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Pituitary and Neuroendocrinology 1

Ipilumumab induced hypophysitis

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Introduction: Immunotherapy has advanced significantly over the past years. Immune-related adverse events (IRAEs) are various and include endocrinological complications such as Ipilimumab-induced hypophysitis (IIH). The incidence of this cytotoxic T-lymphocyte antigen 4 antibody ranges from 0 to 17%. Patients usually present with symptoms secondary to hormonal insufficiencies.

Case report: A 73 year-old lady, known case of metastatic melanoma on immunotherapy presented with a 1 week history of pre-syncopal episodes and nausea. She gave a few week history of non-vertiginous dizziness, lethargy and headache. The patient had received her third course of ipilimumab few days prior to presentation. Cortisol level during admission was 23 nmol/l, from a previously normal level of 993 nmol/l few weeks prior. The patient had low T4 and TSH levels (0.080 mIU/ml and 6.7 pmol/l respectively) together with low FSH (2.4 U/l), LH (0.6 U/l) and prolactin levels (59 mIU/l) in keeping with panhypopituitarism. The patient was started on glucocorticoids and thyroxine with rapid improvement of her symptoms.

Imaging: MRI brain at presentation showed a 1.5×1.4×1.2 cm sellar lesion involving the pituitary gland with mild suprasellar extension. The lesion demonstrated low T1 and mildly hyperintense T2 signal intensity and enhanced avidly following contrast administration, with a central non-enhancing component. The infundibulum was thickened. Repeat MRI after 3 months revealed complete resolution of the sellar and infundibular changes with normalization of the gland confirming the initial hypothesis of hypophysitis.

Discussion: Literature suggests that a high index of suspicion for hypophysitis needs to be kept in mind in patients receiving immunotherapy. It is advised that patients undergo 6 monthly assessment of pituitary function and MR scans should be compared to previous imaging if available to assess for a change in pituitary size. In hypophysitis, the degree of pituitary enlargement should reduce after treatment as was in our case. If this is not observed, alternative diagnoses such as pituitary metastasis should be considered. It is debatable whether patients with IIH should be administered higher dosages of glucocorticoids in contrast to physiological replacement, since there are concerns that

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treatment with high dosages of glucocorticoids may affect the antitumor efficacy of Ipilimumab. In our patient, a physiological replacement dose was sufficient for her to improve clinically and have complete resolution of symptoms after 3 months.

Conclusion: Development of IIH can precipitate acute adrenal failure or crisis. Early diagnosis and management are vital to prevent complications including increased morbidity and mortality rates.

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