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Case Report

Giant Cell Tumor of the Kidney

Kakuhei Kimura[1], Yoshihisa Ohnishi[2], Hideo Morishita[3], Mamoru Amezaki[4], and Hideo Irikura[4]

[1] College of Biomedical Technology, and Second Department of Pathology, Niigata University School of Medicine, Asahimachidori 1, Niigata 951
[2] Second Department of Pathology, Niigata University School of Medicine, Niigata 951
[3] Department of Urology, Niigata University School of Medicine, Niigata 951
[4] Department of Urology, the Prefectural Shibata Hospital, Niigata Prefecture, 957, Japan

Summary. A multinucleated giant cell tumor developed in the left renal pelvis of a 60-year-old man. The tumor was morphologically indistinguishable from giant cell tumor of bone and considered to be both primary and benign, with a follow-up period of one year and no evidence of either recurrence or metastasis.

Key words: Giant cell tumor – Osteoclastoma – Renal tumor – Giant cells

The occurrence of extraosseous multinucleated giant cell tumor has been reported in diverse organs such as soft tissues (Guccion et al. 1972; Alguacil-Garcia et al. 1977), ovary (Veliath et al. 1975; Lorentzen 1980), pancreas (Rosai 1968; Alguacil-Garcia et al. 1977; Trepeta et al. 1981), thyroid gland (Rather 1950; Silverberg and DeGiorgi 1973; Cibull and Gray 1978), liver (Munoz et al. 1980) and breast (Inauen and Gloor 1981) but, to our knowledge, a description of a case arising in the urinary organs is not available. The present report describes a multinucleated giant cell tumor of the kidney which developed in the left renal pelvis and discusses the origin of this tumor.

Clinical History

A 60-year-old man was seen at the Prefectural Shibata Hospital with the chief complaint of sudden gross haematuria in April, 1981. He had neither a past nor a family history of urogenital diseases. Cystoscopy showed no particular change, but intravenous pyelography (IVP) revealed an abnormality of the left renal pelvis. The patient was admitted to the hospital for detailed examination on May 18, 1981. Renal arteriography, retrograde pyelography (RP), drip infusion pyelography (DIP), renal scintigraphy, cytological examination of the urine, etc. were carried out.

Both DIP and RP revealed partial filling defect of the left renal pelvis, and renal scintigram showed a cold area. Renal arteriography revealed no coiling or pooling.

Offprint requests to: K. Kimura at the above address

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No significant laboratory findings on admission were detected apart from blood urea nitrogen 24.1 mg/dl, serum creatinine 0.8 mg/dl and LDH 443 IU/l. Various renal function tests were within normal limits. Several cytological examinations of the patients urine showed no tumor cells.

A nephrectomy was performed, and a renal tumor was confirmed on May 29, 1981. No further tumor was disclosed, throughout the body after intensive examination. The patient improved progressively and was discharged home one month after the operation. He has been seen thereafter at regular intervals, and is still in good health.

Pathological Findings

Gross Appearance

The tumor was pendulous hanging in the left renal pelvis, measuring $4.0 \times 2.5 \times 1.5$ cm (Fig. 1). The consistency of the tumor was slightly soft and the surface was smooth, but partially erodes.

The cut surface was variegated, with solid grayish areas alternating with friable reddish yellow ones. Macroscopically the tumor showed no invasion into the renal parenchyma.

Histological Findings

Light Microscopy

Light microscopic examinations were performed with paraffin-embedded tissues fixed in 10% buffered formaldehyde solution. Every specimen taken from various portions of the tumor disclosed a multinucleated giant cell tumor which was indistinguishable from giant cell tumor of bone. The tumor proliferated in the submucosa of the pelvis, and there were no direct histogenetic relationships between the tumor cells and transitional epithelium in any section examined.

The basic microscopic pattern was that of a vascularized stroma associated with ovoid-shaped or rather plump spindle-shaped cells (stromal cells), interspersed with multinucleated giant cells (Fig. 2).

