Attempts to Localize Tumor Metastases in Long Bones by Mechanical Trauma*

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The medical literature contains many discussions dealing with the influence of trauma on tumor development and numerous reports indicating that in some unexplained manner trauma may be a significant factor in initiating malignant growth, but relatively few articles concerning the influence of trauma on the localization of metastases. Toth (5), who studied 2 patients with generalized carcinomatosis to determine the influence of various mechanical injuries on the formation of metastases, was unable to demonstrate any definite causal relationship (see this article for further references). Lubarsch (4) could not localize metastases in tumor-bearing mice by fracturing bones whereas Ewing (1), on the other hand, cited 5 instances of localization at sites of trauma. Foulds (2), in a critical review on filterable tumors of fowls, stated that in fowls bearing Fujinami sarcoma, secondary growths have been induced by the injection of kieselguhr, lycopodium, powdered charcoal, etc. He also mentioned that, following intravenous injections of filtrates of Rous sarcoma I, tumor formation has been induced at the sites of injection of Scharlach R, tar, embryonic tissues, kieselguhr, histamine, and at points of injury. Jones and Rous (3) were able successfully to transplant a mouse tumor intraperitoneally only after preliminary irritations of the peritoneum by injections of lycopodium, and believed that this irritation was an important factor in causing localization of the tumor.

In view of the conflicting evidence and because of the importance of this problem from the medicolegal standpoint, the following experimental study was undertaken to ascertain whether or not trauma applied to long bones might be influential in the localization of metastases from a transplanted malignant tumor.

The Brown-Pearce rabbit tumor was used throughout this study. This is a highly malignant tumor, readily transplantable into the testes, from which it metastasizes early and, within 3 to 6 weeks from the time of intratesticular transplantation, produces a generalized carcinomatosis.

Attempts were made to localize metastases in long bones by a single mechanical trauma and by chronic irritation. Bone metastases have not been observed in our stock tumor rabbits except in the spinal column, and then but rarely.

However, in order to ascertain whether or not the Brown-Pearce carcinoma grows in long bones, transplants were made directly into the femur in 6 normal male rabbits. The tumor grew well within the marrow spaces in all, soon invaded the periosteum and adjacent muscles, and metastasized extensively.

Trauma to the bones was produced by simple fracture of the humerus. In a series of 21 rabbits the left humerus was fractured and immediately afterward an intravenous injection of a suspension of tumor cells was made into the ear vein. In a second series of 12 rabbits the left humerus was fractured and 14 days later a suspension of tumor cells was injected intravenously into the ear vein. In a third series of 12 animals, tumor was transplanted into the testes (for technic, see Am. J. Cancer, 33:239-295, 1938). Two weeks later, after the testicular tumor was easily palpable, the left humerus was fractured.

Intravenous transplantation was done by the following technic: Portions of fresh sterile tumor tissue were crushed in a tissue press and passed through a fine sieve. The resultant jelly-like mass was then vigorously shaken for 10 minutes in saline and allowed to stand in a vertical position for 10 minutes. The larger particles of tumor quickly settled to the bottom of the flask and the supernatant fluid, consisting of fine particles of tumor suspended in saline, was separated. Ten cubic centimeters of this supernatant fluid was injected into the marginal ear vein of each rabbit.

It may be stressed here that the number of rabbits listed embraces only those which at autopsy disclosed metastases in the various organs, and which obviously died as a result of widespread metastases.

Roentgenograms of the entire skeleton of each rabbit were made after death. At autopsy, in those animals that had received the intravenous transplantation,
most of the metastases were found in the lung, but the kidneys and liver were also involved. The animals in which the tumor was transplanted into the testes showed metastases principally in the inguinal lymph nodes, liver, and kidneys. The region of the fracture was carefully examined by means of roentgenograms in the gross, and a number of blocks were taken from the region of the fracture and the adjacent bone and soft tissue. There was no macroscopic evidence of tumor in this location. The histological examination disclosed tremendous cellular proliferation in the region of the fracture and callus formation, which varied according to the interval between the time of fracture and the death of the animal. In several cases serial sections were cut from the region of the fracture, but in not a single instance were tumor cells encountered.

The second set of experiments was undertaken to determine the influence of chronic mechanical irritation on the possible localization of tumor metastases. To produce such an irritation, a rough piece of a small vitallium screw was placed immediately beneath the periosteum in close contact with the cortex of the distal end of the femur beneath the quadriceps tendon, and held in position by silk sutures. The vitallium screw was placed so that with each movement of the leg the metal rubbed against the bone. In every instance the correct position of the screw was verified by roentgenograms. These experiments were divided into two parts. In the first series 23 animals were used. Six weeks after the vitallium screw had been placed in position, a testicular transplantation of the tumor was made. In the second series (11 animals), intravenous transplantation of tumor cells was done 6 weeks after the vitallium screw had been placed. Again, only those animals that obviously died as a result of a widespread tumor growth are mentioned in this report.

After the animal had died, the position of the screw was studied once more by means of roentgenograms. A thickened periosteum, evidence of mechanical irritation, was almost invariably noted, and again widespread metastases were recorded. In the region of the vitallium screw, the periosteum was greatly thickened and firm, but no gross evidence of tumor was encountered. Multiple sections were taken from the bone in the area of the thickened periosteum and both periosteum and bone were submitted to careful histologic study, but in no case were tumor cells encountered at the site of the mechanical irritation.

SUMMARY

Mechanical trauma or chronic irritation of bones played no role in the localization of metastases from transplanted Brown-Pearce carcinomas in rabbits.

REFERENCES

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