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Meningeal Granulocytic Sarcoma Without Evidence of Leukemia

Light and Ultrastuctural Study of One Case

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Summary. An unusual case of meningeal granulocytic sarcoma without evidence of Leukemia is presented. The patient, a 40 year old female, presented with a chronic subdural haematoma. Three months later a large meningeal tumor was discovered adjacent to the previous haematoma and was found to be a granulocytic sarcoma by the use of electron microscopy.

The tumor was treated by surgical excision followed by radiotherapy and chemotherapy. The patient remains free of symptoms and without evidence of leukemia in the peripheral blood or bone marrow 9 months after the diagnosis was established.

The ultrastructural findings in the tumor and diagnostic difficulties often encountered are emphasized.

Key words: Granulocytic sarcoma – Chloroma – Meningeal sarcoma – Ultrastructure – Myelogenous leukemia

Introduction

Granulocytic sarcoma (GS) usually presents as a rapidly enlarging tumor mass. It is composed of immature cells of the myelogenous series, occurring in extramedullary sites (Rappaport 1966). Other synonyms for this tumor are: Chloroma, due to its frequent greenish appearance, myeloblastoma (Comings et al. 1965) and myeloid sarcoma (Fayemi et al. 1973).

GS are reported in 3 to 7% of the myelocytic and myelomonocytic leukemias and generally appear in the course of or simultaneously with the leukemic process (Krause 1979; Liu et al. 1973; Muss et al. 1973). Although far less numerous, some well documented cases of GS have been reported which preceed

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the leukemic picture by months or years (Mason et al. 1973; Seo et al. 1977). These cases often present serious diagnostic problems to the surgical pathologist and are frequently misdiagnosed as reticulum cell sarcoma, eosinophillic granuloma and other entities (Zimmerman and Font 1975).

Electron microscopic (EM) examination makes the diagnosis obvious by demonstrating the granulocytic nature of the cells. However, there are few reports in the literature with ultrastructural findings (Brugo et al. 1977; Carmichael et al. 1977; McCarty et al. 1980; Mason et al. 1973).

This report describes in detail the light microscopic and ultrastructural findings on a case of a single, intracranial meningeal tumor that developed into a large subdural mass over a period of 3 months. The patient had no evidence of leukemia in the peripheral blood or bone marrow at the time of the initial diagnosis or up to the present.

Clinical History

A 40 year old white female was admitted to hospital in March 1980 with 6 months history of personality changes, gait disturbances and temporo-parietal haedaches of increasing intensity. There was no history of cranial injury.

Physical and laboratory examinations were within normal limits except for the EEG and Computed Tomographic (CT) studies that disclosed a chronic subdural haematoma in the left temporo-parietal region. This was drained and no evidence of tumor was observed by the surgeon. The patient improved and remained asymptomatic until early June 1980 when she was readmitted to the hospital in coma. Laboratory data at this time revealed a haemoglobin of 8g/dl, haematocrit 27%, WBC 4100 with 47% neutrophils, 2% bands, 46% lymphocytes, 4% monocytes and 1% eosinophils. Urinalysis and serum biochemistry were within normal limits.

Sternal bone marrow was normocellular with 73% of normal granulocytic cells, 24% erytrocytic and 3% lymphoplasmocytic elements. Iliac crest bone marrow biopsy was also within normal limits.

Repeated CT scan and angiographic studies revealed a mass in the left fronto-temporal region arising in the meninges obtaining its blood supply from the meningeal arteries and situated anteriorly to the previously drained haematoma. The bone overlying the tumor was not involved. Through the previous temporo-parietal craniotomy a small biopsy of the mass was taken and initially interpreted as a reticulum cell sarcoma-microglioma (Rubinstein 1972).

A few days later a new left fronto-temporal craniotomy was done and a large, lobulated tumor mass was found arising in the Duramater and growing subdurally, displacing but not invading the brain parenchyma. An excisional biopsy was taken and following the pathological diagnosis of GS the patient was treated by external radiation to the head (2000 rads) and a chemotherapeutic regimen consisting of Cytosine Arabinoside and Duxorobicin. Repeated examinations of the peripheral blood and bone marrow has not shown evidence of leukemia and the patient remains asymptomatic 9 months after the diagnosis.

Materials and Methods

Both biopsies were fixed in 4% buffered formaldehyde. From the second biopsy smears were taken fresh and fixed in 95% Methanol. Standard histopathological and cytological techniques were done including Giemsa stain and Leder's chloroacetate esterase. Several 1 mm. cubes were fixed on iced 3% buffered glutaraldehyde, postfixed in OsO_4 embedded in Epon, stained with Lead Citrate and Uranyl Acetate and examined with a Phillips 301 EM.

