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Case Report

Nuclear Bodies in Liver Metastases of an Ileal Carcinoid

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Summary. The present paper describes the existence and the morphology of nuclear bodies in liver metastases of an ileal carcinoid, and their possible role is discussed. Although the patient presented a "flush syndrome", there were few secretory granules in the metastatic neoplastic cells. This fact is correlated with the light microscopic observation that only rarely did the cell of the metastatic carcinoid give a positive argentaffin reaction. This was in accordance with the observed pleomorphism of the carcinoid cells in the liver metastasis.

Zusammenfassung. Lichtoptische und elektronenoptische Beschreibung von 3 Kerneinschlüssen in der Lebermetastase eines Ileum-Carcinoids. Trotzdem der Patient Flush-Symptome aufwies, konnten in den Tumorzellen der Lebermetastasen nur wenige Sekretgranula nachgewiesen werden. Dies stimmt mit der Tatsache überein, daß Carcinoidmetastasen nur selten eine positive Silberreaktion geben.

Nuclear bodies are distinct intranuclear spherical structures. These peculiar bodies have been classified into five types on morphological grounds by Bouteille *et al.* (1967). They have never been reported in a malignant carcinoid or its metastases.

Materials and Methods

The ultrastructure of gastrointestinal carcinoids has been reported by a small number of authors (Black, 1968; Black *et al.*, 1968; Luse and Lacy, 1960; Schumacher and Schultz, 1963; Verley, 1965).

A metastatic nodule was obtained from the liver of a 16 year old white male readmitted with a "flushing syndrome", who four years previously had been submitted to an operation due to an ileal carcinoid. Part of a metastatic nodule was embedded in paraffin and stained in hematoxyline and eosine and according to Fontana's method to demonstrate argentaffin granules. The remaining nodule was double fixed in glutaraldehyde 1,6 or 6% and osmium tetroxide 1% and embedded in Epon 812 (Luft, 1961) or fixed only in glutaraldehyde 1,5% and embedded in Glycol methacrylate (Leduc and Bernhard, 1967). They were stained according to Reynolds (1963).

Results

Light Microscopy of the Metastatic Nodule. This was essentially similar, although more cellular and more pleomorphic to the primary tumor. The argentaffin granules were rare (Fig. 1).

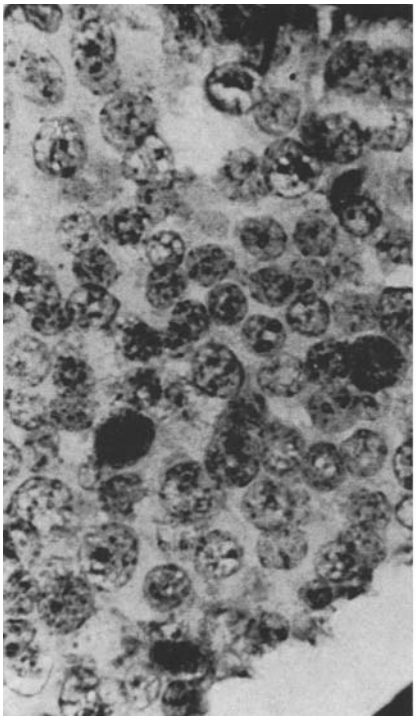

Fig. 1

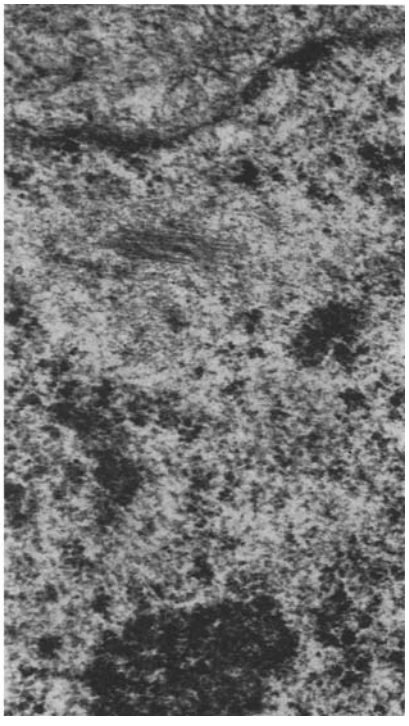

Fig. 2

Fig. 1. The metastatic nodule, argentaffin reaction. Only three cells in the field show argentaffinity. × 750

Fig. 2. Peculiar nuclear inclusion consisting of parallel microtubules. This type of nuclear inclusion has been so far described only in nervous tissue cells. ×20000

