ONCOLOGY

# Peculiarities of Tumor Growth in Pregnant Rats

V. P. Shelepov and Z. G. Kadagidze

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 119, № 6, pp. 640-641, June, 1995
Original article submitted June 7, 1994

The development of a transplantable tumor (Zajdela ascitic hepatoma) is studied in pregnant rats. Pregnancy is shown to retard tumor growth and influence its course. It prolongs the survival of tumor-bearing rats and induces total regression of the tumor in 15-20% of cases; pregnancy causes the ascitic growth to be transformed into a solid form, and prevents the development of hemorrhagic ascites.

**Key Words:** *anemia; pregnancy; tumor development*

It is widely believed that a growing malignant tumor acts as a "trap" of various metabolites and biologically active compounds in the host [4,6]. Efficient competition with the organism's tissues for amine nitrogen, glucose, and vitamins deprives the normal tissues of plastic and energetic resources, inducing a situation of chronic starvation [6,7]. This leads to multiple endocrine-biochemical disturbances, the prime cause of which is the hypoglycemic pressure exerted by the tumor [6]. At the same time, forced feeding and additional administration of glucose neither prolong the survival of tumor-bearing animals nor prevent the development of secondary complications in cancer patients [1-3,5].

In order to verify the hypothesis of the tumor as a metabolic trap, we attempted to analyze the situation on the model of pregnant rats, considering that the growth of embryos fully matches the demands made by the "metabolic trap." A number of biochemical and endocrine parameters of pregnant and tumor-bearing animals were compared. Unexpectedly it was found that tumor development in pregnant animals markedly differs from that in the control. The present report describes such a phenomenon for the first time.

Laboratory of Tumor Biochemistry, Research Institute of Carcinogenesis, Cancer Research Center, Russian Academy of Medical Sciences, Moscow. (Presented by I. P. Ashmarin, Member of the Russian Academy of Medical Sciences)

## MATERIALS AND METHODS

Female outbred albino rats were purchased from the *Kryukovo* animal breeding center. The control group included rats weighing 150-180 g. The experimental group consisted of pregnant females that were injected at various stages of pregnancy with Zajdela ascitic hepatoma (ZAH). Animals received intraperitoneally 0.2 ml of ascitic fluid (cytocrit index equal to 20% of volume). All animals were fed a standard diet. For evaluation of the hematocrit, blood was drawn from the caudal vein under ether anesthesia. The hematocrit was recorded by centrifugation of heparinized blood in glass capillaries on an MTSG-8 microcentrifuge. Hepatoma preparations were fixed with formalin and stained after Romanowsky. The results were statistically evaluated using a standard package for a Hewlett-Packard-97 calculator.

## RESULTS

After intraperitoneal transplantation, ZAH grows in rats in the form of islets of various size (up to 200 cells per islet), does not give rise to solid growths, and practically does not metastasize, due to the rapid death of animals (on average on the 5th day after transplantation). A hemorrhagic ascitis is always observed, its development being

