists to study the pituitary region in greater detail. Magnetic resonance imaging (MRI) is the imaging modality of choice for evaluating hypothalamic-pituitary-related endocrine diseases. The radiographic size of sella is not a sensitive indicator of pituitary gland abnormality, as the empty sella may itself lead to enlargement of size. Thus, the plain radiographs have been replaced by crosssectional imaging techniques such as CT scanning and MRI. MRI is the examination of choice for sellar and parasellar pathologies due to its superior soft tissue contrast, multiplanar capability and lack of ionizing radiation. In addition, MRI also provides useful information about the relationship of the gland with adjacent anatomical structures and helps to plan medical or surgical strategy. The aim of MR imaging is to obtain a high-spatial-resolution image with a reasonable signal to noise ratio. Conventional MRI findings were expressed as the ratio of the Signal Intensity (SI) in the lesions to the SI of the normal white matter and the degree of contrast enhancement. There have been substantial advances in pituitary imaging in the last half-century. In particular, magnetic resonance imaging is now established as the imaging modality of choice, providing high quality images of the hypothalamic–pituitary axis and adjacent structures. MRI is the investigation of choice for evaluating hypothalamicpituitary-related endocrine diseases. MRI not only helps in the diagnostic differentiation of these lesions but also provides useful information about the relationship of the gland with adjacent anatomical structures and helps to plan medical or surgical strategy.

Key words: pituitary gland, lesions, MRI

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INTRODUCTION

Pituitary gland plays a central role in body growth, metabolism, and reproductive function. Pituitary lesions, albeit relatively infrequent, can significantly alter the quality of life [1]. The sellar and parasellar region is an anatomically complex area where a number of neoplastic, infectious, inflammatory, developmental and vascular pathologies can occur. Differentiation among various etiologies may not always be easy, since many of these lesions may mimic the clinical, endocrinologic and radiologic presentations of pituitary adenomas. Pituitary tumors account for up to 15% of all intracranial masses [2], and pituitary adenomas are reported to account for 90% of sellar and parsellar lesions [3, 4]. Clinically active pituitary adenomas occur at a prevalence of 1:1064 to 1:1288 to the general population [5, 6]. The most common indications for pituitary imaging, excluding known mass follow-up, were for evaluation of hyperprolactinemia or hypo-gonadism and Breast and lung cancer are the two most common malignancies that metastasize to the pituitary [7, 8]. The diagnosis of sellar lesions involves a multidisciplinary effort, and detailed endocrinologic, ophthalmologic and neurologic testing are essential. CT and, mainly, MRI are the imaging modalities to study and characterise normal anatomy and the majority of pathologic processes in this region. With advancements in imaging occurring over the past decade as well as the availability of refined endocrine testing techniques, pituitary masses are diagnosed with increased frequency. Increased incidence of pituitary adenomas observed over the second half of an 18-yr study period was due to a 3-fold increased frequency of incidentally discovered pituitary adenomas [9]. Precise imaging with high contrast and topographic resolution is critical in visualizing this small-volume area to determine both location and specific characteristics of masses, which are important for diagnosis [10-12]. Recent advances in neuroimaging helps the radiologists and endocrinologists to study the pituitary region in greater detail. Magnetic Resonance Imaging (MRI) is the imaging modality of choice for evaluating hypothalamic-pituitary-related endocrine diseases. Magnetic Resonance Imaging (MRI) is the examination of choice for evaluating hypothalamic pituitaryrelated endocrine diseases. Pituitary masses are diagnosed with increased frequency with Magnetic Resonance Imaging (MRI) advancements and availability, but indications and diagnostic outcomes of MRI screening for sellar lesions are not defined. Although pituitary adenomas are the most frequently encountered sellar mass lesions, other etiologies should be considered in the differential diagnosis of a sellar mass.

Epidemiology

Pituitary neoplasms represent an estimated 10%–15% of all Central Nervous System (CNS) tumors and are the cause of approximately 25% of all surgical resections for CNS tumors [13-15]. Determination of the incidence and prevalence of pituitary neoplasms is challenging, as a subset of neoplasms are subclinical and discovered incidentally. Autopsy studies suggest pituitary neoplasms occur in approximately 1%–35% of the general population [16-18]. Ezzat et al. performed a systematic review to evaluate the prevalence of pituitary tumors using imaging studies and determined the prevalence to be 22.5%, with a range between 1 and 40% in radiographic studies. In addition, the overall estimated prevalence of pituitary adenomas as assessed by imaging and autopsy studies was found to be 16.7% [19-23]. Incidence appears to increase with age as approximately 3.5%–8.5% of pituitary tumors are diagnosed prior to age 20, while an estimated 30% of individuals between the ages of 50 and 60 harbor inciden talomas [24].

