I would like to analyze here advantages and disadvantages of Japanese medical care for musculoskeletal tumors in my experience, and to describe what we should do in the future in order to enhance the advantages and overcome the disadvantages.

I graduated from university and started my career as an orthopedist in 1977. Also in that year, the Cancer Institute Hospital of JFCR opened the Department of Orthopedic Oncology, and clinical trials of high-dose methotrexate (MTX) therapy commenced in Japan. In 1980, I started working at the Cancer Institute Hospital and have been heavily involved in medical care for bone and soft tissue tumors since then. The following year, 1981, the hospital’s original total knee replacement was first performed for osteosarcoma, showing favorable response to neoadjuvant chemotherapy.

Current medical care system

Tumors that orthopedists often deal with can include the following three diseases: (1) metastatic bone tumors, (2) benign tumors, and (3) sarcoma. While all these diseases develop in the musculoskeletal system, different therapeutic strategies and systems are required to provide proper treatment. In Japan, the three diseases are currently treated in various medical facilities in an uncoordinated manner.

As for metastatic bone tumors, nowadays, it is said that approximately 50% of all people experience cancer during their lifetime. The five most frequent cancers in Japan are lung cancer, gastric cancer, colon cancer, breast cancer, and liver cancer. For the purpose of providing equal treatment for patients with the five major cancers anywhere in Japan, the first basic measures against cancer were formulated. As a result, 397 designated cancer hospitals had been established by 2012. When surgery is required for pathological fracture or spinal cord paralysis caused by metastasis of the frequently seen cancers to bones, orthopedists at the designated cancer hospitals provide the requisite medical care.

The most important part of treatment for benign tumors is to completely exclude the possibility of malignant tumors. If there is even the slightest possibility of malignant tumor in the image, a histological diagnosis is necessary. If sufficient specimens can be obtained by needle biopsy, the histological diagnosis can essentially be made at any facility. On the other hand, if a diagnosis is not or cannot be made by needle biopsy, further histological examination, including incisional biopsy, is mandated. With regard to treatment for a tumor confirmed as benign, there is the option of follow-up. However, if the tumor has already limited the activities of daily living or might limit these activities in the future, surgery is deemed necessary. For instance, even a benign bone tumor requires surgical treatment if there is a risk of pathological fracture. Considering that pathological diagnosis, particularly by frozen section, of bone and soft tissue tumors is difficult, and that benign tumors may have a high rate of local recurrence, even a benign tumor should be treated in a facility with qualified orthopedists and pathologists specializing in bone and soft tissue tumors.

The incidence of sarcoma is said to be just 1% of all malignant tumors, and as such is fortunately one of the rare cancers. However, since sarcoma can develop in any part...
of the body, sarcoma of the bone, some parts of the retroperitoneum and extremities, which are included in the area of orthopedic care, account for almost 70% of all sarcomas. Unfortunately, we cannot state that the treatment of sarcomas in Japan has been systematically carried out in the past. It’s actually the reverse. Surgery is variously performed by a mix of orthopedists, gastrointestinal surgeons, urologists, head and neck surgeons, gynecologists, etc., depending on the site of occurrence of the sarcoma. In terms of chemotherapy care, children may be treated by pediatricians, whereas adults are treated not only by oncologists but by surgeons in several different specialty areas. The reason behind this is that, in Japan, sarcoma cases are dealt with across various clinical and hospital facilities and no progress has been made in the intensification and uniform handling of these cases. If the number of cases per facility is small, it is not possible to create an environment in which oncologists specializing in sarcoma can grow their practices.

In sarcoma treatment by orthopedists, the history of chemotherapy for sarcoma started with the introduction of high-dose MTX therapy for osteosarcoma in the late 1970s. The effectiveness of chemotherapy for Ewing’s sarcoma was reported at around the same time and the necessity for anticancer therapy of primary malignant bone tumors was determined. Since the 1990s, when new drugs such as doxorubicin, cisplatinum, and ifosfamide were released, the survival rate of osteosarcoma patients has almost reached a plateau. With regard to soft tissue sarcomas, the clinical significance of chemotherapy for round cell sarcomas has been well established, while the significance of adjuvant chemotherapy for non-round cell sarcoma remains unclear. With this background, no new medication effective in treating sarcomas has been recently released. Instead, progress in bone and soft tissue tumor treatment after 1990 has been seen particularly in local treatment. This progress in local treatment is supported by the determination of the extent of resection to prevent local recurrence and reconstruction to maintain good function after resection.

