# Hypothyroidism in a child during treatment with nivolumab for a glioblastoma

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## BACKGROUND

The programmed cell death 1 protein (PD1) is a T lymphocyte membrane receptor, which when bound to its ligand PD – L1 inactivates the cytotoxic T lymphocyte, thereby down regulating the immune response. Cancer may upregulate PD – L1 on the cell surface, further downregulating the immune response. Nivolumab, a so called check point inhibitor, is a PD1 antibody, and when bound to PD1 keep the cytotoxic T lymphocyte active. Cytotoxic T lymphocyte activation by nivolumab has proven effective in treating hypermutant tumors. However, activating cytotoxic T lymphocytes may cause hormonal side effects.

## OBJECTIVE

To describe the development of primary hypothyroidism in a child during treatment with nivolumab for an inoperable glioblastoma.

## CASE REPORT

At the age of five years the patient was diagnosed with a frontal malignant nerve sheet tumor. After tumor resection, he was treated with radiation therapy 36 Gy with tumor bed boost of 25.2 Gy. Six years after initial diagnosis, the tumor recurred. At that time, the tumor was subtotal resected, histology showed glioblastoma WHO grade IV, and tumor was hypermutating. Re-irradiation with 36 Gy in 20 fractions and a boost of 18 Gy was initiated with concomitant temozolomide treatment. Four months after initiated treatment MRI showed new tumor progression in the right frontal lobe and the right temporal lobe (figure 1).
Treatment with nivolumab 3 mg/kg every second week was initiated October 2018. After four months MRI showed complete tumor regression (figure 2), but at the same time the child had developed primary hypothyroidism and treatment with tablet L-thyroxin was initiated (table). Apart from growth hormone deficiency no other hormonal deficits were found.

***Figure 1.*** *T1 MRI showing right frontal and temporal tumor (arrows) before treatment.*

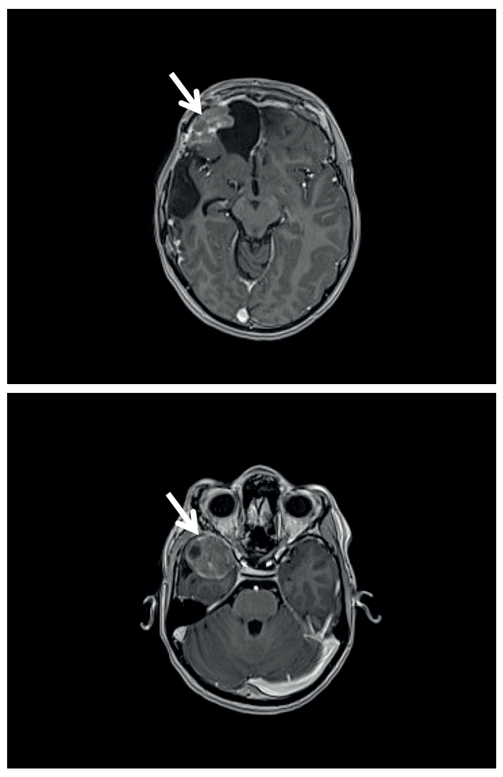
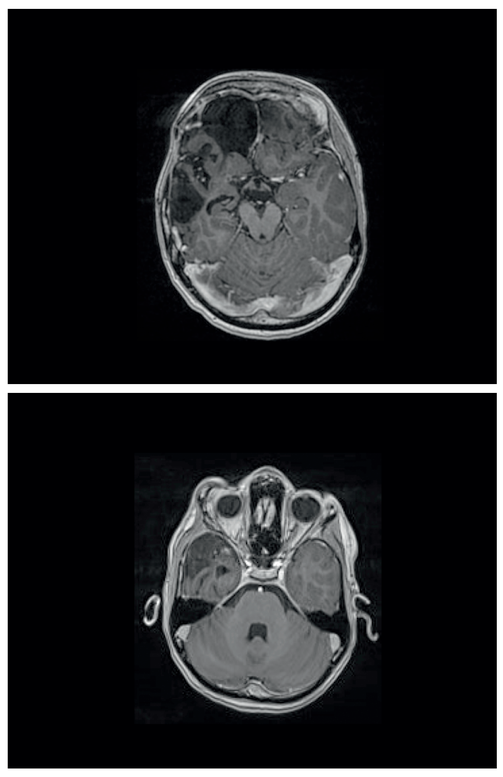


***Figure 2.*** *T1 MRI showing complete tumor regression after four months treatment with nivolumab.*



| | 05.10.17 | 27.12.17 | 12.02.18 | 27.02.18 | 13.03.18 | 11.06.18 |
|---|---|---|---|---|---|---|
| **TSH IU/ L (0.6-4.5)** | 2.9 | 0.74 | 18.4 | 25.3 | 12.7 | 0.6 |
| **Free T3 pmol/ L (3.9-7.7)** | 6.6 | 6.0 | 3.2 | 2.7 | 3.9 | 4.6 |
| **Total T3 nmol L (1.3-3.4)** | 2.4 | 2.3 | 1.1 | 0.9 | 1.45 | 1.4 |
| **Free T4 pmol/ L (13-21)** | 18.6 | 15.8 | 7.2 | 13.3 | 17.8 | 19 |
| **Total T4 nmol/ L (68-185)** | 110 | 128 | 50 | 93 | 106 | 131 |
| **Treatment** | Nivolumab 3mg/kg every two weeks | | L-thyroxin 50 µg | L-thyroxin 75 µg | L-thyroxin 75/100 µg | L-thyroxin 75/100 µg |

***Table.*** *Thyroid hormones and L-thyroxin treatment during nivolumab treatment.*

## CONCLUSION

We describe a child developing hypothyroidism during successful treatment with the check point inhibitor nivolumab for an inoperable glioblastoma. When treating with check point inhibitors, patients should be monitored on regular basis for hormonal deficits, particularly for hypothyroidism and hypopituitarism.

**Duality of interest - none**

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