Normal anatomy

The sellar region is an anatomically complex area bounded by sphenoid sinus anteroinferorly, the paired cavernous sinuses laterally, the suprasellar cistern and its contents, diaphragma sellae and hypothalamus superiorly, and the dorsum sella and brainstem posteriorly [25]. The hypothalamus consists of multiple nuclei regulating the temperature, water balance, drinking behavior, and sexual activity. The hypothalamus and the pituitary gland are functionally and physiologically interlinked contiguous structures and often referred to as the hypothalamic-pituitary axis. Oxytoxin and vasopressin are synthesized in the hypothalamus and transported to the posterior pituitary [26]. The pituitary gland is composed of two anatomically and functionally distinct lobes: the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis) [27]. The anterior lobe comprises 75% of volume of the gland and consists of pars tuberalis (part of the infundibular stalk and median eminence of hypothalamus), pars intermedia (a vestigial structure and common site for developmental cyst) and pars distalis (forms most part of intrasellar adenohypophysis) [28]. Thed imensions o f p i tuitary glands are highly variable, particularly its height. The gland undergoes dramatic changes in size and shape throughout life. A useful guide to the gland's height in relation to age is "Elster's rule" of 6, 8, 10, 12: 6 mm for infants and children, 8 mm in men and postmenopausal women, 10 mm in women of childbearing age and 12 mm for women in late pregnancy or postpartum women [25]. The pituitary stalk has a normal thickness of 2 mm, and it should not exceed a maximum of 4 mm or the width of the basilar artery.

Imaging modalities

Pituitary imaging is important not only in confirming the diagnosis of pituitary lesions but also in determining the differential diagnosis of other sellar lesions. Plain skull radiographs are poor at delineating soft tissues, and infrequently requested these days for diagnosing sellar and parasellar pathologies. The radiographic size of sella is not a sensitive indicator of pituitary gland abnormality, as the empty sella may itself lead to enlargement of size [29]. Thus, the plain radiographs have been replaced by cross-sectional imaging techniques such as CT scanning and MRI. MRI is the examination of choice for sellar and para-sellar pathologies due to its superior soft tissue contrast, multiplanar capability and lack of ionizing radiation. In addition, MRI also provides useful information about the relationship of the gland with adjacent anatomical structures and helps to plan medical or surgical strategy. MRI techniques in diagnosing pituitary lesions have witnessed a rapid evolution, ranging from non-contrast MRI in late 1980s to contrast-enhanced MRI in mid-1990s. Introduction of dynamic contrast-enhanced MRI has further refined this technique in diagnosing pituitary microadenomas [30].

Recently, a variety of advanced MR techniques have been evolved which are particularly helpful in evaluating specific cases. These include 3D volumetric analysis of pituitary volume [31], high-resolution MR imaging at 3 Tesla (T) for evaluating pituitary stalk [32] , diffusionweighted imaging [33], MR spectroscopy [34], magnetization transfer ratio [35], and intraoperative MRI [36]. The aim of MR imaging is to obtain a high-spatial-resolution image with a reasonable signal to noise ratio. Pituitary MRI identifies sellar tumors and pituitary masses and offers high contrast and multiplanar, thin pituitary cuts enabling evaluation of small soft tissue changes [37]. MRI also allows accurate visualization of mass effects on neighboring soft tissues. Although, most adenomas are detected on nonenhanced MRI, microadenomas may become visible only after contrast injection. Dynamic contrast MRI has been proven to be the best imaging tool in the evaluation of pituitary adenomas. Addition of dynamic sagittal plane to the routine coronal study increases the overall detection rate of pituitary microadenomas [35]. Dynamic contrast MRI is not only useful in evaluating the pituitary microadenomas but also has an equally important role in assessing the macroadenomas, invasion of cavernous sinus by the macroadenomas, and differentiating residual/recurrent tumour from postoperative tissues [33–35]. Some microadenomas exhibit maximum lesion-to-gland contrast on unenhanced scan; however, this image contrast begins to diminish the moment the contrast-enhancing agent arrives in the pituitary gland.

In any woman presenting with a sellar mass lesion during pregnancy or in the first postpartum year, LH should be suspected, though it can be diagnosed with certainty only histologically. MR imaging is currently the best noninvasive diagnostic tool to differentiate Lympohocytic Hypo-physistis (LH) from non-secreting macroadenomas, although no single radiological feature is characteristic of the disease. MR features indicative of LH include symmetric enlargement of the gland, homogeneous appearance, intense contrast enhancement, thickening and enhancement of the pituitary stalk, loss of posterior pituitary bright spot, and enhancement of dura adjacent to the pituitary mass and an intact sellar floor.In contrast, pituitary macroadenomas are frequently asymmetric, usually heterogeneous in appearance, have lesser gadolinium uptake, rarely involves the stalk, preservation of posterior pituitary bright spot and eroded sellar floor. Although, a thickened pituitary stalk is typical for LH and strongly favors LH over adenoma, an enlarged pituitary stalk can be found in a variety of diseases, such as germinoma, lymphoma, tuberculosis, sarcoidosis, or Langerhans

