Radiation Therapy of Orbital Inflammatory Lymphoid Pseudotumor

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眼窩炎性リンパ腫型偽腫瘍の放射線治療

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眼窩炎性偽腫瘍の中リンパ腫型にのみ放射線による急速且完全な腫瘍消失が期待できるといわれている．併し本偽腫瘍はありふれた疾患でないので2—3の例に照射を行なった諸報告をみるに過ぎない．著者らはリンパ腫型炎性偽腫瘍10例に高エネルギー電子線を主とした放射線治療を行ない期待以上の好成績をえた．

水晶体の遮蔽のため4種類のコンタクトレンズ型鉛製 shielding disk を作製した．最も薄い厚さ1.9mm の disk の18MeV 電子線による水晶体線量は20%以下である．前方より照射した患者には厚さ3.3mm 以上の disk と10MeV 以下のエネルギーを用いたので白内障の懸念は殆んどない．

6例は腫瘤摘出後ステロイドホルモンの投与を受けたが効果不充分又は再発の例，1例は腫瘤摘出術のみ，3例は試験切除のみの症例である．全て外照射で1例に ^{60}Co を用いた以外は，前方よりの照射には 6～10MeV，側方よりの照射には18MeV の高エネルギー電子線を用いた．照射野は腫瘤に限局して照射した1例を除き眼窩全体を含むように設定した．

全例に腫瘤，眼球突出の何れか又は両方がみられたのでこれら所見の消失を目標として照射を行った．全例目標を達したが総線量は600rad/19日から2,100rad/25日，NSD を計算しえた例では282retから924ret の間である．1回線量としては100, 150, 200, 又は300rad を試みた．又80rad から160rad に至る漸増法も行った．300rad 照射3例中2例に結膜炎を生じ200rad 以下では発生しなかった．

8例は照射終了24カ月から56カ月後再発を認めていないが残りの2例は6及び7カ月後に再発をみた．再発の原因は不明であるが1例は腫瘤に限局して照射しておりこの為かも知れないと考えている．

リンパ腫型炎性偽腫瘍は放射線照射で著効がえられるのでこの型の偽腫瘍には照射を優先することが望ましい．

I. Introduction

Orbital inflammatory pseudotumor is a general term for diseases whose symptoms are similar to genuine tumor of the orbit, but non-specific inflammation is proven histologically[1]. It has been histopathologically classified into 3 types[1)2)] and 8 types[3)], and among these types only the lymphoid type has been reported to disappear rapidly and completely by means of radiation therapy[4)]. Pseudotumor is a comparative rare disease, and there are only a few detailed on its radiation therapy available in the literature.

The authors in treating 10 cases of orbital inflammatory pseudotumor of the lymphoid type with radiation therapy mainly employing high-energy electron beams as radiation source obtained good results.

II. Subjects and Methods

1. Subjects

All cases were histologically proven to be pseudotumor of the lymphoid type. The ophthalmological treatments administered prior to irradiation and the chief signs immediately before irradiation of all 10 cases are shown in Table 1. In six cases tumor excision was made followed by steroid treatment, but this treatment resulted in recurrence of the tumor. One case had been subjected to local excision and the remaining 3 cases were given radiation therapy after biopsy.

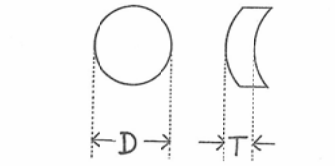
Table 1. Ten cases given radiation therapy with discription of previous treatments given before irradiation and chief signs immidiately before irradiation

Case	Sex	Age	Previous treatments	Chief signs before irradiation
1	M	64	Excision and steroid hormone	Tumor, exophthalmus, disturbance of ocular movement, and diplopia
2	M	43	Excision and steroid hormone	Exophthalmus, disturbance of ocular movement, and diplopia
3	M	68	Local excision	Tumor, disturbance of ocular movement, and diplopia
4*	F	68	Excision and steroid hormone	Tumor, disturbance of ocular movement, and ptosis of the lid
5	M	48	Biopsy	Exophthalmus
6*	M	34	Excision and steroid hormone	Tumor and swelling of the lid
7	M	43	Excision and steroid hormone	Exophthalmus, disturbance of ocular movement, and diplopia
8	M	31	Excision and steroid hormone	Exophthalmus, disturbance of ocular movement, and diplopia
9	M	44	Biopsy	Tumor and exophthalmus
10	F	53	Biopsy	Tumor and exophthalmus

*Cases of recurrence

2. Radiation Source

As sources of high-energy electron beam, betatron was used for Case 1 to 6, a linear accelerator for Cases 8 to 10 and a telecobalt unit for Case 7.



