

Exceptional Case

Vitiligo following a combined liver–kidney transplant

Victoria Bradley¹, Elizabeth Helen Kemp², Claire Dickinson¹, Tim Key³, Paul Gibbs⁴ and Menna R. Clatworthy⁵

¹Cambridge School of Clinical Medicine, ²School of Medicine and Biomedical Sciences, University of Sheffield, Sheffield, ³Tissue Typing Laboratory, Addenbrooke's Hospital, Cambridge, ⁴Department of Surgery, University of Cambridge and ⁵Division of Renal Medicine, Department of Medicine/Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK

Abstract

We report an Afro-Caribbean male who developed vitiligo 10 days following a combined liver–kidney transplant from a Caucasian donor. Neither the donor nor the recipient had any previous history of vitiligo, nor of autoimmunity. The depigmentation gradually resolved by 8 weeks post-transplant with topical corticosteroids and standard maintenance immunosuppression. We propose that the skin depigmentation occurred due to the destruction of melanocytes by donor-derived alloreactive cytotoxic T-lymphocytes or antibody transferred during transplantation. Although vitiligo has been described in patients receiving allogeneic bone marrow transplantation for haematological malignancy, there are no previous reports of vitiligo post-solid organ transplantation.

Keywords: autoimmunity; liver–kidney transplant; vitiligo

Background

The occurrence of *de novo* autoimmunity has been described in a handful of cases following solid organ transplantation. Typically, these autoimmune diseases occur in the context of liver transplantation and include cytopenias [1], hepatitis and inflammatory bowel disease. The aetiology of post-transplant autoimmunity is variable; rarely it occurs due to the direct transfer of an autoreactive antibody or CD8 T cells from a donor with documented autoimmunity [1]. More commonly it may form part of a widespread graft-versus-host response. Vitiligo is a depigmenting disorder of uncertain aetiology characterized by the loss of melanocytes from the skin. Its association with other autoimmune diseases and the demonstration of melanocyte-specific antibodies [2] and cytotoxic T cells [3] in some

patients supports an autoimmune aetiology. We describe a patient who developed vitiligo 10 days after a liver–kidney transplant. Although vitiligo has been described in patients receiving allogeneic bone marrow transplantation (BMT) for haematological malignancy [4], this is the first report of vitiligo post-solid organ transplantation.

Case report

A 60-year-old Afro-Caribbean man with hypertension, insulin-requiring type 2 diabetes, chronic liver disease secondary to alcoholic hepatitis and end-stage renal failure secondary to biopsy-proven IgA nephropathy received a combined heart-beating liver–kidney transplant. The donor was a 2-2-2 mismatch (donor and recipient HLA shown in Table 1) and had a history of hypertension. Maintenance immunosuppression consisted of tacrolimus (0.1 mg/kg/day), azathioprine (1 mg/kg/day) and prednisolone 20 mg/day. The liver allograft functioned immediately; however, he remained oligoanuric for a month following transplantation. Renal transplant biopsies were performed on a weekly basis, the first of which showed moderate acute cellular rejection. This was treated with three 1g doses of intravenous methylprednisolone, and mycophenolate mofetil (500 mg/po/bd) was added to his maintenance immunosuppression in place of azathioprine. Subsequent biopsies showed only recovering acute tubular necrosis and by Week 4 his renal function improved such that he was dialysis independent.

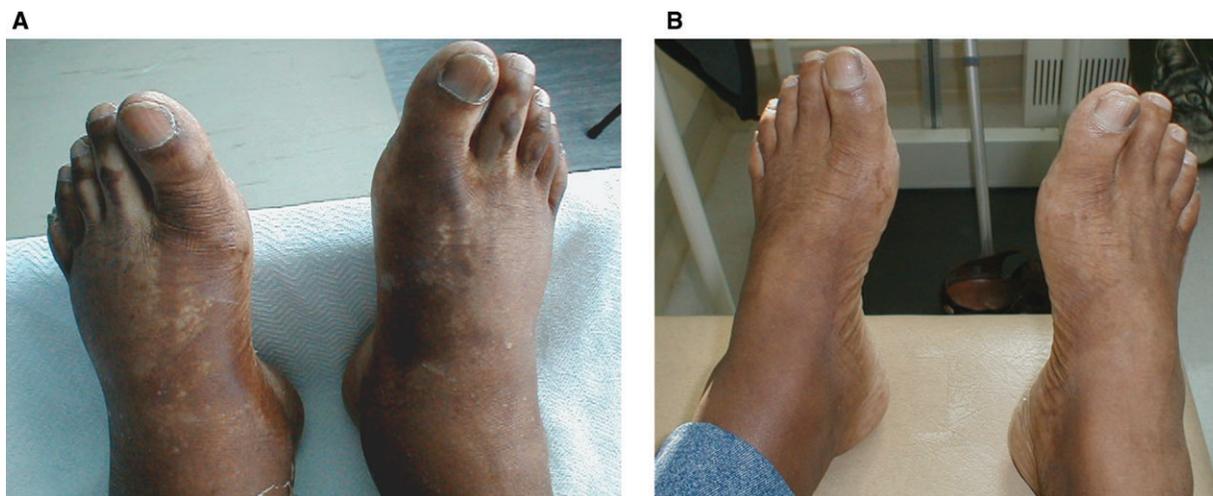
Ten days following transplantation, the patient was noted to have developed areas of patchy depigmentation on both feet (Figure 1a). He was reviewed by the dermatologists who felt this was typical of vitiligo and declined to perform a confirmatory skin biopsy. On their advice, he was commenced on topical corticosteroid cream (betnovate) and continued systemic immunosuppression as described above. Repigmentation occurred over the next 3 weeks and by Week 8 post-transplant, the vitiligo had resolved (Figure 1b).