**Evaluation method of surgical margin and safety surgical margin**

We have seen that what is most important in the resection of tumors is the surgical margin required to prevent local recurrence. “The evaluation of surgical margin” [1] is a method we use to describe the relationship between the tumor and surrounding tissue as seen in surgical specimens. Based on analysis of surgical specimens at the Cancer Institute Hospital, the evaluation method of surgical margin for musculoskeletal sarcoma was approved by the Japanese Orthopedic Association Musculoskeletal Tumor Committee in 1989, which provides a basis for determining safety surgical margins. The evaluation method consists of a macroscopic evaluation of surgical specimens, performed by means of converting not only the actual thickness (distance) of normal tissue removed with a tumor but also tissues (barriers) such as fascia and periosteum, which have resistance to tumor invasion, into “distance.” In respect to fascia surrounding muscles, for example, thick fascia is converted into a “distance” of 3 cm and thin fascia into a “distance” of 2 cm. The surgical margin of the entire circumference of the tumor is evaluated based on this method and the minimal surgical margin determines the presence or absence of recurrence; therefore, the type of surgical procedure is decided by the minimal surgical margin. Researching the relationship between the evaluation method of surgical margin and the subsequent recurrence thus reveals the optimal extent of tumor removal.

We define surgical margins with local control rates of 90% or more, as safety surgical margins. Safety surgical margins in soft tissue sarcoma vary widely depending on whether or not the tumor shows invasive growth. In the case of non-invasive sarcoma, a wide procedure of 2 cm would be safe for high-grade and a wide procedure of 1 cm would be safe for low-grade. Even for high-grade, a wide procedure of 1 cm is acceptable if preoperative treatment is effective. However, in the case of invasive sarcoma, the tumor easily invades surrounding tissue that does not play a role as a barrier, and images cannot show the leading edge of the tumor invasion. Therefore, setting safety surgical margins is difficult and may lead to either excessive or insufficient resection. If we can determine whether or not the tumor is invasive by gene-level analysis and clarify the extent of tumor invasion with bio-imaging in the future, a more reliable determination of safety surgical margins will become possible.

**Surgical procedure for soft tissue sarcoma**

Currently in the US, surgical treatment combined with radiotherapy is the standard treatment for deep, high-grade tumors. However, application of radiotherapy should be limited due to time, cost, and serious complications such as secondary cancers. Thus, surgery based on the concept of safety margins is an important advance. When findings of preoperative images confirm that a safety surgical margin can be obtained by surgery alone, radiotherapy can be excluded. In addition, when the findings cannot determine whether an adequate safety surgical margin can be obtained, there is also an in situ preparation (ISP) method [2] that permits intraoperative evaluation of the safety margin without increased risk of neoplasm seeding. This method
enables resection of the tumor and surrounding healthy tissue while maintaining the major neurovascular supply. For this, after separating the tumor mass from the surgical field by the use of a sterile vinyl sheet, the neurovascular bundle is detached from the tumor and the surgical margin is evaluated. If the bundle is seen to be contaminated by the tumor, it should be excised. However, if the bundle can be isolated, additional procedures including alcohol soaking are performed to preserve it. With the concept of safety surgical margins and the ISP method, unnecessary resection and radiotherapy can thus be avoided.

Reconstruction after bone and soft tissue tumor resection

The development of various skin flaps for treatment of skin defects and improvement in the quality of artificial vessels have played a significant role in improving function after malignant tumor resection. For bone defects, significant progress in tumor prosthesis and bone transplantation has been achieved. Improvements in the quality and form of tumor prosthesis have reduced the loosening or breakage of artificial joints. In addition, improvements have been made in resolving problems with expandable prostheses, such as leg length discrepancy. Allografts used alone or with metallic materials (allograft-prosthetic composite) have played a key role in the reconstruction of bone defects.

