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Observations on the fine structure of interdigitating cell sarcoma

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Summary. In this histo-pathological follow-up study of a case of interdigitating cell sarcoma, intracytoplasmic membrane complexes were seen by electron microscopy within the neoplastic cells. These complexes might correspond to the eosinophilic inclusions seen in the tumour cells by light microscopy; they were not identified in the initial lymph node lesion. Recently, these structures have been found to be a variation of microtubuloreticular complexes. To our knowledge, they have not been previously described in interdigitating cell sarcoma. Their significance remains obscure.

Key words: Interdigitating cell sarcoma – Eosinophilic inclusion – Electron microscopy – Membrane complex

Introduction

Tumours arising from interdigitating cells (dendritic cells located in T-cell domains) are rare lesions first described as interdigitating cell sarcoma by Feltkamp et al. (1981).

We have previously reported the subcellular characteristics of this rare tumour (Nakamura et al. 1988). During histopathological follow-up study of that case, a number of specific structures were found in the cytoplasm of the neoplastic cells in the recurrent lesion. These specific structures had not been detected in the initial lesion despite intensive study and, to our knowledge, have not been reported previously in interdigitating cell sarcoma.

The present communication reports the follow-up study of the fine-structural aspect of interdigitating cell sarcoma and the characteristics of the specific structures in the cytoplasm of the neoplastic cells.

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Materials and methods

A 58-year-old male was diagnosed as having interdigitating cell sarcoma by lymph node biopsy (Nakamura et al. 1988). In spite of chemotherapy, the tumour recurred twice in the jejunum. The recurrent lesions were excised in March and November 1986. The patient was discharged, followed with chemotherapy and was still alive in October 1988 without the metastasis.

Tissue blocks for both light and electron microscopy were obtained from the recurrent jejunal tumour. For light microscopy, specimens were fixed in phosphate-buffered 10% formalin. Specimens for electron microscopy were initially fixed in cacodylate-buffered 2.5% glutaraldehyde for 2 h and then postfixed in 2% osmium tetroxide. After ethanol dehydration, the tissues were embedded in Epon 812. Thin sections were stained with uranyl acetate and lead citrate, and observed with a JEOL 1200EX.

Immuno-histological and enzyme-histochemical studies were done on fresh tissue obtained from the jejunal tumour by the same methods as previously described (Nakamura et al. 1988). Tumour cells possessed intracytoplasmic S100 protein, Leu3a (T4) and HLA-DR antigens. The neoplastic cells also showed membranous ATPase activity. LeuM1, T6, Leu1, Leu2a, B1, lysozyme and immunoglobulin were not detected. Alpha1-antitrypsin and antichymotrypsin were present in the cytoplasm of a minority of tumour cells.

Results

The histological features of this interdigitating cell sarcoma have been reported previously (Nakamura et al. 1988). In brief, histological examination of lymph node biopsy revealed infiltration of pleomorphic cells in the paracortical area. Neoplastic cells exhibited pleomorphic nuclei with abundant cytoplasm. The tumour cells of the jejunal tumours and mesenteric lymph nodes had the same morphological characteristics as those in the cervical lymph node. A number of unusual eosinophilic inclusions were found in the cytoplasm of about 10–20% of the tumour cells at these sites