Both stromal cells and multinucleated giant cells were similar to those of giant cell tumor of bone (osteoclastoma) respectively. The stromal cells consisted of mononuclear round to spindle-shaped cells which showed no obvious cellular atypia, but a few mitotic figures were found. The giant cells had multiple nuclei, occasionally numbering more than 50, which were ovoid or irregularly shaped without or with one to two nucleoli. Mitosis and pleomorphism in the multinucleated giant cells was not seen, but large vacuoles, engulfed cells, and cellular debris were sometimes present in the cytoplasm.

The multinucleated giant cells demonstrated acid phosphatase activity, showing some variation in the degree of activity. Numerous minute granules were observed in the cytoplasm of multinucleated giant cells, and the intensity of acid phosphatase activity in the giant cells was almost parallel to the quantity of these granules. Some of mononuclear stromal cells exhibited

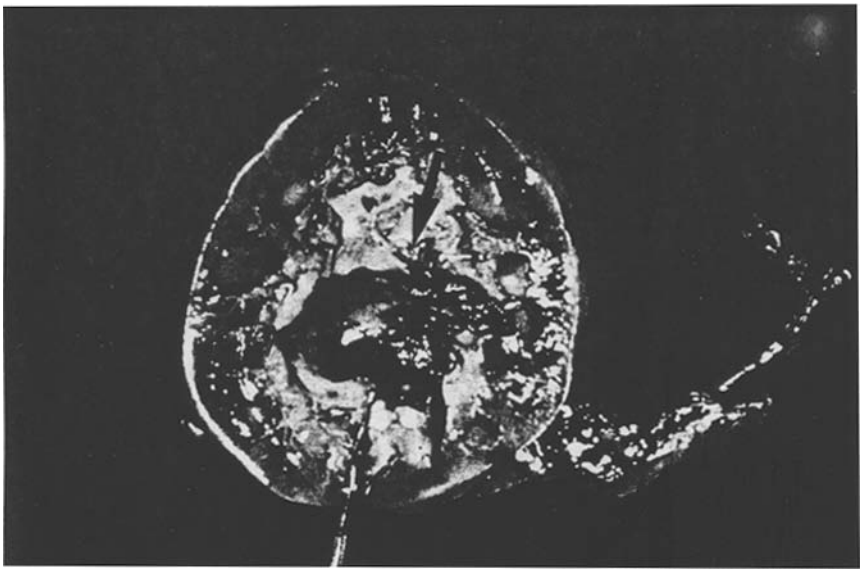

Fig. 1. The renal tumor developing in the left pelvis (*arrow* and *probe*)

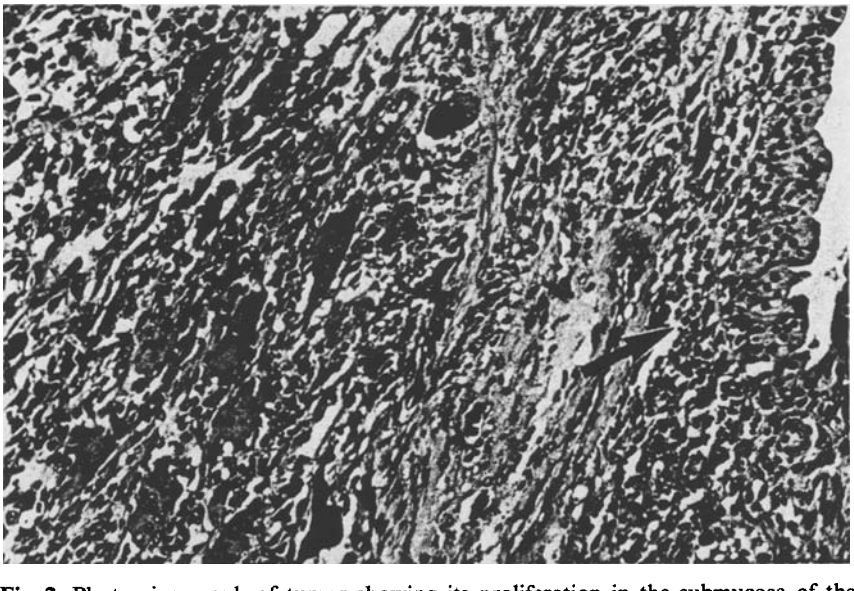

Fig. 2. Photomicrograph of tumor showing its proliferation in the submucosa of the pelvis. The tumor has characteristic histological appearances, composed of stromal cells and multinucleated giant cells. The *arrow* indicates the transitional epithelium of the pelvis (H & E, × 200)