Pathological Findings

Gross Findings. Several fragments of firm, somewhat lobulated tissue with a greenish-pinkish hue were received, measuring altogether $5 \times 5 \times 1.5$ cm.

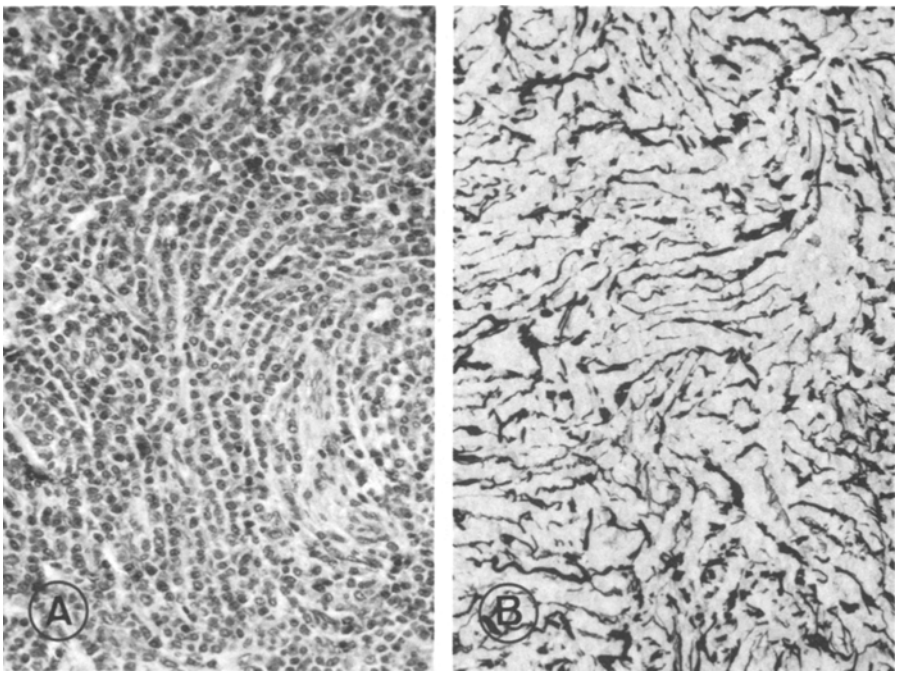

Fig. 1A, B. Uniform tumor cells with round nuclei arranged in a trabecular pattern. **A** HE; **B** Reticulin stain (Obj. 16)

Histological Findings. Both biopsies showed similar features. The tumor was composed of compact sheets of uniform cells with round, oval or somewhat irregular nuclei, some of them bearing inconspicous nucleoli (Figs. 1A, 2A). The cytoplasm was moderately abundant, eosinophillic and granular in many cells. Others with empty looking clear cytoplasm and dense nuclei were seen in some areas (Fig. 2C). Giemsa stain in the sections failed to demostrate cytoplasmic granules. A trabecular, somewhat whorled, pattern was observed in many parts with the cells separated by thin connective tissue septae, clearly shown by the reticulin stains (Fig. 1B). The cells in the smears showed numerous cytoplasmic azurophillic granules with the Giemsa stain (Fig. 2B) but failed to stain with the Leder's chloroacetate esterase technique.

Electron Microscopic Findings. All cells in the numerous grids studied showed numerous lysosomal granules. Most cells had round or ovoid nuclei but nuclear irregularities were common (Fig. 2D). Kidney shaped nuclei, deep clefts and occasional multisegmented nuclei were also observed. Some of the cells had small nuclear appendages and delicate nuclear bridges. One or two central or peripheral nucleoli were seen in many more cells than was appreciated by light microscopy.

The lysosomal granules were round or ovoid and often arranged in small groups near the nucleus and in rows adjacent to the cytoplasmic membrane. Some of these granules showed degenerative changes. Occassionally large granules were observed but no typical Auer rods were identified.

