Though not severely depressed, the patients studied seemed typical of those referred to hospital for antidepressant outpatient treatment, their mean Hamilton depression score being 24.

These findings are similar to the results of several mainly uncontrolled studies. Nistico *et al*¹¹ reported the development of hypomania during treatment with flupenthixol in four out of 32 patients, which by itself strongly suggests that the drug has antidepressant properties. The improvement recorded during our trial, however, may have been due partly to anxiolytic drug effects. This might apply to both flupenthixol and amitriptyline, as it seems to apply to other antidepressants that are effective against primary anxiety and phobic states¹² and to other major tranquillisers, such as thioridazine, effective against some forms of depression.¹³ In fact, the precise nosological relations between anxiety and depression remain not clear.

Within the limits of our present findings, flupenthixol is a useful alternative antidepressant, which acts rapidly, is effective in low doses, and has no serious side effects. With increased dosage the drug has acknowledged antipsychotic properties, and recorded side effects include extrapyramidal features and insomnia. There is no tendency towards dependence, as there is with the benzodiazepines, and toxicity after an overdose is much lower with flupenthixol than with tricyclic drugs.

Several treatment possibilities suggest themselves. Since many outpatients are unreliable in taking oral medication,¹⁴ the effects of flupenthixol given parenterally in depot form to depressed patients would be interesting. The risk of overdose would be reduced and adequate blood levels presumably maintained. The effectiveness of long-acting intramuscularly administered flupenthixol might also be tested as a prophylactic against

frequently recurrent depressive illness. Nevertheless, the possibility of untoward reactions such as persistent dyskinesias cannot be ignored. There are clear structural and pharmacological differences between the thioxanthenes and tricyclic antidepressants, and the mode of clinical action of the two groups of drugs may also differ. Possibly, therefore, the antidepressant effects of combined treatment with flupenthixol and a tricyclic drug may be additive.

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Value of gallium scanning in seminoma of the testis

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Summary

Whole-body scanning using gallium-67-citrate gave consistently accurate tumour localisation in patients with seminoma of the testis. Thirteen out of 15 scans performed in patients with disseminated seminoma in relapse gave good imaging in all disease areas. Scans in patients with teratoma of the testis were less consistently positive; of nine scans performed in patients with disseminated teratoma seven were entirely negative and two scans lightly imaged large disease masses in two patients. In eight patients with combined (seminoma and teratoma) tumours the scan seemed to reflect the dominant tumour type at the time of scanning. In one of these patients the scans changed from positive to negative, being positive

when seminoma was the dominant tumour and negative when a teratoma developed.

Gallium-67-citrate scanning is useful in managing seminoma of the testis, both for determining the extent of disease present at initial presentation and for routine follow-up. It may be useful in the differential diagnosis of combined tumours when tumour masses are greater than 2 cm in diameter.

Introduction

A satisfactory tumour localising agent for the testicular tumours would help in deciding on treatment, localising the tumour for external radiation, and monitoring the response of the disease to treatment.

In seminomas disease localisation is important since this tumour is exceedingly sensitive to radiation, and sites that are usually vulnerable to radiation damage, such as the liver and lungs, can be irradiated to tumouricidal dose levels without prohibitive normal tissue damage. Thus, widespread disease is not necessarily incompatible with cure. In testicular teratomas there is the added problem of staging, which is particularly relevant to a combined irradiation-chemotherapy approach for disease that has spread to the lungs and when it is important to exclude liver disease.

From 1972 we have assessed the tumour imaging agent ⁶⁷Ga-citrate in the whole-body scanning of patients with testicular tumours. ⁶⁷Ga-citrate is prominent among tumour

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imaging agents because of its favourable lesion:background radioactivity ratios in a small range of tumours. For us it has proved valuable in the management of certain clinical conditions in Hodgkin's disease and carcinoma of the bronchus, and others have recommended its use in hepatomas¹ and malignant melanomas.² We report here our experience with ⁶⁷Ga scanning and assess its value in the management of testicular tumours.

Methods

⁶⁷Ga-citrate (Philips-Duphar) 2-3 mCi was injected intravenously and 48 hours later the patients were scanned on a Selo Superscanner DS7. Bowel laxatives were routinely used before scanning, but if any suspicious area of activity was seen in the abdomen the patient was rescanned 24 hours later. The scans were interpreted by two independent observers, and the tumours were classified in the department of pathology, Royal Marsden Hospital, according to the classification put forward by the Testicular Tumour Panel and Registry.³

Results

Twenty-three patients with a pure seminoma were scanned and received a total of 39 scans. Of 15 scans performed when seminoma had been confirmed by other methods or by response to treatment, 13 were positive in every disease site. There was one false-negative scan in a patient with small but affected external iliac lymph nodes which had been diagnosed on lymphography. One patient was classified as having a "partial" false-negative scan. He had relapsed with bilateral hilar deposits and a further deposit in the right upper zone and another peripherally in the left lower zone. The gallium scan was clearly positive in the right hilar and right upper zone deposits, but was negative for the left hilar and left lower zone deposits. The

remaining 24 scans were performed on patients who were disease-free and were negative.

