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Intracranial Granulocytic Sarcoma (Chloroma) in a Nonleukemic Patient

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Chloroma is a granulocytic sarcoma with it's characteristic greenish color. Recently there is an increased number of cases that are apparently aleukemic when the tumor mass is first presented. Recently we experienced a case of granulocytic sarcoma with characteristic green color (chloroma), which showed no evidence of leukemia in the bone marrow and peripheral blood. This patient presented headache, and was diagnosed brain tumor on computed tomography. A left parietal cranietomy was done to remove a large central dome-like mass, 8cm, involving the dura with a slightly dusky greenish solid appearance. Compact nests of moderately mature granulocytes and immature cells comprised the tumor. Histochemical and electron microscopic studies confirmed these tumor cells as myeloid cells in varying stages of maturation. Several days after the operation, left cervical lymph nodes became palpated, and the biopsied lymph nodes revealed same neoplastic cells seen in the skull. However, bone marrow aspiration, biopsy and peripheral blood smears did not show any evidence of leukemia.

Key Words: *Chloroma, granulocytic sarcoma, acute myelogenous leukemia.*

INTRODUCTION

Granulocytic sarcoma (chloroma) is a localized tumor composed of immature cells of the granulocytic series, infiltrating any site of the body. It was first reported by Burns in 1811.

Because of their unusual greenish color which fades on exposure to air, the term "chloroma" was designated by King in 1853. This fading greenish color of these tumors has been known to be due to the presence of myeloperoxidase (verdoperoxidase) in the tumor cells (Agner, 1941). However, Rappaport (1966) suggested to use the term "granulocytic sarcoma" rather than chloroma, because these tumors frequently have no distinct green color.

Till 1893 by Dock, it was not recognized that the granulocytic sarcoma is associated with acute leukemia. Since that time, most reported cases of granulocytic sarcoma have been related to the patients with obvious acute myelogenous leukemia, chronic myelogenous leukemia or other myeloproliferative disorders in impending blast crisis (Longo et al., 1978; Ellman et al., 1979; Morgan et al., 1981). A few case reports of granulocytic sarcomas occurring

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in patients who exhibit none of the peripheral blood or bone marrow manifestations of acute leukemia or other blood dyscrasia have been presented after the paper by Comings et al. in 1965. It has been generally believed that the ultimate development of acute myelogenous leukemia is the rule in these patients. The interval from the initial diagnosis of granulocytic sarcoma to the development of acute leukemia has been variable, ranging from one week (Meis et al., 1986) to 49 months (Neiman et al., 1981). But recently there are cases that treated as acute leukemia have not manifested into systemic leukemia for 3.5 to 16 years (Beck et al., 1984; Meis et al., 1986).

This report describes a case of Korean girl who developed an intracranial chloroma without manifestation of leukemia or other blood dyscrasia, and has not developed leukemia during the subsequent 6 months after the diagnosis.

CASE REPORT

This 16 year old high school girl suffered from left parietal headache since October, 1986. She had been healthy till that time. The headache was intermittent and associated with progressive bilateral visual dimness. In early January, 1987, she visited Yang Chin Hoe Hospital, Seong Nam City, where brain CT was checked and found abnormal. She was transferred to Seoul National University Hospital on January 15, 1987.

Physical examination revealed normal physique and nutrition with good memory and insight. The vital and neurologic signs were not remarkable. Organomegaly or lymphadenopathy was not detectable, but bilateral papilledema with increased blind spots was identified. Repeated brain CT exhibited a large hypervascular mass (Fig. 1), with multiple radiopaque densities in the left high parietal area, suggestive of osteogenic sarcoma. The chest x-ray was negative. The laboratory results were hemoglobin 12.5gm/dl, WBC 6,000/mm^3 (Stab 3%, seg 57%, lymph 33%, mono 7%), platelet $274\times10^3/mm^3$, and ESR 2mm/hr. Other studies including of urine, stool, coagulation study and liver function tests were normal, except slightly increased serum alkaline phosphatase (200 IU/L).

