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Radiation Therapy (RT) of Midline Granuloma

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Seven patients having midline granuloma received local irradiation from March 1983 to June 1986. Clinically, all of the 7 patients had pansinusitis with necrotic destruction of the involved sites and one case revealed colonic lesion.

Each of the patients received a tumor dose of 4,000~5,000 cGy/5~6 wks to the upper aerodigestive tract using a 6-MV linear accelerator.

Complete and partial remission occured in 3 patients each, and in one case, the disease progressed despite of the irradiation.

Key Words: Midline granuloma, Upper air passage, Local irradiation.

INTRODUCTION

Lethal midline granuloma (LMG) is a non-specific term that encompasses a variety of confusing histologic and clinical entities. LMG refers generally to a progressively destructive inflammatory condition that involves the nose, paranasal sinuses, and palate and produces a secondary erosion of contiguous structures[1,2]. The disease was first described in 1897 by McBride, and in 1933 Stewart reviewed its clinical and histologic features. The etiology is debated. The disease is uniformly fatal, with death occuring usually after an extended illness (from months to years) from meningitis secondary to erosive invasion of the meninges, hemorrhage, sepsis and/or inanition. Even though fatal, most of the destructive lesions respond to a high-dose local irradiation, and many remaining controlled for several years. This communication will report the result of a 3-year study of 7 patients with LMG who received local irradiation.

Table 1. Histopathologic Findings in 7 Cases with LMG

Case No.	Histopathology
1	Multiple biopsies of medial wall of antrum and necrotic mucosa of nasal cavity showing chronic inflammation with extensive necrosis
2	Multiple biopsies of soft palate showing polymorphic reticulosis/chronic inflammation with necrosis ; Biopsy of ileum, appendix, cecum, and ascending colon showing polymorphic reticulosis, diffuse with ulcer
3	Multiple biopsies of larynx showing marked chronic inflammation with large necrosis
4	Multiple biospes of nasopharynx showing marked chronic inflammation with necrosis/lethal midline granuloma (malignant midline reticulosis)
5	Multiple biopsies of soft palate margin, left posterior pillar, left inferior turbinate region showing marked acute and chronic inflammation, necrosis, and focal clusters of atypical cells
6	Biopsy of right nasal mucosa showing marked acute and chronic inflammation with large areas of necrosis
7	Biopsy of nasal cavity, right showing malignant lymphoma lymphocytic, poorly differentiated

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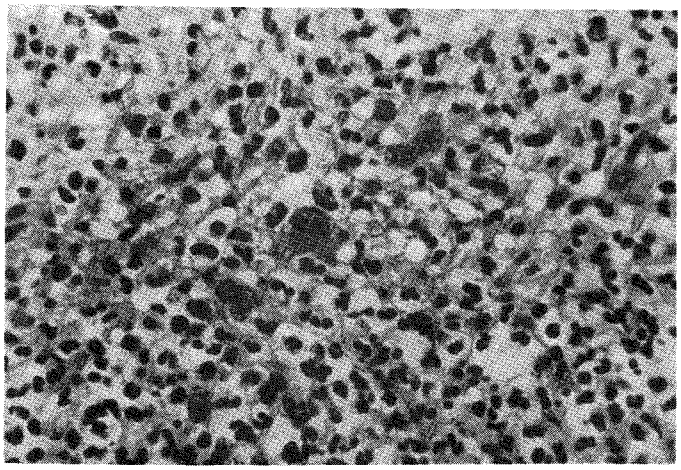

Fig. 1. This fields shows marked acute and chronic inflammation, and focal clusters of atypical cells (X100) (Case No. 5).

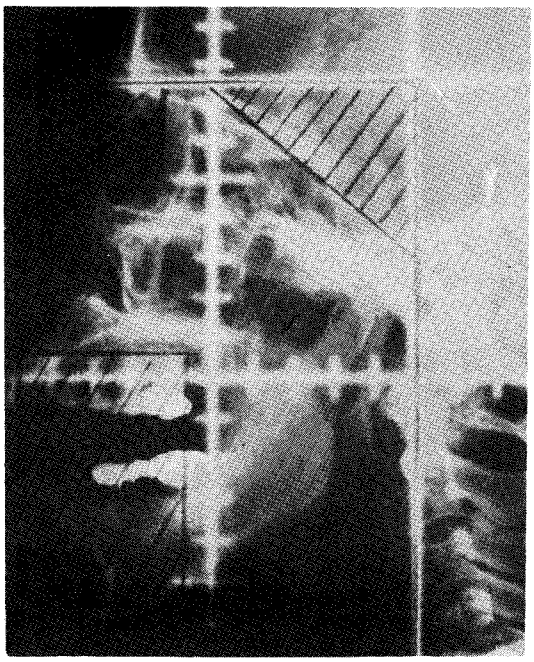

Fig. 2. Lateral simulation film for radiation therapy (Case No. 7).