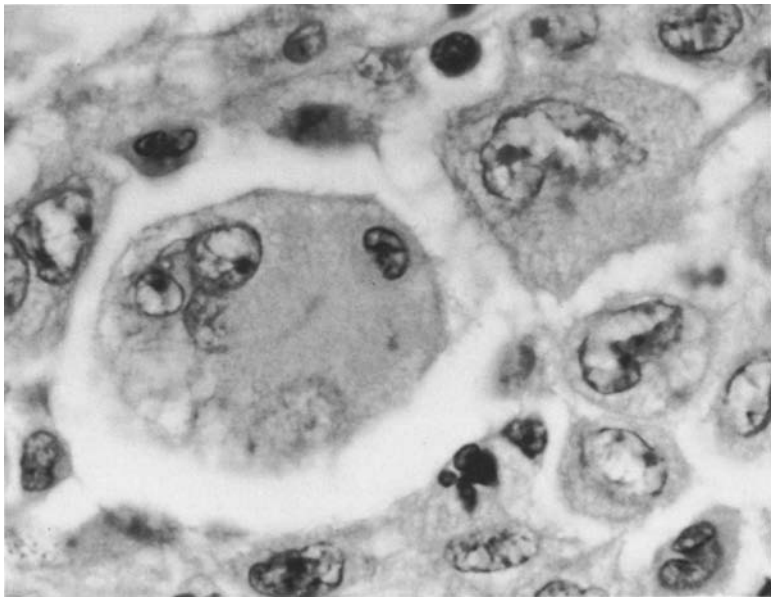


Fig. 1. Jejunal tumour. Interdigitating cell sarcoma. Note the eosinophilic inclusions in the cytoplasm of the neoplastic cells. Haematoxylin and eosin. (×1000)

(Fig. 1). They were round or spindle-shaped and located in the center of the cell or near the nucleus. On electron microscopy the fine structure of the tumour cells from the cervical lymph node and jejunal tumour resembled each other in their main features (Figs. 2, 3). The cells had markedly elongated and complex cell processes, and invagination and bladelike indentation of the plasma membrane (Figs. 2–5). The cytoplasm of most cells was electron transparent. The nuclei were located centrally and occupied a relatively large part of the cell. Their contours were pleomorphic with deep invagination of the nuclear envelope and enlarged nucleoli. Some cells appeared to be multinucleated (Fig. 7). The finely dispersed chromatin was condensed in a thin rim against the nuclear envelope. The cytoplasm contained variable amounts of cell organelles, such as rough and smooth endoplasmic reticulum, mitochondria, Golgi apparatus, and ribosomes. These were dispersed around the nuclei. A few endoplasmic reticulum profiles were present as a variable forms of concentric membranous bodies or confronting cisternae, and were identified in the neoplastic cells from the jejunal tumour but not the cervical lymph node (Figs. 11, 12). They were associated with intracytoplasmic inclusions, which are referred to as membrane complexes in this paper and described in detail later (see Ghadially 1982). Some cells showed a moderate number of granules and lysosomes. One unusual cell had an annulate lamella-like structure in the cytoplasm (Fig. 13). Intracytoplasmic microtubules, associated with centrioles, and a few intermediate filaments were occasionally irregularly arrayed and undulated around cell organelles (Fig. 14). A small number of phagosomes were recognized in a few cells. Junctional complexes, Birbeck granules, basal lamina or thickening of cytoplasmic membranes were not identified.

Lymphocytes were intermixed in close contact with neoplastic cells through their branched cytoplasmic projections (Figs. 2, 3).

In about one fourth of the tumour cells in one section of specimen embedded for electron microscopy, membrane complexes were observed in the cytoplasm (Fig. 3). They were located near the nuclei apart from the Golgi apparatus, sometimes surrounded by rough endoplasmic reticulum and found in the neighborhood of confronting cisternae (Figs. 3, 8, 10, 11). They measured from 2.2 to 6.4 μm in length. The membrane complexes were intermixed with slightly-distended rough endoplasmic reticulum and appeared to be composed of undulating paired membranes showing an irregular pattern of loops or circles, or a combination of these configurations (Figs. 6, 7, 9). There were a very small number of circular profiles acceptable as sections through fine tubular structure (Fig. 9). The paired membranes of the complex measured 25 nm in thickness and maintained a uniform separation throughout their three-dimensional configuration. At the periphery and interior of the complex, the membranes were in direct communication with and appeared to be derived from rough endoplasmic reticulum (Figs. 6, 7, 9, 10). At the point of transition, two apposing membranes of the endoplasmic reticulum abruptly converged to form membrane complexes (Fig. 7). The paired mem-