Disk No.		Diameter(D)	Thickness(T)
Pb	1	12.6 mm	1.9 mm
	2	12.2	2.6
	3	13.0	3.3
	4	12.0	3.5

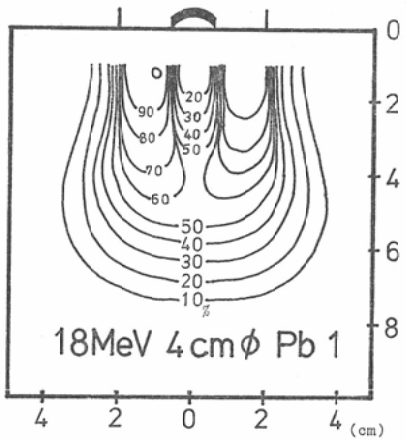


Fig. 1. Sizes of shielding disks made of lead and isodose curves shielded with Disk No. Pb 1 using an energy of 18 MeV and a field size of 4 cmϕ

3. Shielding of the Lens

For shielding the lens from high-energy electron beams, 4 kinds of shielding disks of the contact lens type were fabricated (Fig. 1). Fig. 1 shows the isodose curves obtained by the film method with the thinnest disk, No. Pb 1, irradiated with an energy of 18 MeV, a field size of 4 cmϕ, and Mix DP Phantom. The special property of the electron beams that spread in a fan shape provided a dose distribution suitable for the treatment of intraorbital tumors. During irradiation the disk was applied to the eye after surface anesthesia, and after irradiation an antibiotic drug was dripped to prevent infection.

4. Energy, Field Size, Dose, and Overall Time of Irradiation

As all the subjects showed either a palpable tumor or exophthalmus or both, the selection of

Table 2. Physical factors of irradiation and time/dose relationship

Case	Source and energy	Field size (cm)	Dose (rad)	Overall time (days)	NSD (ret)
1	10 MeV E*	4 cmϕ	600	19	282
2	10 MeV E	4 cmϕ	600	19	282
3	8 MeV E	6 cmϕ	2100	25	924
4	10 MeV E	4 cmϕ**	1800	18	
	18 MeV E	3 cmϕ			
5	10 MeV E	4 cmϕ	1200	13	
6	6 MeV E	2 cmϕ	1970	45	
7	Cobalt 60	5×5 cm***	2000	14	860
		5×4 cm			
8	10 MeV E	6 cmϕ	1000	27	400
9	8 MeV E	6 cmϕ	2050	45	
10	10 MeV E	4 cmϕ	1200	14	584

*E; Electron beams from betatron or linear accelerator
**10 MeV; A. P. field, 18 MeV; lateral field
***wedge-pair technique

total dose and overall time was based on the guideline for the disappearance of these symptoms. The irradiation field was selected to cover the entire orbit, but in Case 6 it was localized on the tumor. The energy used was varied from 6 to 10 MeV depending on the position and extension of the tumor (Table 2).

Cases 1 and 2 were treated with electron beams of 10 MeV through the anterior portal in a field size of 4 cmϕ. The daily dose at a depth of 3 cm was 100 rad and a total dose of 600 rad was given in 19 days with an NSD of 282 ret.

Case 3 was treated with electron beams of 8 MeV through the anterior portal in a field size of 6 cmϕ. The daily dose at a depth of 2.5 cm was 300 rad and a total dose of 2100 rad was given in 25 days with an NSD 924 ret.

Case 4 was first treated with electron beams of 10 MeV through the anterior portal in a field size of 4 cmϕ. The daily dose at a depth of 3 cm was 300 rad. When a dose of 900 rad was given in 7 days, the patient complained of congestion of the conjunctiva, lachrymation, and pain resulting from acute changes in his chronic conjunctivitis due to trichiasis. The beam direction was then changed to the lateral portal, the energy and field size were also changed to 18 MeV and 3 cmϕ, respectively, and a dose of 900 rad was given in 11 days. The total dose was 1800 rad in the overall irradiation period of 18 days.

Case 5 was treated with electron beams of 10 MeV through the anterior portal in a field size of 4 cmϕ. At the start of treatment 300 rad per day at a depth of 3 cm was given. When a dose of 600 rad was given in 3 days, mild conjunctivitis appeared but it disappeared by pause and medication for 3 days. Irradiation was resumed with a dose of 80 rad, which was gradually increased to 100, 120, 140, and 160 rad, but conjunctivitis did not occur. The total dose was 1500 rad in 13 days.

Case 6 was treated every other day with electron beams of 6 MeV through the anterior portal in a field size of 2 cmϕ localized on the tumor. The daily dose at a depth of 1 cm was 150 rad. After the third treatment, edema appeared on the lower eyelid and irradiation was discontinued until its disappearance one week later. Irradiation was resumed with a dose of 80 rad which was gradually increased to 100 and 120 rad. The total dose was 1970 rad in the overall irradiation period of 45 days.

