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Shizuo Oi

Recent advances and racial differences in therapeutic strategy to the pineal region tumor

An editorial

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S. Oi
Department of Neurosurgery,
Tokai University School of Medicine,
Bohseidai, Isehara, Kanagawa,
259-11 Japan
Tel.: (81) 463-93-1121
Fax: (81) 463-91-1295

Abstract The therapeutic modalities for pineal region tumors in Western countries differ from those in Japan, mainly because of the different patient populations. The majority of pineal region tumors in Japan are radio- and/or chemosensitive, and adjuvant therapy rather than extensive surgery plays the main part in the treatment of these tumors. The specific clinical features of and therapeutic modalities for pineal region tumors, together with racial differences, were analyzed at the joint symposium of the Japanese Society for Pediatric Neurosurgery and the Korean Society for Pediatric Neurosurgery. The results of a cooperative study, together with the collective experience in Korea, confirmed that this specific patient population is nearly identical to the Japanese one. The new therapeutic approaches to pineal region tumors recommended included neuroendoscopic or stereotactic biopsy as a "minimally invasive" initial procedure. The adjuvant therapeutic modalities were further analyzed and neoadjuvant chemotherapy, mainly with cisplatin or carboplatin with or without etoposide (VP-16), was recommended for the treatment of germinoma and nongerminomatous malignant germ cell tumors. "Target radiation therapy" with extensive chemotherapy is a hopeful regimen and a future subject of research.

Key words Pineal region tumors · Japan · Korea · Treatment

Historical trends in therapeutic modalities for pineal region tumors (Table 1)

Until the late 1970s, there was a tendency to select radiation therapy as the initial procedure in the treatment of pineal region tumors before attempting radical resection [1, 8]. However, along with the recent advances in microneurosurgical technique and instrumentation, it has become generally accepted in North America and Europe that in the management of pineal region tumors the histological diagnosis should be obtained before radiotherapy and/or chemotherapy [2, 3, 5]. The evidence in support of this tactic includes the following [2, 3, 5]: 36–50% of pineal tumors are either benign or radioresistant; there is increasing evidence that even low doses of radiation may be harmful to the developing brain; advances in diagnostic and surgical techniques have significantly lowered the mortality and morbidity rates associated with surgery in the pineal region; and histological diagnosis permits the rational development of histology-specific therapy.

In Japan, it was first recognized by Araki and Matsumoto [4] in their extensive survey that pineal region tumors are very common in Japan. It then became generally accepted that the majority of these tumors are radiosensitive and likely to be germinomas, and that a low-dose radiation test should be performed as the initial procedure [9]. Recently, however, the standard therapeutic regimens for tumors of the pineal region have changed around the world, most particularly in North America, for the reasons described, but the appropriate therapeutic regimen remains controversial in Japan and some other countries. In 1992, we therefore performed a worldwide survey of the management of pineal region tumors [6], in order to gather in-

Table 1 Historical trends in therapeutic modalities for pineal region tumors

Reference	Neuroimaging		Initial procedure
[5]	Dissemination		
Tumor marker (AFP)	(–)	(–)	Surgery
	(+)	(–)	Surgery
		(+)	Chemotherapy
[9]	Calcification/irregularity/cyst		
	(–)	(–)	Radiation (local, 20 Gy)
Tumor marker (AFP, hCG)		(+)	Surgery
	(+)		Surgery

formation regarding the collective experience in and treatment regimens for pineal region tumors in different patient populations. The results demonstrated again that there were significant racial differences in the epidemiology. The therapeutic modalities also differed with the different patient populations. Determination of tumor histology as an initial procedure was strongly supported by the majority of neurosurgeons in North and Central America and in Europe, whereas all but one of the neurosurgeons in Asia and Egypt emphasized initial application of the radiation test.

It is of vital importance to determine whether this specific racial difference of the patient population in Japan is also applicable to that in Korea and how this would affect the current therapeutic modalities in pineal region tumors.

Racial difference in epidemiology and differences in standard therapeutic modalities for pineal region tumors around the world (Fig. 1)

Since the extensive survey performed by Araki and Matsumoto [4], it has become well recognized that pineal region tumors are much more common in Japan than in Western countries and China. In a nationwide survey, the Brain Tumor Registry in Japan collected a total of 861 cases of pineal region tumor between 1969 and1981, i.e., in the era of computed tomography (CT) and microneurosurgery. In 504 (58.5%) of these cases the histological type was verified, and there were 301 cases of germinoma (59.7%) and 75 of teratoma (14.9%). Gliomas was seen in only 43 cases (8.5%), and pineoblastoma or pineocytoma in 24 (4.8%). The majority of the unverified tumors and germinomas (658 cases in total: 76.5%) were treated mainly by radiation therapy. The age distribution in the germinoma cases was specific, with the overall peak incidence occurring in the second decade of life. Among the pineal region tumors occurring in patients 15–35 years of age germinomas constituted the majority, up to 84% in same-age groups. The incidence of germinomas was not as high in patients aged

