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Introduction: Evidence pertaining to new-onset endocrine dysfunction in patients with COVID-19 is currently limited and extrapolated from prior SARS epidemics. Further, identifying whether the quantum of this dysfunction is associated with the severity of disease in patients with COVID-19 is unknown. We aimed to to comprehensively explore the prevalence, nature and degree of endocrine dysfunction stratified based on disease severity at a dedicated COVID care centre.
Patients and Methods: Consecutive patients enrolled at PGIMER Chandigarh, were stratified on the basis of disease severity as: group I (moderate to severe disease including oxygen saturation <94% on room air or those with comorbidities) and group II (mild disease, with oxygen saturation >94% and without comorbidities). Hypothalamo-pituitary-adrenal, thyroid, gonadal axes and lactotroph function were evaluated. Inflammatory and cell-injury markers were also analysed.
Results: Patients in group I had higher prevalence of hypocortisolism (38.5 vs 6.8%, p=0.012), lower ACTH (16.3 vs 32.1pg/ml, p=0.234) and DHEAS (86.29 vs 117.8µg/dl, p= 0.086) as compared to group II. Low T3 syndrome was a universal finding, irrespective of disease severity. Sick euthyroid syndrome (apart from low T3 syndrome) (80.9 vs 73.1%, p= 0.046) and atypical thyroiditis (low T3, high T4, low or normal TSH) (14.3 vs 2.4%, p= 0.046) were more frequent in group I than group II. Male hypogonadism was also more prevalent in group I (75.6% vs 20.6%, p=0.006) than group II, with higher prevalence of both secondary (56.8 vs 15.3%, p=0.006) and primary (18.8 vs 5.3%, p=0.006) hypogonadism. Hyperprolactinemia was observed in 42.4% patients, without significant difference between both groups.
Conclusion: COVID-19 can involve multiple endocrine organs and axes, with a greater prevalence and degree of endocrine dysfunction in those with more severe disease. Involvement of multiple axes, particularly at hypothalamo-pituitary level suggests the possibility of hypophysitis as an underlying etiology. We also observed less characterised findings like atypical thyroiditis and normal DHEAS despite secondary hypocortisolism. Follow-up surveillance of these patients at periodic intervals and estimation of anti-pituitary antibodies could be considered to elucidate viral cytopathic effect or inflammation as the major underlying mechanism of endocrine dysfunction.

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Gonadotropin-Releasing Hormone Agonist Induced Pituitary Apoplexy

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Background: Gonadotropin-releasing hormone agonists (GnRHa), used in the treatment of prostate cancer (PC) and for reproductive purposes in women, have been implicated as the cause of pituitary apoplexy (PA), a potentially life-threatening condition. The pathophysiology of PA after GnRHa has not been completely elucidated. Proposed mechanisms include a stimulatory effect of GnRHa on pituitary adenoma cell metabolism, causing mismatched blood supply prompting hemorrhage or infarction. Prior documentation of PA associated with GnRHa has been scarce and limited to case reports.
Methods: This is a detailed clinical case series of GnRH-induced PA from a single institution, obtained by a Research Patient Data Repository query. Clinical characteristics of the patients including demographics, detailed history, time interval between GnRHa and PA, physical exam, biochemical data, pituitary imaging and pathology were reviewed.
Results: Seven cases were identified between 1990-2020; six men (aged 55 – 83 years) receiving treatment for PC and one woman (aged 22 years) receiving GnRHa for oocyte donation. All patients presented with headache; four within 48 hours of, one >1 month after, and one 5 months after, receiving GnRHa. One patient had insufficient data on time between GnRHa and PA. Most patients (86%) presented with nausea and vomiting. Other symptoms included ophthalmoplegia (43%), visual field defects (17%), and altered consciousness (29%). All patients had sellar masses and/or evidence of hemorrhage on MRI. Five patients underwent pituitary surgery while the others were managed medically. Of those who underwent surgical resection, 80% had positive histopathological staining for gonadotropins. Five patients with reliable hypothalamic-pituitary-adrenal (HPA) axis testing had impairment of this axis after PA; 40% recovered adrenal function. Central hypothyroidism occurred in 60% of whom 66% recovered. Hyponatremia occurred in 43%.
Conclusions: Patients with gonadotrope-secreting adenomas may develop PA in response to GnRHa, more frequently in elderly men who are receiving GnRHa treatment for PC. This may be due to older age and higher prevalence of GnRHa use in this group. However, as demonstrated here and in prior case reports, women are not exonerated from this complication. Headache and adrenal insufficiency are typically present. HPA axis recovers in a subset. While most patients present <48 hours after GnRHa treatment, delayed presentations may occur. Therefore, a history of prior GnRHa exposure should be ascertained in patients presenting with PA. While the incidence of PA after GnRHa is low, this case series and prior case reports suggest that this serious potential complication should be recognized prior to treatment, especially in patients with known pituitary macroadenomas.

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