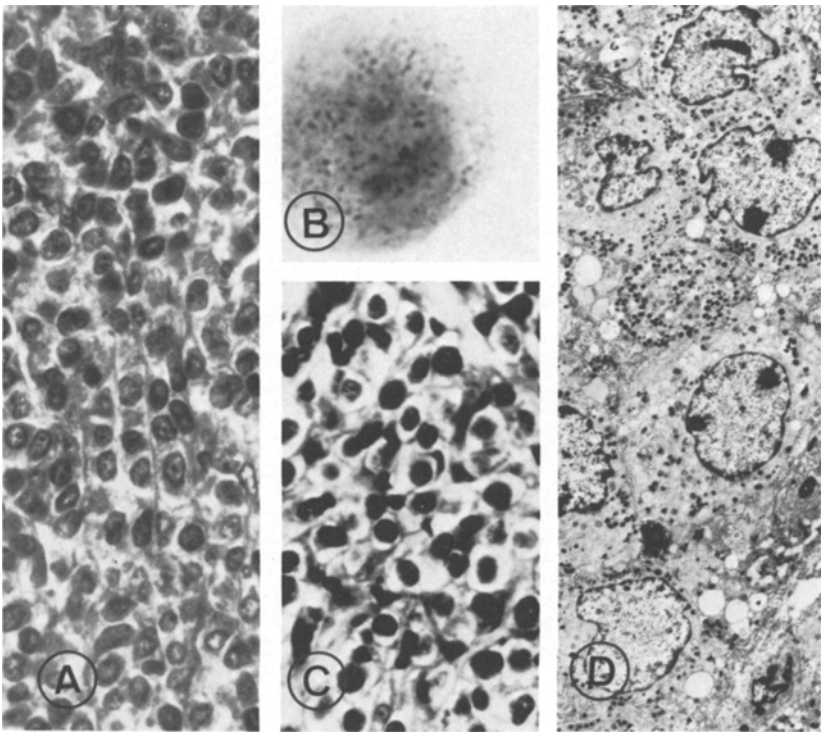

Fig. 2.A Tumor cells with round or ovoid nuclei and granular eosinophillic cytoplasm (HE Obj. 25). **B** Smear of tumor cells with numerous cytoplasmic azurophillic granules (Giemsa Obj. 100). **C** Cells with empty looking cytoplasm and dense nuclei. (HE Obj. 25). **D** Cells with round irregular nuclei, small nucleoli and numerous lysosomal granules (H.M. $\times 1{,}800$)

The number of granules seemed to bear no relation with the maturiry of the nucleus. The Mitochondria were abundant and normal in size and shape and often polarized near the nucleus. Some of the cells contained dilated cisternae of Endoplasmic Reticulum filled with granular material while in others parallel arrays of Rough Endoplasmic Reticulum were prominent.

The cytoplasmic membranes had smooth contours without specialized unions. Fragments of cytoplasm with or without granules and isolated lysosomal granules were often seen detached from the cells and admixed with the connective tissue fibers.

Discussion

GS are reported in 3–7% of surgical and autopsy series of patients with acute or chronic myelocytic leukemias, without a significant difference between the acute and the chronic forms (Krause 1979; Liu et al. 1973; Muss et al. 1973).

The tumors mainly affect children with a peak incidence at 5 to 7 years of age. The most common form of clinical presentation is that of unilateral proptosis due to a retro-orbital tumor mass (Zimmerman and Font 1975). Other

