OSTEOSARCOMA : A STUDY OF 100 CASES.

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ABSTRACT

One hundred cases of osteosarcoma were studied clinically, pathologically and treated with preoperative intraarterial chemotherapy with or without preoperative irradiation and followed by surgery. Prophylactic lung irradiation was administered for every case after surgery. Sixty two patients belonged to Enneking's stage IIB and 11 cases were in stage III. The acturial three years survival rate of 25 cases was 48 percent.

INTRODUCTION

Osteosarcoma is the most common primary malignant bone tumor in Thailand. The incidence was 39.9 percent of all malignant bone tumor or comprised of 2.2 percent of all cancer cases in the year 1992 and 1.01 percent in 1993 in Ramathibodi Hospital.[1-3] Before 1986, osteosarcomas of the long bone, in the Faculty of Medicine, Ramathibodi Hospital, were treated exclusively by amputation, adjuvant chemotherapy while radiation were aimed at palliative treatment for advanced and affordable cases.[4] However, the results were poor, all cases died within the first 2 years. In the light of the effectiveness of adjuvant chemotherapy for osteosarcoma; as reported in Western countries, our institute pioneered the multidisciplinary treatment of osteosarcoma in this country when our program commenced in 1986. They were adapted partly to suit our socioeconomic conditions.[5-12] Local irradiation treatment including prophylactic lung irradiation was adjuncted with the purpose of enhancing the chemotherapeutic response.[13-15]

MATERIALS AND METHODS

From January 1988 to January 1994, 100 cases of osteosarcoma were enrolled in the study. There were 52 males and 48 female patients. The age of the patients ranged from 7 to 45 years old. Sixty four percent was in the second decade. Twenty one patients were belonged to the third decade and 10 were below ten and only 5 cases had the age over 30 (Fig. 1). Fifty nine patients presented with pain and 31 cases experienced pain after some kinds of trauma. Every patients had visited physicians at least two times before the diagnosis of osteosarcoma was given. They were diagnosed as sprain in 82 cases with 5 osteomyelitis and 4 tendinitis. Lump only was detected in 10 cases, the other 31 cases had lump followed by pain one or two weeks later (Fig 2A, B). Twenty patients had pathological fracture prior to the diagnosis, mostly belonged to the telangiectatic subtype. There were 60 osteoblastic, 19 chondroblastic, 13 telangiectatic and 8 fibroblastic subtype. Primary skeletal distributions were 49 femur, 24 tibia, 10 humerus 6 fibula, 2 pelvis and others as shown in Fig 3. The roentgenographic appearence were mostly osteolytic (Fig. 4A, B).

The treatment started after routine blood test including erythrocyte sedimentation rate (ESR), serum alkaline phosphatase (AP), and lactic acid dehydrogenase (LDH). The roentgenologic study included plain film of primary lesion and chest, linear or computerized tomogram of the lung and computerized scan of the primary tumor for the diagnosis of any soft tissue extension and intramedullary metastasis (Fig. 5). Bone scintigraphy was also requested for detecting skip metastasis and metastatic disease outside the bone.

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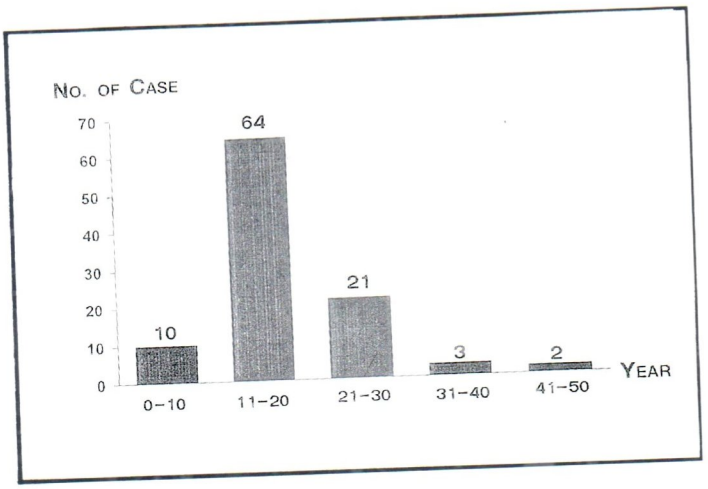

Fig. 1 Age at diagnosis for 100 cases of osteosarcoma.

