NIVOLUMAB INDUCED THYROID DYSFUNCTION

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ABSTRACT

Nivolumab acts by blocking ligand activation of programmed cell death 1(anti-PD-1) receptor on T cells. Its effects on thyroid gland can result in hypothyroidism (7%), hyperthyroidism (1%), and thyroiditis (<1%), mostly developing around week 12 after start of therapy.We report a case of nivolumab-induced thyroid dysfunction.

CASE REPORT

A 41 year old male came with diagnosis of adenocarcinoma lung with leptomeningeal metastasis. Patient received chemotherapy with nivolumab at 240mg dose weekly for 4 weeks.Following 4th cycle of nivolumab,patient developed weight loss, progressive fatigue, excessive sweating, palpitations and tremors.On examination tachycardia with tremors and nontender diffuse goitre noted. Investigations revealed TSH<0.005mcIU/ml, T4 > 24.9mcg/dl,T3 4.37ng/ml.Thyroid scintigraphy revealed decreased uptake s/o thyroiditis. Patient was started on propranolol following which symptoms subsided.After 5^{th}cycle of nivolumab patient developed giddiness, easy fatigability, anorexia and reduced alertness. Ankle edema and bradycardia noted with no focal neurological deficits. Investigations revealed TSH 62.32miu/ml, T4-4.02 mcg/dl. Patient was started on levothyroxine 50 mcg/day. But, patient again presented with similar symptoms after 6 cycles of nivolumab. TSH done was 40.58 and T4-4.86mcg/dl. An 8 am cortisol was 10.2mcg/dl. Hence nivolumab induced hypophysitis was ruled out.Levothyroxine dose was increased to 75mcg/day.Presently patient is better with levothyroxine 75 mcg and TSH 2.69mciu/ml.

DISCUSSION

Because of high incidence of hypothyroidism incourse of anti-PD-1 treatment, monitoring TFTs is of value. Mechanisms underlying immune-related thyroid dysfunction is not fully characterised. This can be ascribed todisinhibition of CTLA-4 and PD-1 which might exacerbate hypothyroidism and/or thyroiditis. Adrenal insufficiency is uncommon with PD-1 antibodies, hence no recommendation for routine monitoring

CONCLUSION

Since the number of patients treated with nivolumab is expected to increase in due course of time, our case report createsawareness of this endocrine effect.