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The Effect of Hyperbaric Oxygen on Uterine Cervical Cancer

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INTRODUCTION

The majority of studies on the use of Oxygen at High Pressure (OHP) therapy for the treatment of cancer of the uterine cervix have reported primarily as a radiotherapeutic adjuvant.^{1)~3)} There are, however, few reports on the use of OHP in combination with chemotherapy.^{4)~6)} This paper is concerned with histological changes which result from OHP therapy, and some of their implications for combination of OHP with chemotherapy.

MATERIALS AND METHODS

From October 1974 to February 1978, 17 patients with Stage II and III epidermoid carcinoma of the uterine cervix were treated with OHP at the Ryukyu University Department of Obstetrics and Gynecology. Specimens were obtained before, during, and after the treatment and also immediately after operations of radical hysterectomy. The specimens were stained by the hematoxylin-eosin methods. The stages of the uterine cancer at the time of treatment were divided as follows:

Stage II: 6 patients,

Stage III: 11 patients.

The patients' ages ranged from 37 to 59, with an average mean age of 45.7 years.

The histological types at the time of treatment were:

Transitional cell type: 12 patients,

Spindle cell type: 5 patients.

For OHP treatment we used a Nihon Sanso INC. type KS-305 pressure chamber. This chamber has a capacity of 8 atmospheres absolute (ATA) and is large enough to accomodate the performance of an operation. The pressure schedule called for 10 minutes of compression, 50 minutes of full pressure maintenance, and 15 minutes of decompression. Each patient remained for a total of 75 minutes in the chamber which was pressurized at 2 ATA.

The chamber itself was pressurized with air rather than pure oxygen as a safety precaution to prevent explosion. Within the chamber the patients respired 100% oxygen at 15 liters per minute, by means of a mask from the beginning of the compression period to the end of the decompression period. The patients' condition was continuously monitored through the chamber window.

RESULTS

The histopathological findings of the cancer cells and histological manifestation of the tissue which were observed after OHP therapy are summarized in Table 1.

Table 1. Summary of the Histopathological Findings

		Transitional cell type	Spindle cell type	
Changes in the cancer cell	Cytoplasm	Vacuolation	3/12	1/12
		Swelling	4/12	1/12
		Condensation	1/12	0
		Necrosis	5/12	0
	Nucleus	Pyknosis	4/12	2/12
		Enlargement	3/12	0
		Polymorphism	5/12	0
		Karyoklasis	2/12	0
Histological manifestation of the tissue	Dilatation of intracellular space	3/12	2/12	
	Progression of cornification	6/12	1/12	
	Dissociation and Falling of cells	3/12	0	
	Coagulation and Necrosis	1/12	0	

In some cases of the transitional cell type, we found swelling and vacuolation of the cytoplasm, pyknosis and polymorphism of the nucleus, and dilatation of intracellular space and progression of cornification in cancer tissue. Characteristic histopathological findings after OHP therapy were progressive cornification and interstitial fibrosis in the cancer tissue.

Figure 2 shows the histological pattern in transitional cell type at 8 days after treatment; cytoplasm and nucleus of the cancer cells were enlarged markedly, and the tendency of cornification was progressive. In Figure 4, some nuclei of the cancer cells were found to be enlarged but others showed pyknosis on the 5th days after treatment.

In the spindle cell type, the above changes were observed only in a few cases, and the degree of pyknosis of the nucleus and dilatation of intracellular space were much lesser degree than in the transitional cell type. (Fig. 1, 2, 3, 4)

DISCUSSION

In this study, histological changes of uterine cervical cancer treated with oxygen at high pressure (OHP) were investigated. Seventeen patients were divided into two groups: 6 patients in Stage II and 11 patients in Stage III. The histological types of 12 patients were transitional cell type and the rest were spindle cell type. Specimens for histological investigation were obtained before, during and after the OHP treatment. The condition of OHP was scheduled at 2 ATA air pressure, inhaling pure oxygen at 15 L./min. by means of a mask once a day for ten days in the cabin. The total time required for OHP treatment from compression to decompression was 75 minutes.

The following conclusion about the changes in the nucleus and cytoplasm of cancer cells after OHP therapy may be drawn. Histologically, the mass of cancer cells of the transitional cell type

