MALIGNANT GRANULOMA*

By E. J. GILROY GLASS (Nottingham)

WHEN I was invited to take part in this discussion I was very conscious of my limited personal experience of malignant granuloma. The condition is, however, so rare that perhaps I need not excuse myself on that score. The four cases on which I base these remarks have had one merit; they occurred so close together that one has been able to compare the response to treatment in a way that is hardly possible in the sporadic cases which are the more normal experience.

There is something very sinister about malignant granuloma, in some ways almost worse than cancer. Seen early, and in an accessible position, we generally have some hope in cancer, but with malignant granuloma the patient seems all too often to be doomed to mutilation and death from its earliest recognition.

Breckenridge and others (1954), reviewing the condition state, "The prognosis is grave. Until 1941 only four patients had recovered. Two had been treated with radium and X-ray irradiation, and one was believed to have recovered spontaneously; the other case was atypical. Since 1941, there have been a few instances of recovery; the follow-up period on some of these cases, however, has been too short to classify them as cures."

In addition to this rather gloomy statement, there is the fact that such cures, or apparent cures, as are recorded, have borne no clear relationship to the line of treatment and, indeed, there seems to be little uniformity of opinion as to what constitutes the best line of treatment. Let us hope that this discussion to-day will help to clarify the position.

In 1933, J. P. Stewart, in his classic description of this condition, states: "Deep radiotherapy promises more success, and deserves further trial." To judge from the literature this advice has not, perhaps, had the attention that it deserves. To some extent this may be due to an unwarranted, or possibly, warranted fear of sequestration and X-ray necrosis.

The references to radiotherapy in the treatment of malignant granuloma which I have been able to find, have either not mentioned the dosage, or have suggested a fairly large dosage such as one might use in the treatment of malignant disease. The cases on which I base these remarks were, however, dealt with by minimal dosage, something in the level of 80-100 r weekly, over a period of 6 to 10 weeks.

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In the past 27 years only six cases of malignant granuloma had been seen in the Nottingham General Hospital. The first two were in the pre-war years, and I was only too thankful that the responsibility for their treatment rested with those older and more experienced than myself. Both were treated with radiotherapy among other measures, and both were fatal. In the post-war years there have been four cases, three of which were seen personally, and the fourth is included here by courtesy of my colleague, Mr. Macleod.

The remarks which follow are based on the post-war cases.

P.K., a man in his early thirties, was in his young days an enthusiastic boxer, with the result that his nose had been badly damaged. The bridge was flattened and the septum badly twisted. Some years ago I advised him to have a submucous resection, but his business commitments prevented him from taking this advice for the time being. When seen again in October, 1952, he had what appeared to be an idiopathic perforation of the septum, but it was still felt that he would benefit by a submucous resection. It was only during operation that I got a clear view of the inferior turbinals and floor of the nose; both of which areas were found to be ulcerated and covered with granulation tissue and crusts. A biopsy report from this tissue was "non-specific granulation tissue". The possibility of malignant granuloma seemed very real.

The effect of operation on his symptomatology was so satisfactory that he did not report for some 10 weeks, despite requests to the contrary. By that time the condition looked ominous. Almost the whole remaining septum was eaten away, the inferior turbinals were ulcerated, there was a minute perforation of the palate, and the granulations had spread out over the oral surface. A Wassermann was negative, bacteriological investigations inconclusive, blood investigations negative and the histopathology consistent with malignant granuloma.

As a first line of treatment we tried intensive antibiotic therapy, both locally and generally, including penicillin, chloromycetin, streptomycin and aureomycin. I had the impression that chloromycetin reduced the crust formation, but beyond that there was no improvement. A course of A.C.T.H. relieved the pain, and I got the impression that it stayed the progress of the ulceration, but as soon as it was stopped the condition continued its slow, vile and relentless course, until ulceration had spread right back to the nasopharynx, and the palatal perforation was a centimetre in diameter.