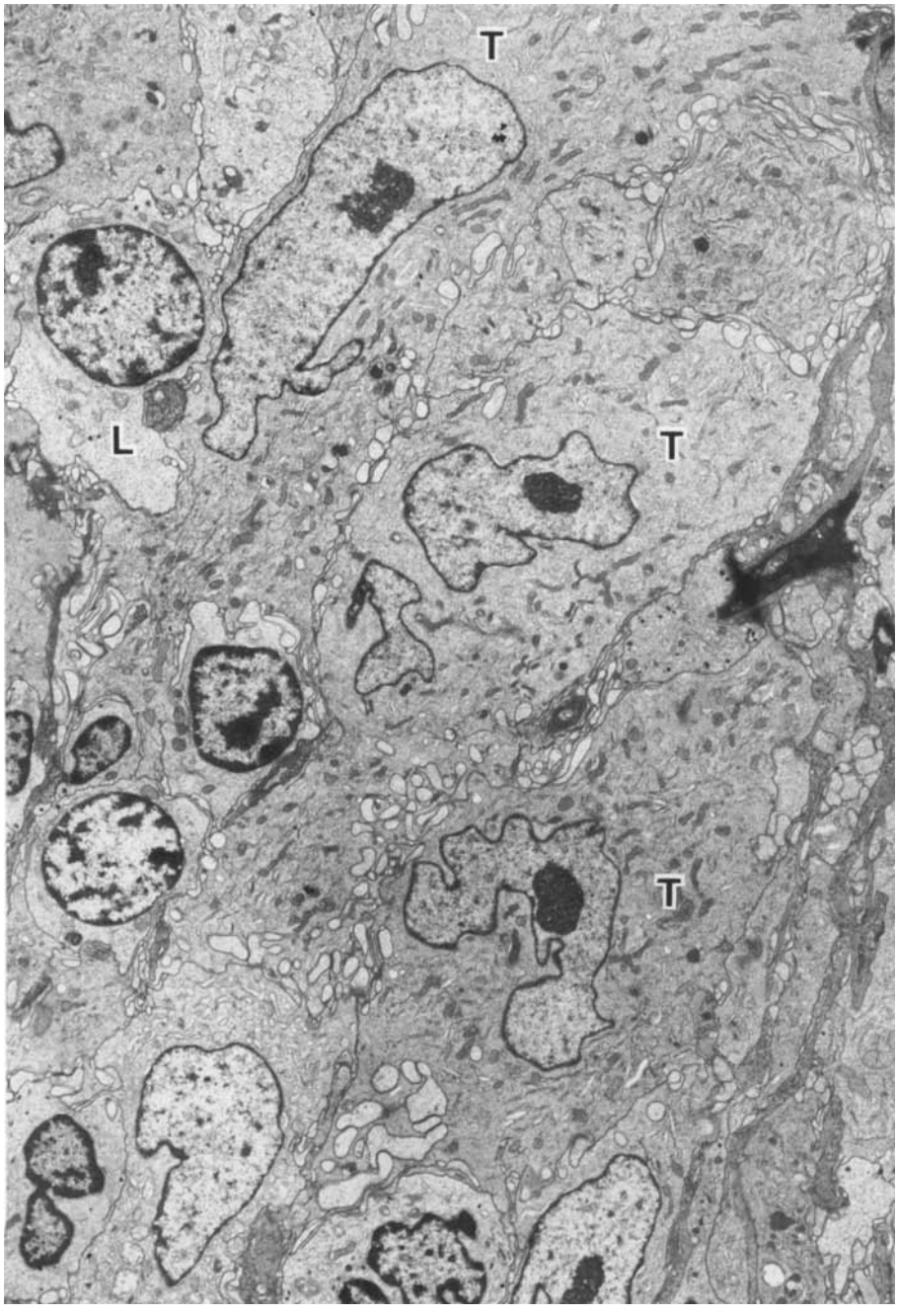


Fig. 2. Cervical lymph node biopsy. The neoplastic cells (T) have prominent cytoplasmic processes interdigitating with the processes of adjacent cells and scanty cell organelles. Lymphocyte (L). (× 3800)

branes of the complexes resembled the interdigitation and invagination of the surface membrane observed in the cytoplasm of the tumour cells, but were not confirmed to be continuous with the latter by serial sectioning. Furthermore, unlike the description of Chandra and Stefano (1976), the complexes were neither found to be continuous with the confronting cisternae nor to lie within the dilatation of the endoplasmic reticulum.

Coated vesicles were observed within the complexes. In addition, some membrane-limited spherical particles, ranging from 0.07 to 0.16 μm in outside diameter were observed within all complexes (Figs. 6, 9). They contained an electron-opaque material and no core. Continuity of particles with the complexes was not confirmed.

These specific structures were identified in cytoplasm from the neoplastic cells of the jejunal tumour, but not of the cervical lymph node despite intensive investigation. No were they detected within the endothelial cells or lymphocytes in the jejunal tumour.

