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LETTER TO THE EDITORS

Pancreas rejection after pandemic influenzavirus A(H_1N_1) vaccination or infection : a report of two cases

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Influenza infection was proved to be rejectogenic several decades ago [1]. Killed or subunit influenza vaccine is currently recommended in solid organ transplant recipients [2]. Despite immunosuppressive medications, it is possible to induce both humoral and cellular responses although at a lower extent than in healthy controls. Organ rejection is probably the most feared dysimmune complication of flu vaccination, but it has been reported to date exclusively in corneal [3] and kidney [4] transplant recipients.

We report here two type I diabetes mellitus patients who had received pancreas transplant alone (PTA) in 2001 and 2005, respectively using basiliximab induction and triple maintenance immunosuppression with tacrolimus, mycophenolate mofetil and short-course steroid. Both suddenly experienced pancreas rejection shortly after influenzavirus A(H_1N_1) vaccination (patient 1) or infection (patient 2) during the 2009–2010 flu season.

Patient 1 was a 52-year-old man (typed A*02, 08, B*18, DRB1*03; panel reactive antibody (PRA) 0%) who received a PTA (portal-enteric drainage) in April 2001 from a 19-year-old cadaveric donor (typed A*02, 32, B*18,35, DRB1*11,14). Being a Jehovah witness, the recipient never received blood component transfusions. A follow-up study of serum in January 2009 by Screening Luminex™ assay (One Lambda, Inc., Canoga Park, CA, USA) showed no anti-HLA IgGs. Patient 2 was a 39-year-old man (typed A*03,26, B*08, B*27, DRB1*03,16; PRA 0%) who received a cadaveric PTA (portal-systemic drainage) in August 2005 from a 15-year-old cadaveric donor (typed A*24, A*33, B*14,51, DR*01,11). In April 2008, a follow-up study of serum by Screening Luminex™ assay (One Lambda, Inc.) showed no anti-HLA IgGs. In December 2009, shortly after H_1N_1 vaccination (patient 1) and infection (patient 2; confirmed by serology on convalescent sera), both patients reported hyperglycemia and hyperamylasemia, and lost insulin-independence. Blood levels of tacrolimus were within normal ranges, and pancreatic biopsies were finally performed: histologies showed septal inflammatory infiltrates and diffuse positive C4d stainings, so the recipients were finally diagnosed with acute rejection.

At the time of rejection, Single-Antigen Luminex™ (One Lambda Inc., Canoga Park, CA, USA) testing showed a broad sensitization against >18 different HLA class I and >13 HLA class II antigens in both patients (including donor-specific antibodies). Both patients also had a strikingly similar anti-HLA antibody pattern, suggesting a common antigen exposure, and steady autoantibody titers, excluding diabetes recurrence as the leading cause of rejection. We then performed an HLA MatchMaker analysis. Reactive epitopes for patient 1 were 82LR on A32 and 163LW on B35; 56PPA, 57PV and 74SV on DQB; 56RR5 and 47ERW on DQA. For patient 2, reactive epitopes were 62EE and 79ERI on A24, and 163LW + 79ERI on B51. Despite anti thymocyte globulins and plasmapheresis, the 8-month follow-up confirmed both rejections as irreversible, and donor specific antibodies persisted in serum.

The safety of flu vaccination has been assessed in several clinical trials. Candon *et al.* reported that during the 2005–2006 vaccination campaign with A/H_1N_1 and A/H_3N_2 strains, vaccination of kidney transplant recipients did not change pre-existing or *de novo* anti-HLA sensitization and did not cause any episode of allograft rejection [5]. We finally mined the Food and Drug Administration/Center for Disease Control Vaccine Adverse Event Report System (VAERS) database using the query ''rejection'' since January 2009 until April 2010, and we could find only two cases of cornea rejection after pandemic H1N1 flu vaccination. However, systematic reporting of adverse events following influenza vaccination in transplant recipients should be encouraged.

Conflicts of interest

We declare that we have no conflict of interest related to this manuscript.

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