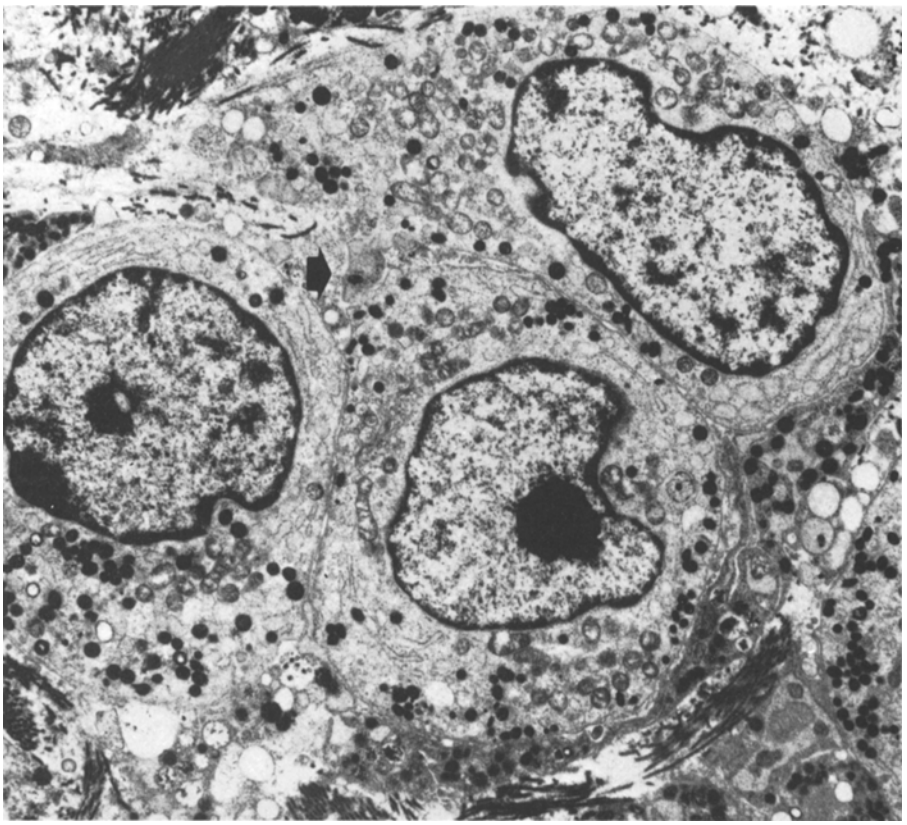

Fig. 3. Cells with round or ovoid irregular nuclei, abundant lysosomal granules, polarized mitochondria and moderately abundant rough endoplasmic reticulum. Cytoplasmic membranes with smooth contour. Fragments of cytoplasm (*arrow*) and isolated granules appear detached from the cells. (E.M. ×4,300)

frequent location include the subperiosteal regions of vertebrae, sternum, ribs, pelvis and femur (Liu et al. 1973; Rappaport 1966; Zimmerman and Font 1975). Less frequently they appear in the ovaries (Chorlton et al. 1974) breasts (Wiernik et al. 1970; Krause 1979), gastrointestinal tract (Brugo et al. 1975), scalp (Comings et al. 1965) and cervix (Seo et al. 1977).

Central nervous system (CNS) involvement in acute myelocytic leukemia is not uncommon with approximately 20% of the patients having microscopical meningeal involvement at the time of presentation (Meyer et al. 1980). Tumoral involvement of the meninges, particularly in the paraspinal regions, is also described in a significant number of patients with multiple GS in the course of leukemia (Liu et al. 1973; Rappaport 1966). Intracranial GS preceding leukemia, however, are most uncommon (Hurwitz et al. 1970; Ragins et al. 1950; Sowers et al. 1979). The clinical manifestations of these tumors are those of a space occupying lesion. Invasion of the underlying brain in GS of the CNS is exceptional (Sowers et al. 1979) and was not present in our case.