On January 26, 1987, craniectomy was done, and a well circumscribed dark greenish dome-like mass, measuring 8cm in the diameter of base and 4cm in height (Fig.2) was removed. It penetrated the attached dura mater and tightly adhered to the inner surface of removed calvarium. The cut surface of the mass

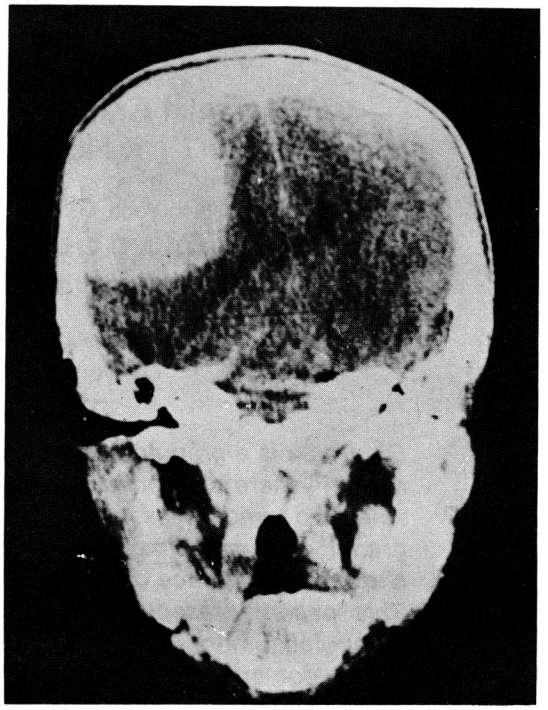

Fig. 1. Brain C-T scan shows a large well demarcated intracranial mass in the left parietal area.

also showed relatively homogeneously dark green color without necrosis. The attached calvarial bony cortex and medulla were infiltrated by the greenish neoplastic tissue and showed sunburst appearance on X-ray film (Fig. 3). The overlying outer periosteum, measuring 7.5×7cm in surface dimension, was also involved. The color faded only slightly on exposure to air during the procedure, but light green color was maintained in the formalin solution. Giemsa stain of touch prints of the tumor showed immature granulocytes, mainly myelocytes and promyelocytes with reniform or ovoid nuclei and plump eosinophilic or amphophilic cytoplasm. The ovoid nuclei revealed more delicate and fine hromatin pattern with suggestive nucleoli. Some of the granules in the cytoplasm were coarse and azurophilic, and occasionally Auer rods were seen (Fig. 4). The H&E stain of the mass after formalin fixation exhibited the same characteristics of the Giemsa preparation and showed individual cell necrosis (apoptosis), with preservation of the architecture without tumor necrosis. Macrophages, containing brownish tan or eosinophilic granules, resembling large eosinophils, were scattered (Fig. 5). Mitotic figures were infrequent,

Fig. 2. A dome-shaped chloroma showing characteristic greenish hue on cut surface. (Upper margin of this mass was continuous to the dura mater and overlying skull bone).

