

Brief reports

Cancer chemotherapy: Hormonal changes and recurring asthma

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The recurrence of persistent respiratory symptoms in a young woman with severe steroid-dependent asthma in childhood, but asymptomatic without medication for more than 16 years,¹ was suggestive of a possible asthma-provoking role of chemotherapy, (administered for breast cancer) or of the secondary hormonal changes that followed it. The extraordinary event of a second menarche, after a 12-month iatrogenic amenorrhea, was then associated with a second remission of asthma.

CASE REPORT

This 36-year-old woman is now practically asymptomatic, having experienced a rapid remission of her asthma for the second time in 16 years after her recovery from an amenorrhea of nearly 12 months, induced by intensive chemotherapy for breast cancer. In the past time, asthma had required almost continuous medication, including daily bronchodilators and oral corticosteroids for 17 years. When she was 6 years old, the little girl was admitted to the Children's Asthma Research Institute and Hospital CARIH in Denver for long-term residential care and was included in a study of steroid-induced growth suppression.² After her discharge, she continued to have severe asthma, but between the ages of 17 and 19 years, she improved, and no more

hospitalizations were required.¹ Then, after a clinical trial of triamcinolone acetonide aerosol therapy, and possibly in connection with the use of an oral contraceptive, asthma subsided almost completely, and pulmonary function remained satisfactory without medication.

No significant asthma was noted for about 15 years.¹ At the age of 35 years, the patient had a mastectomy for adenocarcinoma of the right breast, followed by chemotherapy with methotrexate, cyclophosphamide, and 5-fluorouracil for 6 months. Prednisone, 60 mg daily, was also administered in four 14-day courses but was then stopped because of the patient's insistence.

Leukopenia, hair loss, and amenorrhea resulted, with menopausal blood levels of follicle-stimulating hormone of 100 to 140 mIU/ml. Wheezing with episodic dyspnea recurred. After about 5 weeks, increasing asthma necessitated a course of systemic steroids, added to the theophylline, adrenergic aerosol, and triamcinolone acetonide (Azmecort inhaler; Rorer Pharmaceuticals, Ft. Washington, Pa.) inhalational therapy. Clinical improvement was gradual, and forced expiratory flow rate of 25% to 75% of FVC remained low (Table I). Almost 12 months later, the patient again had a menstrual period, and a regular cycle has been resumed in the year since that time. A significant amelioration of asthma occurred, and currently, symptoms have practically disappeared.

DISCUSSION

The extreme changes in a young woman's asthma could be attributed to (1) chance, (2) fluctuations in sex hormone levels, (3) toxicity of, or hypersensitiv-

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TABLE I. Spirometric (PFT) data during extended remissions and relapses of chronic asthma

	Date	FVC (L)	% PRED	FEV ₁ (L)	% PRED	PEF ₂₅₋₇₅ (L/sec)	% PRED
Last typical PFT during a 16-year remission	5/6/87	3.33	97	2.16	72	2.06	59
First PFT after relapse	6/5/89	2.89	86	1.54	53	0.70	20
Follow-up PFT	8/16/89	3.20	93	1.84	63	0.90	26
After epinephrine	8/16/89	3.43	100	1.83	62	0.90	26
PFT after second remission (typical of a series)	2/22/90	3.43	100	2.27	76	1.93	55

PFT, Pulmonary function tests; FEF₂₅₋₇₅, forced expiratory rate of flow, 25% to 75% of FVC (midexpiratory flow).

ity to, chemotherapy, and/or (4) changes in corticosteroid administration. The often unpredictable variations in the course of asthma do demonstrate certain nonrandom patterns. In >50% of children with asthma, all symptoms may subside in the second decade of life.³ Puberty, however, is not a reproducible phenomenon. The occurrence of menarche twice in the same young woman has provided an opportunity to observe this duplication of a remission of asthma associated with a normal mature female hormonal cycle. The recurrence of fairly severe asthma during a 12-month iatrogenic amenorrhea and a rapid remission as soon as a regular menstrual cycle was reestablished can be taken as more than suggestive of an etiologic relationship. A deterioration of asthmatic symptoms and a drop in the average morning peak expiratory flow from the follicular to the luteal phase of the menstrual cycle has been demonstrated, although the reactivity to methacholine did not change significantly.⁴ The sudden termination of a high-dose adjuvant chemotherapeutic regimen with prednisone could not be blamed directly for the recurrence of asthma in this case because of the different timing, but the effect of sudden steroid withdrawal on pulmonary function will require further documentation. Antineoplastic chemotherapy can cause amenorrhea by suppressing normal ovarian function. A compensatory pituitary overactivity results in elevated blood

levels of pituitary follicle-stimulating hormone. Among the many other adverse effects of chemotherapy for malignant growths are hypersensitivity reactions, including pneumonitis, but there was no evidence of such a reaction in this case. Chemotherapy is not a very uncommon therapeutic modality, and it appears surprising that little reference to it could be found in the current allergy literature. Only the presumed beneficial effects of "low-dose" methotrexate for subjects with steroid-dependent asthma have received some attention,⁵ but no mention of amenorrhea was made in these communications.

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