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Using the complexity of hypopituitarism aetiology to understand and teach hormone function in endocrinology

Abstract

Hypopituitarism is a multifaceted medical disorder with a complex aetiology Endocrinology remains a content heavy discipline and places great focus on understanding the transition from normal to the abnormal. Especially during the clerkship and clinical years, expectations are high regarding the understanding of the basic function of pituitary gland and clarity and reference to the function and physiology, as and when required, is expected. Various aetiological causes when taught methodically, including developmental, genetic and acquired causes can form an ideal scenario regarding complete review of embryology and functional anatomy leading to a better prediction of clinical manifestations, and thus, an improved management plan.

Keywords: hypopituitarism, panhypopituitarism, aetiology, hormone, deficiency

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Abbreviations: ADH, antidiuretic hormone; GH, growth hormone; GHRH, growth hormone releasing hormone; POMC, proopiomelanocortin; TSH, thyroid stimulating hormone; LH, luteinizing hormone; FSH, follicle stimulating hormone; ACTH, adrenocorticotropic hormone; TBI, traumatic brain injury; AIDS, acquired immune deficiency syndrome

Introduction

The complexity of aetiology of Hypopituitarism presents the ideal scenario for reviewing and teaching various hormones, embryology and anatomy and physiological function at both the undergraduate and postgraduate level. With the proper approach, Hypopituitarism, as a disorder, can be the missing link in developing a clear understanding of the entire Endocrinology as a discipline. In this review, I will attempt to highlight how and where to focus on the different aspects of the aetiology of this disorder.

Description

Hypopituitarism is a complex, uncommon condition with a prevalence of ~46 per 100 000[1] and defined as either partial or complete deficiency of anterior or posterior pituitary hormone secretion or both.[2] The incidence rate (12 to 42 new patients per million per year) and the prevalence rate (300 to 455 patients per million) seems to underestimate the actual incidence of this disorder keeping in mind that 30% to 70% of patients show decreased diminished pituitary secretion post trauma.[3]

Aetiology of Hypopituitarism determines not only how the disorder presents but also the speed and degree of loss of hormone, clinical manifestations, management and the complications that may arise. Thus, to begin with, distinction should be made between Panhypopituitarism and partial hypopituitarism. For instance, a partial hormone deficiency may progress slowly in the initial stages, going undetected for years, however, the sudden and complete loss of hormone secretion may result in an emergency situation that requires immediate medical attention.[3]

To understand the aetiology better, there can be two approaches: distinction can be made between Panhypopituitarism and hypopituitarism or distinction can be made between Primary and secondary hypopituitarism.[4] Panhypopituitarism refers to the deficiency of all anterior pituitary hormones. Vasopressin (ADH) and oxytocin secretion will be considerably affected only if the hypothalamus is involved, whether by a hypothalamic tumour or a major suprasellar extension of a pituitary lesion, or if there is inflammation. Similarly, Primary hypopituitarism is caused by defect in the Pituitary gland itself, which may be due to loss, damage, or dysfunction of pituitary hormone-secreting cells. While secondary hypopituitarism is caused by disorders of the hypothalamus or pituitary stalk interrupting the nerve or vascular communication with the pituitary gland, thus decreasing the secretion of the pituitary hormones.[4]

Another approach involves distinction between developmental and genetic disorders. This provides an excellent opportunity to review embryology and developmental biology, with focus on genetic disorders as well. Pituitary development follows midline cell margination from Rathke's pouch, thus, impaired anomalies lead to structural anomalies e.g. failed forebrain cleavage and anterior commissure and corpus callosum defects. Similarly in infants surviving craniofacial developmental anomalies, as anencephaly, lifelong appropriate pituitary replacement therapy for life is required. Opportunity can also be availed to remind the trainee/student that children with mild forms of midline anomalies are also more prone to growth hormone deficiency. In fact, with sensitive MRI techniques for pituitary visualization, several anatomic features such as the an absent infundibulum, decreased gland size and volume or disturbed sella turcica architecture and absent or transected pituitary stalk can be carefully correlated to the developmental defect, with the added advantage of being able to predict and manage the clinical manifestations.[5]

While discussing the heritable disorders of Pituitary failure, special focus should be placed on mutations at each level, including hormones,

receptors, and transcription factors that determine anterior pituitary development, such as PROP1, HESX1 and POUIFI. Furthermore, it should be kept in mind that mutations in specific genes, including those for GH, GHRH receptor, POMC, TSH, LH, and FSH, all lead to single-hormone deficiencies.[6]

Several recognized mechanisms of hormone deficiency include the direct pressure onto or trauma to the tissues surrounding the tumour, mechanical compression of the portal vein by the pituitary stalk, raised intrasellar pressure, and focal necrosis due to prolonged portal vein interruption.[7] The resilience of the individual pituitary cells to compression, inflammation, radiation and vascular damage vary and it is interesting to note that growth hormone (GH) secreting cells are the first to be affected followed closely by the follicle stimulating hormone (FSH) cells, luteinizing hormone (LH) cells, thyroid stimulating hormone (TSH) cells and finally the corticotroph cells. In fact, the corticotroph cells secreting the adrenocorticotropic hormone (ACTH) is particularly resistant to hypothalamic or pituitary destruction, and it is usually the last cell to lose function.[8]

In addition, causes such as complications from surgery (postsurgical hypopituitarism varies from 10 to 25%),[9] or radiation therapy for pituitary adenoma,[7] radiation exposure for treatment of head and neck tumours[8] (another excellent opportunity to discuss a variety of hormone deficiencies related to treatment of pituitary tumour with radiotherapy, with stress upon the fact that hormone deficiency frequency is greater than 50% at 10years after radiation exposure),[7] and viruses (including cytomegalovirus superimposed on AIDS virus,[9] tuberculosis meningitis and haemorrhagic fever).[4]

While discussing causes of secondary hypopituitarism, focus should be on head and neck injuries with frequent review of functional anatomy involved. Recently, idiopathic hypopituitarism prevalence has increased but that is thought to be most likely due to traumatic brain injury (TBI) or hypothalamic damage.[3]

Conclusion

Aetiology of Hypopituitarism in itself is a vast topic. I have barely managed to touch it superficially. If approached methodically and constant links made continuously, clinical manifestations can be predicted fairly accurately and management planned accordingly. It can, in fact, be used at both the clerkship (postgraduate) and undergraduate level to assimilate and comprehensively understand Endocrinology.

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Conflict of interest

Author declares that there is no conflict of interest.

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