Fungal infections among Renal transplant recipients

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Incidence of IFI in SOT

Population	Incidence (%)	Overall mortality (%)
Heart	3.5–26.7	36–66.7
Kidney	1.2–4	4–25
Liver	1–4.7	83–88
Lung	8.3–23.3	4.2

Neofytos *et al. BMC Infectious Diseases* (2021) 21:296

Table 2. No. (%) of Invasive Fungal Infection (IFI) Cases in the Surveillance Cohort, by Transplant Type

IFI type	Kidney (n = 332)	Liver (n = 378)	Pancreas (n = 128)	Lung (n = 248)	Heart (n = 99)	Small bowel (n = 22)
Candidiasis	164 (49)	255 (68)	97 (76)	56 (23)	48 (49)	19 (85)
Aspergillosis	47 (14)	42 (11)	6 (5)	109 (44)	23 (23)	0 (0)
Zygomycosis	8 (2)	9 (2)	0 (0)	8 (3)	3 (3)	0 (0)
Other mold	10 (3.0)	9 (2.4)	4 (3.1)	49 (19.8)	7 (7.1)	0 (0.0)
Unspecified mold	7 (2.1)	8 (2.1)	0 (0.0)	7 (2.8)	2 (2.0)	0 (0.0)
Cryptococcosis	49 (15)	24 (6)	6 (5)	6 (2)	10 (10)	1 (5)
Endemic mycoses	33 (10)	17 (5)	8 (6)	3 (1)	3 (3)	0 (0)
Pneumocystosis	5 (1)	0 (0)	1 (1)	4 (2)	3 (3)	0 (0)
Other yeast	6 (1.8)	9 (2.4)	5 (3.9)	0 (0.0)	0 (0.0)	1 (5)
Unspecified yeast	3 (0.9)	5 (1.3)	1 (0.8)	6 (2.4)	0 (0.0)	1 (5)

Table 3. Fungal pathogens causing invasive fungal disease.

Invasive Fungal Infection	No. (%) of Patients	Days from Transplantation
Invasive Candidiasis	17 (23.6%)	181 (38–3423)
Candida Albicans	5	
Candida Tropicalis	4	
Candida Glabrata	2	
Candida Parapsilosis	1	
Invasive Aspergillosis	26 (36.1%)	161 (32–697)
Aspergillus Fumigatus	7	
Aspergillus Terreus	1	
Aspergillus Niger	1	
Aspergillus Flavus	1	
Cryptococcosis	2 (2.8%)	1834 (1444–2225)
Trichosporonosis	2 (2.8%)	870 (445–1295)
Scedosporiosis	1 (1.4%)	99