Case 7 was treated with a ^{60}Co source through a pair of wedge filter portals perpendicular to each other. The anterior and lateral field sizes were 5×5 cm and 5×4 cm, respectively. The daily dose was 200 rad and a total dose of 2000 rad was given in 14 days with an NSD of 860 ret.

Case 8 was treated with electron beams of 10 MeV through the anterior portal in a field size of 6 cmϕ. The daily dose at a depth of 3 cm was 100 rad and a total dose of 1000 rad was given in 27 days with an NSD of 400 ret.

Case 9 was treated with electron beams of 10 MeV through the anterior portal in a field size of 4 cmϕ. The daily dose at a depth of 2 cm was 100 rad for the first ten irradiations and 150 rad for the following seven irradiations. The total dose was 2050 rad during the overall period of 45 days.

Case 10 was treated with electron beams of 10 MeV through the anterior portal in a field size of 4 cmϕ. The daily dose at a depth of 3 cm was 200 rad and a total dose of 1200 rad was given in 14 days; the NSD was 584 ret.

III. Results

Both the tumor and the exophthalmus disappeared in all cases. Follow-up observations were made for from 24 months to 56 months, and relapse was seen in only 2 cases. Case 4 showed tumor recurrence 6 months later, and surgery was performed. Case 6 showed signs of a tumor and exophthalmus 7 months later, but the symptoms improved by administration of steroids. Disturbance in eye movement (6 cases) and diplopia (5 cases) improved in all instances, but complete elimination was not possible in 2 and 3 cases, respectively. Swelling of the eyelid (1 case) disappeared, but blepharoptosis (1 case) persisted.

Table 3. Effects and side effects resulting from irradiation

Case	Residual symptoms	Follow-up period (months)	Side effects	
			Conjunctivitis	Cataract
1	Negative	56	Negative	Negative
2	Disturbance of ocular movement and diplopia	56	Negative	Negative
3	Negative	54	Negative	Negative
4	Ptosis of the lid Tumor recurred 6 months later		Positive	Negative
5	Negative	53	Positive	Negative
6	Tumor and exophthalmus recurred 7 months later		Negative	Negative
7	Disturbance of ocular movement and diplopia	52	Negative	Negative
8	Diplopia	45	Negative	Negative
9	Negative	44	Negative	Negative
10	Negative	24	Negative	Negative

Conjunctivitis occurred as a side effect in 2 cases. In one of these cases, it was exacerbation of chronic conjunctivitis caused by trichiasis. In both cases, the conjunctivitis was cured within 1 week after suspension of irradiation. No other post-therapeutic disturbances, including cataracts, were observed during the follow-up period. The therapeutic results and side effects are shown in Table 3.

IV. Discussion

Generally, pseudotumor is treated by surgery, chemotherapy mainly using steroids, and radiation therapy. It is difficult to surgically remove the tumor completely in many cases. In administration of drugs, only temporary improvement in symptoms is usually observed. In this method of therapy, therefore, recurrences often occur. In irradiation, only temporary relief of symptoms is usually obtained as same as chemotherapy in many types of pseudotumor[5)5)6)], except only pseudotumor of the lymphoid type can be treated with a low incidence of recurrence.

Radiation therapy has been employed against orbital inflammatory pseudotumor in some facilities and with various doses. CHENG *et al.*[5)] have reported 20 cases of inflammatory pseudotumor. Here in one case of the lymphoid type, together with the administration of nitromin, X-rays were applied