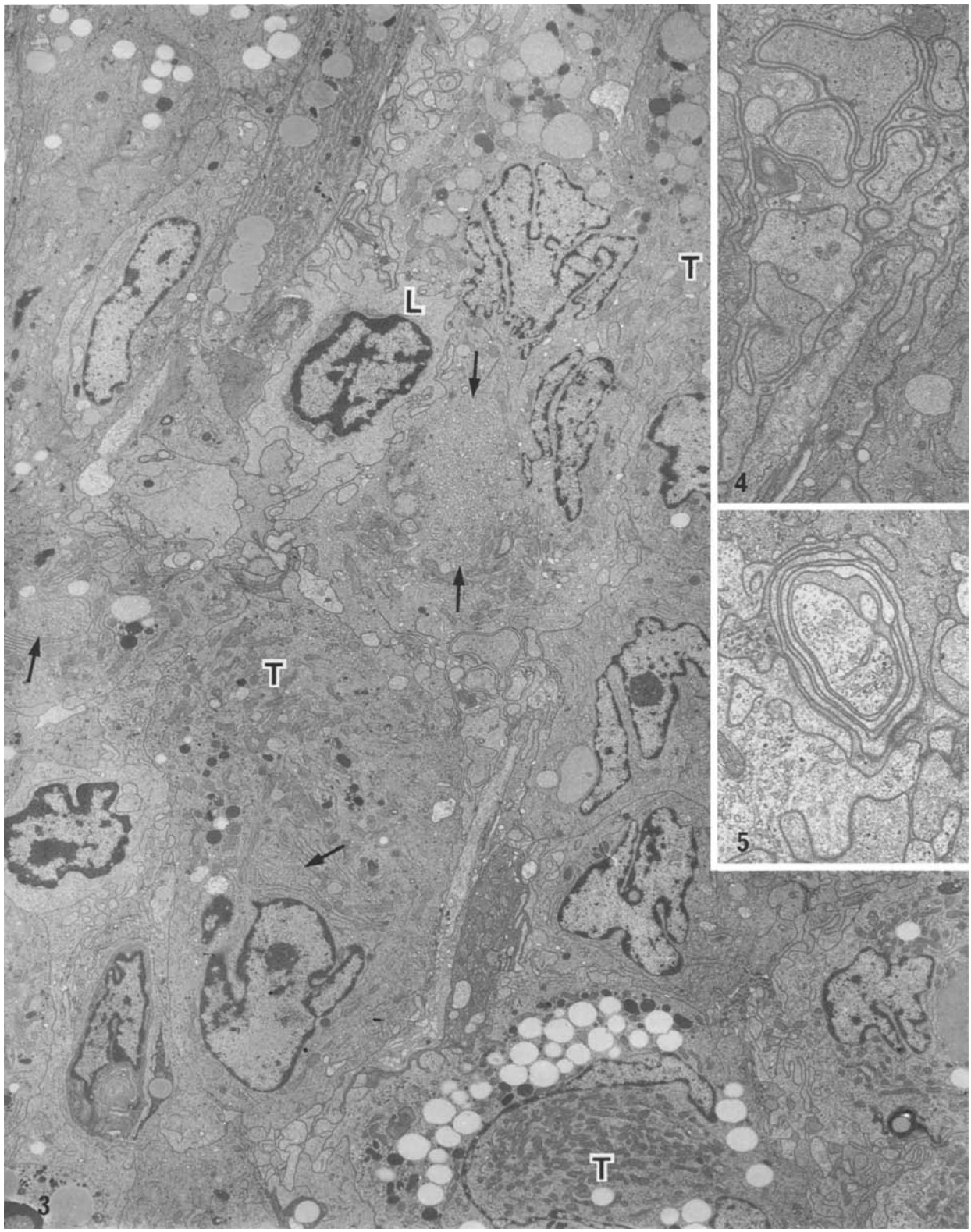


Fig. 3. Jejunal tumour. Note the membrane complexes (*arrows*) in the cytoplasm of tumour cells (T) with prominent interdigitation and invagination of the plasma membrane. Lymphocyte (L). (×4300)

Fig. 4. Higher magnification of the interdigitation of Fig. 3. (×11000)

Fig. 5. A cell showing glia-like interdigitation. (×11000)

Discussion

Interdigitating cells are defined by their fine structural appearance (Friess 1976; Veerman 1974; Veldman 1970; Kaiserling and Lennert 1974; Fuse et al. 1983; Heusermann et al. 1974; Kaiserling et al. 1974; van Ewijk et al. 1974). This emphasizes the need for fine structural examination in the investigation of interdigitating cell sarcoma (Chan and Zattari 1986; Feltkamp et al. 1981; Turner et al. 1984).

