RESULTS

A human cell line derived from a nonmalignant endometrium can produce tumors when inoculated into newborn hamsters i.p. In addition to the epithelial cells that were originally transplanted, the tumors also contained bone marrow; their origins were investigated using isozyme patterns by glucose 6-phosphate dehydrogenase. This observation indicates that xenotransplantation of human cells accompanied by ossification in nonimmunosuppressed hamsters is not a unique phenomenon seen only in the prostatic cells as Richman reported.

INTRODUCTION

It has been known that many human tissue culture lines have been successfully transplanted into immunosuppressed or nonimmunosuppressed hamsters. We have maintained an epithelial cell line, designated OE, for more than 100 passages in culture. This cell line has been derived from nonmalignant tissue of a 65-year-old patient with endometrial hyperplasia; its very specific biological characteristics have been published elsewhere (1). While we were examining its xenotransplantability, we encountered findings very similar to those of Richman et al. (3).

MATERIALS AND METHODS

OE cells have been maintained with Eagle’s minimal essential medium supplemented with 20% bovine serum. This was trypsinized and was appropriated to a 0.9% NaCl solution containing 10^7 cells/ml. One-tenth ml of this solution was then injected i.p. into golden hamsters less than 48 hr old and which had received no immunosuppressive treatments. These animals were then sacrificed weekly; their abdominal cavities were examined grossly, and certain organs and tissues were removed for histology and enzyme analysis. An isozyme, G6PD, was examined according to a modified technique of Davis using a polyacrylamide gel electrophoresis (4).

A few animals died within 1 week and the remaining 12 hamsters were used for the experiments up to the end of the 3rd month after inoculation. One week after inoculation 2 animals were killed, and there were several, almost hemispherical and hardly recognizable nodules scattered on the peritoneum. Histologically, inoculated, rapidly proliferating and aggregated epithelial cells were surrounded by scanty mesenchymal tissues. In the 2 hamsters killed 2 weeks later, we also found several ivory-white nodules on the peritoneum that were larger than those in the first 2 animals. These nodules measured approximately 1 to 3 mm in diameter. Some nodules were conglomerated on the retroperitoneum and diaphragm and infiltrated further into their muscles; even, bony, hard, apparent calcium depositions were noticed. These nodules were removed aseptically and were dispersed into the medium described above. Cultured cells from the nodules, designated as OEH, proved to show morphologically the same characteristics as the OE cells originally established in culture. All the inoculated animals had thus grown as excellent as controls (i.e., noninoculated group) up to the end of the 3rd week. After that time they started to deteriorate gradually; 4 hamsters were found dead within 2 months after inoculation. Autopsy showed that all 4 animals had developed bone formation around the retroperitoneum and diaphragm, as in the 2 hamsters killed 2 weeks after inoculation. There were also bony adhesions between the liver, kidneys, and diaphragm that apparently were a direct cause of death resulting from respiratory distress. In 2 of the 4 hamsters, inoculated epithelial cells had survived well, had proliferated, and had coexisted with newly formed bone components (Figs. 1 to 3). The remaining 4 hamsters had survived for more than 3 months, and nothing significant was found on autopsy.

While we found a vigorous hematopoiesis with megaloblasts in the above newly developed bone marrows (Fig. 4), no significant changes were found in the peripheral blood. Regarding the isozyme patterns by G6PD, the nodules as a whole, in which inoculated OE cells were rapidly growing, showed a mixture of the human and hamster types. Some bony, hard nodules in which inoculated OE cells were no longer growing had only the hamster type of isozyme pattern. Furthermore, cultured cells from the nodules (OEH as described above) proved to be of the human type, the same as the OE cells originally established (Fig. 5).
As we stated earlier, OE cells have been established from the endometrium free of cancer. Thus, it is quite natural to assume that these OE cells have been transformed into malignant cells in vitro through continued cultures as Fraley demonstrated in his MA-160 cells. We have successfully observed a sequence of events in which cell aggregates followed by infiltrating tumors with ossifications caused deaths in hamsters. This was achieved by injecting OE cells i.p. into newborn hamsters. In view of the isozyme patterns by G6PD in the nodules, the epithelial component is considered to be of human rather than hamster origin. In contrast, the bony component would be of the hamster origin as the nodules showed merely the hamster type of isozyme pattern after the disappearance of epithelial cells. As far as the ossifications are concerned, it is not a unique phenomenon seen only in the prostatic cells as described by Richman. The argument against his conjecture is simply that our OE cells came from glandular epithelia of the human endometrium. The elucidation of the factors involved in ossifications accompanied by hematopoiesis demonstrated in a xenotransplantation of the human cell line will need further investigations.

**REFERENCES**


**DISCUSSION**

Fraley (2) reported recently about his MA-160 cells derived from a benign prostate adenoma. This was an established cell line from the human nonmalignant tissue. Richman (3) has produced tumors by inoculating these cells s.c. on newborn hamsters and has found, after a short period of apparent disappearance of these tumors, regrowths accompanied by ossification with hematopoiesis. He surmised that a heterotransplantability of the human-derived culture cell line was caused by serum globulin, an antibody, attached to the cultured cell surfaces. The hosts, then, might be unable to recognize these inoculated cells foreign to themselves. He further suggested a relationship of ossifications with the cellular features derived from the prostate.
Xenotransplantation of Established Human Endometrial Cells into Newborn Hamsters

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