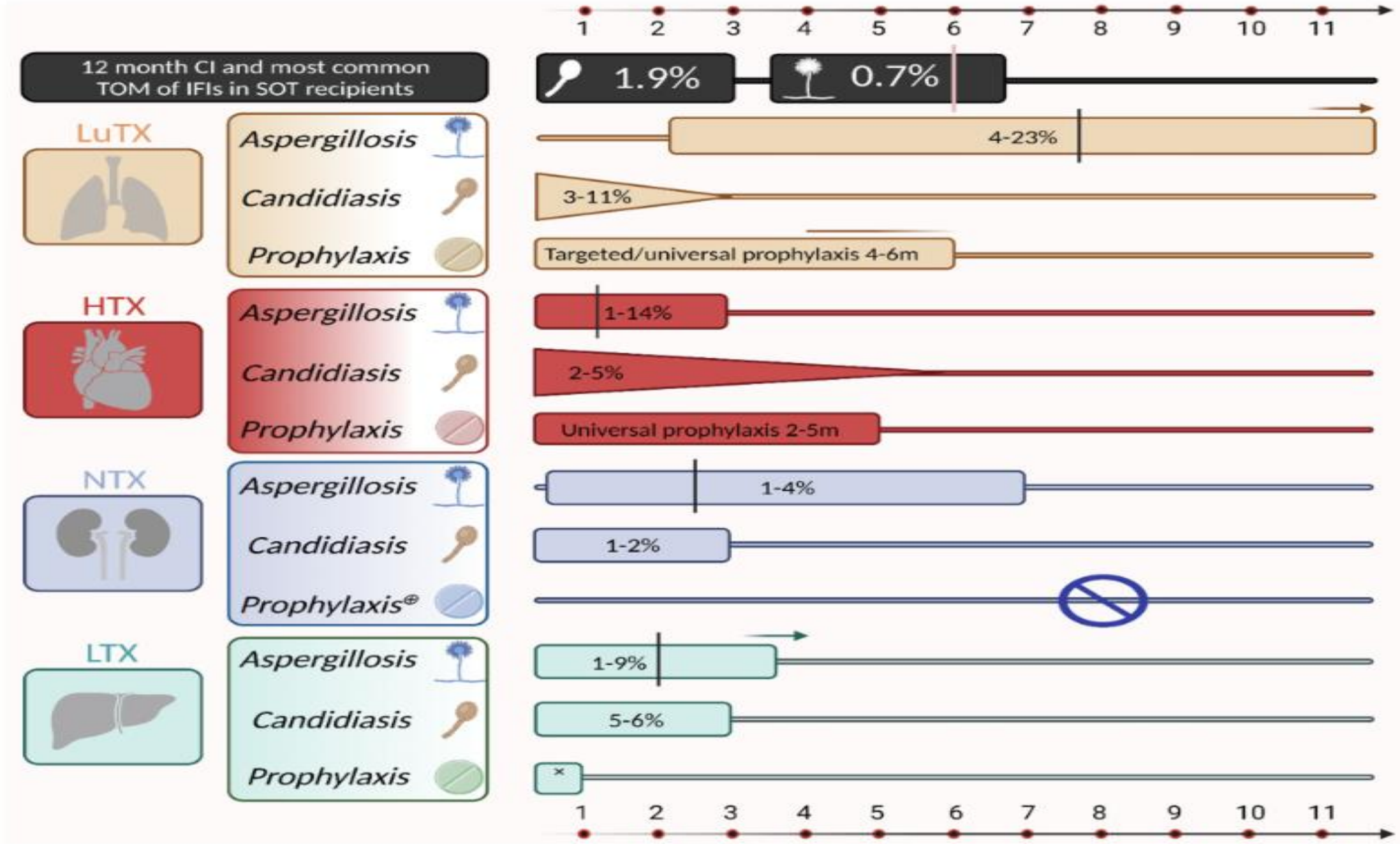
12 month CI and most common TOM of IFIs in SOT recipients
1 2 3 4 5 6 7 8 9 10 11
LuTX
Aspergillosis
Candidiasis
Prophylaxis
1.9%
0.7%
4-23%
3-11%
Targeted/universal prophylaxis 4-6m
HTX
Aspergillosis
Candidiasis
Prophylaxis
1-14%
2-5%
Universal prophylaxis 2-5m
NTX
Aspergillosis
Candidiasis
Prophylaxis⊕
1-4%
1-2%
LTX
Aspergillosis
Candidiasis
Prophylaxis
1-9%
5-6%
1 2 3 4 5 6 7 8 9 10 11

Table 2. Risk factors for the development of invasive fungal disease (IFD) in patients after kidney transplantation (KT).

Variables	OR (95% CI)	*p* Value	Adjusted OR (95% CI)	*p* Value
Age	1.04 (1.01–1.07)	0.005	1.03 (0.99–1.06)	0.101
Sex	0.57 (0.28–1.16)	0.121	0.61 (0.25–1.48)	0.274
Diabetes Mellitus	3.50 (1.49–8.21)	0.004	3.72 (1.34–10.31)	0.011
Dialysis-Dependence	0.72 (0.24–2.17)	0.564	0.48 (0.12–1.89)	0.292
ABO Incompatibility	0.89 (0.39–2.02)	0.784	0.81 (0.29–2.24)	0.678
Deceased Donor	1.77 (0.86–3.63)	0.123	2.10 (0.88–5.03)	0.095
Re-Transplantation	2.17 (0.46–10.27)	0.331	1.39 (0.27–7.08)	0.696
Lymphocyte-Depleting Antibody Usage *	1.05 (0.49–2.25)	0.898	0.46 (0.17–1.26)	0.132
Delayed Graft Function ‡	2.56 (0.81–8.10)	0.109	4.02 (0.74–21.98)	0.108
Acute Rejection §	2.23 (1.09–4.58)	0.028	3.41 (1.41–8.21)	0.006

* Lymphocyte-depleting antibodies include anti-thymocyte globulin, basiliximab, and alemtuzumab, used according to each treatment indication. ‡ Delayed graft function was defined as the use of dialysis within 7 days of transplantation. § The diagnosis of acute rejection was confirmed by graft biopsy.