All these patients were randomized to different arms of the study as shown in figure 6. Chemotherapy was repeated every 3 weeks if WBC was normal, total WBC $\geq$3000/ul or total PMN $\geq$ 1500/ul for 8 courses. Most of the patients received 4 courses of intraarterial chemotherapy followed by 4 intravenous routes after surgery, concomittant with prophylactic whole lung irradiation (Fig. 7). Total treatment time was about 32-52 weeks according to WBC and clinical status. Patients who also received methyl progesterone acetate (MPA) seemed to have shorter treatment time.

In the group of patients who were randomized to receive radiation to the affected primary tumor, the radiation treatment began on the next day after the last intraarterial chemotherapy. Treatment was done by Co-60 teletherapy or 6 MV linear accelerator. A total dose of 30 Gy in 10 fractions over 12 days was given using two opposed fields with the doses specified at midplane. Radiation port included only primary bone disease, abnormal vessels, and also intramedullary extension. No safety margin was given due to the concept that microscopic disease could be destroyed by intraarterial chemotherapy and to preserve normal tissue as much as possible especially in the limb salvage group. Two to 4 weeks after radiation, the patients were reevaluated to decide on limb salvage surgery or amputation. After surgery, the specimens were reveiwed to plan for further treatment (Fig. 8A, B). If tumor necrosis in the surgical specimens was less than 80 percent, the patient with limb salvage was advised to have amputation. Patients with poor tumor response had to receive a change in the chemotherapeutic regimens. For prophylactic whole lung irradiation, each lung was irradiated 150 cGy every other day to the total dose of 2550 cGy to each lung at midline depth without correction for the lung inhomogeneity, concurrented with intravenous chemotherapy.

RESULTS

For the total cases of one hundred, 27 cases refused treatment and continued to have traditional medicine. Sixteen patients had incomplete treatment, twelve of them returned to the hospital again with either lung metastases or severe progression of primary tumor. All were dead within the next other year after diagnosis. Other 11 cases terminated from either lung or bony metastases, 4-24 months after initial visit. Limb salvage surgery after preoperative intraarterial chemotherapy with or without radiation was performed in 22 cases. Other 19 patients underwent amputation or disarti-

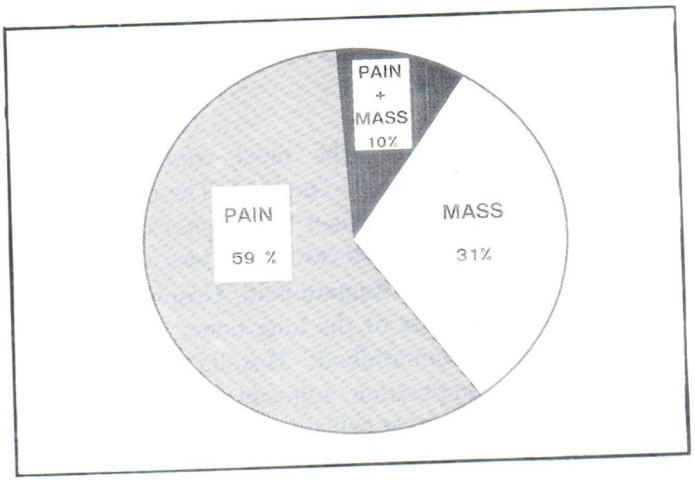

Fig. 2A Presenting symptom of 100 cases of osteosarcoma.