In Japan, allografts have been difficult to obtain and autogenous bone grafts (using autoclaved bone, boiled bone, etc.) have long been performed. Since the Cancer Institute Hospital started using pasteurized autogenous bone graft [3] in the 1980s, research on recycled autogenous bone graft techniques has become popular in Japan. However, there are problems with recycled autogenous bone grafts that are still to be resolved. The problems include that the complete death of tumor cells cannot be confirmed, the histological analysis of surgical specimens may be insufficient, and the techniques cannot be used for osteolytic lesions. In Japan, various recycled bone graft techniques are developing even now, but more efforts should be made to establish an allograft bone bank first, rather than spending time and money on developing recycled bone graft techniques.

Improvement of medical care system for musculoskeletal tumors

The surgical procedures for bone and soft tissue sarcoma may be significantly changed in the future, as evidenced by the fact that the introduction of new drugs, including molecular target drugs, has totally changed surgical treatment for frequently seen cancers including breast cancer. Although it remains in the distant future that extended surgery and reconstruction will not be necessary at all, there is a high possibility that the requirement for extensive surgery will be reduced in the near future.

Medication-based treatment for bone and soft tissue sarcomas is not necessarily considered to require its own special attention but instead should be regarded as part of the larger field of chemotherapy for sarcomas in general. It is essential to establish a system of medical care for musculoskeletal tumors as a way to reduce medical costs and provide efficient medical care. Medical facilities can be categorized as general hospitals, designated cancer hospitals, specialized hospitals for bone and soft tissue tumors, and specialized hospitals for sarcomas (sarcoma centers). The role of general hospitals is to keep an eye out for tumors and refer patients to appropriate hospitals as necessary. Designated cancer hospitals provide diagnosis and treatment for metastatic bone tumors. In specialized hospitals for bone and soft tissue tumors, pathologists and clinicians experienced in bone and soft tissue tumors provide diagnosis and treatment. In specialized hospitals for sarcomas, medical care for sarcomas not only in the musculoskeletal system but also in the whole body is given systematically. The staff members are engaged in diagnosis and treatment for sarcomas as well as study and education.

Sarcoma center

If sarcoma, which can appear in any part of the body, develops in a location that makes it hard to remove, it is extremely difficult to improve the patient’s prognosis. New chemotherapy treatment inhibiting the growth of sarcomas, etc., is vital to treat unresectable sarcomas. In recent years, new medications such as trabectedin, pazopanib, etc., have finally been released in the field of sarcomas; however, those medications may have adverse reactions different from those of traditional anticancer drugs, therefore treatment by specialists in chemotherapy is recommended. Also, in the field of musculoskeletal tumors, since orthopedists provide both surgery and chemotherapy in the traditional system, they will have difficulty in dealing with the plethora of new medications being released one after another. It is thus essential to establish a system in which oncologists specializing in sarcomas are in charge of medication-based treatment for sarcomas. This requires concentrating sarcoma patients in several facilities across Japan and providing treatment. To achieve this, sarcoma centers need to be established with the role of providing systematic treatment for sarcomas. As for surgically based treatment, surgical departments with the most anatomical knowledge should provide treatment depending on the site.
of occurrence, and form the team to perform surgery as needed. In respect to medication, oncologists specializing in sarcomas should provide the treatment. It is also required that research and clinical departments cooperate with each other to develop new diagnostic treatment methods using a wealth of surgical findings and accurate clinical data. Such centers should be set up in Japan as early as possible.

Finally, our Cancer Institute Hospital annually holds the forum of the Surgical Society for Musculoskeletal Sarcomas. Young orthopedists responsible for the next generation of medical care for bone and tissue tumors and international specialists participate in the forum. I recall very well the words of the renowned orthopedist, Professor Franklin H. Sim of the Mayo Clinic who said, “I am fortunate because I do not have to prescribe anticancer drugs.” Orthopedists in Japan should be dedicated to performing surgery and analyzing postoperative function and the prognosis of patients. In addition, medication treatment should be provided by specialists. To achieve these conditions for optimum medical practice, it is essential to establish specialized centers for sarcoma treatment.

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