Candida

Candidiasis in kidney transplant recipients

- Oral candidiasis
- Bloodstream infection
  - HD, surgical procedures and dysbiosis secondary to antibiotic use.
  - Mortality is high.
  - Echinocandin therapy was associated with improved survival.
- Chorioretinitis
  - a complication of candidemia
  - Importance of fundus examination.
- Early graft candidiasis
  - 1 in 1000 renal transplants following contaminated perfusion fluid

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ORIGINAL ARTICLE

NEPHROLOGY WILEY

Oral/oesophageal candidiasis is a risk factor for severe infection after kidney transplantation

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Abstract

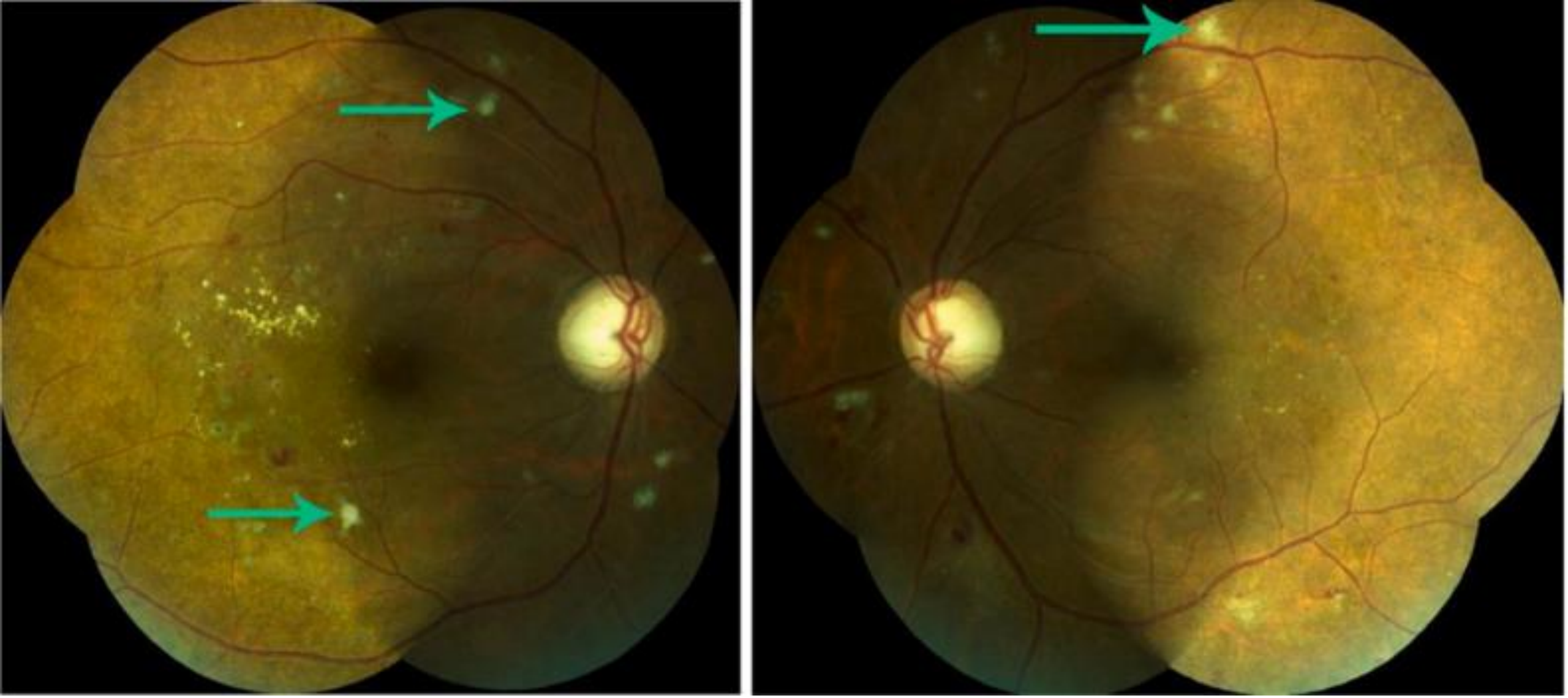
Aim: Bacterial and fungal infections are serious, life-threatening conditions after kidney transplantation. The development of oral/oesophageal candidiasis after kidney transplantation is not a reported risk factor for subsequent severe infection. This study was performed to investigate the relationship between oral/oesophageal candidiasis after kidney transplantation and the development of subsequent infection requiring hospitalization.

Methods: This retrospective study included 522 consecutive patients who underwent kidney transplantation at Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital from 1 January 2010 to 1 February 2019. Ninety-five percentage of patients were living donor transplant recipients. Visual examination was performed to detect oral candidiasis, beginning immediately after kidney transplantation; upper gastrointestinal endoscopy was performed 8–10 months after kidney transplantation. Twenty-five patients developed candidiasis (Candida-onset group) and 497 did not (non-Candida-onset group). The follow-up periods were 67 (37–86) months in the Candida-onset group and 55 (34–89) months in the non-Candida-onset group. Severe infection was defined as bacterial or fungal infection requiring hospitalization; viral infections were excluded.

