Pseudopuberty in a young girl with Adrenocortical Carcinoma during Mitotane therapy.

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Background:

The Adrenocortical Neoplasm (ACN) is a rare condition in childhood (0,3 cases/1000000). In paediatric age, ACN at stage 1 is cured by complete resection by surgery, while at stages 2 and 3 surgery is followed by adjuvant treatment with Mitotane. Chemotherapy is required in metastatic cases (stage 4).

Objective and hypotheses:

Mitotane is an adrenal cytotoxic agent which has both adrenolytic action on ACN cells and inhibition on steroid hormone synthesis apparently without cellular destruction. Furthermore Mitotane appears to modify the peripheral metabolism of steroid. It was hypothesized that the Mitotane also has a partial suppressive effect on pituitary ACTH-secreting cells.
Gynecomastia has been described as a side effect of Mitotane in men and in one little boy. It has been associated with increased binding capacity of SHBG in the plasma compartment modulating hormonal disposal for target cells.

Methods:

In the 2008-2016 period we observed 8 patients affected by ACN (3 males and 5 females, aged 0-32 months at diagnosis). Histologic results: malignant lesion in 5 cases, neoplasm with uncertain behaviour in 2 cases, and adenoma in 1 patient. All children affected by malignant or uncertain lesions underwent surgery, followed by Mitotane adjuvant treatment. One child was also treated with chemotherapy due to advanced disease (stage 4).

Results:

We report a young girl, affected by ACN with uncertain behaviour (stage 2), who, at the age of 2.5 years, underwent Mitotane therapy developing adrenal insufficiency - which was treated with hydrocortisone - and progressive telarche. The full hormonal testing (LH-RH Test, basal 17-Beta-estradiol, progesterone, adrenocortical hormones and their precursors) showed a normal pre-pubertal panel. The telarche reverted after the stop of Mitotane therapy (2 gr/m2/daily for 1 year).

Conclusion:

To our knowledge this is the first reported case of abnormal breast development in a young female child treated with Mitotane for adrenocortical neoplasm.

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