Tumours of the pancreas as a sequel to abdominal irradiation

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Summary: Two cases of tumours arising in or near the pancreatic head are reported in patients previously treated with abdominal irradiation for testicular tumours. These are only the third and fourth such cases to be reported and they suggest that second cancers may develop as a result of abdominal irradiation for malignant disease.

Introduction

The development of new tumours many years after apparently successful treatment of malignant disease is not rare. Although delayed recurrence of the first tumour is always possible, tumours may arise as a consequence of the original treatment. Chemotherapy and radiotherapy used in the treatment of malignancies are immunosuppressive and may be carcinogenic.¹

We report here two cases of carcinoma originating in the upper alimentary tract several years after abdominal irradiation for the treatment of primary testicular neoplasms.

Case reports

Case 1

A telephone operator born in 1953 was admitted to Guy's Hospital for the first time in December 1966 at the age of 14 years complaining of a 3-month history of painless swelling of the right testicle and gynaecomastia. The right testis was excised and histology showed 'teratoblastoma' (malignant teratoma, intermediate, – British Testicular Tumour Panel classification) (Figure 1). Three weeks later a metastatic deposit was removed from the right lung and subsequently the patient was treated with radiotherapy, 4000 rads being administered to the pelvis and thoracolumbar spine over 4 weeks. Later he received a further 4000 rads to the chest. In 1968 the left lower lobe was removed because it contained a second metastasis.

The patient was well until 1979 when he was admitted to the hospital with a 5-year history of diarrhoea, steatorrhoea and weight loss. Investigations showed extensive small intestinal changes and two strictures in the sigmoid colon, all attributed to radiation damage. He was treated with a low fat diet, nutritional supplements and loperamide with good results until 1983. During the next two years he had four surgical interventions for ileal perforations and/or obstruction, with the removal of a total of 85 cm of ileum. Histology of the resected gut showed changes compatible with radiation damage, including mucosal inflammation and ulceration, replacement of muscle by fibrous tissue and vascular endarteritis obliterans. There was no evidence of tumour.

He remained well on a low fat diet, nutritional supplements and anti-diarrhoeal agents until March 1987 when he was admitted with acute diarrhoea and vomiting. The diarrhoea resolved spontaneously but the vomiting became more voluminous. Barium meal revealed obstruction at the second part of the duodenum. Upper gastrointestinal endoscopy showed oedematous and friable mucosa at the site of obstruction. A few days later obstructive jaundice developed. Abdominal ultrasound revealed a dilated biliary tree and two lesions in the liver. Histology of duodenal and liver biopsies revealed a poorly differentiated mucin secreting adenocarcinoma with a dense fibrous stroma, compatible with a pancreatic origin. Percutaneous transhepatic drainage of the biliary tree was performed, followed by a gastrojejunostomy some days later. Bile duct surgery was impossible because of multiple adhesions. The patient's condition deteriorated and he died several days later.

Post-mortem examination revealed the pancreas to be replaced by a mass of hard white tissue with

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Figure 1 Malignant testicular teratoma with adenocarcinoma and malignant stroma (haematoxylin and eosin $\times 225$)

involvement of the para-aortic nodes. Tumour was present in the right lobe of the liver. Histology of the main tumour mass was similar to that of the liver biopsy performed earlier (Figure 2).

Case 2

A physician born in 1924 was admitted to hospital for the first time in 1974 at the age of 50 years complaining of testicular enlargement for several months. The left

testis was excised and a diagnosis of seminoma was made (Figure 3). He was treated with radiation receiving 4000 rads over 4 weeks to an inverted 'Y' field covering the pelvis and lumbar spine, after which he was well for the next 8 years.

In 1982 he presented with post-prandial fullness and vomiting and, on examination, the stomach was distended and a splash was present. A dilated pylorus and obstruction of the second part of the duodenum beyond the ampulla of Vater was seen on endoscopy

Figure 2 Pancreatic tumour at post-mortem with poorly cohesive signet ring cells in fibrous stroma (haematoxylin and eosin $\times 324$)

Figure 3 Testicular seminoma with focal lymphatic and granulomatous infiltrate (haematoxylin and eosin $\times 114$)

Duodenal biopsies showed adenocarcinoma. Abdominal ultrasound and CT scan revealed a tumour in the head of the pancreas but no metastatic lesions and a Whipple's resection was performed. Examination of the resected specimen revealed a tubular adenocarcinoma with infiltration between fibres of muscularis propria (Figure 4).

Following this he remained relatively well but six years later a CT scan showed a left-sided retroperitoneal mass, which was removed at laparotomy. Histology showed lymph nodes containing adenocar-

cinoma identical to that removed by the Whipple's procedure.

Discussion

In both our patients the second tumour was different morphologically from the original primary and the histology was compatible with a pancreatic origin in each case.

In case 2 examination of the resected specimen

Figure 4 Tubular adenocarcinoma showing infiltration between fibres of muscularis propria (haematoxylin and eosin $\times 282$)

revealed a tumour situated distal to the ampulla of Vater, making a periampullary origin unlikely. The tumour in the first case was so extensive as to preclude precise localization of its origin.

In recent years the frequency of pancreatic cancer has increased in many areas of the world and the rates are higher in Western industrialised countries.² A variety of risk factors, including age, race and diabetic state, together with smoking and exposure to certain chemicals, such as β -naphthylamine and benzidine, have been implicated in the aetiology of the disease.³⁻⁵ The two patients described did not have obvious predisposing factors since they were both Caucasian, non-smokers and had not been exposed to any chemical carcinogens.

Age is perhaps the principal known risk factor for pancreatic cancer as it chiefly develops after 60 years of age.⁶ It has been calculated that the annual incidence is approximately 2/100,000 for the 40-44 year age range with a 50-fold increase (i.e. 100/100,000) for the 80-84 year age range.⁷ It is possible that there is a causal relationship in these two patients between abdominal irradiation and the development of a pancreatic carcinoma which is strengthened by the fact that both were relatively young.

Two well documented case reports^{1,8} describe two

relatively young patients with no known risk factors who developed pancreatic carcinoma 5 and 13 years after radiotherapy for lymphoma. Furthermore, in a review of the records of 14,554 patients with ankylosing spondylitis who had been treated with radiation there was a two-fold increase in deaths from pancreatic cancer in comparison with a non-irradiated population, as well as a high level of deaths from cancers originating in other heavily irradiated tissues. There have also been suggestions of excess pancreatic cancer among British radiologists and Japanese survivors of the atomic bombs,^{10,11} although in these groups the increase was small and of marginal statistical significance. Radiation is an accepted carcinogen and a number of years are required for the malignancy to develop (in the two cases reported here the time interval was 20 and 8 years).

In conclusion, we report two cases of adenocarcinoma, probably of pancreatic origin, developing in the field of irradiation for primary testicular tumours and suggest that the irradiation was responsible.

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