Fig. 2B One boy with a very huge shoulder mass, he was disarticulated with all his 15 axillary nodes negative for osteosarcoma.

culation. The rest of 5 patients, received incomplete treatment at the time of evaluation due to severe neutropenia and poor general condition.[4,16-20]

There were 25 cases who were followed up for longer than 3 years (15 limb salvage, 10 amputated cases). Three years survival rate was 48%, three of them had lived longer than 5 years now.

For the cost of treatment, excluding professional fee, was 125,000 baht or about US$ 5000 per case.

DISCUSSION

In this study we had approximately the same incidence between male and female patients. Peak incidence was in the second and third decade of life which was the period of very high bony activity. The first diagnosis was mostly that of sprain, osteomyelitis or tendinitis. Very few patients were diagnosed to be osteosarcoma at the first visit, so definitive treatment was delayed in almost every case. Early X-ray of the primary site would be of much help for early detection of osteosarcoma. Other cause of treatment delay was refusal to have amputation of the limb. The patients and their parents tried to seek other chances including traditional medicine, and most of them returned to have treatment after metastases has already established. Limb salvage procedure was the other chance to comfort the patient and their parents. This study, therefore, suggested that adjuvant chemoradiotherapy and limb salvage benefit patients in terms of quality of life and disease free survival. The outcome shown in our study was satisfactory; it was observed that disease-free survival, especially in the limb-salvage group, was better than historical control. Cost of the entire treatment was approximately 125,000 baht (US$ 5000) per case, which might be considered appropriate for the economic status of Thai patients. It is therefore advocated that limb-salvage procedure with preoperative intraarterial chemotherapy and radiotherapy be the treatment of choice for early cases of osteosarcoma in this country. Overall significance in terms of cure rate, however, awaits further follow up.

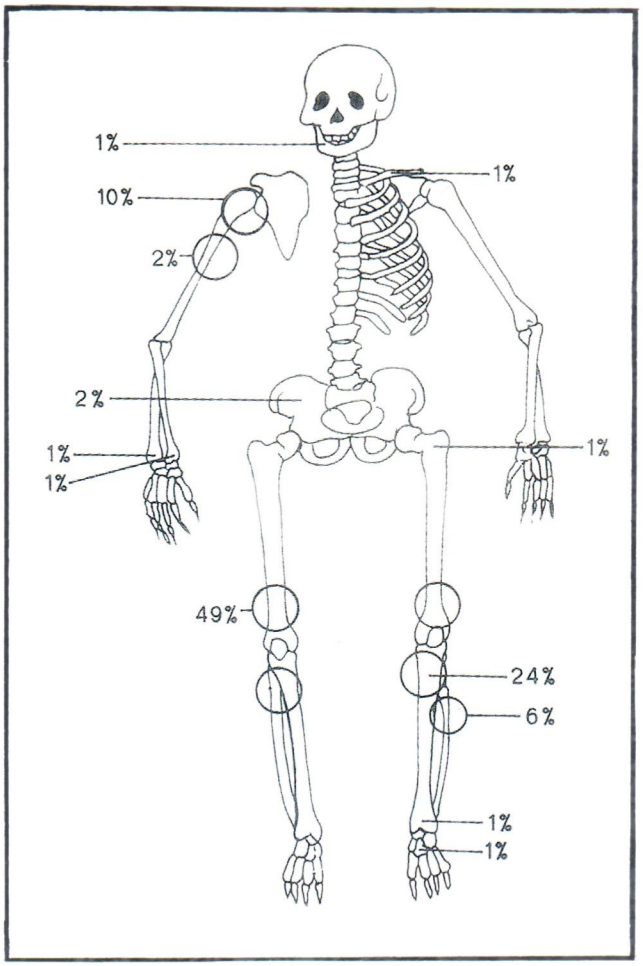

Fig. 3 Location of the primary lesion.