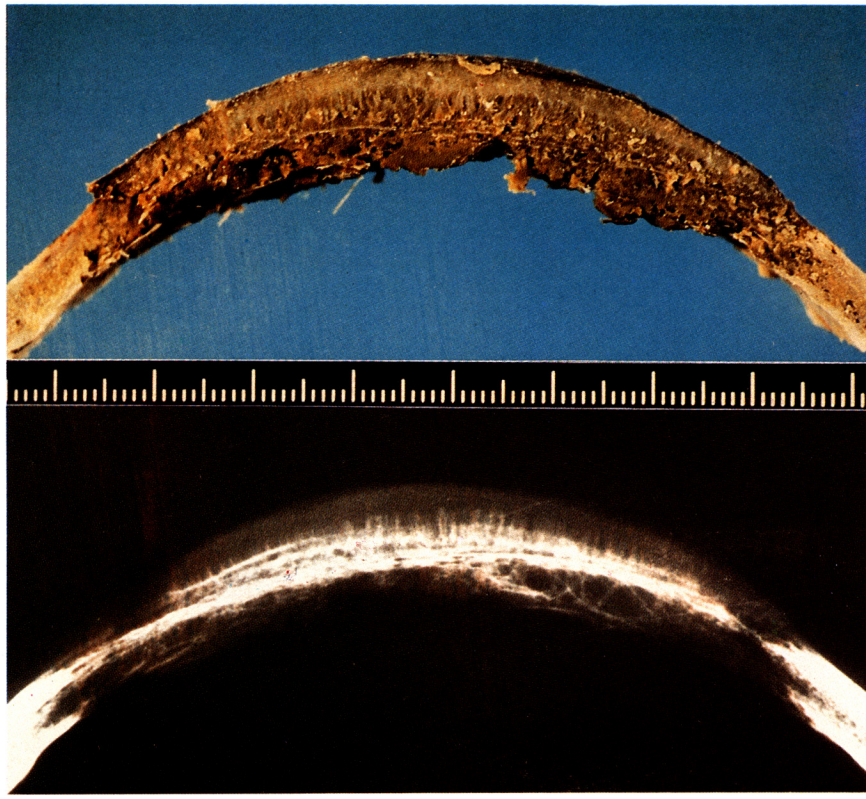

Fig. 3. (upper) Cross section of the involved calvarium exhibiting greenish tumor mass with involvement of entire marrow cavity and tables. (lower) Sunburst-like appearance in the x-ray film.

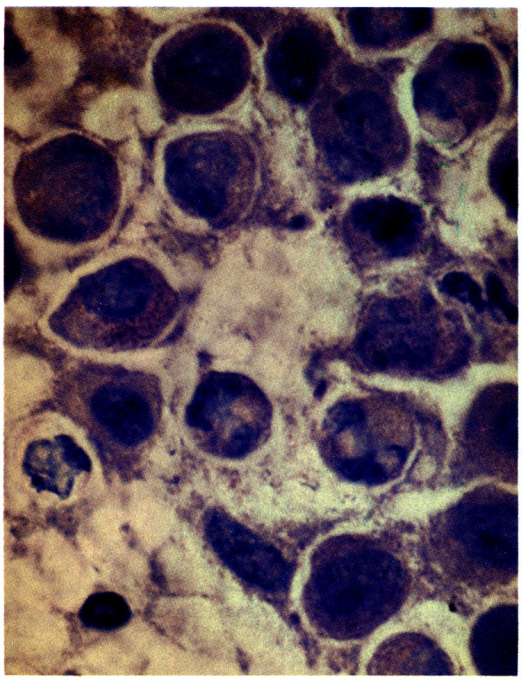

Fig. 4. Touch print of chloroma, showing myelocytes and promyelocyte with azurophilic granules and suspicious Auer rod. (Giemsa stain x1,000).

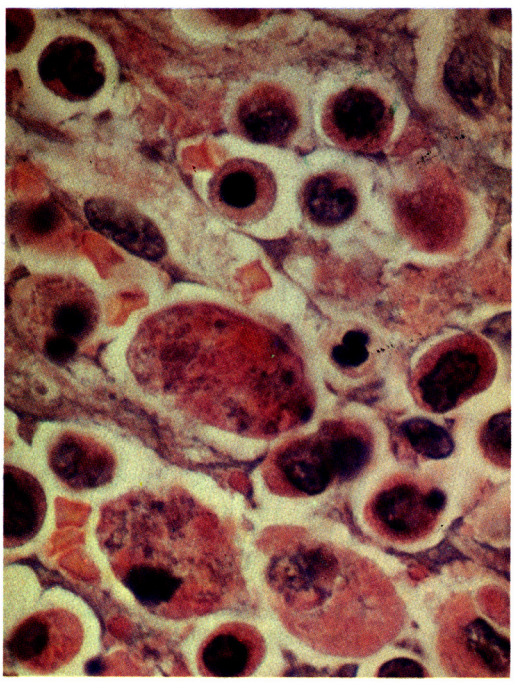

Fig. 5. Photomicrograph of chloroma, showing immature granulocytes and macrophages with tingible eosinophilic granules. (H & E x1,000).