MATERIALS AND METHODS

We reviewed 7 patients who received curative external radiation therapy (RT) for pathologically proven LMG from March 1983 to June 1986 at the Division of Therapeutic Radiology, Kangnam St. Mary's Hospital, Catholic Medical College. Six of 7 cases were referred from Department of Ear, Nose and Throat and one from the Department of Internal Medicine. All patients had pretreatment work-ups including paranasal and chest X-rays and neck CT scanning. Biopsies were made of the involved areas in each patients, and the histopathologic findings were as listed in Table 1. Typical nonspecific acute and chronic inflammation with necrosis was noted in 6 cases (Fig. 1), and malignant lymphoma in 1 case.

We classified biopsy findings according to Halperin[4] into (1) idiopatic midiline granuloma, (2) polymorphic reticulosis, and (3) extranodal lymphoma. Prior to RT, one patients underwent Caldwell operation of PNS and another one received 3 courses of chemotherapy consisting of Vincristine, Cytoxan, and prednisone. Tumor dose of 4,000~5,000 cGy was delivered in an elapsed time of 5-6 weeks. with daily fraction of 180 cGy using a 6-MV linear accelerator. Because of the nasal stuffiness and pansinusitis in most patients, a wide field irradiation including the upper air passage was used. Technically, combined anterior plus lateral wedge fields (case No. 1, 6, 7) or bilateral parallel opposing portal (case No. 2, 3, 4, 5) (Fig. 2) were used.

RESULTS

1. Age and Sex

The ages of the patients ranged from 16 to 54 years at the time of diagnosis. There were 3 males

and 4 females.

2. Clinico-pathological Classification

Clinico-pathologic diagnosis was non-Wegener's granuloma in all cases. Among the types of non-Wegener's granuloma, idiopathic midline granuloma was 4 cases (1, 3, 5, 6), polymorphic reticulosis 2 cases (No. 2, 4), and extranodal lymphoma 1 case (No. 7) (Table 2).

3. Sites of Involvement and Clinical Findings

In all patients, the upper air passage was involved. Exceptionally, case 2 showed colonic involvement in conjunction with the upper air passage lesion. Involved sites in decreasing order were nasal cavity (5 cases), maxillary sinus (3 cases), palate (3 cases), larynx (1 case), nasopharynx (1 case), and colon (1 case). All of the 7

Table 2. Clinical Data of 7 Cases with LMG

Case No	Age of onset sex	Site of involvement	Clinical manifestation	Clinicopathologic criteria
1	18/F	Nasal cavity maxilla antrum	Nasal obstruction with foul odored nasal discharge	Idiopathic midline granuloma
2	16/M	Nasal cavity, palate maxillary sinus GI tract (colon)	Nasal stuffiness, nasal bleeding sore throat, abdominal pain	Polymorphic reticulosis
3	19/M	Larynx	Throat pain, swallowing difficulty necrotizing ulceration of larynx	Idiopathic midline granuloma
4	54/F	Nasopharynx maxillary sinus	Frequent epistaxis, nasal stuffiness swallowing difficulty, easy bleeding exophytic mass on Lt. Rosenmuller fossa	Polymorphic reticulosis
5	40/M	Nasal cavity soft palate	Nasal stuffiness with crust formation	Idiopathic midline granuloma
6	45/F	Nasal cavity nasopharynx soft palate	Pain & foul odor from Rt. nose, necrosis on Rt. nasal alar with perforation, erythematous change of soft palate	Idiopathic midline granuloma
7	54/F	Nasal cavity	Nasal obstruction, swallowing difficulty perforation of soft palate, polypoid mass in nasal cavity	Extranodal lymphoma

Table 3. Results of Radiation Therapy in 7 Cases with LMG

Case No.	Tumor Dose/RT technique	Clinical response	Comment
1	4,500 cGy/5 weeks, combined anterior plus lateral wedge fields	PR	Died of unknown cause, 11 mo, later after initial RT
2	Initial RT 4,620 cGy/5 – 6 weeks, Second course of RT is administered, bilateral parallel opposing portal	Progression, 1.5 months later since initial RT	Rt. hemicolectomy, 4 months later after initial RT
3	4,500 cGy/5 weeks, bilateral parallel opposing portal	CR	5 mo. NED
4	5,040 cGy/5 – 6 weeks, bilateral parallel opposing portal	CR	4 mo. NED
5	4,500 cGy/5 weeks, bilateral parallel opposing portal	CR	2 mo. NED
6	4,940 cGy/5 – 6 weeks, combined anterior plus lateral wedge fields	PR	1 mo. NED
7	3,960 cGy/4 weeks, combined anterior plus lateral wedge fields	PR	2 mo. NED prior RT, chemotherapy

CR : Complete remission, PR : Partial remission, mo : month(s), NED : No evidence of disease

patients had pansinusitis, with necrotic destructive lesions of the nasal septum and/or palate, larynx. Perforation of the soft palate was developed in case 7 (Table 2).

