Granulocytic Sarcoma of the Uterine Cervix Preceding Myelogenous Leukemia

Chan Il Park, Tae Seung Kim and Yoo Bock Lee

Department of Pathology, Yonsei University College of Medicine, Seoul, Korea

A case of granulocytic sarcoma involving the uterine cervix as the primary manifestation, before the peripheral blood and bone marrow showed evidences of overt leukemia, is presented. Six weeks after the onset of the genital tract symptom the patient developed acute myelogenous leukemia. The uterine tumor was initially believed to be a histiocytic lymphoma. The diagnosis of granulocytic sarcoma was confirmed by the naphthol AS-D chloracetate stain for esterase, which was performed on the uterine cervix and obturator lymphnodes taken by hysterectomy and pelvic node dissection. The literature was reviewed with emphasis on the differential diagnosis of granulocytic sarcoma and histiocytic lymphoma, and the clinical and pathological problems that arise when the tumor presents at an unusual location and without peripheral blood manifestation of leukemia.

Granulocytic sarcoma is a term applied to localized malignant tumors composed of immature cells of the myelogenous series, and is also known as a chloroma, chloromyeloma (Wintrobe et al, 1974), chloromyelosarcoma, granulocytic leukosarcoma, myeloblastoma, myelocytoma and myelosarcoma (Rappaport, 1966). The curious term chloroma is derived from the observation that the cut surface of such a tumor transiently turns green when exposed to light, a phenomenon that probably reflects the myeloperoxidase content of the cellular lysosomes (Schultz and Schwartz, 1959).

It has been pointed out that the tumor may develop during the course of, or as a presenting sign of, myelogenous leukemia, usually of the acute form (Burns, 1963). The organs that have been reported to be involved by the granulocytic sarcoma are the breast (Blackwell, 1963), the ovary (Hinkamp and Szanto, 1959; Chorlton et al, 1974b), central nervous system (Hurwitz et al, 1970), orbit (Mortada, 1962) and the uterus including the cervix uteri (Hartford, 1968; Chorlton et al 1974a; Seo et al, 1977; Kapadia et al, 1978).

The renal cortex, thyroid gland, thymus, lung, gastrointestinal tract, pancreas and urinary bladder are less commonly involved (Bran- nan, 1926).

We present a case of granulocytic sarcoma in a 36 year-old woman who initially had postcoital vaginal bleeding. A punch biopsy from the uterine cervix was misinterpreted as malignant lymphoma, histiocytic type or cervical involvement of the mixed mesodermal tumor. There are problems in the differential diagnosis between granulocytic sarcoma and other undifferentiated tumors, when the

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former occurs in an unusual site such as in our case.

CASE REPORT

A 36 year-old woman was admitted to the Department of Gynecology, Yonsei University College of Medicine, because of abnormal vaginal bleeding.

She was well until one month ago, when she began to experience postcoital vaginal spotting. Fifteen days before admission a cervical cone biopsy was performed, which revealed solid and diffuse infiltration of undifferentiated cells. The neoplastic cells had round to oval hyperchromatic nuclei with frequent prominent nucleoli, and scanty to moderate amount of amphophilic cytoplasm. Mitosis was frequent. Very fine, delicate reticulin fibers were found between groups of tumor cells. The overlying cervical mucosa was eroded focally, but largely spared by the malignant infiltration. The biopsy was initially interpreted as malignant lymphoma, histiocytic type.

On admission, the pelvic examination revealed the cervix in the state of post conization with serosanguinous discharge. The uterine fundus and both adnexae were not remarkable. The liver, spleen and lymphnodes were not palpable. No tumor or pathology was found in skin, soft tissue or other viscera.

The temperature was 36.6°C, the pulse 94/min, and the respiration 22/min. The blood pressure was 120/80mmHg. The urine was normal. The hematocrit was 33 per cent and the white cell count was 2,700/mm³ with 34% neutrophils, 62% lymphocytes and 4% eosinophils. Platelet count was normal. A bone marrow aspiration showed a M:E ratio of 5:1 with a moderate shift to the left of myeloids and megaloblastoid forms. The changes in the bone marrow were thought to be a result of chronic irritation or possible preleukemia.

Radical hysterectomy with bilateral pelvic lymphnode dissection and splenectomy was done. The uterine cervix was infiltrated by poorly differentiated round cells similar to those found on cervical biopsy, with small numbers of lymphoid and plasmacytoid cells. Eosinophilic precursor was not discernable. The corpus uteri and vagina were free of tumor extension. The obturator lymph nodes showed massive sinusoidal infiltration, especially subcapsular, of poorly differentiated cells with partial obliteration of the normal architecture. Focally the cells were also found infiltrating into the perinodal soft tissue, where they were aggregated or scattered between fat and connective tissue cells.

Since the findings of bone marrow aspiration were unusual, a histochemical staining was done for naphthol AS-D chloracetate esterase which is characteristically active in myeloid cells, differentiating them from the histiocytes. Many of the immature cells infiltrated into the cervix uteri, obturator lymphnodes and the perinodal soft tissue were stained positively and were proved to be granulocytic myeloid cells.

Thirteen days following operation a spiking fever developed and the white blood cell count was 20,000/mm³ with a typical peripheral blood picture of acute blastic leukemia. The differential count revealed 82% blasts, 8% myelocytes, 1% band form, 4% lymphocytes, 1% neutrophil and 4% monocytes. The bone marrow was almost completely replaced by immature blastic cells, which showed occasional Auer bodies and were positive for the peroxidase stain. The erythroid and megakaryocytic cells were hardly seen. The final diagnosis was acute myeloblastic leuke-
mia initially appearing as a granulocytic sarcoma of the cervix uteri.