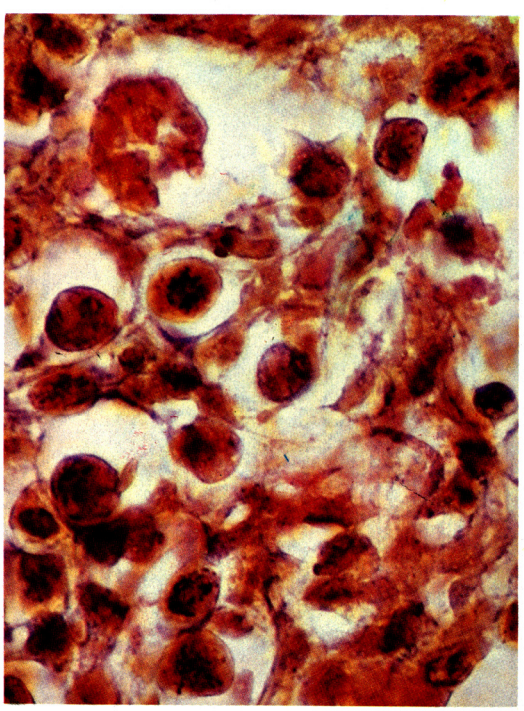

Fig. 6. Naphthol AS-D chloroacetate esterase stain of the chloroma section, showing positive reddish to darkish granules in most cells (X1,000).

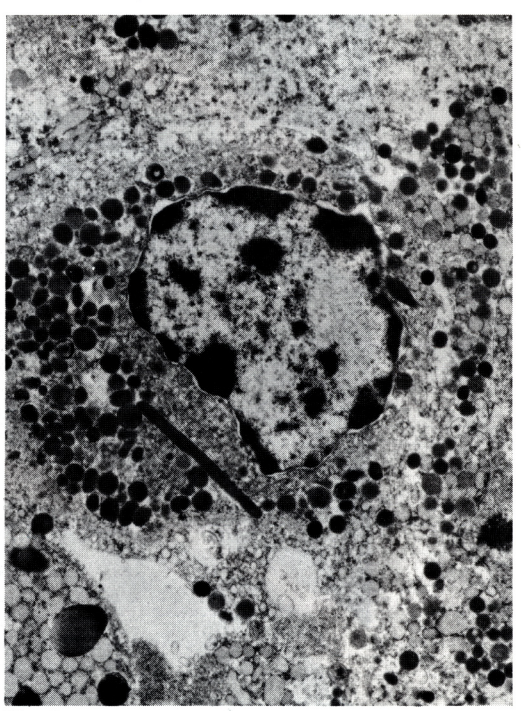

Fig. 7. Electron micrograph of a promyelocytic tumor cells, revealing an Auer rod (3.60x0.27 μm) and numerous granules. (TEM x6,000).

suggestive of group III, well differentiated pattern, classified by Meis et al. (1986), although eosinophils in myelocytic or segmented form were hardly observable. To confirm these immature granulocytes to be myelogenous origin, naphthol AS-D chloroacetate esterase (Fig. 6) and antilysozyme immunoperoxidase stains were performed. Both stains disclosed positive granules in over 90% of neoplastic cells. In the former, reddish brown to darkish, and in the latter, yellowish brown color was noted in the cytoplasm. Electron micrographs of the formalin fixed tissue was processed. Most cells contained many primary and secondary granules in the cytoplasm, indicating intermediate stages of neutrophils. The size of primary granules ranged from 0.17 to 0.50μm, with the mean of 0.31μm, and that of secondary was 0.18 to 0.59μm, with the mean of 0.33μm, respectively. In a suspective promyelocyte by nuclear figure, the Auer rod (3.6x0.27μm) was identified (Fig. 7).

Immediately after the surgery and the histopathologic diagnosis, bone marrow study was done, showing M:E ratio of 3.5:1, myeloblast (2.0%), and promyelocyte (1.8%) in the background of normocellularity (50-70%). No evidence of granulocytic leukemia was present.

One week after the operation it was found that a few neck lymph nodes were swollen and the nodes were biopsied. The nodes revealed chloroma cells packed in paracortical areas and medullary cords. These cells were positive for anti-lysozyme immuno peroxiodase stain.

After 24 days of the operation, 4,500 rads were given to the operated left parietal area and ipsilateral neck, respectively. And the patient is well until the time of report.

