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Tuberculosis in kidney transplant patients: a Tunisian single center experience

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Introduction:

Tuberculosis (TB) is a major public health issue in the world. Its prevalence in Kidney transplant (KT) patients is estimated higher than in the general population. It poses a great diagnostic and therapeutic challenge in KT recipients due to its atypical presentation leading to diagnostic delay and the risk of toxicity and drug interactions. Our study aimed to evaluate the epidemiology, risk factors, clinical manifestations, management and impact of TB in KT recipients.



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Methods:

A retrospective and descriptive study was conducted in our department between November 2007 and November 2018. Were included, all KT patients who presented a post-transplant TB disease with bacteriologically confirmed or clinically diagnosed cases.



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Results :

Among the 274 KT recipients evaluated, four patients developed post-transplant TB i.e., a prevalence of 1.45%. The mean age was 34.5 years with male predominance. Half of cases were diagnosed during the first-year post-transplantation with bacterial documentation in two cases. Pulmonary TB was predominant (3 cases) with frequent extra-pulmonary localizations. The diagnosis was delayed in most cases by one month. Circumstances were prolonged fever (3 cases), deterioration of general condition (2 cases), cough (2 cases), night sweats (2 cases), isolated diarrhea (1 case), bi or pancytopenia (2 cases) and acute kidney injury (2 cases). All patients had a quadruple drug regimen with a total therapy duration between 6 and 20 months. Underdosage of calcineurin inhibitor or sirolimus and hyperuricemia were the most noticed drug side effects. No graft or patient survival was compromised. However, chronic graft dysfunction was observed in 2 cases. All patients were screened for latent TB infection before transplantation. One case was identified using QuantiFERON test. Risk factors associated with post-transplant TB were mainly the male gender, the use of depleting antibodies, the use of calcineurin inhibitors with overdose and the presence of concomitant infections (Cytomegalovirus, Epstein-barr virus and pneumonia).

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	23	49	36	30
Sex	M	F	M	M
Socioeconomic level	Good	Good	Bad	Good
Diabetes millitus	No	No	No	No
Hepatitis C or B	No	No	No	No
Duration of dialysis (months)	0.5	1	3	20
Prior TB disease	No	No	No	No
Contact with a TB case	No	No	No	No
Chest x-ray	Normal	Normal	Normal	Normal
QFT	Not done	Not done	Not done	Positive
Sputum AFB smear and culture	Negative	Negative	Negative	Negative
Type of donor	Living	Living	Living	Living
Number of HLA mismatches	6	4	4	3

	Patient 1	Patient 2	Patient 3	Patient 4
Year of transplantation	2013	2010	2011	2016
Induction Therapy	MTP + Thymoglobulin	MTP + Thymoglobulin	MTP + Thymoglobulin	MTP + Thymoglobulin
Maintenance Therapy	Prednisone + MMF + Tacrolimus	Prednisone + MMF + Tacrolimus	Prednisone + MMF + Tacrolimus switched to sirolimus	Prednisone + MMF + Cyclosporin switched to Tacrolimus
Infections in the 3 months preceding TB diagnosis	EBV and CMV infection + Pneocystis pneumonia	Pleuro- Pneumopathy	No	No
Other associated diagnosis	Large B cell lymphoma	No	No	No
Acute rejection in the 6 months preceding TB diagnosis	No	No	No	No
Tacrolimus overdose at the time of TB diagnosis	Yes	No	No	No
Diabetes after-transplantation	No	Yes	No	No
Time to TB diagnosis	5 months	10 months	45 months	19 months
Time between symptoms onset- TB diagnosis	1 month	2 months	1 month	20 days
TB localizations	Pulmonary + mesenteric lymph nodes+ hepatic	Pulmonary+ Thoracic lymph nodes	Pulmonary +pleural	Digestive (intestine)
Discovery circumstances	Pancytopenia +fever+acute kidney injury	Fever+cough	Fever+cough +nights sweats+DGC	Fever+DGC+diarrhea+AKI +bicytopenia
TB diagnosis methods	BALF+liver biopsy	BAFL	Pleural biopsy	Colon biopsy

	Patient 1	Patient 2	Patient 3	Patient 4
TB regimen	2 HRZE/ 15 HR	2 HRZE/ 18 HR	2 HRZE/ 10 HR	2 HRZE/ - HR
Total Therapy duration (months)	17	20	12	6
Side effects of drugs	None	Hyperuricemia+Peripheral neuropathy+ underdosage of Tacrolimus	Underdosage of Sirolimus	Hyperuricemia+ Underdosage of Tacrolimus
Serum creatinine before treatment (μmol/l)	140	70	190	131
Serum creatinine after treatment (μmol/l)	117	69	121	99
Chronic graft dysfunction	Yes	No	Yes	No
Graft Survival	Yes	Yes	Yes	Yes
Patient Survival	Yes	Yes	Yes	Yes



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Conclusion:

Our study underlined the difficulties of TB diagnosis and management in KT patient. Risk factor resumed mainly in intense immunosuppressive state. Drug-drug interactions and chronic graft dysfunction were the most observed impact.