**DISCUSSION**

Acute myelogenous leukemia (AML) may on occasion present initially as tumors composed of immature myeloid elements and be referred to as granulocytic sarcoma (Rappaport, 1966).

The diagnosis of granulocytic sarcoma may be difficult, since there are factors that mislead the interpretation (Brugo et al., 1975); 1) the neoplastic cells are poorly differentiated, 2) the tumor presents without a leukemic picture in the peripheral smear and bone marrow aspirate, 3) the tumor arises in an unusual location and 4) the tumor frequently appears without green discoloration.

Since the granulocytic sarcoma commonly shows marked histological similarity on hematoxylin-eosin to the other undifferentiated round cell sarcoma, especially the histiocytic lymphoma (Laszlo and Grode, 1967; Hurwitz et al., 1970; Scott and Horn, 1970; Wiernick and Serpick, 1970; Mason et al., 1973; Chorlton et al., 1974b) and the neoplastic cells are often more immature than those in the peripheral blood and in bone marrow aspirates of leukemic patients, several special methods such as Giemsa stain, periodic acid Schiff stain, naphthol AS-D chloracetate stain for esterase and occasionally electron microscopic study may be required (Liu et al., 1973; Seo et al., 1977). Although histiocytic lymphoma may terminate in acute myelogenous leukemia, the diagnosis of histiocytic lymphoma in the presence of AML must be viewed with suspicion and strong evidence must be presented to show the immature cells are not myeloid elements (Marin-Padilla et al., 1964; Mason et al., 1973). In the present case, the tumor cells in the uterine cervix, obturator lymph nodes and perinodal soft tissue revealed strong positivity with naphthol AS-D chloracetate for esterase, and thus the cone biopsy, with which the diagnosis of histiocytic lymphoma was made, proved to be incorrect.

Clinically granulocytic sarcomas are frequently silent and discovered unexpectedly at postmortem examination (Muss and Moloney, 1973). On rare occasions symptomatic granulocytic sarcomas may precede blood and marrow involvement (Lusher, 1964; Comings et al., 1965; Chorlton et al., 1974b). It may also occur concomitantly with AML (Rappaport, 1966; Ti et al., 1974; Sears and Reid, 1976), or occur in a patient with known AML (Hinkelamp and Szanto, 1959). Granulocytic sarcoma developing during the course of leukemia can be explainable as a massive infiltration of leukemic cells, but it has not been explained why certain patients develop the tumor nodules preceding overt leukemia. Liu et al. (1973) suggested that the granulocytic sarcoma represents extramedullary foci of malignant granulopoiesis. The length of time from the initial diagnosis of granulocytic sarcoma to the onset of leukemia varied from five weeks to over three years (Mason et al., 1973; Chorlton et al., 1974a; Brugo et al., 1975). In our case it was about 6 weeks from the appearance of genital bleeding to the second peripheral blood smear and bone marrow aspiration, when morphological diagnosis of leukemia was made.

The granulocytic sarcoma rarely occurs before the age of one year or after the age of sixty (Laszlo and Grode, 1967; Chorlton et al., 1974b). In our case the patient was 36 when she first presented with vaginal spotting.
It was reported that the incidence of tumor formation occurring in patients with AML is 3~8% at autopsy (Scott and Horn, 1970; Liu et al., 1973), and the involvement of the female reproductive tract by leukemia as a part of a generalized process is well known (Hartford, 1968). However, initial presentation of clinically unrecognized reticuloendothelial malignancy especially leukemia in the vagina, cervix or corpus uteri is very rare, and when the female genital organ is involved, the ovary is the most frequent site (Edgerton, 1947). Chorlton et al. (1974a) and Seo et al. (1977) reported 2 and 1 cases of granulocytic sarcoma of the uterine cervix respectively with symptoms of vaginal discharge and a vaginal mass. Initially their cases did not show peripheral blood manifestation of granulocytic leukemia and the latter developed postoperatively as in our case. This suggests that the surgery itself may accelerate the course of the disease.

The survival of the patients with granulocytic sarcoma is similar to that of acute myelogenous leukemia without tumor formation (Ross, 1955) and uniformly fatal as seen in Chorlton’s cases (1974a) of cervical granulocytic sarcoma, in which death occurred at 8-14 weeks.

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Fig. 1. Microscopic view of uterine cervix diffusely infiltrated by neoplastic cells. Note the nuclear pleomorphism and fine reticular fibers by which the tumor cells are grouped. H-E, ×430

Fig. 2. Higher magnification of tumor cells showing hyperchromatic nuclei, prominent nucleoli, and moderate amounts of amphophilic cytoplasm. Frequent mitosis and occasional indented nuclei are noted. H-E, ×1000

Fig. 3. Tumor cells similar to those seen in Fig. 1 and 2 occupy the subcapsular sinusoid, forming a mass. Right lower field shows unaltered paracortex of the lymph node. H-E, ×430
Fig. 4. Perinodal soft tissue (right two thirds) is infiltrated by tumor cells. A small portion of lymph node is also infiltrated by the same neoplastic cells. H-E, ×430

Fig. 5. The cytoplasm of neoplastic cells stains red brown by the naphthal AS-D chloroacetate method for esterase. This is one from the perinodal soft tissue. ×430