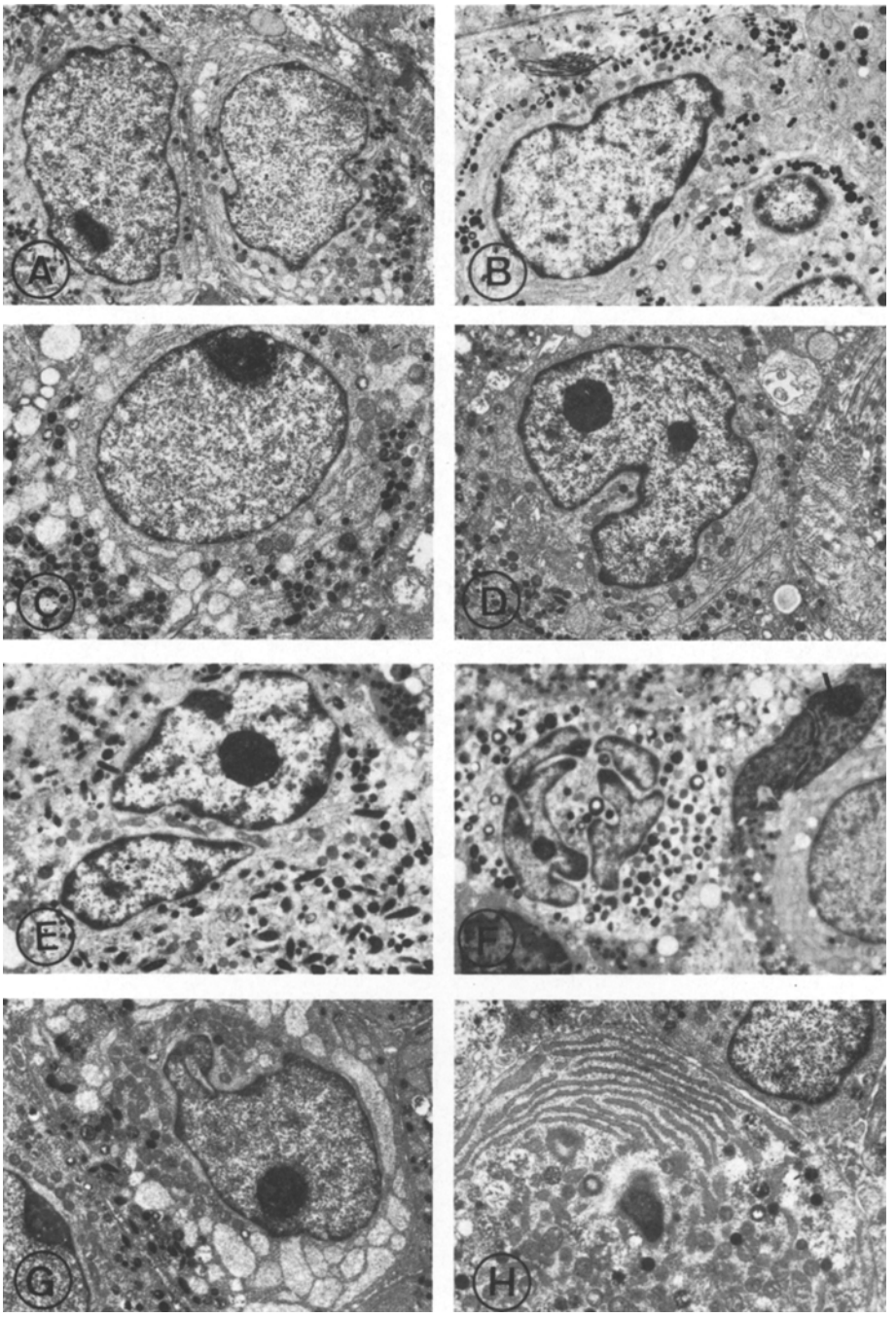

Fig. 4A–H. (E.M. ×3,400). Detailed nuclear and cytoplasmic appearance of the different types of cells. **A** Primitive nucleus and granules in small groups. **B** Ovoid nucleus and peripheral granules adjacent to cytoplasmic membrane. **C** Primitive nucleus with prominent nucleolus and numerous granules. **D** Cell with kidney shaped nucleus and nucleolus. **E** Bilobed nucleus and numerous fusiform granules. **F** Multisegmented and elongated nuclei. **G** Cell with abundant distended endoplasmic reticulum. Nuclear appendage and thin bridge. **H** Parallel arrays of rough endoplasmic reticulum

Although there is no documentation we feel that the subdural haematoma that initiated this patient's symptoms might have been in relation to the presence of a small focus of tumor not visualized at the time of the surgical procedure (histological examination of the haematoma was not performed).

The overal prognosis in GS is similar to that of the accompanying leukemic process. From the different therapeutic approaches it appears that external radiotherapy is the most effective with complete, although short lived, remissions (Brugo et al. 1975; Comings et al. 1965; Wiernik et al. 1970). When the GS precede the leukemia and appear in uncommon locations, as in our case, they are often misdiagnosed, even by experienced pathologists. The green color that they often present may be absent or may dissappear on exposure to air.

Giemsa stains and specific esterase techniques in tissue sections may not reveal the granulocytic nature of the tumor (McCarty et al. 1980; Zimmerman and Font 1975).

Reticulum cell sarcoma or histiocytic lymphoma is the most frequent misdiagnosis. Eosinophillic granuloma, undifferenciated sarcoma, Ewing's sarcoma, neuroblastoma, non-secretory myeloma and atypical carcinoid are some other alternative diagnosis collected from the literature (Brugo et al. 1977; Carmichael et al. 1977; Washburn and Dittes 1962; Zimmerman and Font 1975). To these we would add oligodendroglioma, a diagnosis bassed on the histological ap pearance of some areas of the tumor.

EM examination is the definitive study in the diagnosis of these tumors. In our case the granulocytic nature of the tumor cells was clearly demonstrated and marked asynchrony between the maturation of the nucleus and of the cytoplasm and cytoplasmic organelles was prominent. The appearance of tumor cells is basically similar to that of the cells of acute mielogenous leukemia (Bessis 1972)

It is likely, as previously pointed out by some authors (Laszlo and Grode 1967; Mason et al. 1973) that some cases diagnosed as histiocytic lymphomas, particularly when they develop in the course of leukemias, may be GS.

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