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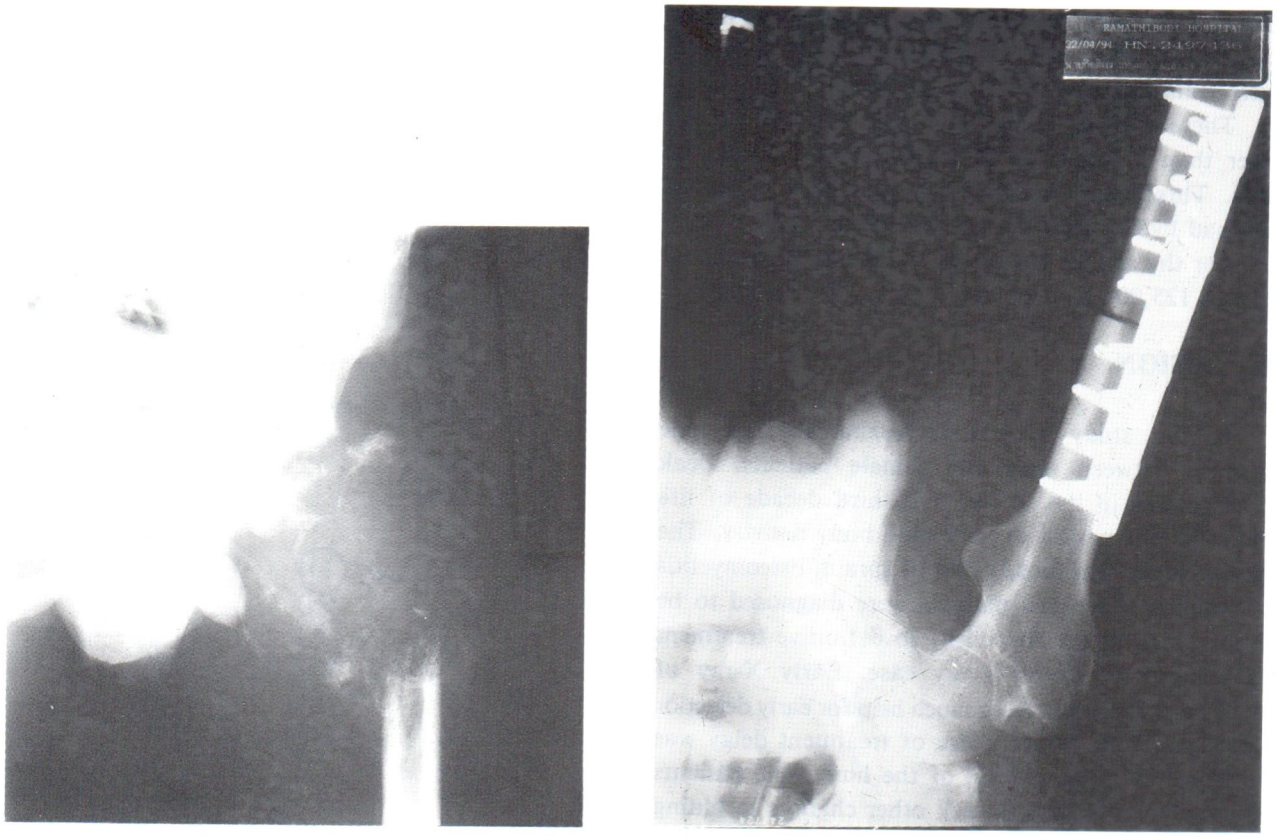

Fig. 4A,B Plain film of a patient with upper femur lesion, he was undergone preoperative chemotherapy with limb salvage surgery.