Eleven patients with a testicular teratoma were each scanned once, and of nine who had disseminated disease with sizeable tumour deposits only two patients showed light uptake in the disease areas. The other two patients scanned had stage 1 disease and were negative.

Eight patients with combined (seminoma and teratoma) tumours were studied. These eight patients between them received 16 scans, one patient being scanned seven times. On three scans which were negative no tumour was found with other investigations, and the absence of disease was confirmed by the patients continuing in clinical remission. Tumour masses were present at the time of the other 13 scans, and five of these scans were performed on patients with tumours that were histologically and clinically like pure seminomas. These scans were positive in all disease areas. Two patients subsequently developed teratomas, but unfortunately only one was rescanned. This patient had a mediastinal tumour, which previously had imaged very well with ⁶⁷Ga-citrate but could no longer be seen on scanning. Five patients with known combined tumours failed to respond to conventional treatment for seminoma and developed large masses of teratoma which also failed to image with ⁶⁷Ga-citrate. Altogether eight scans were performed when teratomas were present, but none of these scans were positive.

We scanned one patient with a mixed teratoma-choriocarcinoma probably of mediastinal origin, and this tumour did image clearly with ⁶⁷Ga-citrate.

Three cases in the series are discussed more fully below to illustrate the value of gallium scanning in seminoma of the testis.

Case 1—This patient was found to have extensive intra-abdominal seminoma in 1969 for which he received radiotherapy. He relapsed in 1972 with deposits of seminoma in the right neck, para-aortic region, and prostate gland. Chemotherapy was restarted and the patient went into complete remission (fig 1A) until October 1974, when he suffered from severe abdominal pain. From November 1973 ⁶⁷Ga-citrate scans had been performed regularly as a follow-up procedure. An abnormal area of ⁶⁷Ga uptake was noted five months before the onset of symptoms, but no action was taken then because of lack of corroborative evidence (fig 1B). A scan performed at the onset of his symptoms showed that the mass had enlarged (fig 1C At).

FIG 1—Case 1. Serial scans of upper abdomen. (A) December 1973. Normal liver image showing area where seminoma deposit later develops (arrowed). (B) May 1974. Abnormal area of ⁶⁷Ga uptake below right lobe of liver. (C) October 1974. Abnormal area has increased. Laparotomy revealed recurrent seminoma below right lobe of liver. (D) April 1975. Further recurrence in upper abdomen to left of midline (arrowed).

FIG 2—Case 2. Serial chest scans. (A) January 1972. Upper mediastinal mass of seminoma extends into right and left upper zone of chest. (B) February 1972 during radiotherapy. Mediastinal seminoma has shrunk and extends into left upper zone only. (C) March 1974. Large paravertebral and right lower zone deposit, which subsequently turned out to be teratoma. Only normal blood background can be seen and masses have not imaged with ^{67}Ga .

operation an 8-cm mass of tumour below the liver was found. No other investigation before laparotomy had indicated disease. The patient was put on chemotherapy and the mass was irradiated. He remained well until April 1975, when a further area of abnormal uptake was noted in the left upper abdomen (fig 1D).

Case 2—This 37-year-old patient had an orchidectomy for seminoma in the summer of 1972. There was no evidence of a combined tumour at that time. He was referred to the Royal Marsden Hospital in 1973 after relapsing in the mediastinum and was treated with radiotherapy. A gallium scan was highly positive in the mediastinum (fig 2A and B). He responded to treatment and the scan returned to normal. In 1974, however, he developed a lower mediastinal mass that did not respond to treatment. This large mass failed to image with ^{67}Ga -citrate. He died from widespread deposits of teratoma. A tumour that had previously taken up ^{67}Ga no longer did so, which suggested that the character of the tumour had changed.

Case 3—A 47-year-old man presented with a tumour in the left testis in 1973. In September 1974 he was referred to us complaining of backache and with evidence of extensive recurrent disease. A malignant teratoma was initially diagnosed, but, on review, the appearances were more those of seminoma. There was radiological evidence of collapse of the 9th and 12th dorsal vertebrae and the first three lumbar vertebrae. There were also

metastases in the right 10th and the left 5th and 6th ribs. The scan taken in September 1974 (fig 3A) showed increased uptake in the head of the left humerus, the dorsal and lumbar spine, and in the ribs on both sides. There was also uptake in the ilium and right pelvic lymph nodes. After chemotherapy and radiotherapy the abnormal areas showing gallium uptake returned to normal (fig 3B). At the time of writing the patient remained well controlled on cyclophosphamide.