DISCUSSION

The most frequently involved site of the granulocytic sarcoma was described to be the soft tissue surrounding bone as in this case, by Neiman et al. (1981) among 61 biopsied cases and by Liu et al. (1973) among 23 autopsied cases with myelogenous leukemia. But Meis et al. (1986) reported involvement of skin and subcutis in 16 patients without evidence of leukemia. The age range was 2 to 81 years (mean 48 years) (Neiman et al., 1981).

The first report of granulocytic sarcoma in Korea was made by Park et al. (1980), describing a tumor involving the uterine cervix before the manifestation of overt leukemia in a 36 years old woman. The uterine tumor was initially believed to be histiocytic lymphoma with the punch-biopsied material, but the subsequently removed uterus revealed infiltration by poorly differentiated round cells in the cervical portion, which was confirmed to be granulocytic sarcoma by naphthol AS-D chloroacetate esterase stain. Two weeks after the hysterectomy, signs of acute myeloblastic leukemia developed in the peripheral blood and bone marrow. No other report on granulocytic sarcoma without leukemia could be searched in Korean literature.

The diagnosis of granulocytic sarcoma is not difficult when the tumor is grossly green or shows relatively well differentated granulocytes in touch prints. However, it can be confused with other diagnoses in many cases (Neiman et al., 1981; Meis et al., 1986), such as malignant lymphoma of large cell type, Burkitt's lymphoma, Ewing's tumor or eosinophilic granuloma (Wiernik and Serpick, 1970; Ersbøll et al., 1980).

The accompaniment of eosinophils infiltration may be helpful in differential diagnosis. Meis et al. (1986) found in those 16 cases that the infiltrating frequency of eosinophilic myelocytes generally paralleled the degree of granulocytic maturation. However, present case showed no eosinophils. Therefore naphthol AS-D chloroacetate esterase and the immunohistochemical stain of anti-lysozyme were crucial for the confirmation of the diagnosis. Electron microscopic study is often required for the diagnosis and to identify the exact degree of main cell maturity, because the myelogenous granulocytes have specific respective granules in the development of 3 stages (Scott and Horn, 1970). Electron microscopic findings of this case are generally compatible with the descriptions of Scott and Horn (1970) except that the secondary granules were slightly smaller than those of theirs.

As of management, in non-leukemic granulocytic sarcoma like this case, aggressive management as in the acute leukemia is advocated for the prevention of leukemic manifestation, using irradiation for the local lesion or combined chemotherapy (Wiernik and Serpick, 1970; Conran et al., 1982; Beck et al., 1984; Meis et al., 1986). Ersbøll et al. (1980) asserted that, as the sarcoma is very sensitive to irradiation, 1,000 to 2,000 rads seem to be sufficient for inducing local remission, in addition to the combination chemotherapy. And Conran et al. (1982) introduced that the harvest and store of patient own leukemia-free marrow should be available for rescue in the preceded granulocytic sarcoma.

It is evident that the green color produced in the

chloroma is due to the myeloperoxidase, by the experimental evidence in the rats (Schultz, 1958; Ioachim et al., 1972). But the reason why some of the tumors possess the green color and others do not is questionable. For the explanation, Duttera et al. (1972) proposed the amount of the enzyme present. Schultz (1958) verified that the content of myeloperoxidase in rat chloroma cells is three times as high. Muss and Moloney (1973) suggested the oxidation state of the enzyme in addition to the amount is important. Ioachim et al. (1972) inferred spontaneous mutation in their experimental rat chloroma, but they observed that the white tumor occurred spontaneously during the successive transplantations of the chloroma did not differ microscopically from the chloroma line. The peroxidase activity is known to be present in the primary and secondary granules (Yamada, 1966; Scott and Horn, 1970). Even to the presence of the evident green color and the granules identified by electron microscopy in our case, we failed to demonstrate peroxidases in the tumor cells with the formalin-fixed tissue by the blood smear method (o-tolidine & H_2O_2 method). With the formalin-fixed tissue, the verification might be impossible due to the oxidation state or to other causes. It seems very important to procure touch prints of fresh tumor or frozen section for this purpose.

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