0007-4888/95/0006-0617$12.50 

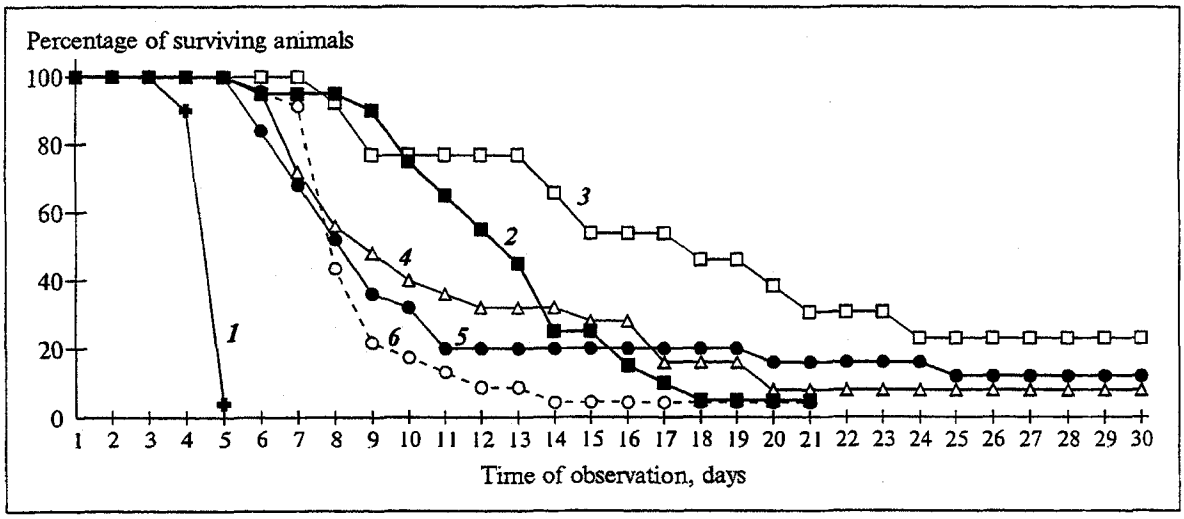


**Fig. 1.** Effect of pregnancy on the survival of ZAH—bearing rats. *1*) control animals (virgin females); *2—6*) tumor transplanted on different days of pregnancy: *2*) 1st—5th day; *3*) 5th—9th day; *4*) 9th—11th day; *5*) 7th—18th day; *6*) 22th—24th day. Each group consisted of 25—28 animals.

accompanied by increasing anemia (on the 5th day of tumor growth the hematocrit drops to 20-25% of the control level).

However, it turned out that the main parameters of tumor growth (short survival, ascitic form of growth, and development of anemia) undergo marked changes against the background of pregnancy (gestation lasts 24-26 days; on average the two uterine horns contain 13 embryos). The effect of pregnancy on the survival time of ZAH-bearing rats is presented in Fig. 1. This parameter slightly differs from the control if the tumor is transplanted at early (1st-5th day) or late (23rd-25th day) stages of pregnancy (series 5 and 6). The survival time is a bit longer when delivery occurs 3 days after tumor transplantation (series 4). (It is worth noting here that tumor growth did not affect lactation, although delayed weight gain was observed in the littermates of tumor-bearing mothers, as compared to the intact control). The maximal survival time (series 2) was observed in the rats that were injected with ZAH on the 9th-11th day of pregnancy. The females receiving a tumor transplant on the 5th-9th day of pregnancy (series 5), as a rule, died while giving birth due to physical weakness apparently caused, by the combined effect of pregnancy and tumor growth.

Three points are to be noted here. First, within the group of females that successfully bore and nursed their offspring, in 15-20% cases a disappearance of the ascitic fluid and complete remission were observed (no relapse during the following 8 months). However, in most females of this group the ascitic fluid, absent at the moment of delivery, reappeared 4-5 days later and simultaneously the symptoms of anemia increased.

Second, it is interesting that females receiving the tumor transplant on the 7th-18th day of pregnancy did not develop hemorrhagic ascites. Upon autopsy, we observed only serous fluid without signs of hemorrhage. The spleen of such animals was within normal size limits. However, tumor cells persisted in the ascitic fluid for a long period, as was confirmed by the following experiment. On the 12th day postpartum, the abdominal cavity of females was punctured, and ascitic fluid was injected to males in a dose of 0.2 ml. The recipients developed tumors, and died at the usual time and with the usual symptoms (development of anemia and presence of hemorrhagic ascites).

Third, it was found that in the females with ZAH that had died during pregnancy or at delivery, the tumor was growing in solid, not ascitic form. It formed a solid mass in the region between stomach, pancreas, and spleen. The tumor weighed about 20-40 g, was well vascularized, and sometimes showed small foci of necrosis.

The findings suggest that ZAH growth in pregnant rats markedly differs from the process in intact animals, and that this model may be fruitful for further study of tumor-host interactions and for elucidation of the factors preventing tumor development.

## REFERENCES

1. R. W. Begg, *Adv. Cancer Res.*, № 1, 54 (1958).
2. I. L. Cameron, *Cancer Treat. Rep.*, **65**, Suppl.5, 93-99 (1981).
3. E. Kwong, M. C. Nesheim, and W. L. Dills, *J. Nutr.*, **114**, № 12, 2324-2330 (1984).
4. G. B. Mider, *Cancer Res.*, **11**, № 6, 821-827 (1951).
5. M. B. Popp, A. K. Kirkemo, S. D. Morrison, and M. F. Brennan, *Ann. Surg.*, **199**, № 2, 205-210 (1984).
6. V. S. Shapot, *Adv. Cancer Res.*, **30**, 89-150 (1979).
7. J. Van Eys, *Cancer Bull. (Wash.)*, **34**, № 4, 136-139 (1982).