In August, 1953, Dr. Cross, the surgeon in charge of the Hogarth Radiotherapeutic Centre, suggested that we might try very small doses of X-ray therapy, without holding out much hope of success. The recommended dosage was 80 r weekly. Treatment was commenced in early September and almost immediate improvement became evident. By the time this first course was completed on October 15th, the whole ulcerated

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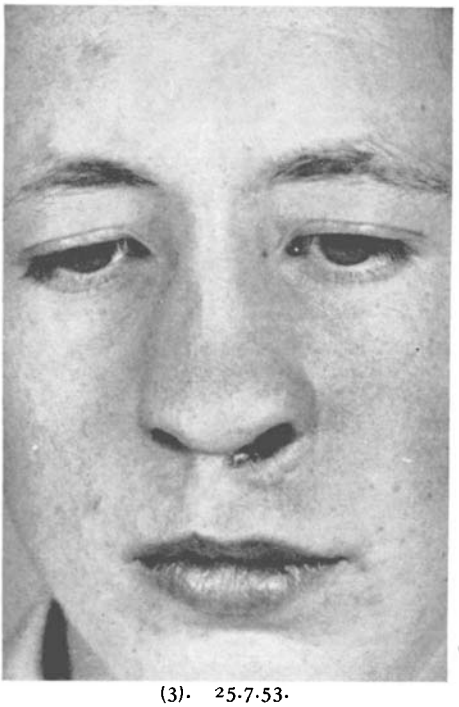
Case 2.—A.H. Showing the response to treatment over a period of six weeks.



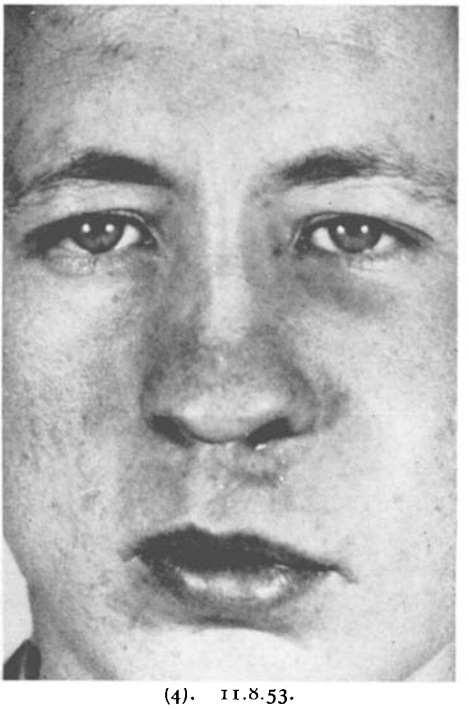
(1). 1.7.53.



(2). 11.7.53.



(3). 25.7.53.



(4). 11.8.53.

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area had healed, the mucosa was restored and the edges of the palatal perforation clean-cut and healthy looking. He had, however, some discomfort, which suggested a lesion on the upper surface of the soft palate, although we could see none, and it was felt wise to give a second course of radiotherapy, which was completed on December 23rd, by which time he was completely relieved of pain and all discomfort.

In February of this year there was some pain in the laryngeal region and a tiny white ulcer, no bigger than a rice grain, appeared over the arytenoid. Although not typical, we again gave a course of radiotherapy with very rapid healing, and all went well till the beginning of October of this year, when he developed a recurrence in the floor of the nose, the left inferior turbinal and, soon after, a tiny patch on the right arytenoid. A further course of Deep X-ray Therapy in similar dosage has had equally good effect, and when seen during the last few days (4.12.54) healing was complete and there was no discomfort.