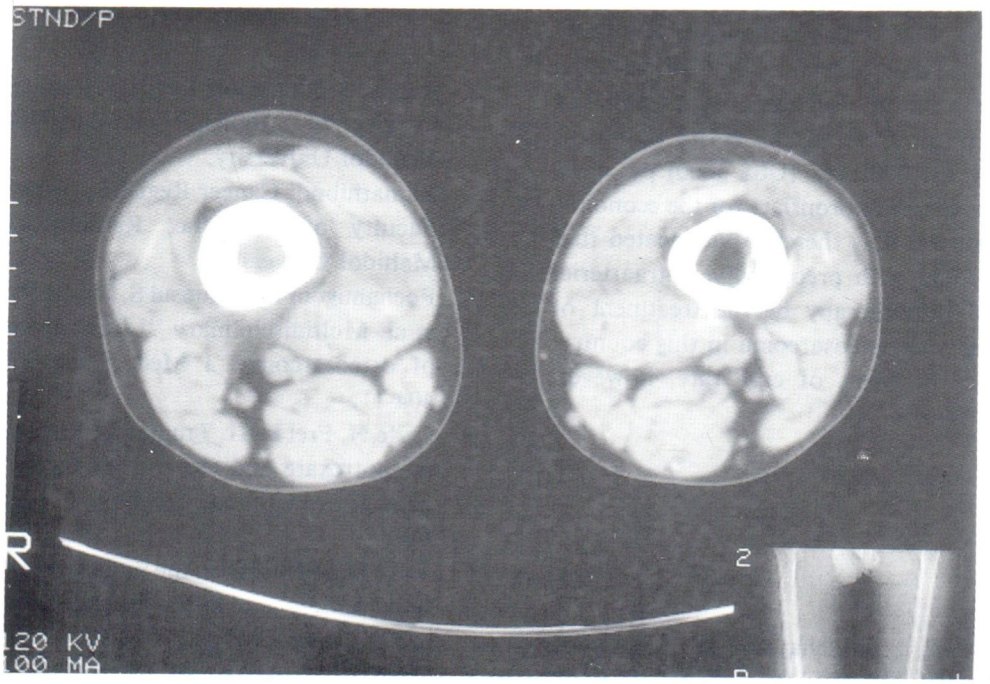

Fig. 5 Computer tomography of the bone showed intramedullary extension, in some patient the extension was 13-19 cms from the primary lesion.

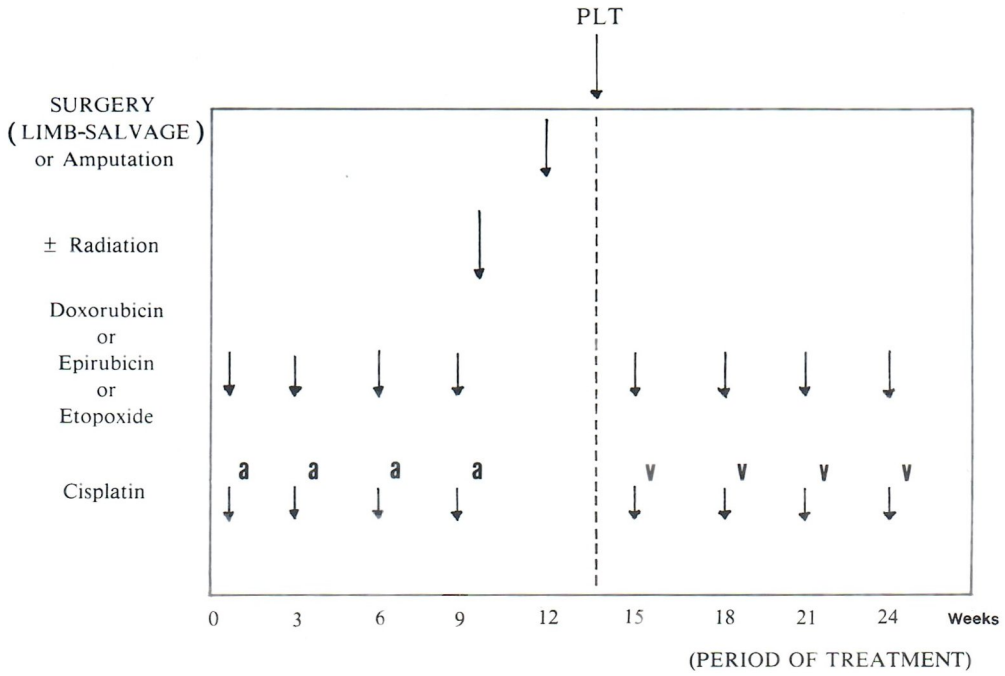

Fig. 6 Schedule of adjuvant treatment : PLI = prophylactic lung irradiation.