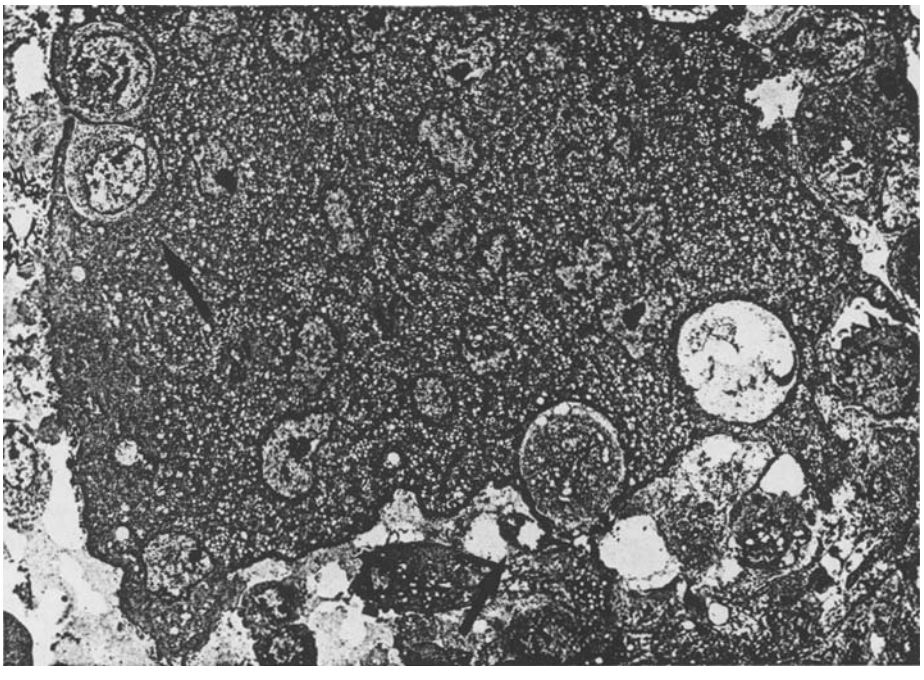

Fig. 3. Electron micrograph of a multinucleated giant cell. The nuclei show the variety in shape and are with and without nucleoli. Three cells (*arrow*) appeared to be nearly engulfed in the cytoplasm (× 1,500)

acid phosphatase activity. Multinucleated giant cells, binuclear, trinuclear and cells with several nuclei also showed this staining.

Alkaline phosphatase activity was not detected in either giant cells or stromal cells.

A cloudy substance was observed in the stroma, particularly in the loosely structured portions of the tumor. This substance consisted of acid mucopolysaccharides, especially hyaluronic acid as demonstrated by an apparently positive reaction for both toluidine blue (pH 7.0) and colloidal iron. This reaction which was highly susceptible to testicular hyaluronidase (pH 7.0), weakly positive reaction for alcian blue stain (pH 2.5). There was no production of metachromasia by the toluidine blue stain (pH 2.5).

Neither osteoid nor cartilaginous tissues were demonstrated.

Electron Microscopy

The electron microscopic study was performed on small segments of the tumor fixed immediately in 10% neutral buffered formaldehyde solution, thereafter following the ordinary procedure for electron microscopy.

Multinucleated giant cells and mononuclear stromal cells predominated in every section examined. The nuclei of giant cells varied from oval to highly irregular in shape with or without one or two prominent nucleoli (Fig. 3).