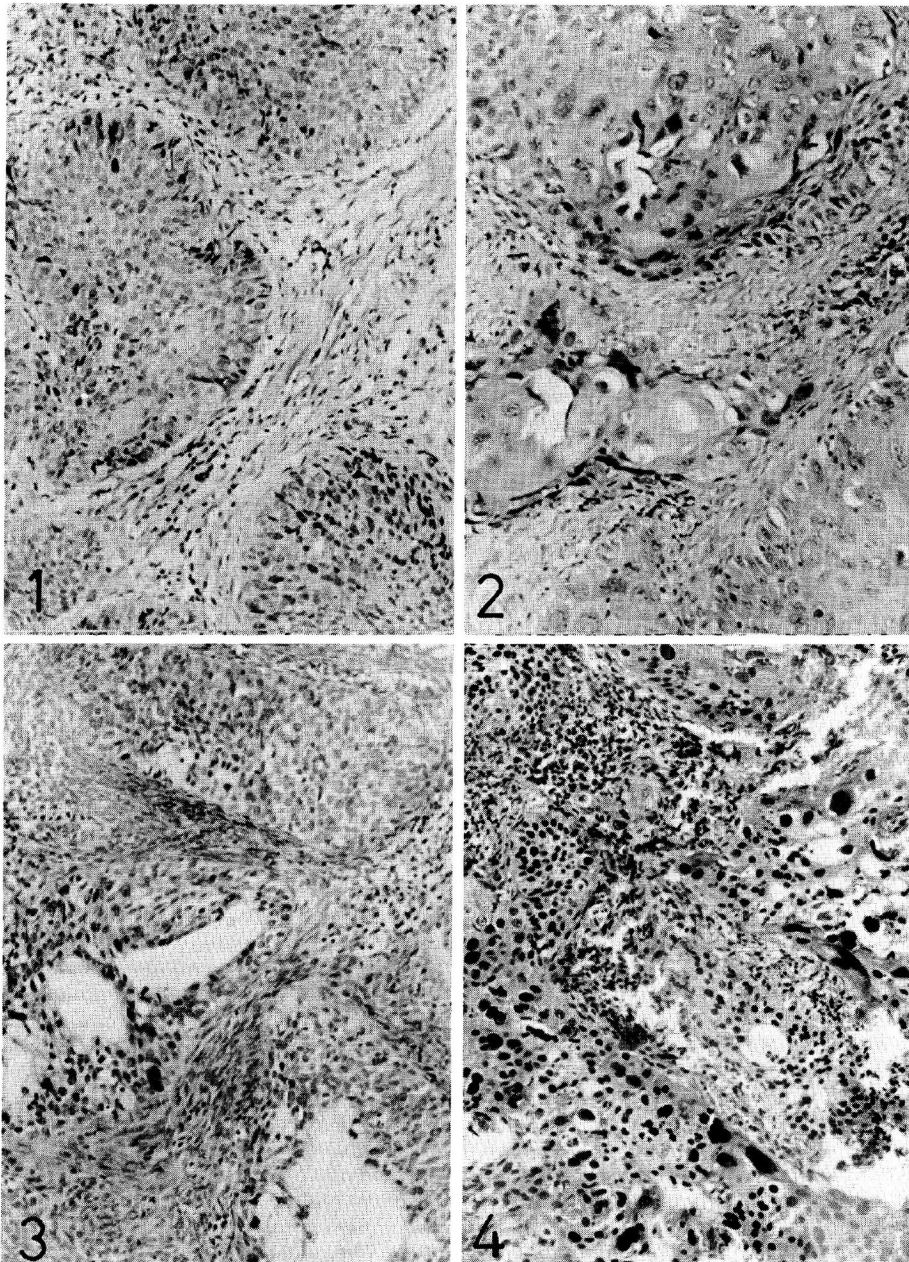


Fig. 1. 45 Yrs. Female. Picture shows the histological pattern of the tumor before treatment. Transitional cell type. x 200.

Fig. 2. Same case as Fig. 1. 8 days after treatment. Cytoplasm and nucleus of the cancer cells are markedly enlarged. Tendency of cornification was progressed. x 200.

Fig. 3. 53 Yrs. Female. Picture shows the histological pattern of the tumor before treatment. Transitional cell type. x 200.

Fig. 4. Same case as Fig. 3. 5 days after treatment. Some nucleus of the cancer cells are enlarged and others show pyknosis. x 200.

showed pyknosis, enlargement and deformation of the nuclei, necrosis, swelling and vacuolation of cytoplasm, and also showed enlargement of intracellular space, cornificational changes, and falling off of cells. Spindle cell types showed less clear changes than transitional cell types. In general, the changes of the cytoplasm in the cancer cells followed the nuclear change.

Although the cancer cells have presumably adapted themselves to the OHP, the metabolism in the cytoplasm was moderately retarded. Recently, Chance⁷⁾ indicated that as soon as the tissues were exposed to OHP, the inhibitory action of oxygen was immediately observable on the electron system, and was followed by a gradual decrease in mitochondrial oxidative enzyme activities. Also Asano⁸⁾ has described the reaction of HeLa cells to exposure to OHP, when the cells were subsequently removed from the pressurized chamber and returned to normal atmospheric pressure, the morphological changes returned to normal. Bean⁹⁾ has likewise described the reaction of Ehrlich ascited cell, and attributed those morphological changes to alteration of the cell membrane, and/or osmotic factors within the cell. It was suggested that the metabolism of the cancer cell was damaged by OHP therapy. But these metabolic changes were reversible and recovered under normal atmospheric conditions. Therefore, excluding the entry of another variable, such as administration of drugs, the metabolic changes due to OHP presumably are reversible.

Our hypothesis is that if anti-tumor drugs were administered while the cells are in this retarded condition (i.e. while under OHP), the cells may be permanently damaged.

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