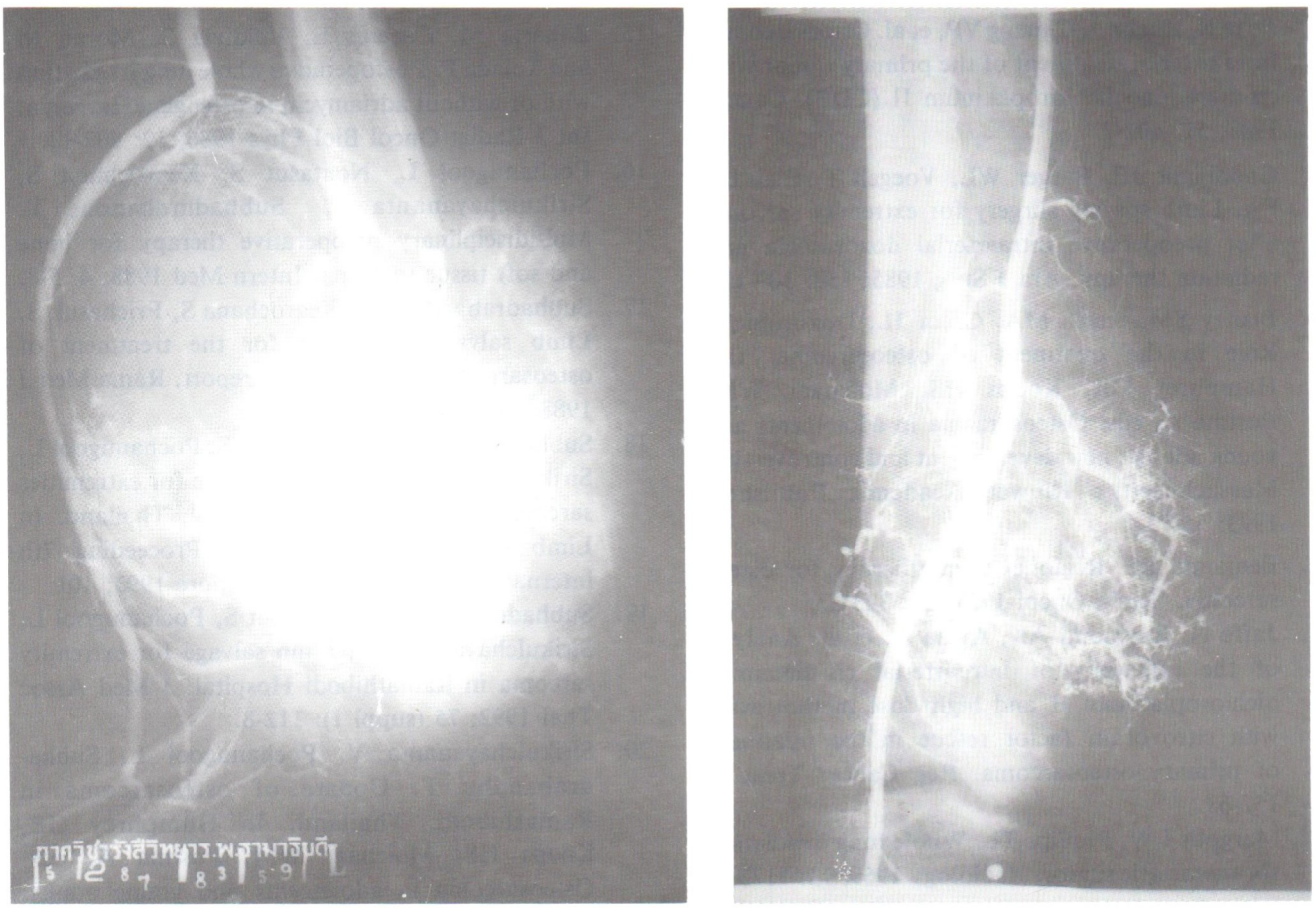

Fig. 7A,B Intraarterial cisplatin after femoral angiography.

