Editorial

Hypopituitarism in the tropics

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Pituitary disorders, including hypopituitarism and hypothalamic pituitary insufficiency (HPI), are common conditions seen by endocrinologists in tertiary/referral centers. The important causes of hypopituitarism are pituitary tumors (including craniopharyngioma), postoperative and postradiotherapy states, vascular conditions, autoimmune diseases such as hypophysitis, and infectious/inflammatory lesions. The exact prevalence of pituitary diseases in India is not known, but Kochupillai *et al.* have estimated that 4% of the Indian population suffers from clinically significant growth and pituitary disorders.[1]

The etiology of hypopituitarism is different in tropical countries as compared to the West. Awareness of the various etiologies of pituitary dysfunction, as well as recognition of their subtle clinical features, is necessary for optimal management of the patient. Chatterji *et al.*, presenting a profile of 86 patients with hypopituitarism from east India, have shown that, after adenomas, Sheehan syndrome and snake bite are important etiological factors.[2] Garg *et al.* have recently highlighted the poor recognition of hypopituitarism in clinical practice.[3] Till recently, hypopituitarism caused by infectious diseases were reported as case reports or in retrospective studies only".[4,5] The infectious agents that can cause HPI are *Mycobacterium tuberculosis* and non-mycobacterial agents such as bacteria, fungi, spirochetes, viruses, and protozoa. Human immunodeficiency virus (HIV) infection is a common cause of pituitary endocrinopathy in the tropical setting. Pituitary infection by *Toxoplasma gondii* and cytomegalovirus (CMV) have been documented in patients with HIV.[6]

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Most often described among these infectious diseases is tubercular meningitis (TBM). TBM has been reported to be a cause of HPI, especially in children. Prospective studies on this subject are few. Dhanwal *et al.* have described 75 patients with TBM who had HPI at presentation"?.[7] The most common hormonal finding in these patients was hyperprolactinemia, followed by adrenal insufficiency. A significant number of patients also had structural abnormality on MRI. Similar reports on HPI as a sequel of acute central nervous system (CNS) meningitis have been published in case reports or in small retrospective studies.[8]

In the present issue, Dhanwal *et al.* have, in a systematic study, evaluated the pituitary hormone profile in 30 patients with non-mycobacterial acute CNS infections.[9] The most common infectious organisms were bacteria, followed by viruses and fungi. Adrenal insufficiency was seen in 23.3% and hyperprolactinemia in 30.0% of the patients. Thirty percent of patients had abnormal levels of luteinizing hormone (LH) and/or follicle stimulating hormone (FSH). All these abnormalities normalized after treatment of the CNS infection. These findings are similar to those reported by Tsiakalos *et al.*[8] The Dhanwal study should motivate researchers from India and other tropical countries to carry out further research on this subject.

The causes of hypopituitarism in tropical countries include pituitary abscess, snake bite, HIV infection, Sheehan syndrome, road traffic accidents, iron overload states, etc.[2] Primary pituitary abscesses of various etiologies are encountered in tropical medicine, and have been reported in this issue of IJEM.[10] The pituitary abscess must be considered in the differential diagnosis of a parasellar mass. They usually occur in immune-compromised subjects, and are caused by *Aspergillus*, *Nocardia*, *Candida albicans,* or *Pneumocystis jeroveci*. The endocrine manifestations include diabetes insipidus, hyperprolactinemia, and gonadal dysfunction.[11] The posterior pituitary is more often involved because it receives its blood supply directly from the systemic circulation via the internal carotid arteries.

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At times, these infections, including tuberculosis, may lead to central precocious puberty.[12] This may occur because of increased intracranial pressure, which activates the hypothalamo-pituitary- gonadal axis, or because of irritation of the basal hypothalamus.

Pseudocyesis is a condition often encountered in cultures that place a high premium on fertility and fecundity.[13] In this functional hypothalamic disorder, non-pregnant women develop all the symptoms of pregnancy, including amenorrhea and weight gain. This conversion reaction usually occurs in social settings where the woman is pressurized to bear children. It may be associated with elevated prolactin and LH levels.

Snake bite has been known to cause pituitary failure during the acute stage or after months to years.[14] Russell's viper, *Vipera russelli* (Shaw), is a leading cause of fatal snake bite in Pakistan, India, Bangladesh, Sri Lanka, Burma, and Thailand. Acute pituitary infarction is common in reports of snake bite from Burma and south India.

Sheehan syndrome is a vascular cause of hypopituitarism and has been discussed in detail by Shivprasad in this issue of IJEM.[15] There are a few important studies published from India on the epidemiological aspects and autoimmunity in Sheehan syndrome.[16,17] In this issue of IJEM, Laway *et al.* describe the varied manifestations of Sheehan syndrome, as encountered in India.[18]

Severe head injuries lead to varying degrees of hypopituitarism, especially in patients who have been unconscious for several days and in those who have associated skull fractures.[19] Diabetes insipidus occurs in a third of these cases. Though head injury is not confined to the tropics, the relatively higher incidence of road traffic accidents in developing countries makes this a significant cause of unrecognized HPI.

Iron-overload states such as thalassemia and hemochromatosis (treated with frequent blood transfusions) may be a cause of pituitary disease.[20] Frequent transfusions lead to pituitary siderosis, reduction in pituitary cell number, and hyposecretion. The most affected axis is the gonadotropin axis, followed by the growth hormone (GH) and adrenocorticotropic (ACTH) axes. Iatrogenic Cushing syndrome, due to corticosteroid misuse is often encountered in the tropics due to the large number of quacks who practice medicine in these countries.[13] At times, the traditional medicines prescribed by practitioners of alternative medicine may contain glucocorticoids.

The spectrum of conditions causing hypopituitarism in tropical countries is quite different – and more varied – from that in the West. There are also a large number of unrecognized and undiagnosed cases of pituitary deficiency. It is hoped that the coverage of 'tropical' pituitary disorders in the current issue of IJEM will sensitize endocrinologists, physicians, and medical students to maintain a high index of suspicion for these conditions in appropriate clinical settings.

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