cell histiocytosis, but its presence in the absence of systemic infections suggests a diagnosis of hypo-physitis. Hence, MR imaging increases the probability of diagnosing LH and plays a very important role in the management of patients with LH, who are benefited more from medical as opposed to surgical treatment. Until a specific antibody for this disease or a characteristic MR feature has been identified, the diagnosis of this entity must rely only on the histologic study [37]. 3-Tesla MRI with stronger magnetic field strength offers an improved image quality and spatial resolution under conditions with subtle differences between normal and abnormal tissue.

Preoperative localization of pituitary microadenomas in Cushing's disease is relatively better with 3T MRI compared to 1.5T MRI, although some of these lesions were missed even on 3T MRI [38]. Wolfsberger et al. used 3T MRI to study the invasion of cavernous sinus by the adenomas in 42 patients [39]. Moreover, the knowledge of normal pituitary gland volume and normal imaging appearance of the pituitary stalk is important for diagnosing different lesions of the gland and infundibulum. Accurate assessment of the stalk and subtle changes in gland volume is better with 3T MRI than with 1.5 T MRI [40,41]. Although pituitary adenomas can be well delineated on plain and contrast-enhanced MR sequences, the differentiation between secreting and non-secreting adenomas is not possible using classical MRI. In addition, the role of MRI in evaluating residual tumor in postoperated cases is also limited. The MT technique can also be used in postoperative assessment and follow-up of patients with pituitary adenomas, especially when classical MRI is negative for residual tumor. Increased MTR values are highly suggestive of persistent adenomatous tissue. Future prospect of MT imaging includes other pituitary disorders such as pituitary insufficiency and precocious puberty [42].

Currently, MRI is the examination of choice for sellar and parasellar pathologies due to its superior soft tissue contrast, multiplanar capability and lack of ionizing radiation. In addition, MRI also provides useful information about the relationship of the gland with adjacent anatomical structures and helps to plan medical or surgical strategy. The role of Diffusion-Weighted Imaging (DWI) in early detection of acute pituitary infarction has been evaluated by some authors. Pituitary apoplexy which results from either hemorrhage or infarction of the pituitary gland may be associated with high mortality and morbidity. It has been documented that DWI assists in the early diagnosis of acute pituitary infarction with timely intervention and excellent outcome. Diffusion-weighted imaging and Apparent Diffusion Coefficient (ADC) maps can characterize tumor components within microadenomas and provide information about the consistency of macroadenomas.

Diffiusivity in creasing leads to in crease in the amount of ADC and, therefore, increasing in signal on ADC map that this behavior in signal intensity is in the invert of diffusion images [43]. Tumors demonstrate a low signal intensity on DWI and have a relatively high ADC value of $(1.363 \pm 0.259) \times 10^{-3}$ mm^2/sec. DWI should become a part of routine assessment of macroadenomas for planning the surgical approach.

Pituitary adenomas are among the most common central nervous system tumors. Extension of pituitary adenomas can occur in a suprasellar, retrosellar, or lateral fashion. Suprasellar extension of macroadenomas is the most common direction of extension and can result in penetration of the floor of the third ventricle and hypothalamus [44-46].

Headache is a common clinical indication for imaging leading to discovery of incidental pituitary masses [47]. Pituitary tumor-related headaches may improve in up to 70% of patients after adenoma resection [48,49]. Furthermore, the presence of headaches does not necessarily correlate with the mass size. Several mechanisms have been proposed for the cause of headaches in patients harboring pituitary masses [50, 51], although these have not been uniformly substantiated [48,52]. Regardless, the higher rate of headache occurrence observed for non-adenomatous lesions vs. both nonfunctioning and functioning adenomas suggests that non-adenomatous lesions are more likely to cause headache ($P<0.001$).

Headache (57%) was the most common presenting symptom in patients with nonadenomatous masses identified by MRI.

Dedicated pituitary MRI is the preferred diagnostic imaging modality for evaluation of sellar and parasellar tumors, including adenomas. In particular, when functioning adenomas are suspected, a dynamic pituitary MRI, which obtains images within seconds after gadolinium contrast injection, may be more useful because it has higher sensitivity than other imaging modalities for detecting small microadenomas. Overall, given the compelling list of possible diagnoses, when a non-secreting pituitary mass is observed by MRI, a high clinical suspicion and thorough endocrine and possible pathological assessment is required to exclude the presence of a nonfunctioning pituitary adenoma.

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