Electron Microscopy. The size and shape of the cells varied considerably. Their nuclei were lobulated. The chromatin was condensed under the nuclear membrane or in clumps. The nuclear bodies appeared as spherical masses of amorphous or fibrillar material (type I) or as spiral structures with or without granules (type II or III), well demarcated from the surrounding nucleoplasm and surrounded by a clear halo (Fig. 4). Types IV or V were never observed. Sometimes clumps of chromatin were attached at the periphery of the nuclear body. In glycol methacrylate embedded material the halo was missing or was very limited. Up to four nuclear bodies were found in a single nucleus. When multiple they were of different types. They were composed of two concentric granular leaflets (Fig. 3). Very rarely a peculiar intranuclear inclusion was noted, namely microtubules running parallel to each other (Fig. 2). The secretory granules were seen only in some of the cells, they were generally few (Fig. 4). There was no relation between the number of the secretory granules and the presence or the number of nuclear bodies.

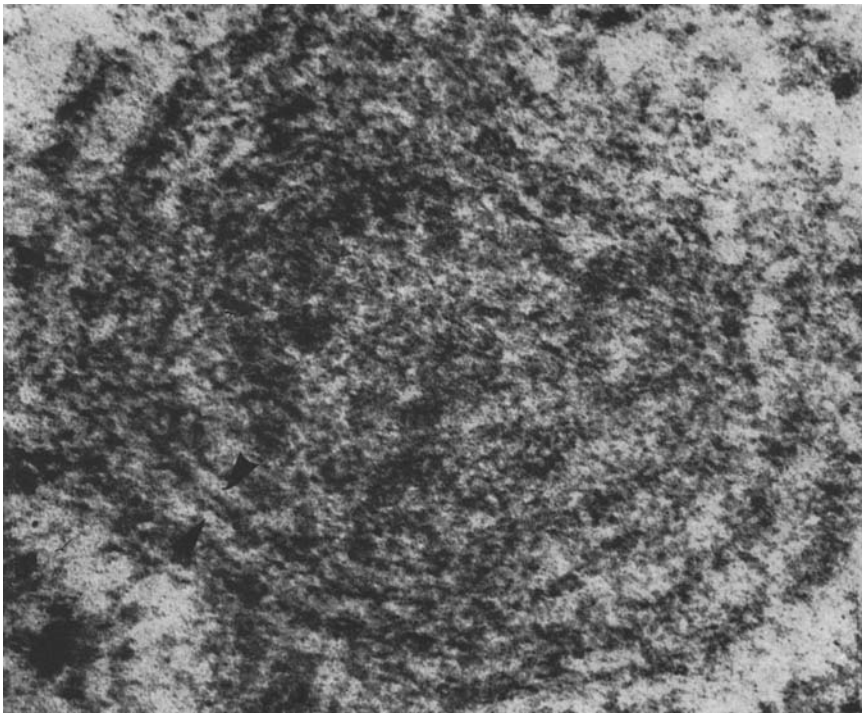

Fig. 3. Nuclear body at high magnification. The two leaflet structure is apparent at the arrows. ×180000

Discussion

Nuclear bodies are peculiar spherical intranuclear structures ranging in size from 0,5 to 1,8 microns. They have been described, among others, by Bouteille *et al.* (1967) who classified them according to their structure and size to five types: Type I is a spherical structurless or fibrillar body 0,5 microns in diameter. Type II is 0,8 microns in diameter composed of concentric fibrils in an onion like configuration. Type III is also 0,8 microns in diameter but with a center occupied by osmiophilic granules surrounded by a fibrillar cortex. Type IV is large up to 1,8 microns, resembling in structure nuclear bodies type III. Type V is composed of a fibrillar cortex surrounding small globules. These types seem to be according to Kierszenbaum (1969) morphological variations.

Nuclear bodies have been described in normal or deseased tissues and in animal tumors including human (Bouteille *et al.*, 1967; Kierszenbaum, 1969; Krishan *et al.*, 1967; Popoff and Stuart, 1968). A peculiar type of fibrilar intranuclear body has been described in nervous tissues (Hirano and Zimmerman, 1967; Popoff and Stuart, 1968, Seite, 1970).

Nuclear bodies have been recorded in numerous tissues under a great variety of conditions making it impossible to correlate them with any one condition in