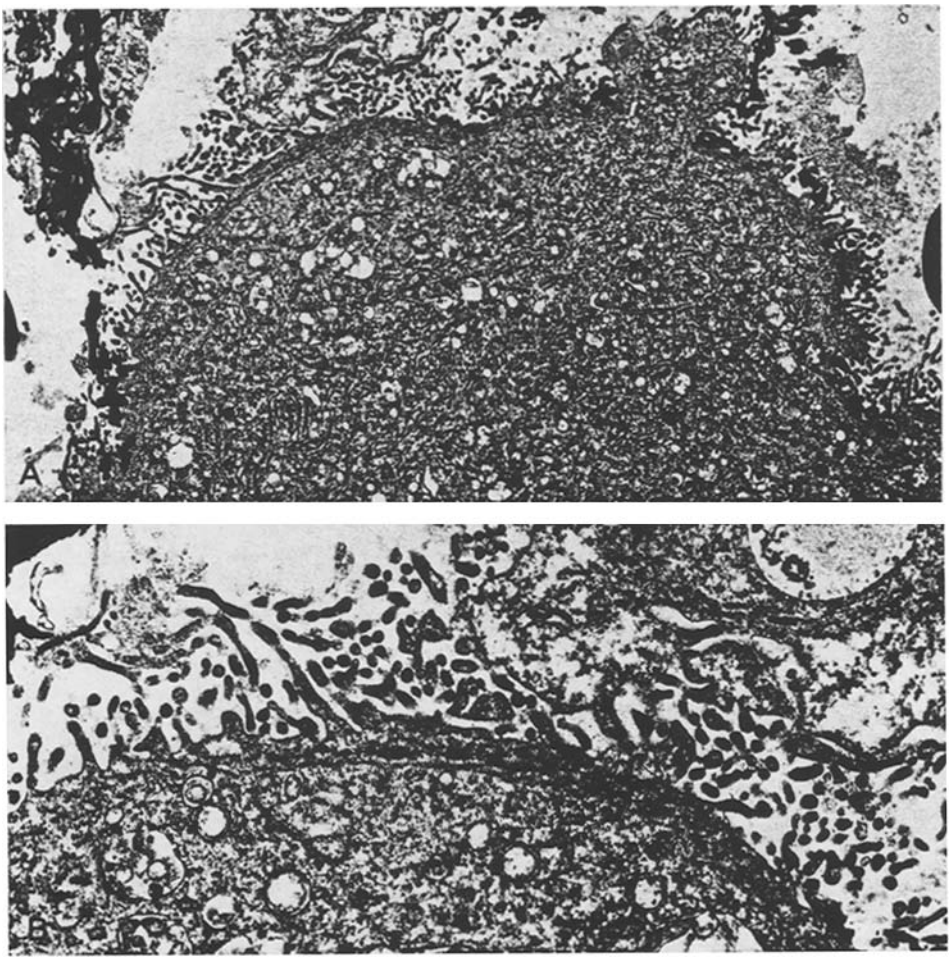

Fig. 4. A (*top*) Electron micrograph showing microvilli of a giant cell, which is on the border of a vascular space (×6,600). **B** (*bottom*) Higher magnification of **A**. Numerous microvilli were seen in the cytoplasm of a giant cell (×15,400)

Pseudopod-like projections and microvilli, which seemed somewhat like those of osteoclasts were occasionally seen in the cytoplasm of giant cells especially where they bordered on a vascular space or loosely arranged regions of the cells (Fig. 4A and B). Relatively organelle-free areas were also noticed at the marginal zone of the cytoplasm (Fig. 5).

The giant cells contained a substantial amount of mitochondria in the cytoplasm, but the most prominent feature was the presence of numerous vesicles and vacuoles (Fig. 6), which seemed to correspond to those vacuoles and granules observed in multinucleated giant cells which demonstrated intense acid phosphatase activity in light microscopic sections. A Golgi apparatus was frequently found adjacent to the nuclei, and rough-surfaced endoplasmic reticulum (RER) was usually placed at the periphery of the

