Malignant melanoma following heart transplantation: A cautionary tale

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A Nandi, AR Groves. Malignant melanoma following heart transplantation: A cautionary tale. Can J Plast Surg 1994;2(4):173-174. The incidence of neoplasia in patients on immunosuppression after organ transplantation is 100 times greater than that of the general population. Skin tumours and malignant lymphomas are most common. Such tumours are more aggressive than their counterparts in the general population. A higher incidence may be expected in patients receiving heart transplants since they receive the most vigorous immunosuppressive regimens. A case of malignant melanoma developing five years after cardiac transplantation is reported. The need for increased vigilance towards detection of skin cancers in this risk group is highlighted.

Key Words: Heart transplantation, Immunosuppression, Malignant melanoma

Mélanome malin suite à une transplantation cardiaque : mise en garde

RÉSUMÉ : La survenue de néoplasies chez des patients immunocompromis après une transplantation d'organe est 100 fois plus fréquente que dans la population en général. Les tumeurs cutanées et les lymphomes malins sont les plus fréquents et sont plus agressives que leurs contreparties dans la population en général. Une incidence plus grande peut être prévue chez les patients qui reçoivent des transplantations cardiaques, étant donné qu'ils reçoivent les régimes immunosuppresseurs les plus énergiques. Un cas de mélanome malin survenu cinq ans après une transplantation cardiaque est présenté ici. La nécessité de surveiller davantage les cancers de la peau dans ce groupe à risque est mise en évidence.

A 25-year-old man underwent a cardiac transplant for end-stage heart failure due to hypertrophic cardiomyopathy in 1986. He was placed on cyclosporin 250 mg per day, azathioprine 25 mg bid, and prednisolone 5 mg od for immunosuppression.

Five years after transplant he noticed that a nevus, which had been present unchanged on his right cheek since birth, had enlarged in size, changed colour and become more irregular in outline over six months. He brought the matter to the notice of his family doctor, who suspected malignant change and referred him to our care.

On examination the 0.5 x 1.0 cm lesion appeared suspicious with an irregular edge and variegated pigmentation. It was excised with a wide margin. Subsequent histopathological examination showed this to be a superficial spreading malignant melanoma Clarke's level 3, 1.5 mm in thickness arising in a pre-existing nevus, which had been completely removed. During the same operation, two other skin lesions were removed from his right and left knees; these lesions proved to be completely excised benign intradermal nevi.

The patient is being followed up closely. There is no evidence of local, regional or distant spread of the tumour in the last 12 months.

DISCUSSION

Cardiac transplantation is an effective means of treating end stage refractory heart failure and is being offered to an increasing number of patients, many of whom are fairly young. Data from the Cincinnati Transplant Tumour Registry (CTTR) shows the average age of the transplant patient to be 40 years. The average time of appearance of the tumour is 58 months after transplantation (1-4).

The incidence of de novo malignant tumours reported from major transplant centres in the USA, Europe and Australia varies from 1 to 16% (mean 4%), which is approximately 100 times greater than that of the matched general population (5).

Interestingly, carcinomas commonly observed in the general population, such as those of the lung, prostate, colon and rectum, female breast and uterine cervix, are not increased in incidence in transplant recipients. In contrast, however, an increased incidence of skin cancers, non-Hodgkins lymphomas and hepatobiliary cancers are observed after renal and cardiac transplantation (6-8).

Skin cancers are the most frequently encountered neoplasms in transplant recipients, forming 39% of the total carcinomas reported to the CTTR (1-4). This incidence is four to seven times that of a matched general population; in regions of abundant sunshine the incidence rises to 21 times that of the general population of that area (9).

In an Australian series, 80% of the tumours following

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transplantation were skin cancers. Most tumours are squamous cell carcinomas, in contrast with the general population in whom basal cell carcinoma is the most frequently encountered tumour. The tumours tend to occur in individuals who on the average are 30 years younger than their counterparts in a general population. A higher incidence of multiple tumours (43%) is also noted.

An important consideration is that these tumours are far more aggressive in their behaviour and metastasized more frequently. Seven per cent of all deaths from cancer in immunosuppressed patients were from skin cancer, which contrasts sharply with the rate of 1 to 2% in general (10).

In the general population skin cancer deaths are mainly from melanomas, whereas 65% of the deaths in the CTR report are due to squamous cell carcinomas and 32% from melanomas (1-4). Melanomas are, however, more common in transplant recipients, and Sheil et al (11) report a fivefold increase in the incidence of melanomas in their Australian study. Such tumours are aggressive and cause death in nearly 40% of cases.

Homograft recipients commonly show an increase in de novo cancers while on immunosuppressive therapy (2,9,12,13). This case was unique because malignant transformation occurred in a preexisting nevus, presumably due to immunosuppression. The latency period of five years is similar to that of 58 months reported in the literature (6).

The high incidence of malignant tumours is almost certainly related to pharmacologic suppression of the immune system. Immunosuppression may impair the immune surveillance mechanisms that destroy malignant cells (14-16).

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Drugs such as azathioprine are known to cause chromosomal breaks and nuclear abnormalities and have been shown to potentiate action of oncogenic stimuli (17). The donor organ itself may cause prolonged antigenic stimulation of the lymphoreticular system leading to the development of neoplasia (18,19). Oncogenic viruses may be encouraged to cause neoplastic change, since immunosuppression increases susceptibility to viral infection (20-22). Feedback mechanisms that hold oncogenesis in check are interrupted by immunosuppression, leading to tumour proliferation. It is possible that immunosuppressive agents potentiate the effects of other carcinogens such as sunlight and ionizing radiation. Various cancers probably arise from a complex interplay of multiple factors.

Recipients of heart transplants are more prone to neoplastic change than renal transplants since immunosuppression in such patients is more vigorous (23).

CONCLUSION

This report draws attention to the fact that skin cancer is more likely in a patient on immunosuppressive therapy following organ transplantation, and these tumours are more likely to be aggressive. Immunosuppressed patients should be monitored closely for signs and symptoms of malignant change. A high index of suspicion should be maintained and all suspicious lesions examined by biopsy. If malignant, they should be widely excised without delay. Follow up should be rigorous. In sunnier climates, transplant recipients should be instructed to avoid excessive sun exposure and protect exposed skin with clothing or sun-screening lotions.