The second case, A.H., a miner, aged 18, was referred from an outlying clinic in June of last year, with a history of ulceration of the nasal vestibule for some three months. The columella, the inner surface of the alae, the anterior septum, inferior turbinals and an area of the upper lip, were ulcerated and covered with crusts. Once more all investigations were negative, and a biopsy was again consistent with the diagnosis of malignant granuloma. Aureomycin and penicillin did not influence the condition at all, and he in turn was referred for Deep X-ray Therapy in July. The granuloma healed almost miraculously and he remained well until the beginning of October, when he reported again with soreness in the mouth and swelling of the face. The uvula and pharynx were superficially ulcerated, and there was some crusting in the right side of the nose. A further course of X-ray therapy was commenced immediately and continued till December 22nd, by which time the ulceration had again healed, but the patient was pyrexial and appeared in bad shape. He was given a further course of aureomycin and A.C.T.H., which seemed to improve his condition for a day or two, then he went into a rapid decline in his general health and death supervened. The cause of death was considered by the pathologists to be agranulocytosis, and there was a suspicion that sensitivity to aureomycin might well have been a factor.

The third case, D.L., is, as far as I know, the youngest recorded case of malignant granuloma, being only 2 years and 11 months when first seen. The granulomatous ulcer affected the whole vestibule of the nose, with erosion of the columella and spread out to the upper lip. The usual tests were carried out, with negative findings, and again a biopsy was consistent with malignant granuloma. Encouraged by the previous case, he was treated by Deep X-ray Therapy, without any antibiotics or other treatment. The period of therapy was from November 12th to January 13th, and the response to treatment was very rapid. Half-way through the

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course the active area seemed to be confined to a small part of the alae nasi, and by the end of treatment the whole mucosa and skin surface looked clean. He has been kept under close observation and there has been no sign of recurrence.

The fourth, and last case, Mrs. C., who is a private patient of my colleague, Mr. Macleod, was a woman aged 66, who was first seen in April of this year with a history of seven weeks sore throat, and an ulceration involving the soft palate, fauces, tonsils and the greater part of the naso-pharynx, the uvula being completely eroded. The same series of tests was again negative, and she was treated by radiotherapy from May 3rd to June 29th, by which time the whole lesion had healed and it has remained so to date.

Such has been the recent experience of Dr. Cross and myself in the treatment of malignant granuloma. Looking back on these four cases, we are inclined to feel that in the first two we did not irradiate a sufficiently wide field. This defect was remedied in the last two cases and, to date, we would feel that this has been justified.

Summary of Treatment

Case	Date	Treatment
1. P.K.	20. 8.53	80 r. Twice Weekly for 5 weeks—6 × 8 cms. field to nose
	8.11.53	80 r. Weekly for 6 weeks— Large fields
	22. 3.54	80 r. Weekly for 8 weeks—Larynx
	5.10.54	60 r. Twice weekly for 5 weeks—nose and larynx
2. A.H.	8. 7.53	100 r. Twice weekly for 6 weeks—5 cm. circle field
	13.11.54	60 r. Twice weekly for 6 weeks—neck bridge
3. D.L.	23.11.53	50 r. Weekly for 8 weeks—neck bridge
4. A.C.	3. 5.54	80 r. Weekly for 8 weeks—large fields

With regard to our choice of minimal dosage in treatment, this was done because we felt that such low dosage could not possibly lead to either sequestration or to irradiation necrosis. Moreover, it would be possible to repeat a course of treatment if the condition broke out in another area, as it did, in fact, in the first case. We were by no means certain that it would have the desired effect, we could but try.

If you would level the criticism that it is too early to assess the results, I would agree. If your criticism is that the experience of four cases is insufficient to assess the value of minimal radiotherapy, I would once more agree, but I feel that Dr. Cross and I have some justification for presenting these cases. Their affect on me, personally, has been to change my attitude to this vile disease from one of despair to, at least, a guarded optimism.

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When one looks through the literature the despair is, perhaps, not unfounded, and even this little ray of hope looks like a beacon by contrast.

Before concluding, I would like to express my thanks to Dr. Cross for his interest, and for the part which he played in treating these four cases, and to Prof. Ormerod and Dr. Friedman for much help and advice freely given, and gratefully accepted.

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