4. Results of Irradiation

All patients received a tumor dose of 4,000~5,000 cGy to the upper aerodigestive tract area, and tolerated well. Complications other than oral mucositis were not observed. Clinically, complete remission was noted in 3 cases, partial remission in 3 cases, and progression in 1 case. One patient (case 7) had right hemicolectomy because of right colon involvement, 4 months after the initial RT. This patient also showed recurrence of the destructive lesion in the nasal cavity and hard palate, and a second course of RT was administered. The remaining 5 patients showed no evidence of disease during the months following the initial RT (1 to 5 months) (Table 3).

DISCUSSION

The term LMG has been used to encompass the many disorder which produce midfacial destruction, and described as several clinico-pathologic entities. But strictly speaking, LMG is a pure clinical term lacking histopathologic information. LMG is classified into Wegener's and non-Wegener's granuloma by clinico-pathological criteria[4,9].

Wegener's disease is characterized by necrotizing granuloma with vasculitis of the upper and lower respiratory tract, systemic vasculitis, and glomerulitis.[4,7] Non-Wegener's granuloma can be distinguished as 3 different pathological entities: (1) idiopathic midline granuloma, (2) polymorphic reticulosis(PR)/lymphomatiod granulomatosis (LG), and (3) extranodal lymphoma. Idiopathic midline granuloma, in contrast to PR, has no systemic symptoms despite of the extensive destruction of the upper airway unless secondary infection intervenes. Idiopathic midline granuloma does not have the angiocentric infiltrate of atypical cells characterisitic of PR/LG. PR/LG is locally invasive, has the potential for distant spread, and may porgress to lymphoma. There, this entity should be grouped with the lymphoproliferative disorders[4]. PR was coined by Eiche in 1966 and named as LG by Liebow in 1972. While the term PR has been used for a disease with local midfacial symptoms, LG may be localized one site or diseminated to lung, GI tract, kidney, and central nervous system[5,8,10].

In ordinary malignant lymphoma, an inflammatory cell infiltrate may be found near an area of necrosis. But in PR, the inflammatory infiltrate tends to be dispersed more extensively throughout the tumor tissue. PR exhibits more extensive mucosal ulceration, tissue necrosis, bone destruction, and fistular formation in contrast to malignant lymphoma[11].

Regarding the result of RT, Fauci et al. had remarkable success utilizing 4,000~5,000 cGy with long term remission in 7 of 10 patients with a mean survival of 7.4 year[12]. Also, patients with localized upper airway disease have been reported to respond to RT in about 75% without local recurrence or peripheral dissemination[13]. Since in most instance the disease is extensive, radiation treatment is difficult to plan and carry out. Generally, we should include area of nasal cavity, paranasal sinus, and palate for radiation field.

CONCLUSION

During a 3 year period, 7 patients having midline granuloma received local irradiation. Clinico-pathologic diagnosis was non-Wegener's granuloma in all cases. In all patients, the upper air passage was involved. Involved sites in decreasing order were nasal cavity, maxillary sinus, palate, larynx, nasopharynx, and gastrointestinal tract (colon). All patients received a tumor dose of 4,000~5,000 cGy to the upper aerodigestive tract area using the treatment technique of combined anterior plus lateral wedge fields or bilateral parallel opposing portals. Clinically, complete remission was noted in 3 cases, partial remission in 3, and progression in 1.

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= 국문초록 =

중앙성육아종의 방사선치료

가톨릭의대 강남성모병원 방사선치료실

권형철 • 오운경 • 길학준 • 윤세철 • 박용휘

중앙성육아종 환자 7예에 대하여 가톨릭의대 강남성모병원 방사선치료실에서는 1983년 3월부터 1986년 6월까지, 사이에 외부방사선치료를 시행하였다.

임상증상으로서, 모든 환자에서 침습부위에 궤사를 동반한 부비동염 증세를 보였고, 1예에선 대장(결장)병변도 나타냈다.

방사선치료는 6 MV 선형가속기를 사용하여 비강 및 부비동 부위를 포함하는 상기도 부위에 2~3문 조사를 실시하여, 총선량 4,000~5,000 cGy/5~6주를 조사하였다.

방사선치료 반응으로서 방사선치료 종료후 1.5~20개월 추적관찰한 결과 완전 및 부분관해가 각각 3예, 대장부위에 병변을 보였던 1예에선 병이 진행되고 있음이 관찰되었다.