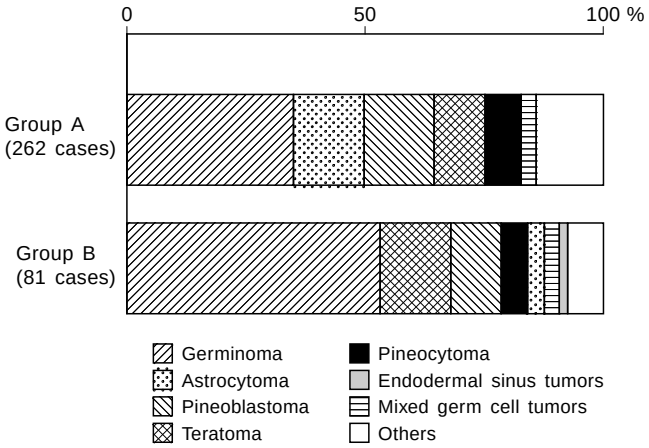

Fig. 1 Racial differences in epidemiology and different standard therapeutic modalities for pineal region tumors around the world. Note the obvious differences between the two groups: *A* Canada, Mexico and Europe; *B* Korea, Egypt, Japan, and Republic of China. Total 408 cases, 343 confirmed, 65 unconfirmed by histology. (From [6])

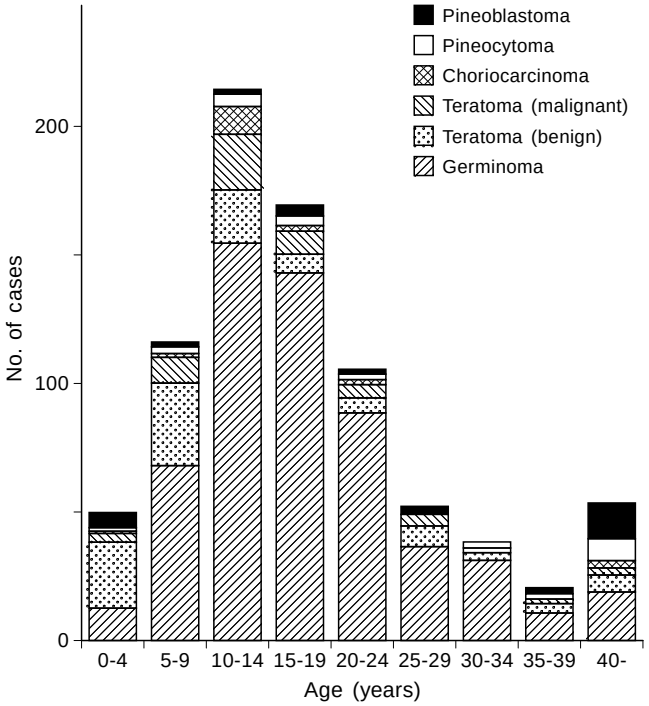

Fig. 2 Incidence of individual tumor types and age distribution of intracranial germ cell tumors and other pineal region tumors. (Data from the Brain Tumor Registry in Japan, vol 6 [6])

14 years or less and 36 years or more. Germinoma was a rare occurrence in infants and preschool children, and teratoma accounted for the majority of these cases. Based on the results of a worldwide survey performed in 1992, Oi et al. [6] emphasized that the epidemiological characteristics in Fig. 2 should be regarded as some of the most impor-

tant factors in selection of the therapeutic modalities. The major treatment role is that of adjuvant therapy in these patient populations in Japan, but in Western countries radical resection is the major procedure more often chosen for management of the glial tumors and nongerminomatous germ cell tumors (GCT) predominantly seen in these countries. Figure 2 summarizes the initial procedures included in the treatment plan for patients with pineal region tumors, as reported in the 1980s in the official journals of neurosurgical societies in Japan [7] and the United States [5]. This summary points to the differences in the concepts underlying the choice of therapeutic modalities for pineal region tumors in Japan and in Western countries.

Topics addressed at the Symposium (Table 2)

Based on these historical trends and the racial specificity in the therapeutic modalities, the following topics were proposed for discussion at the joint symposium of the Japanese Society for Pediatric Neurosurgery and the Korean Society for Pediatric Neurosurgery: major and minor varieties of histological types and racial differences between Japan and Korea; role of initial procedure in the therapeutic modality (focusing on indications for extensive surgery and major treatment modalities in Japan and in Korea); recent advances in therapeutic regimen: initial procedure, operative technique, and adjuvant therapy in Japan and in Korea.

Table 2 Subjects at the joint JSPN and KSPN symposium

1. Variety of histological types and racial difference
   What are the most and least frequent in Japan and Korea?
2. Role in therapeutic modality
   Initial procedure; is extensive surgery indicated in all?
   Which treatment has the major role in Japan and Korea?
3. Recent advances in therapeutic regimens
   What's new in initial procedures in Japan and Korea?
   What's new in operative techniques in Japan and Korea?
   What's new in adjuvant therapy in Japan and Korea?

The participants discussed these topics in the light of their experiences and cooperative studies. Almost identical epidemiological and clinical features of pineal region tumors in Japan and Korea were delineated. Among the new treatment modalities, minimally invasive neurosurgery [7], including neuroendoscopic and stereotactic surgical procedures, was favorably regarded by the participants as the initial procedure in the management of pineal region tumors. Chemotherapy was also well regarded as the major procedure in the treatment of germ cell tumors, and cisplatin (CDDP) and carboplatin (CBDCA) with or without etoposide (VP-16) were the main agents used for chemotherapy by the majority of the neurosurgeons.

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