New Technologies

Role of Positron Emission Tomography in the Evaluation of Endocrine Tumors

K Pacak
Bethesda, United States
Contact e-mail: karek@codon.nih.gov

Tumors of endocrine tissue differ from most other tumors in that their functional characteristics can produce large clinical effects despite small size. Conventional imaging methods (e.g. CT and MRI) can fail to visualize such tumors or their metastases and do not depict their specific endocrine nature. Endocrine tumor cells take up hormone precursors, express receptors and transporters, and synthesize, store and release hormones. Novel imaging techniques are now exploiting these characteristics, and with functional information derived from images, helping to define or predict histological features, identify metastases, or guide therapy. Combinations of imaging approaches, especially with data from positron emission tomographic (PET) scanning, are providing increasingly accurate diagnosis. For example, recently developed techniques for imaging pheochromocytomas and carcinoid tumors take advantage of the specific amine precursor uptake and decarboxylation pathways and storage systems that characterize these tumors (Figure 1B-C). For instance, 6-18F-fluorodopamine is taken up into pheochromocytoma cells by cell membrane catecholamine transporters and then concentrated in storage vesicles. Similarly, 11C-hydroxytryptophan is taken up by carcinoid tumor cells, decarboxylated, and then stored in vesicles as 11C-serotonin. Another basis for visualization of endocrine tumors by PET scanning is binding to receptors (Figure 1D). Binding of 11C-methylspiperone and 11C-raclopride to dopamine type 2 receptors in pituitary tumors or 68Ga-labeled somatostatin receptor analogs illustrate this type of application. Expression of specific nuclear receptors provides another potential target for the development of PET agents. Future applications will increasingly exploit cell type-specific functional characteristics of endocrine tumor cells, to visualize transporters, cell membrane and nuclear receptors, enzymes, and even gene expression.

Ultra-Sensitive Determination of Serum Estrogen and Androgen Bioactivity in Children

C Sultan, F Paris, N Servant, C Jeandel, P Balaguer, J C Nicolas
Unité d’Endocrinologie-Gynécologie Pédiatiques, Service de Pédiatrie 1, Hôpital Arnaud de Villeneuve, INSERM U 540 and Service d’Hormonologie, Hôpital Lapeyronie, Montpellier, France
Contact e-mail: chsultan@u439.montp.inserm.fr

The evaluation of estrogen and androgen status can be helpful in a wide range of clinical conditions in children. The diagnosis and treatment of various pediatric endocrine diseases such as premature thelarche (PT), precocious puberty (PP), and Turner syndrome (TS), as well as gynecomastia, micropenis, and other disorders of male sexual differentiation related to the estrogenic properties of environmental pollutants, would benefit from a sensitive determination of both estrogen and androgen bioactivities. We thus developed two new recombinant cell biosays for ultra-sensitive measurement of serum estrogen and androgen bioactivity. Using the Hela cell line stably transfected by ER-a along with an estrogen-responsive promoter fused to the luciferase gene, total estrogen bioactivity (expressed in pg of E2 equivalent) in normal pre-pubertal girls was significantly higher than in pre-pubertal boys: 3.53 ± 2.23 pg.ml vs. 1.44 ± 0.87 pg.ml, respectively. A significant difference was found between pre- and post-pubertal girls: 3.53 ± 2.23 pg.ml vs. 26.77 ± 18.32 pg.ml (p< 0.01). In 9 pre-pubertal girls with isolated PT, estrogen activity was increased: 12.6 ± 6 pg.ml, whereas RIA showed serum estradiol < 9 pg.ml. In a group of 15 girls with central PP, LHRH analogue treatment was unable to lower estrogen activity to pre-pubertal values: 44 ± 15 pg.ml in the untreated group vs 10 ± 4 pg.ml after 1 year of treatment. In a group of 9 pre- and peri-pubertal girls with TS, estrogen bioactivity was dramatically low: 0.6 ± 0.3 pg.ml. This new information may have some therapeutic impact. In 14 pre-pubertal boys with male pseudohermaphroditism and normal testosterone production, the mean estrogen bioactivity was slightly increased: 3.1 ± 2.5 pg.ml; in one boy who had most likely been exposed in utero to environmental pesticides, it was drastically increased (16 pg.ml). In 17 pre-pubertal boys with isolated micropenis (and normal testicular function), the mean estrogen bioactivity was slightly elevated: 3.1 ± 2 pg.ml. In 4 boys with pre-pubertal gynecomastia and 7 boys with pubertal gynecomastia, estrogen bioactivity was increased: 12 ± 8 pg.ml and 21 ± 14 pg.ml, respectively, suggesting either aromatase enzyme overactivity or, more likely, the presence of environmental contaminants with estrogen activity in the serum. Using the CHO cell line stably transfected by AR along with a luciferase reporter gene, we established a bioassay system for evaluating total androgen bioactivity in the serum. We demonstrated a significant difference, expressed in testosterone equivalent, between pre- and post-pubertal boys: 0.6 ± 0.2 ng.ml vs. 12.4 ± 2 ng.ml. Application of this assay in pediatric endocrine diseases is now under investigation. A key advantage of these two assays is that they are capable of evaluating total estrogen and androgen bioactivity. They should thus help to elucidate various physiological phenomena in pediatric endocrinology and to provide considerable insight into pathological processes.