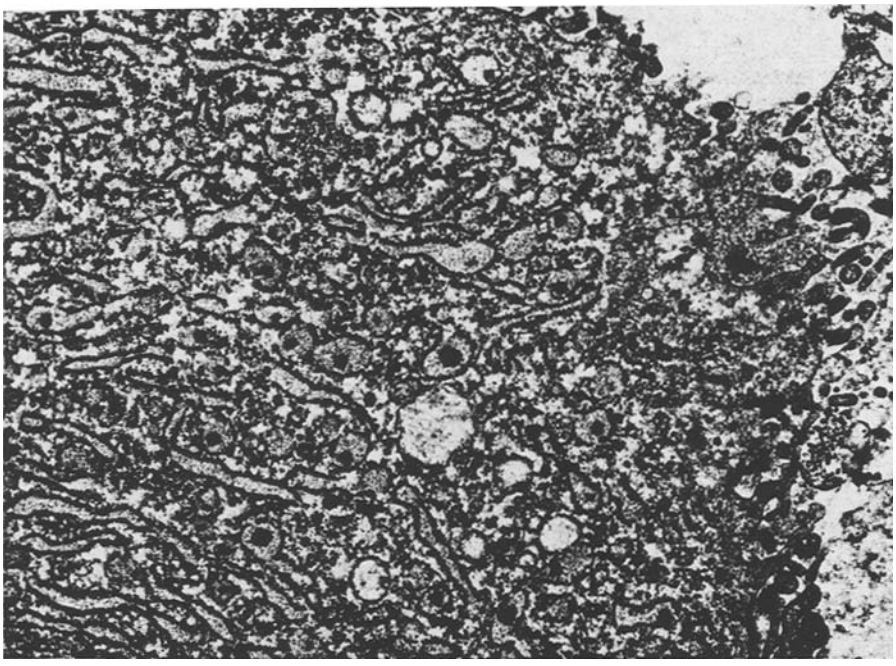

Fig. 5. Electron micrograph showing the dilated cisternae of the RER, containing amorphous substance with an intracisternal granule, and the relatively organelle-free zone of the cytoplasm of a multinucleated giant cell (× 15,400)

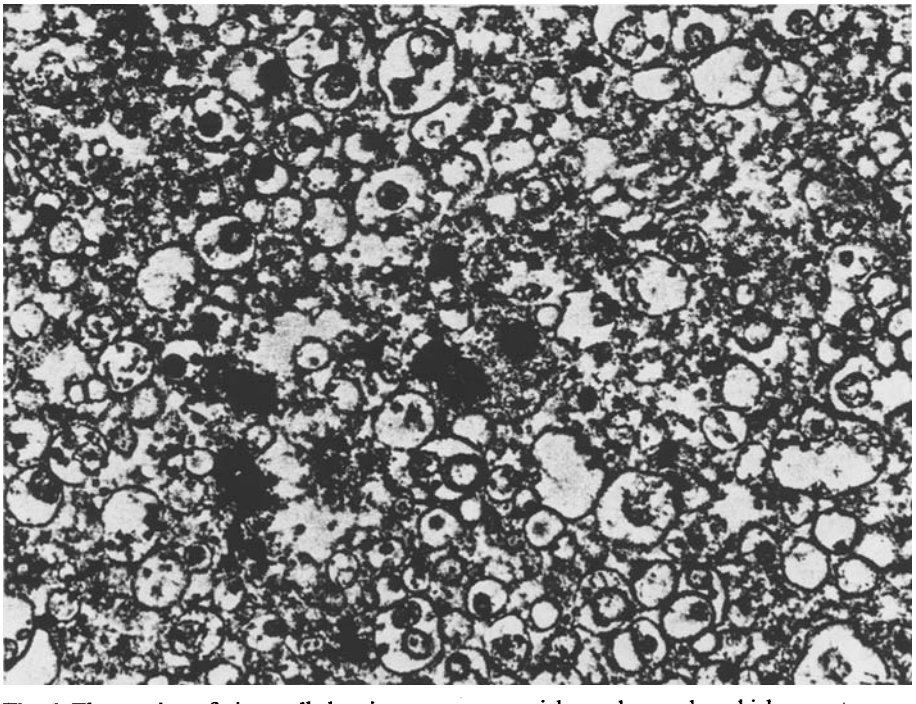

Fig. 6. The portion of giant cell showing numerous vesicles and vacuoles which seem to correspond to secondary lysosomes (× 15,400)

cytoplasm. Some of the RER appeared to have enlarged cisternae, containing amorphous material with one or two intracisternal granules (Fig. 5). Dismosomes were not found.