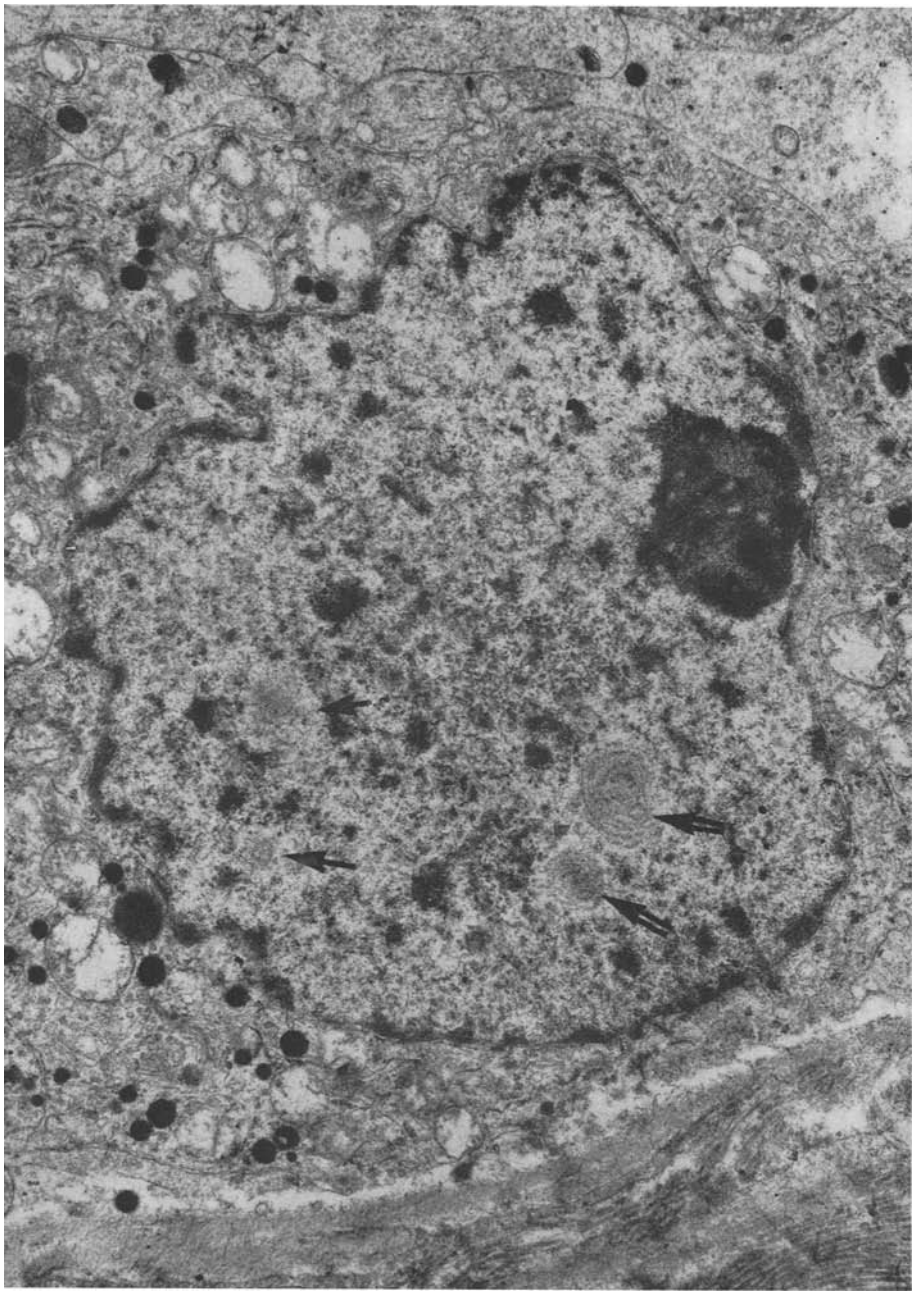

Fig. 4. Cell with four nuclear bodies: type I (single arrow) and type II (double arrow). A clear halo surrounds the nuclear bodies. There are few round, deep black secretory granules. ×10000

particular. Some authors believe that they reflect cellular hyperactivity (Bouteille *et al.*, 1967) and others an "altered" or "special metabolic state of the nucleus" (Krishan *et al.*, 1967). In our material the nuclear bodies observed had no relation to the secretory activity of the cell; in fact many of the cells without secretory granules or with very few of them had multiple nuclear bodies (Fig. 4).

Very few cells showed in light microscopy the argentaffin reaction (Fig. 1). This was confirmed by electron microscopy where cells with an appreciable number of secretory granules were rare. This paucity of secretory granules according to Sokoloff (1968) should indicate immature cells. If we assume that secretory granules reflect cellular activity, then these cells should contain nuclear bodies if the hyperactivity theory of Bouteille *et al.* (1967) were correct, unless the presence of secretory granules within the cytoplasm does not indicate an hyperactive state but rather a storage phenomenon.

Concidering the polymorphism of the cells in the liver metastases of this ileal carcinoid, in contrast to the other carcinoids described (Black, 1968; Black *et al.*, 1968; Luse and Lacy, 1960; Schumacher and Schultz, 1963; Verley, 1965), we are tempted to agree with Krisham *et al.* (1967) that the nuclear bodies are due to an altered or special metabolic state of the nucleus.

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