positive changes of the bioelectrical activity of the brain. But this method cannot be considered as being universally applicable, as was well demonstrated in our research. For instance, the procedure is not indicated for patients with a depleted reserve potential of the activating systems of the brain stem, with increased convulsive readiness, or with grave forms of essential hypertension. In such cases human fetal tissue transplantation may turn out to be a factor strong enough to provoke intensification of pathological foci of impulsation.

REFERENCES

- 1. N. A. Puchkovskaya and S. P. Muchnik, Control of Premature Aging [in Russian], Kiev (1968), pp. 134-141.
- 2. O. V. Korkushko, E. T. Kalinovskaya, and S. V. Litovchenko, Tissue Therapy after Filatov [in Russian], Odessa (1977), pp. 127-129.
- 3. N. M. Tkachenko and E. M. Il'ina, Akush. Ginekol., No
- 3, 24-27 (1985).
 V. P. Smetnik, A. A. Kangel'dieva, and V. G. Kolod'ko, Ibid., № 5, 45-47 (1991).
- 5. F. Schmidt, Cell Therapy, 455 (1983).
- 6. R. F. Casper, J. Clin. Endocr. Metabol., 60, №1, 34-36 (1985).

Status of the Breasts in Patients with the Postcastration **Syndrome Treated by Transplantation of Human Fetal Tissue**

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> Clinical and x-ray examinations of the breasts were carried out in 45 women with the postcastration syndrome before and after treatment by human fetal tissue transplantation. The results indicate that a drastic drop of the steroid hormones level and increased gonadotropin secretion occurring in patients with the postcastration syndrome lead to the intensification of involution processes no matter what the patient's age. Benign hyperplastic changes in the breasts induced by previous neuroendocrine gynecological diseases gradually regress. Breast examinations carried out 6-8 months after transplantation of human fetal tissue showed no deterioration of any kind. Clinical examinations and interviews of patients showed an improved turgor of breast skin, although mammography failed to detect any changes in the volume of the glands.

Key Words: transplantation of human fetal tissues; postcastration syndrome; breast

The function and architecture of the breasts are closely related to the status of the hypothalamopituitary-ovarian system. Persistent disorders in one of the components of the chain of hormonal interrelationships may lead to marked morphological changes in the organ. Since the mammary glands are a target organ for sex steroid hormones, a study of their reaction to the cessation of ovarian function in women undergoing bilateral oophorectomy is of practical interest.

Our aim was to study clinical and x-ray features of the breasts in patients with the postcas-

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tration syndrome after human fetal tissue transplantation as well as to elucidate the role of gynecological diseases necessitating oophorectomy in the formation of breast structure.

MATERIALS AND METHODS

Forty-three women aged 29 to 43 who had undergone bilateral oophorectomy 2-3 years before transplantation of human fetal tissues (THFT) were examined to assess the status of the breasts after THFT. 70.4% of these patients were operated on for external genital endometriosis, in 17.9% operations were carried out for inflammatory diseases of the uterus and fallopian tubes, 7.3% were operated on for common follicular and serous ovarian cysts, and the other 4.7% were patients with a history of gonadal cystomas.

The patients were followed up for a year using control x-ray mammography.

The control group consisted of 20 women aged 30 to 40 with a normal cycle.

Patients with the postcastration syndrome did not complain of mastodynia in 44.7% of cases. Only 21.9% of women noted a moderately increased sensitivity, pain, or tension of the breasts. At the same time, a more in-depth interview revealed that 63.7% of patients felt sexual discontent because of reduced skin turgor and changed shape and elasticity of the breasts.

Mammography showed that involutional changes were in progress in the large majority (88%) of the examinees. These changes were paralleled by total fatty transformation in 30.1%. In 44.4% manifest fatty infiltration was associated with moderate stromal fibrosis and fibrocystic deformation, and in 25.5% with glandular hyperplasia of the adenosis type or glandular-fibrous mastopathy. Only in 11.6% of examinees were manifest forms of fibrocystic mastopathy without signs of involution revealed.

Analysis of x-ray features and gynecological diseases which lead to oophorectomy showed that changes characterized by the adenosis or glandular-fibrous transformation type of glandular hyperplasia were observed in 75.9% of cases in the patients operated on for ovarian endometrial cysts, endometriosis being frequently combined with hyperplastic involvement of the uterus (adenomyosis, myomas). Total fatty transformation in such cases was observed in only 24.1% of patients.

Total fatty transformation in the breasts predominated in women who had had uterine and tubal inflammatory diseases and a history of ovarian follicular and serous cysts. Hence, the results of clinical and x-ray examinations of the breasts showed a drastic reduction of the level of steroid hormones in patients with the postcastration syndrome and, as a result, increased gonadotropin secretion, leading to the development of involution processes regardless of the patient's age. Benign hyperplastic changes of the breasts induced by previous neuroendocrine gynecological diseases regress, although residual changes may persist for a long time.

