Infectious Complications Following Pancreatic Islet Cell Transplantation

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Background

- Pancreatic islet cell transplantation improves glycemic control in people with Type 1 diabetes complicated by frequent severe hypoglycemic unawareness or labile serum glucose levels
- Approximately 40% of North American islet cell transplants occur at University of Alberta Hospital in Canada[1,2]
- Post-transplantation infections have not been well characterized in this population

Objectives

- To describe the incidence, timing and outcomes of opportunistic and non-opportunistic infections in pancreatic islet cell transplant recipients

Methods

- Single center retrospective review of pancreatic islet cell transplant recipients at the University of Alberta Hospital between February 2006 and December of 2015
- Electronic Medical Records were reviewed in order to collect data on patient demographics, immunosuppressive regimens, CMV status, infectious syndrome, pathogens, timing of infection post-transplantation, and outcome
- Antiviral prophylaxis with ganciclovir or valganciclovir:
  - 3 months for all D+/R-
- - 3 months CMV seropositive recipients (R+) that received lymphocyte-depleting antibodies (alemtuzumab or thymoglobulin).
- - R+ recipients without lymphocyte-depleting antibodies induction received preemptive therapy.
- Immunosuppression protocols Induction and maintenance immunosuppressive protocols have evolved in our program over time:

– Initially daclizumab combined with tacrolimus and sirolimus (the “Edmonton Protocol”)

– Subsequently, basiliximab has replaced daclizumab, with the combination of TAC and mofetil mycophenolate

– Other protocols: Infliximab + Daclizumab or Basilixumab + etanercept or thymoglobulin (ATG) for induction

– In most recent years protocols based on alemtuzumab

Statistical analysis: All statistics were calculated with SPSS statistical package (Chicago, IL) version 26. Categorical variables are summarized as percentages. Continuous variables are summarized as mean and standard deviation

Results

	N=143(%)				
Gender M (%)	67 (47)				
Median Age (1st transplant (SD))	50 (11)				
SOT pre- islet	Kidney 8 (6) SPK 1 (1)				
Number of transplants					
n=1	18 (13)				
n=2	78 (54)				
n=3	32 (22)				
n=4	14 (10)				
n=5	1 (1)				
CMV serostatus					
D+/R-	61 (43)				
D+/R+	52 (36)				
D-/R+	17 (12)				
D-/R-	13 (9)				
Induction*	Tx1	Tx2	Tx3	Tx4	Tx5
• **Alemtuzumab**	111(78)	70 (56)	30(64)	8 (53)	1
• **ATG**	23 (16)	6 (5)	6(13)	5(33)	
• **Basiliximab**	7(5)	41 (33)	10 (21)	2(13)	
• **Daclizumab**	2(1)	7(6)	1(2)		

Table1:Demographics
() indicates percentage unless otherwise specified
*induction: Alemtuzumab +/- Etanercept +/- Anakinra, ATG: thymoglobulin +/- Etanercept +/- Anakinra, Basiliximab+/- Etanercept +/- Anakinra, Dacluzumab +/- Etanercept
Abbreviations: SOT: solid organ transplant, CMV cytomegalovirus

OI	Incidence	Syndrome	Number of transplant prior to OI	Timing from last transplant	Outcome
CMV	21(15%)	CMV DNAemia 20 CMV D+/R- 6 (30%), CMV D+R+ 11(55%), CMV D-/+ 3 (15%) CMV Syndrome 1 CMV D-/R+	1.5 1	5 months (SD1) 4 months	Survived
VZV	7(4.9%)	6 Shingles (2 pcr, 4 clinical diagnosis) 1 (Meningitis)	2.3 2	19 months (SD10) 51 months	Survived
Nocardia	3(2.1%)	1 Cutaneous 1 Pneumonia 1 Dissemination	4 2 2	17 months 8 months 4 months	Survived Survived IS stopped
PJP	1	1 Pneumonia (clinical diagnosis)	1	17 months	Survived

Table2: Opportunistic Infections (OI): Incidence and timing after transplant
Abbreviations: CMV: cytomegalovirus, VZV: Varicella Zoster Virus, PJP: pneumocystis jirovecii pneumonia, pcr: polymerase chain reaction

Results

Syndrome	Pathogen	Frequency
Skin and Soft tissue infection	MSSA	4
	Unknown	10
	Nocardia	1
Urinary tract infection	E.coli	6
	P mirabilus	1
	E.fecalis	3
	S gallolyticus	1
Upper respiratory tract infection	Enterovirus-rhinovirus	3
	Influenza A/B	3
	Human metapneumovirus	1
	Coronavirus	1
	Parainfluenza	1
Pneumonia	Nocardia	2
	MSSA	1
	Influenza	2
	RSV	2
	Pneumocystis	1
	No pathogen	2
Bacteremia	Salmonella	2
	E.coli	1
	E. cloacae	1
Gastroenteritis	Clostridium	4
	Norovirus	2
	Rotavirus	1
	D. fragilis	1
	Salmonella	1
Others		

Table 3: Infectious complications post islet transplantation
Abbreviation: MSSA methicillin sensitive staphylococcus aureus, VZV varicella -zoster virus
Others include herpes simplex virus, urethritis, ocular disease, septic arthitis /osteomyelitis, and infected hematoma

Conclusion

- There is a lower frequency of opportunistic and non-opportunistic infections in pancreatic islet cell transplant recipients compared to other hemopoietic and solid organ transplant recipients
- Opportunistic infections such as CMV infection, however, are not uncommon and should still be considered in these patients

References

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