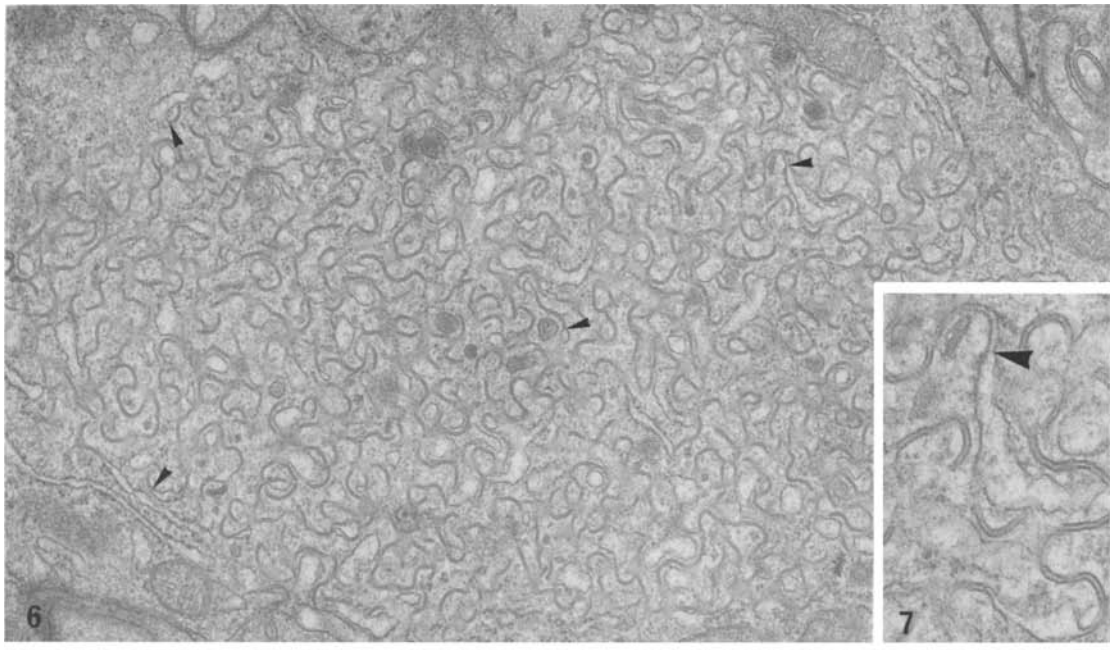
Electronmicroscopy of tumour cells in the present study revealed prominent interdigitation between the neoplastic cells, and between the neoplastic cells and the lymphatic cells. These findings, combined with the cytoplasmic architecture, indicated the fine-structural resemblance of the tumour cells to normal interdigitating cells, although the former were much more variable in cell size than their normal counterparts, and also have multinucleated cells and enlarged nucleoli.

The most striking feature observed in this study was the frequent presence of membrane complexes, which were found in the cytoplasm of the neoplastic cells of the jejunal tumours, but not in the initial cervical lymph node lesion. With light microscopy, eosinophilic intracytoplasmic inclusions were identified in the tumor cells of the jejunal tumour. We speculate that the zones of membrane complexes represent the eosinophilic inclusions in cytoplasm at the light microscopic level since the frequency, location and size of the eosinophilic inclusions in the cells correspond to those of membrane complexes at the fine structural level. In general, the fine structure of the eosinophilic inclusions consists of proteinous substances such as thin and intermediate filaments and microtubules and/or membranes (Ghadially 1982; Cain and Kraus 1977). Accumulation of filaments and membranes other than membrane complexes were rarely seen in the present case. Furthermore, the reduction of ribosomes within the complexes might result in eosinophilic staining.

