NATURE OF THE MULTINUCLEAR CELLS IN GIANT-CELL TUMORS OF BONE

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A histochemical and cytochemical study was made of 25 giant-cell tumors of bone. Activity of the following enzymes was determined: succinate dehydrogenase, NAD- and NADP-diaphorases, and nonspecific phosphatases. Parallel tests for the same enzymes were carried out in foreign body giant cells and in normal osteoclasts from human embryos and young rats aged 6 days receiving parathyroid extract. The histochemical similarity between the multinuclear cells of the giant-cell tumor and osteoclasts was demonstrated.

Existing views on the nature of giant-cell tumors of bone are reflected in the many different names given to them (myeloplax tumor, giant-cell tumor, osteoblastoclastoma, osteoclastoma, etc.).

The histogenesis of giant-cell tumors of bone has been investigated by Soviet and other workers [4-7, 12]. Histochemical methods occupy an important place in these studies [1, 3, 8-11].

The object of this investigation was to compare the results of histochemical and cytological studies of giant-cell tumors with the results of a study of osteoclasts and foreign body giant cells.

EXPERIMENTAL METHOD

The activity and localization of oxidation-reduction enzymes connected with the function of the Krebs' cycle (succinate dehydrogenase – SDH), with electron transport (NAD- and NADP-diaphorases) were studied in 25 human giant-cell tumors of bone. The enzymes were detected by the methods described by Pearse [10] in his text book, with slight changes in the concentration of certain reagents and in the incubation times [2]. Nonspecific phosphatases also were determined by the simultaneous azo-coupling method [5].

Foreign body giant cells were investigated in material from the operating theater (from the region of surgical sutures) and also from pieces of glass inserted under the skin of mice.

Osteoclasts were studied from six human fetuses of different ages and also from 20 rats aged 6 days to which parathyroid hormone had been given in order to stimulate osteoclast formation. The parathyroid extract was given in a total dose of 75 units at intervals of 6 h and the rats were decapitated 8-12 h after the last injection. Activity of SDH, NAD- and NADP-diaphorases, and nonspecific phosphatases was investigated in the femora and vertebrae and the results compared with the control (rats aged 6 days not receiving parathyroid).

EXPERIMENTAL RESULTS

High SDH activity was found in the multinuclear cells in the giant-cell tumor, in agreement with the observations of Raikhlin and Solov'ev [3]. Active multinuclear cells were distributed among inactive mononuclear stromal cells (Fig. 1a). High SDH activity could also be seen in multinuclear cells in squash preparations (Fig. 1b). SDH activity was higher in some mononuclear cells than in most of the others.

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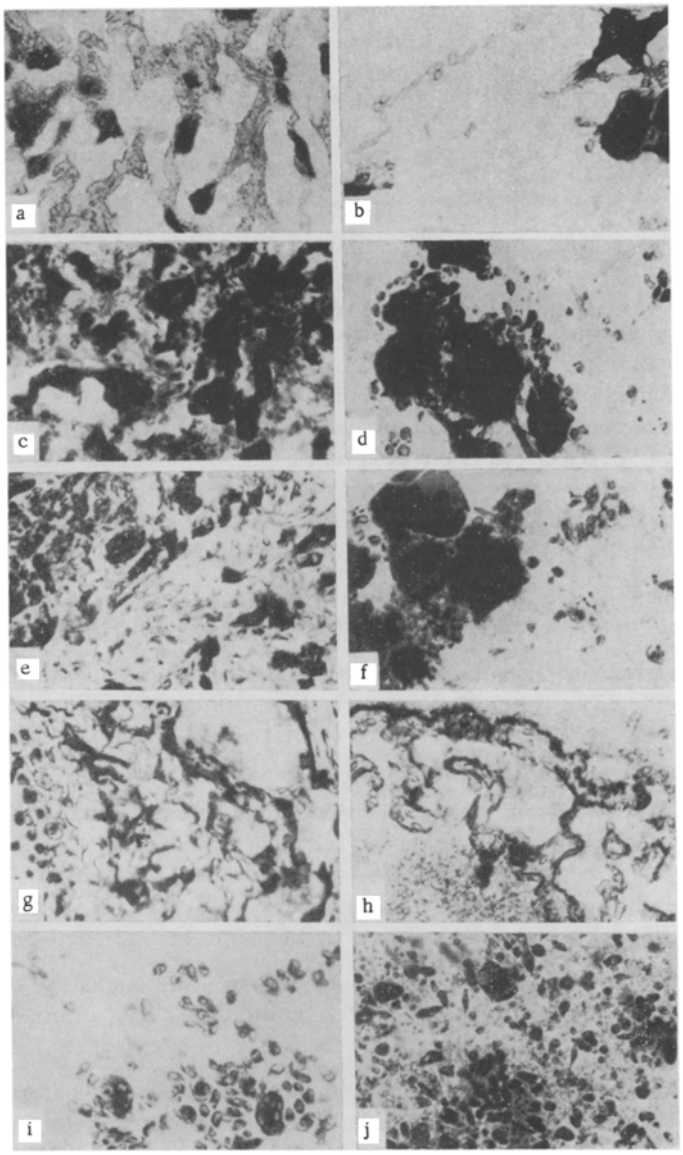