The development of effective methods for the treatment of patients suffering from the postcastration syndrome is still one of the pressing problems in clinical medicine [4,5,8]. Hormone replacement therapy is one of the principal approaches currently used in this condition. However, some authorities are still debating the risk of endometrial hyperplastic processes (U. M. Vikhlyaeva, 1986), breast cancer, thromboembolic complications due to activation of clotting factors, and of cholelithiasis during estrogen therapy for ovarian insufficiency (L. R. Laufer, 1982).

A prolonged follow-up of this patient population showed that in grave forms of the postcastration syndrome hormone therapy is not sufficiently effective, and in 30-40% of patients this treatment causes allergic reactions (V. P. Smetnik et al., 1987). Moreover, it was revealed that prolonged therapy with sex hormones in high doses markedly reduces adrenocortical function (L. Sateen, 1992).

The search for a new treatment modality has led scientists to trials of THFT therapy. In the 40s-50s Russian scientists V. P. Filatov and G. E. Rumyantsev used tissue therapy in patients with burns and diseases of the CNS, liver, pancreas, and ovaries. Later fetal tissue transplantation was used in therapy of diabetes mellitus (grafts of pancreatic islet cells) by V. I. Shumakov, an eminent Russian specialist in transplantation.

Human fetal tissue transplantation is a method permitting treatment of an organism by initiating regeneration. Pathogenetic treatment of the post-castration syndrome starts at the molecular and cellular levels.

THFT helps deliver to the body biochemical substrates, proteins, and inorganic elements contained in fetal tissues; it has become possible to repair structural disorders and functional defects and thus to revitalize disordered functioning of the organism, opening up new vistas of THFT use in patients with the postcastration syndrome.

Analysis of the early results of THFT showed a marked reduction of gonadotropin levels in response to adrenal stimulation and the appearance of peripheral estradiol and progesterone, whose levels normalized. Examination of the breasts 6-8 months after THFT revealed no deterioration: the glandular matrix structure was intact and there were no signs of nodular proliferates.

Thorough clinical examinations and patient interviews showed that along with improved wellbeing, decrease of feverishness, sweating, and irritability, and increased work capacity, an improvement of skin turgor was observed, including that of the breasts. The breast became more elastic and plastic, even though mammography did not detect any increase in the volume of glandular structures.

The preliminary results of the use of THFT in the treatment of patients with the postcastration syndrome permit us to regard with optimism the potentials of this method to correct the serious aftereffects of bilateral oophorectomy.

REFERENCES

- L. V. Kilasoniya, A. N. Kerova, V. P. Smetnik, and N. D. Fanchenko, Akush. Ginekol., № 7, 48-50 (1986).
- 2. V. P. Smetnik, Ibid., № 5, 61-64.
- V. P. Smetnik, A. A. Kangel'dieva, and V. G. Kolod'ko, *Ibid.*, № 5, 45-47 (1991).
- A. V. Basdevant and B. Gay Gren, Rev. Prat. (Paris), 34,
 № 25, 1365-1370 (1984).
- J. R. Bercovici and L. V. Schenkel, Contracept. Fertil. Sex., 15, № 11, 1095-1103 (1987).
- 6. R. F. Casper, J. Clin. Endocr. Metabol., 60, № 1, 34-36 (1985).
- 7. L. Dennerstein, Obstetr. Gynec. Clin. N. Amer., 14, № 1, 33-48 (1987).
- 8. P. C. Ho, G. W. U. Tang, M. C. Fan, and J. W. M. Lawton, J. Obstetr. Gynec., 71, № 4, 622-626 (1988).
- L. C. Huffert, Med. Clin. N. Amer., 71, № 1, 23-39 (1987).
- C. Lauritzen, Horm. Metab. Res., 19, № 11, 579-584 (1987).

Experimental Treatment of Habitual Abortion of Adrenal Etiology by Transplantation of a Tissue Culture of Newborn Pig Adrenals

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Transplantation of an adrenal tissue culture from newborn pigs was performed in patients with habitual abortions. The advantages of this method as compared to the traditional treatment with adrenocortical hormones consist in the absence of effects on the fetus and of side effects in pregnant women. Monitoring of the serum level of adrenocortical hormones is not required. Healthy children were born to 22 patients out of 23. Three clinical cases are described.

Key Words: transplantation of fetal tissues; treatment of habitual abortion; adrenal hypo-function

Habitual abortion due to impaired adrenal function is frequent among cases with a late diagnosis (26.6%) [1] as well as with an early diagnosis and

Department of Gynecology and Pregnancy Pathology, Research Institute of Obstetrics and Pediatrics, Rostov—on— Don; International Institute of Biological Medicine, Moscow when treatment is begun prior to conception (15-20%) [3].

The most common adrenal diseases, causing habitual abortion are congenital dysfunction of the adrenal cortex, namely its mitigated forms with 21-hydroxylase or 11-hydroxylase deficiency, and