Circular or looped patterns in electron images of the complexes, depending on the plane of section, suggest undulating membranes as the predominant element. The close topolographical relationship of the complexes with rough endoplasmic reticulum indicates formation by fusion of two apposing membranes of the endoplasmic reticulum. Similar structures were described as "unique cytoplasmic membranes" by Smith and Deinhardt in Rous sarcoma of a subhuman primate and/or "undulating membranous structures" by other authors, although the present complexes were more remarkably irregular (Chandra 1968; Ghadially 1982; Grimley and Schaff 1976; Smith and Deinhardt 1968; Rabson et al. 1973). In man, "undulating membranous structures" have been reported in cell lines derived from fetal spleen or thymus and in a line of lung carcinoma cells (Chandra 1968; Grimley and Schaff 1976; Rabson et al. 1973). To our knowledge, however, these structures have not been previously described in clinical material. Furthermore, the particles observed within the present complexes were characteristic only of this case. Undulating membranous structures are now thought to be membrane complexes and both are variants of the microtubuloreticular complexes which include innumerable other structural variations (Chandra 1968; Ghadially 1982; Chandra and Stefano 1976; Grimley and Schaff 1976; Smith and Deinhardt 1968; Schaff et al. 1972; Uzman et al. 1971). The preference of the microtubuloreticular complexes for cells belonging to the reticuloendothelial system further supports the idea that the origin of this tumour is in the interdigitating cells (Grimley and Schaff 1976; Schaff et al. 1972; Uzman et al. 1971).

An elaborate complex of narrow tubules and vesicles, probably related to the Golgi apparatus, has been reported in interdigitating cell sarcoma (Chan and Zattari 1986; Feltkamp et al. 1981). However, the architecture differed from the complex described here, judging from the compositions and the tridimensional configuration suggested by the present observations.

Although the true significance of fine structural modifications of the endoplasmic reticulum remains obscure, they may be the endoplasmic reticulum's response to a variety of pathological processes, including viral diseases, neoplastic states and drugs (Ghadially 1982; Grimley and Schaff 1976; Uzman et al. 1971). They also occur in rapidly dividing cells and are more frequent in neoplastic and virus infected cells than in normal cells (Ghadially 1982; Grimley and Schaff 1976; Uzman et al. 1971). In the present case, morphological changes in the endoplasmic reticulum, such as membrane complexes, concentric membranous bodies and confronting cisternae, were observed in the jejunal tumour after chemotherapy and were not found in the initial biopsy of the cervical lymph node. This suggests that they were produced as a result of chemotherapy, since ultrastructural modifications of the endoplasmic reticulum (such as whorl-like formations) have been reported to be induced occasionally by certain chemicals (Ghadially 1982; Goldblatt 1973; Hruban et al. 1972). Another interpretation of the membrane com-