Giant cells were occasionally observed engulfing mononucleated cells and erythrocytes in the cytoplasm (Fig. 3). No mitotic figures were detected in giant cells. The stromal cells seemed to be classified into three cellular types morphologically, but they could not be analyzed in detail because of fixation unsuitable for electron microscopy.

Discussion

The present renal tumor is obviously different in histological appearance from previously described tumors of renal origin, and is considered to be a neoplasm, composed of multinucleated giant cells and stromal cells, morphologically indistinguishable from giant cell tumor of bone.

Despite its characteristic histopathological features, the histogenesis of giant cell tumor of the bone still remains controversial and there are several opinions about its origin. However, the majority of authors support an origin from undifferentiated mesenchymal cells. However, even among those who agree on an undifferentiated mesenchymal cell origin, there is diversity in the conception of these mesenchymal cells; one group is destined to differentiate into osteoclasts (Geschickter and Copeland 1949; Willis 1967) another is presumed to be related to the supporting connective tissue of the bone marrow (Jaffe 1958; Schajowicz 1961; Lichtenstein 1972; Steiner et al. 1972). Hanaoka et al. (1970) suggested that the giant cells are formed by fusion of mononucleated stromal cells, which may originate from macrophages.

Similarly, there is no unanimity of opinion on the histogenesis of extraosseous giant cell tumor; some authors indicated an origin from undifferentiated mesenchymal cells (Lorentzen 1980; Cibull et al. 1978) which are interpreted by some authors as histiocytic cells (Guccion and Enzinger 1972; Alguacil-Garcia et al. 1977) others are of the opinion that they are epithelial in origin (Trepeta et al. 1981; Silverberg and DeGiorgi 1973) especially from acinar cells (Rosai 1968; Alguacil-Garcia and Weiland 1977). The endothelium of vascular channels (Rather 1950), and reticuloendothelial cells (Kupffer cells) (Munoz et al. 1980) have also been suggested as possible origins.

In the present tumor, we observed the dilated cisternae of RER, filled with amorphous material with granules (Fig. 5). The most prominent feature of the giant cells is the presence of innumerable vesicles and vacuoles with intense acid phosphatase activity (Fig. 6), which is regarded as a lysosomal enzyme and a reliable marker of lysosomes (De Duve 1969). Schajowicz (1961) indicated the different histochemical properties of giant cells from stromal cells, but in the present case, some of mononucleated stromal cells exhibit almost the same acid phosphatase activity as multinucleated giant cells; moreover, there are also binucleated and trinucleated cells and cells with several nuclei which have the same morphological and histochemical

properties as multinucleated giant cells. Aparisi et al. (1977 and 1978) demonstrated the same reaction product of acid phosphatase in stromal cells and in multinucleated giant cells electron microscopically. These findings lead us to presume that there exists a certain cell line which originates from some type of stromal cell, possesses intensive phagocytic activity, and which is capable of developing into multinucleated giant cells.

Munoz et al. (1980) observed an osteoclastoma-like giant cell tumor of the liver, and considered their case arose from the hepatic sinusoidal RE component, i.e., the Kupffer cells. Some recent studies (Meuret et al. 1974; Nichols et al. 1971; Nichols and Bainton 1973; Van Furth et al. 1972; Cline 1981) suggest that monocytes, histiocytes, macrophages in various organs and Kupffer cells of liver are same cell line (or the mononuclear phagocyte system).

The histogenesis of the present tumor is not difinitely established, but the morphological and histochemical studies lead us to presume that the giant cells are formed by one type of stromal cell which arises from some undifferentiated mesenchymal cells of the mononuclear phagocyte cell line.

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