Characterization of Natural and Induced Human Xenophile Antibodies Before and After Transplantation of the Fetal Porcine Endocrine Pancreas

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IN the context of future attempts at pig-to-man islet transplantation, an important question is whether there is any difference between fetal and adult tissue when it comes to the expression of natural xenophile antibody (NXA) target epitopes. The binding of such antibodies to porcine islet cells in various stages of ontogeny was tested with indirect immunofluorescence[1] using pancreatic tissue sections from Swedish and German landrace pigs as target.

RESULTS AND CONCLUSION

Sera from type 1 diabetic patients (n = 10) with strong anti-islet NXA reactivity with adult tissue (titer ≥ 1:32) reacted positively with fetal (70 days of gestation), neonatal and newborn (1-week old animals) islet tissue, and were mainly of immunoglobulin (Ig)G isotype. However, binding on these three non- or poorly insulin-secreting tissues was "weak" (serum titer ≤ 1:4), compared with "strong" (serum titer ≥ 1:32) binding to insulin-secreting, adult islet cells. Binding increased from weak to strong when fetal tissue was cultured in vitro. This strong binding persisted when the cultured fetal tissue was grafted underneath the kidney capsule of nude mice. Weak and strong binding correlated with weak and strong insulin staining of the fetal islet cells, and thus seemed to correlate with the degree of differentiation of the fetal endocrine pancreas.

In diabetic patients (n = 5) given an intraportal injection of porcine fetal islet-like cell clusters, the serum titer of xenophile antibodies (IgG) against porcine tissue increased promptly.[2] When sera from these patients were added to sections of adult pig pancreas these antibodies were found to be mainly directed against the vascular endothelium and not against the endocrine or exocrine pancreatic tissue.

Thus, pretransplant NXA bound only weakly to immature pancreatic tissue, but strongly to mature and functional tissue. Xenophile IgG antibodies induced in diabetic patients grafted with pig cells and were mainly directed towards epitopes on porcine endothelial cells. These findings should be taken into consideration when it comes to human porcine xenografting.

REFERENCES

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0041-1345/94/$3.00/+0