Fig. 1. Succinate dehydrogenase activity in tumor and foreign body cells and in osteoclasts: a) giant-cell tumor: high SDH activity in multinuclear cells (75×); b) the same, in squash preparations (120×); c) giant-cell tumor: high NAD-diaphorase activity in all types of cells (75×); d) the same in square preparations (120×); e) giant-cell tumor, focus of fibrosis: high NADP-diaphorase activity in multinuclear cells (75×); f) giant-cell tumor in square preparations: high NADP-diaphorase activity in both types of cells (120×); g) bones of rats treated with parathyroid extract: high SDH activity in osteoclasts (75×); h) bones of rats not treated with parathyroid; fewer osteoclasts present, high SDH activity in them (75×); i) foreign body giant cells and mononuclear cells surrounding them; moderate SDH activity (75×); j) foreign body giant cells and mononuclear cells surrounding them: high NAD-diaphorase activity (75×).

Activity of NAD- and NADP-diaphorases in the multinuclear cells was higher than in mononuclear cells both in frozen sections and in squash preparations (Fig. 1c-f).

Acid phosphatase activity in the multinuclear cells was raised in most cases. Alkaline phosphatase could not be detected in the mononuclear cells of the giant-cell tumor and it was moderately increased in some of the multinuclear cells.

In some preparations multinuclear cells in foci of fibrosis and necrosis still retained NAD- and NADP-diaphorase activity (Fig. 1e). High activity of these enzymes was not found in the endothelium of the blood vessels. SDH activity was either absent or very low in osteoblasts from foci of reactive osteogenesis. SDH activity in osteoclasts in preparations from rats treated with parathyroid extract was high and corresponded to the activity of the multinuclear cells in the giant-cell tumor (Fig. 1g). In the control there were fewer cells with high SDH activity (Fig. 1h).

Activity of NAD- and NADP-diaphorases in the osteoclasts was higher than in the osteoblasts. In some mononuclear cells the activity of these enzymes was the same as in osteoclasts. These cells were presumably precursors of osteoclasts.

High alkaline phosphatase was found in the osteoblasts along the edge of the bone trabeculae. The reaction for acid phosphatase was positive in the osteoclasts. Similar results were obtained with the human embryos.

As a rule foreign body giant cells differed morphologically and histochemically from the multinuclear cells of the giant-cell tumor and their SDH activity was lower than that of the giant-cell tumor (Fig. 1i). Activity of NAD- and NADP-diaphorases was high both in the giant cells and in most of the surrounding mononuclear cells in the tumor (Fig. 1j). In some areas the activity of the enzymes was low in both types of cells.

Multinuclear cells of giant-cell tumors of bone are thus similar in their histochemical properties to the developing cells of the osteoclast series, so that they probably share the same origin.

The mononuclear cells differed from normal osteoblasts (alkaline phosphatase). The presence of cells with high enzyme activity among them (in the square preparations) can be taken as evidence that they include precursors or multinuclear cells.

The multinuclear cells with high enzyme activity, which they preserve not only in unchanged areas of the tumor but also in foci of fibrosis and necrosis, are an essential component of the neoplasm and largely determine its histogenesis.

Multinuclear cells of giant-cell tumors differ morphologically and histochemically from foreign body giant cells and from the endothelium of blood vessels, with which their histogenesis is sometimes linked.

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