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Postgrad Med J (1993) **69**, 883–885

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Carcinoma of the breast at the site of migrated pacemaker generators

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Summary: We report two patients in whom breast malignancy developed in the proximity of 'migrated' pacemaker generators. These cases and the similar ones reported in the literature raise concerns whether this association is merely coincidental or whether the pacemaker generator is responsible for the occurrence in some inexplicable manner. We urge for a routine, careful examination in all patients with implanted pacemaker generators at follow-up visits. This would help in (a) timely detection of migration of the pacemaker generators and (b) earlier diagnosis of any mass developing close to the migrated generators.

Introduction

We report, in two women, the development of breast cancer in the proximity of pacemaker generators, a rare association. Both the generators had migrated to a sub-mammary position from their original sites of implantation.

Case reports

Case 1

During a follow-up visit to the pacemaker clinic an 83 year old woman was detected to have a lump in

her left breast. Thirteen years previously she underwent implantation of a Cordis Omni pacemaker to treat symptomatic sinus bradycardia and cardiac pauses. The pacemaker generator was changed to a Cordis 337A VVI type 6 years later. On both these occasions the generators were placed in left infra-clavicular pockets. The lump noticed was situated in the outer, lower quadrant, was firm, ill-defined and free from the underlying structures. The overlying skin was tethered to it. The axillary or supraclavicular nodes were not palpable and the abdominal examination was unremarkable. Serum biochemical parameters were within normal limits. A plain X-ray of the chest (Figure 1) showed the pacemaker generator to be lying over the ribcage on the left side. This site corresponded with the clinically palpable lump. A fine-needle aspirate diagnosed it to be an adenocarcinoma. In view of

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Accepted: 16 March 1993

Figure 1 Arrow (→) points to the migrated pacemaker generator (Case 1).

her age, the patient was treated with anti-oestrogen therapy in the form of tamoxifen.

Case 2

An 84 year old woman was found to have a hard mass in the right breast at a follow-up visit to the pacemaker clinic. Her original pacemaker generator (Teletronics, VVI model 120B) had been inserted over the right precordium 12 years ago for sinus pauses. The system was replaced 10 years later with a Optima MP 580 VVI generator. The lump palpable was situated directly overlying the pacemaker generator which had migrated to an infra-mammary position. A fine-needle aspirate showed it to be an adenocarcinoma. In view of her age and her general poor condition, the patient was treated with tamoxifen.

Discussion

Carcinoma of the breast occurring in relation to a pacemaker generator is rare, and only four similar cases have been reported.¹⁻³ Zafiracopoulos,¹ who reported the first two cases, raised a question whether the association between breast malignancy

and pacemaker generator was merely coincidental or that the two were correlated. Hamaker⁴ who reported a case of a plasmacytoma occurring in a pacemaker pocket proposed three possible explanations for the occurrence. He suggested that either: (a) the titanium cover of the generator was tumorigenic; (b) the electrochemical stimulation was responsible; or (c) it was due to inflammatory oncotoxicity,⁵ a phenomenon in which chronically inflamed tissues or those lying close to a focus of constant irritation facilitate and trap tumour cells.

Our patients carried their initial pacemakers in the infraclavicular pocket and over the precordium, respectively, and presumably the changed generators also remained *in situ* for a few years. Later a malignancy was observed to develop in close proximity to each of the generators; both having migrated under the breast. In the two cases reported by Zafiracopoulos¹ the generators had been placed 'under the breast', as indeed was the practice in the past. A woman² in whom a pacemaker generator had been implanted over the right pectoral region was found to have an infiltrating breast carcinoma adjacent to it. She underwent a simple mastectomy. Two years later, with the generator still in place, a recurrence developed at the site of previous operation. In the only man reported to have developed breast malignancy in relation to a pacemaker generator, the generator had migrated to beneath the nipple.³

In view of the relatively high incidence of breast cancer, some tumours would be expected to develop in women in whom a pacemaker had been inserted. All the above mentioned cases have in common the placement of a pacemaker generator under the breast, by choice or by chance, and development of an adjacent malignancy. A pacemaker generator lying close could possibly be responsible for enhancing, by some ill-understood mechanism, the inherent potential of the breast tissue to develop malignancy. We urge the physicians involved in the care of patients with implanted pacemakers to be aware of this rare association. In these patients routine and careful examination at follow-up visits would allow (a) timely detection of migration of the pacemaker generators and (b) earlier diagnosis of a suspicious mass developing in the breast close to such migrated generators.

Acknowledgement

The authors wish to thank Ros Hirst, Chief Pacemaker Technician at the Manchester Royal Infirmary, for her help.

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Postgrad Med J (1993) **69**, 885–887

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First use of G-CSF in chlorpromazine-induced agranulocytosis: a report of two cases

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Summary: Chlorpromazine-induced agranulocytosis is an uncommon disorder associated with a high frequency of fatality. We describe two patients with chlorpromazine-induced granulocytosis in whom granulocyte colony stimulating factor (G-CSF) administration enhanced the speed of neutrophil recovery. No toxicity was noted with G-CSF and both patients made a successful recovery. We propose there is a role for such cytokine therapy in patients with life-threatening agranulocytosis in order to speed the recovery of neutrophils.

Introduction

Idiosyncratic non-cytotoxic drug-induced agranulocytosis is an unpredictable adverse reaction to a variety of drugs in hypersensitive individuals. Chlorpromazine-induced agranulocytosis is associated with a reported 50% mortality rate.¹ The period of agranulocytosis may be extensive and during this period the patient is at considerable risk of developing serious infections requiring prolonged hospitalization.²

Neutrophil production is under the control of several glycoproteins including granulocyte colony stimulating factor (G-CSF). Clinical trials have demonstrated that treatment with G-CSF reduces the duration and incidence of agranulocytosis with fever in patients who have received cytotoxic chemotherapy.³ Furthermore the use of G-CSF is a proven benefit in the treatment of congenital or

cyclic agranulocytosis and neutrophils obtained from individuals treated with G-CSF function normally *in vitro* and *in vivo*.^{4,5}

We report two cases of chlorpromazine-induced agranulocytosis which were reversed following therapy with G-CSF.

Case reports

Case 1

A 35 year old female with a long history of depressive illness was admitted 3 weeks after commencing chlorpromazine 40 mg daily and procyclidine 5 mg daily with a fever of 39°C associated with a sore throat.

Physical examination revealed aphthous ulceration of the buccal mucosa and an inflamed throat. A blood count showed a haemoglobin of 10.4 g/dl, a platelet count of $204 \times 10^9/l$ and a white blood count of $0.3 \times 10^9/l$. On the blood film only lymphocytes were detected. A bone marrow aspirate

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Accepted: 14 April 1993