We tested the recipient's serum for the presence of melanocyte-specific antibodies immediately prior to transplantation using a radiobinding assay, as previously

Correspondence and offprint requests to: Menna R. Clatworthy, Lab 4.15 CIMR, Box 139 Addenbrooke's Hospital, Cambridge CB2 2XY, UK. Tel: +44-1223-762639; Fax: +44-1223-762640; E-mail: mrc38@cam.ac.uk

Table 1. Donor and recipient HLA typing

	HLA-A	HLA-B	HLA-Bw	HLA-Cw	HLA-DR	HLA-DRB1	HLA-DRB3–5	HLA-DQ	HLA-DQB1
Donor	24 (9) 31 (19)	60 (40) 62 (15)	6	10 (3)	4 13 (6)	04 13	53 52	8 (3) 6 (1)	0302/0308 0604/0606
Recipient	1 2	53 81	4,6	4 8	12 (5) 10	12 10	52 –	5 (1) –	0501 –

**Fig. 1.** (A) Areas of patchy depigmentation in the skin on both feet at 10 days post-transplant (pictures taken at day 14). (B) Repigmentation at 2 months post-transplant.

described [5]. The sample was negative for antibodies to tyrosinase, TRP-1, TRP-2, Pmel17 and MCHR1. Unfortunately, there was no donor serum available for testing, but he had no history of vitiligo, nor of any other autoimmune disease. The recipient of the donor's second kidney did not develop vitiligo or any other autoimmune complication post-transplantation.

Discussion

Both humoral and cell-mediated autoimmunity are likely to play a role in melanocyte destruction in vitiligo. Specific antibodies to a variety of melanocyte-specific antigens have been identified in patients with vitiligo, and disease severity correlates with antibody titre [2]. These antibodies can induce the destruction of melanocytes both *in vitro* and *in vivo* [2]. Other studies have identified melanocyte-specific cytotoxic T cells in the skin and peripheral blood of patients with vitiligo [2,3].

There are a number of possible explanations for the development of vitiligo post-transplantation in the patient we have described. The first, and most likely, is that there was a transfer of recipient-specific anti-melanocyte antibodies or CD8 T cells during liver–kidney transplantation. The early occurrence of depigmentation within 10 days of transplantation and its subsequent rapid resolution are in favour of this hypothesis. The second possibility is that the vitiligo occurred as part of a florid graft-versus-host dis-

ease (GVHD), as described in a number of allogeneic BMT recipients [4]. However, our patient had no other manifestations of GVHD and presented very early post-transplant (the earliest time point at which vitiligo was observed in BMT recipients with GVHD was 3 months [4]). Finally, the case we have described is unlikely to represent a case of *de novo* autoimmune vitiligo both because of its timing and the absence of melanocyte-specific antibodies in the recipients serum prior to transplantation. Furthermore, he does not have the typical HLA genotype associated with the development of vitiligo in Afro-Caribbeans (HLA-DR4, HLA-DR6 and HLA-DQ3) [6].

The transfer of vitiligo has been described following allogeneic BMT from a donor with vitiligo [7]. Similarly, vitiligo has also been reported in melanoma patients treated with infusions of melanocyte-specific cytotoxic T cells isolated from vitiligo patients [8]. However, in the case we have described, the donor did not have a history of vitiligo nor of any other autoimmune disease (verified with the donor's general practitioner). Unfortunately, we did not have donor serum or lymphocytes to allow testing for melanocyte-specific antibodies and T cells. Given the absence of a history of vitiligo in the donor, melanocyte destruction may have occurred as part of an alloimmune response. Of note, the development of depigmentation coincided with the occurrence of acute cellular rejection in the renal allograft. Melanocytes can express MHC class I and class II molecules and present antigens to T cells [9]. In the case we have described, melanocytes may have presented

donor antigen and been destroyed as part of an alloimmune response.

The donor was Caucasian, and the recipient Afro-Caribbean. Skin colour is mainly determined by melanin, of which there are two main types: eumelanin, which is black/brown in colour, and pheomelanin, which is red/yellow in colour [10]. Differences in the number, size and composition of melanin-containing granules (melanosomes) lead to pigmentation differences. In the case we have described, the recipient would be likely to have predominantly eumelanin-containing melanosomes, and the donor pheomelanin. Therefore, in addition to MHC differences between donor and recipient, there were also likely differences in melanosomal antigens.

In summary, we have described the development of vitiligo in an Afro-Caribbean male following a combined liver–kidney transplant from a Caucasian donor. We propose that the skin depigmentation occurred due to the destruction of melanocytes by donor-derived alloreactive cytotoxic T-lymphocytes or antibody transferred during transplantation. This is the first report of vitiligo post-solid organ transplantation.

Acknowledgement. MRC is funded by a Wellcome Trust Intermediate Fellowship (081020/Z/06/Z).

Conflict of interest statement. None declared.

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Received for publication: 30.10.08

Accepted in revised form: 3.11.08