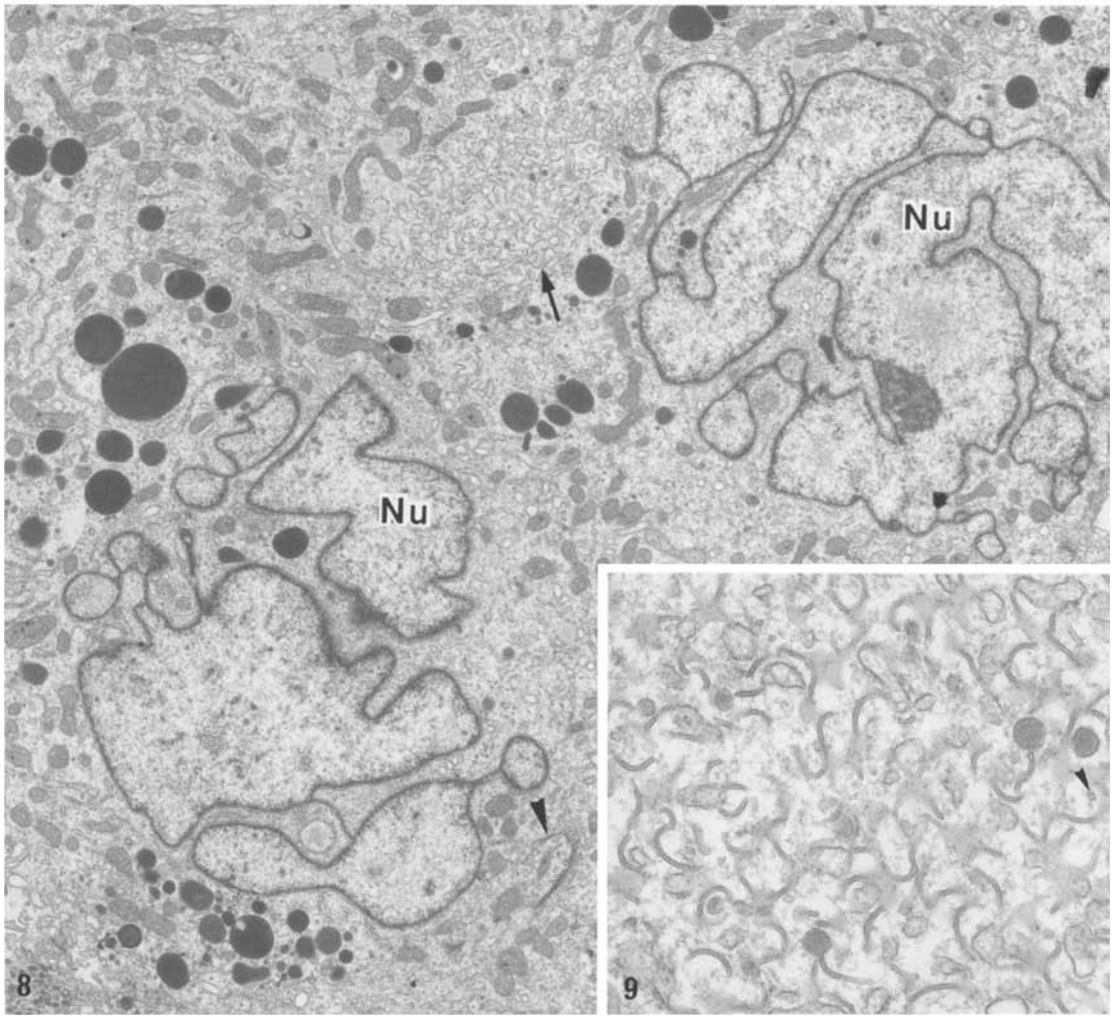


Fig. 6. The large body of the membrane complex in Fig. 3 at a higher magnification exhibits various images of a system of undulating membranes. The complex consists of paired membranes, spherical particles and dilated endoplasmic reticulum. Note continuity of the paired membranes with the endoplasmic reticulum (*arrowheads*). (× 27000)

Fig. 7. Higher magnification of the continuity of the paired membranes with the endoplasmic reticulum of Fig. 6. At the point of transition (*arrowhead*), the two apposing membranes of the endoplasmic reticulum converge abruptly. (72000)