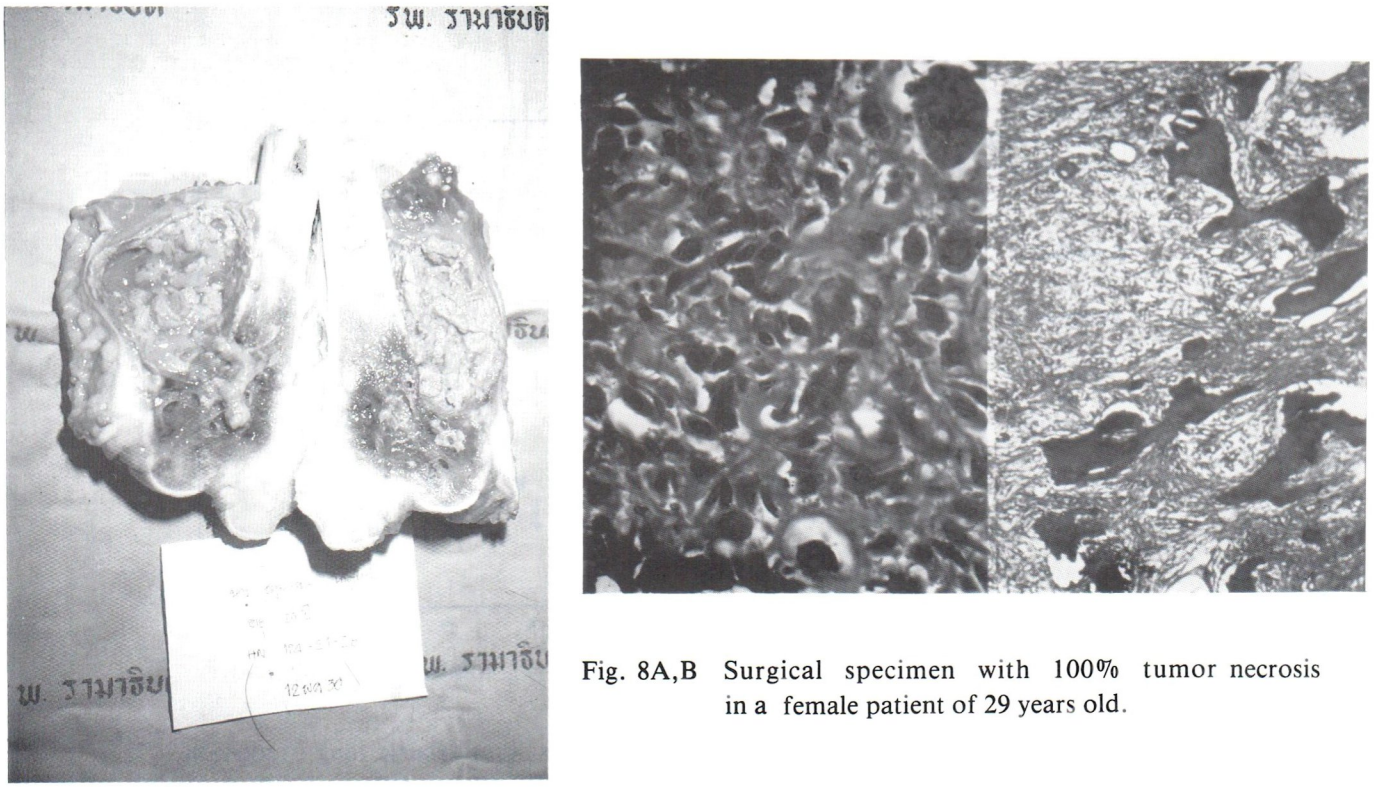

Fig. 8A,B Surgical specimen with 100% tumor necrosis in a female patient of 29 years old.

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