4 times at a dose of 200 r and 3 times at a dose of 150 r for a total of 1250 r to bring about cure. In one case of myositis, together with metazorone therapy, X-rays were applied 6 times at a dose of 50 r and 6 times at a dose of 80 r for a total of 780 r to bring about improvement. In one case of chronic dacryoadenitis, together with the administration of metazorone and Tanderyl, X-rays were applied 3 times at a dose of 50 r and twice at a dose of 100 r for a total of 350 r to bring about cure. KONNO *et al.*[6] have reported that a case belonging to Birch-Hirschfeld's Class 3 was exposed to a daily dose of 212 r for 9 consecutive days together with dexamethasone treatment, and the exophthalmus was completely cured. In these cases, however, radiation therapy was combined with chemotherapy so that the real effect of radiation therapy alone could not be as certained. TAKADA *et al.*[7] applied X-ray therapy with 3 portals to a case of non-specific chronic granulomatous inflammation: X-rays at a dose of 338 r were given 23 times for a total surface dose of 7774 r and the symptoms showed some improvement. Irradiation was then resumed at a dose of 376 r and a corneal ulcer developed at the 10th irradiation. The therapy was suspended at the 17th irradiation when the total surface dosage reached 6392 r. It was concluded that reirradiation had been ineffective. In this case, since the KVp was not reported, the exposure dose to the lesion could not be estimated, but it does suggest that even excessive irradiation to a degree of causing corneal ulcer may prove ineffective against some histological types of pseudotumor. MORGAN, G.[8] reported that in 18 cases initially diagnosed as benign lymphoma, the tumor disappeared by therapy, but that during the 5 to 18 years of follow-up 16 of these cases were found to be non-disseminating tumor. Regarding the 6 cases given radiation therapy, the dosage was described in only 2 cases, i.e., 300 r and 1500 r in 32 days. STÄRK, N. *et al.*[9] employed radiation therapy on 4 cases of benign small cell lymphoma. In the first case, the electrom beam was irradiated from 2 portals at a dose of 200 rad for a total of 2400 rad with an energy of 15 MeV and a field size of 6 cmϕ through the anterior portal, and in dose of 200 rad for a total of 2600 rad with an energy of 20 MeV and a field size of 6 cmϕ through the lateral portal. The tumor disappeared after 4 weeks without recurrence in 3 years. In the second case, electron beam therapy was performed with an energy of 20 MeV and a field size of 8 cmϕ at a dose of 200 rad for a total of 600 rad, and with a beam of ^{60}Co in a field size of 6×6 cm at a dose of 200 R for a total of 4400 R; but after 1 month, exophthalmic relapse and corneal erosion occurred. In the third case, ^{60}Co was irradiated through the anterior portal in a field size of 5×11 cm to each eye at a dose of 200 R for a total of 4000 R, and no relapse was observed in the follow-up observations made 2 years and 5 years later. In the fourth case, ^{60}Co was irradiated through the anterior portal in a field size of 5×11 cm at a dose of 200 R for a total of 5000 R, and no relapse has been seen for 5 years. It was concluded that radiation therapy proved to be more effective than surgery and that electron beam produced fewer side effects than ^{60}Co. It was also stated that with regard to depth dose irradiation from two directions perpendicular to each other was superior to irradiation from one direction alone.

As radiosensitivity is considered to be relatively low on other types of pseudotumor, only cases of the lymphoid type were given radiation therapy. As the present authors aimed at the elimination of tumors or exophthalmus, the doses used were not uniform, but the NSD was from 282 to 924 ret, which was considered to be adequate in view of both the direct effects and the side effects. Such therapy should be applied only to tumors of suitable histological type, and for cases in which the effects

are not satisfactory, excessive irradiation should be avoided.

In protecting the healthy eye, irradiation through the anterior portal is more advantageous than irradiation through the lateral. However, since radiation cataract poses a problem in the former, in order to reduce the radiation dose to the lens it will be necessary to employ either the high energy photon beam having the greager depth of build up or the electron beam with partial shielding by eyeshields. Comparing these two sources the authors have adopted the electron beam in which protection of the healthy tissue behind the orbit is possible. MORITA *et al.*[10] reported that cataract would not induced by 1400 rads in 6 weeks but that a slight visual impairment would develop with 3000 rads in 6 weeks. According to the International Commission on Radiological Protection[11], 15 Sv or lower is the threshold of safety for protracted irradiation during an overall working period. By using a lead shielding block 1.9 mm in thickness the dose to the lens was reduced to 20% when compare with the case without the shielding block. To most patients, a lead block 3.5 mm thick can be used, and moreover, the energy used is lower than 10 MeV. Thus, the risk of cataract due to radiation can be avoided. In the 2 cases that showed conjunctivitis, a dose of 300 rad was applied but it is preferable to use a dose lower than 200 rad.

V. Conclusion

1. Irradiation mainly with electron beam was applied to 10 cases of orbital inflammatory pseudotumor of the lymphoid type, and in all cases the tumor and exophthalmus disappeared. In 2 cases, however, recurrence was observed after 6 and 7 months, respectively.

2. The electron beam treatment is one of the adequate methods of choice and the optimum energy was found to be about 10 MeV and a dose lower than 2000 rad, i.e., below 900 ret, was evaluated to be adequate.

3. To prevent conjunctivitis, it is preferable to use a dose lower than 200 rad. Gradual increase in dosage from 80 rad was found to be effective in cases where conjunctivitis presented a problem.

4. The lens was shielded with a lead block of the contact lens type. During the follow-up of from 24 to 56 months, development of cataract was not seen in any case of this series.

5. For pseudotumor of the lymphoid type, radiotherapy is the treatment of choice.

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