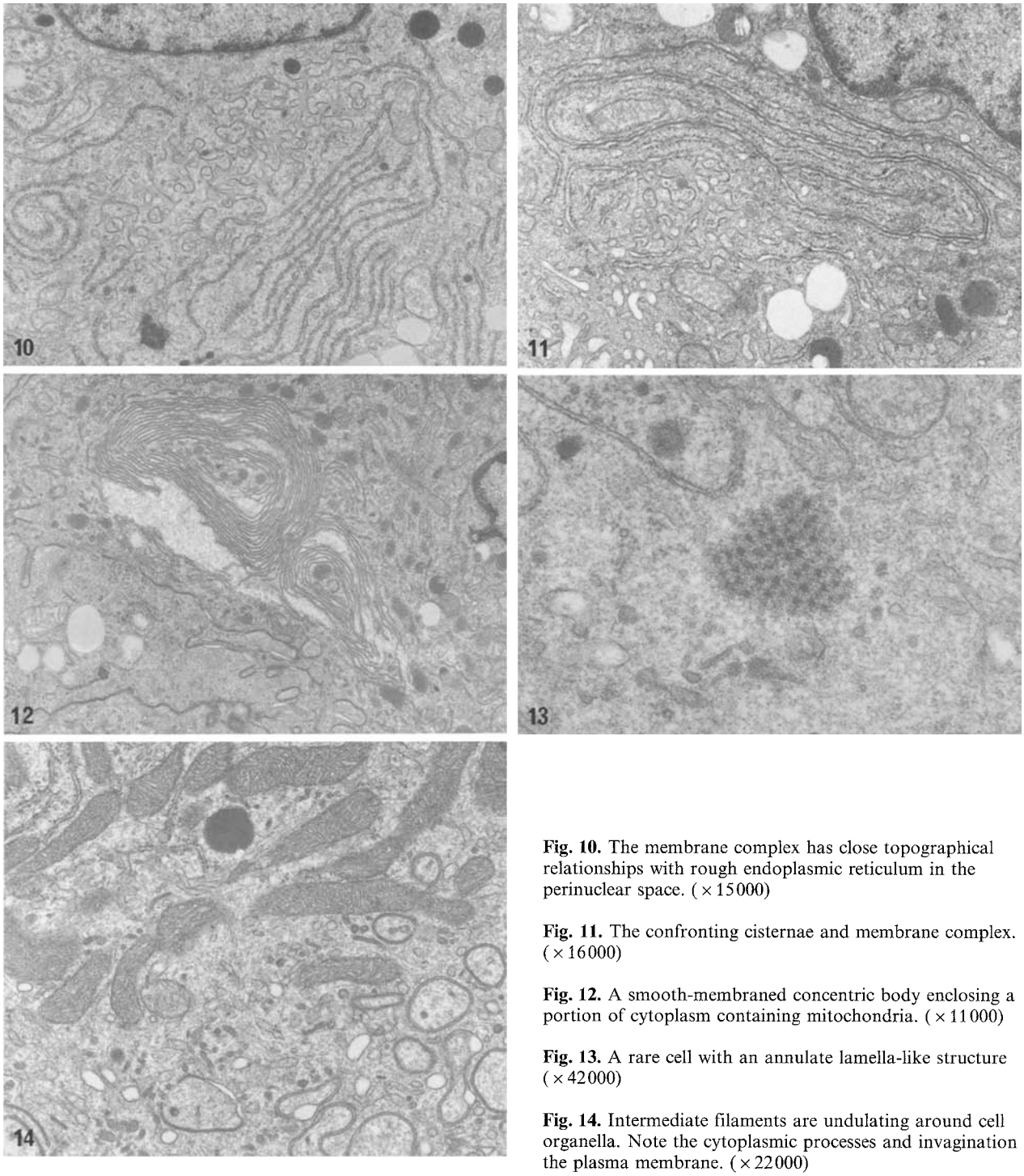


Fig. 10. The membrane complex has close topographical relationships with rough endoplasmic reticulum in the perinuclear space. (×15000)

Fig. 11. The confronting cisternae and membrane complex. (×16000)

Fig. 12. A smooth-membraned concentric body enclosing a portion of cytoplasm containing mitochondria. (×11000)

Fig. 13. A rare cell with an annulate lamella-like structure (×42000)

Fig. 14. Intermediate filaments are undulating around cell organella. Note the cytoplasmic processes and invagination of the plasma membrane. (×22000)

Fig. 8. This tumour cell appears to be multinucleated and contains the membrane complex (*arrow*) apart from the Golgi apparatus (*arrowhead*). Nucleus (Nu). (×8700)

Fig. 9. Higher magnification of the membrane complex of Fig. 8 demonstrating paired membranes and spherical particles. Circular profile (*arrowhead*) reveals the cross-section of a tubule. (×41000)

plexes is that they might reflect atypical or exaggerated growth and/or cellular proliferative states associated with tumour cells because, in this case, they were present only in neoplastic cells. Electron microscopy revealed prominent interdigitation and invagination of the plasma membrane, indicating enhanced membrane production corresponding to the enlarged surface area of the plasma membrane. In general, endoplasmic reticulum is involved in synthesizing membrane proteins and lipids for export to other parts of the cell, and plasma membrane receives both its proteins and lipids together in the form of small vesicles (Palade 1975; Wirtz 1974). Under normal conditions, membrane components are recycled by vesicle-mediated transport to maintain a steady-state distribution of membrane among the various cellular compartments (Palade 1975; Wirtz 1974). In this case, one might speculate that membrane complexes indicate exaggerated production of plasma membrane or an imbalance among the production, redistribution and consumption of plasma membrane. This speculation is supported by our observation that the membrane complexes were accompanied by coated vesicles and spherical particles.

Although a few papers have dealt with the fine structures of interdigitating cell sarcoma, the membrane complexes described here have not previously been reported (Chan and Zattari 1986; Feltkamp et al. 1981; Turner et al. 1984). Therefore, the present observation can not confirm whether or not these membrane complexes are pathognomonic of interdigitating cell sarcoma and are related to excessive production of plasma membranes. Further investigation is needed.

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