Discussion

Gallium scanning provides a convenient and safe means of whole-body screening in the management of patients with seminoma of the testis. Deposits of seminoma may arise in areas not easily accessible to other diagnostic techniques. Differences in uptake of ^{67}Ga in tumour subgroups has not been emphasised. For example, the uptake characteristics of squamous cell carcinoma of the bronchus seem to be no different to those of

FIG 3—Case 3. (A) Before treatment for disseminated seminoma. Increased uptake at head of left humerus and in dorsal and lumbar spine, left ribs, right lower ribs, ilium, and right pelvic lymph nodes. There is also uptake in faeces in proximal colon, which disappeared on rescanning after a laxative. (B) After chemotherapy and radiotherapy these abnormal areas of ^{67}Ga uptake have returned to normal. Again, there is faecal uptake in the proximal colon.

oat-cell carcinoma.⁴ The evidence we have presented here suggests that in the testicular tumours ⁶⁷Ga may be more consistently taken up by seminoma than by teratoma. In patients who are suffering from what it presumed to be a pure seminoma the change from a positive scan to a negative scan together with a change in the clinical course of the disease suggests that a teratoma may have come to dominate the clinical picture.

Pinsky *et al*⁵ have recorded the largest series of ⁶⁷Ga-citrate scans in patients with testicular tumours. Only abdominal scanning was performed, but this proved useful in assessing the spread of tumour to the abdominal lymph nodes. Embryonal carcinomas (anaplastic teratomas) tended to give positive scans, but there were no patients in the series who had disseminated seminomas and few who had more differentiated teratomas.

It is not known why seminomas, like lymphomas, have a high affinity for ⁶⁷Ga. Swartzendruber *et al*⁶ performed electron microscopic autoradiography on thymus and lymph node tissue of leukaemic mice and found that ⁶⁷Ga activity was predominantly in "lysosomal-like" granules within tissue macrophages. Inflammatory cells are known to have a high level of lysosomal activity. Seminomas are tumours characterised clinically by a good response to treatment and often histologically by the presence of granulomata and lymphocytic infiltration, whereas teratoma of the testis is not generally characterised by either of these features. These characteristics may contribute to the particularly good imaging properties of seminoma.

Case 1 illustrates how useful this technique is in following up patients with seminoma of the testis. The deposit of seminoma below the right lobe of the liver was noted six months before his clinical condition demanded exploratory laparotomy; the gallium scan was the only test that detected the tumour recurrence.

Case 2 illustrates a difficult problem in managing patients with seminoma of the testis. When a patient who has been diagnosed as having a pure seminoma then develops a recurrence in a previously treated area or responds poorly to standard treatment careful consideration is needed about whether a teratoma has developed. In case 2 a tumour that had taken up ⁶⁷Ga no longer did so, which suggested that the character of the tumour had changed. Case 3 illustrates the value of gallium scanning in the initial staging of a patient and in monitoring the response to treatment.

In conclusion, we have found this technique to be of great value in diagnosing seminoma of the testis and following up patients. The apparent difference in imaging characteristics between seminoma and teratoma requires confirmation and if proved may have some value in the differential diagnosis of patients with combined tumour of the testis.

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Controlled trial of oxygen in uncomplicated myocardial infarction

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Summary

Two-hundred consecutive patients thought to have suffered a myocardial infarction were admitted to a randomised, double-blind controlled trial of oxygen or air administered by MC mask throughout the first 24 hours in hospital. Forty-three patients in whom myocardial infarction was not subsequently confirmed were excluded from the analysis. The remaining air and oxygen groups were comparable except for a significantly higher PaO₂ and serum aspartate aminotransferase level in the oxygen group. There was no significant difference in mortality, incidence of arrhythmias, use of analgesics, or systolic time intervals between the two groups, although a higher incidence of sinus tachycardia was found in those given oxygen. There appears to be no

evidence of benefit from the routine administration of oxygen in uncomplicated myocardial infarction.

Introduction

The use of oxygen in "severe angina pectoris" was first described in 1900 by Steele.¹ Clinical improvement after oxygen inhalation in four patients with acute myocardial infarction was reported by Levy and Barach in 1930.² Since then the use of oxygen in myocardial infarction has been advised in most standard medical texts.³⁻⁴ The discovery that patients with myocardial infarction usually have a degree of arterial hypoxaemia that may be corrected with oxygen has lent support to this advice.⁵ It has been suggested that increasing the arterial oxygen tension may reduce the area of ischaemia around an infarct⁶ or reduce the incidence of arrhythmias, and such effects have been shown in animals after coronary artery ligation.⁷ Early workers also reported that oxygen reduced the pain of myocardial infarction.⁸⁻⁹ Despite these various claims the efficacy of oxygen in myocardial infarction has received remarkably little attention, although the haemodynamic and metabolic effects have been studied. Only two controlled trials of oxygen treatment have been carried out, and these were under hyperbaric conditions; the results were inconclusive, although neither trial showed a significant reduction in mortality.¹⁰⁻¹¹ A study to determine the efficacy of oxygen

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