Results: Severe infection developed in 9/25 (36%) patients in the Candida-onset group and in 77/497 (15%) patients in the non-Candida-onset group ($p = .006$). Binomial logistic analysis revealed that Candida infection (odds ratio [OR] 2.53, 95% confidence interval [CI] 1.06–6.06; $p = .037$) and use of rituximab (OR 1.81, 95% CI 1.12–2.93; $p = .016$) were significant predictors of subsequent severe infection.

Conclusion: Oral/oesophageal candidiasis is a risk factor for severe infection after kidney transplantation and suggests an over-immunosuppressive state, which should prompt evaluation of immunosuppression.

KEYWORDS
immunosuppression, kidney transplantation, oesophageal diseases, oral candidiasis, rituximab



Colour fundus photographs of the right and the left eye: the arrows show creamy-white, cotton-like retinal lesions that are compatible with Candida chorioretinis.

OPEN ACCESS

Management of early graft candidiasis in a kidneytransplant recipient

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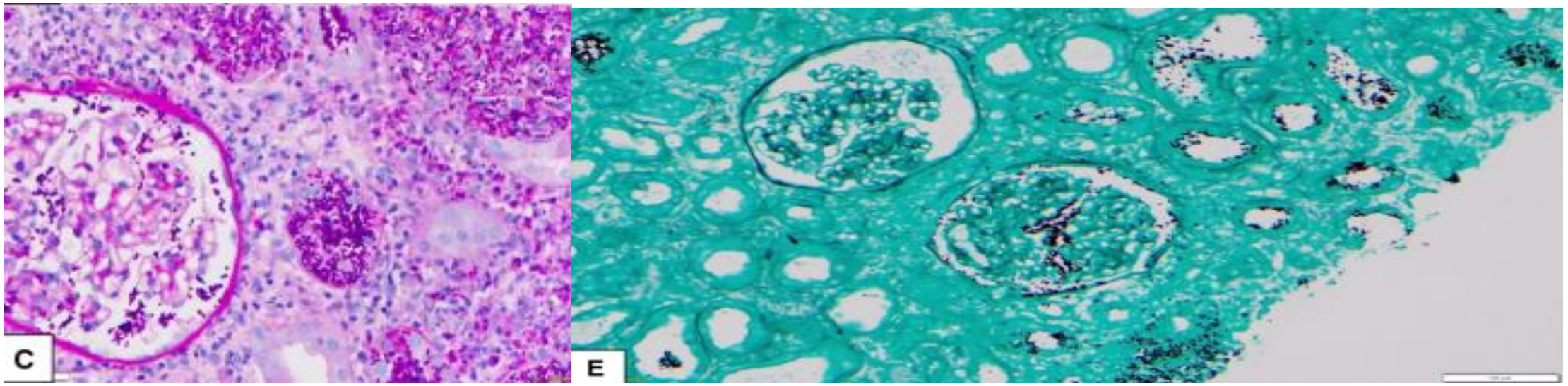


(C) PAS (magnification ×40)—numerous organisms within tubules, the interstitium and in Bowman's space. The organisms are ovoid, showing mild size variation and are intensely and uniformly PAS-positive.

(E) Grocott (magnification ×20)—the organisms stain positively for Grocott stain.

Aspergillosis

Risk factors of IA after kidney transplantation

Risk factor	Random-effect estimation	Significance
Living vs deceased donor	OR: 0.65 (95% CI: 0.46-0.93)	*P* value = .02
Recipient age	Mean difference 5.96 (95% CI: 3.91-8.01)	*P* value < .0001
Previous chronic lung disease	OR: 7.26 (95% CI: 1.05-50.06)	*P* value = .04
Diabetic nephropathy	OR: 1.65 (95% CI: 1.10-2.48)	*P* value = .01
Induction therapy	OR: 1.19 (95% CI: 0.78-1.83)	*P* value = .42
Previous bacterial infection	OR: 7.51 (95% CI: 4.37-12.91)	*P* value < .0001
Previous respiratory tract viral infection	OR: 7.75 (95% CI: 1.60-37.57)	*P* value = .01
Previous CMV infection and/or disease	OR: 2.67 (95% CI: 1.12-6.32)	*P* value = .03
Posttransplant hemodialysis	OR: 3.69 (95% CI: 2.13-6.37)	*P* value < .0001
Surgical reintervention	OR: 6.28 (95% CI: 1.67-23.66)	*P* value = .007
Acute graft rejection	OR: 3.01 (95% CI: 1.78-5.09)	*P* value < .0001

Am J Transplant. 2021;21:703–716.

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03871-2

ORIGINAL ARTICLE

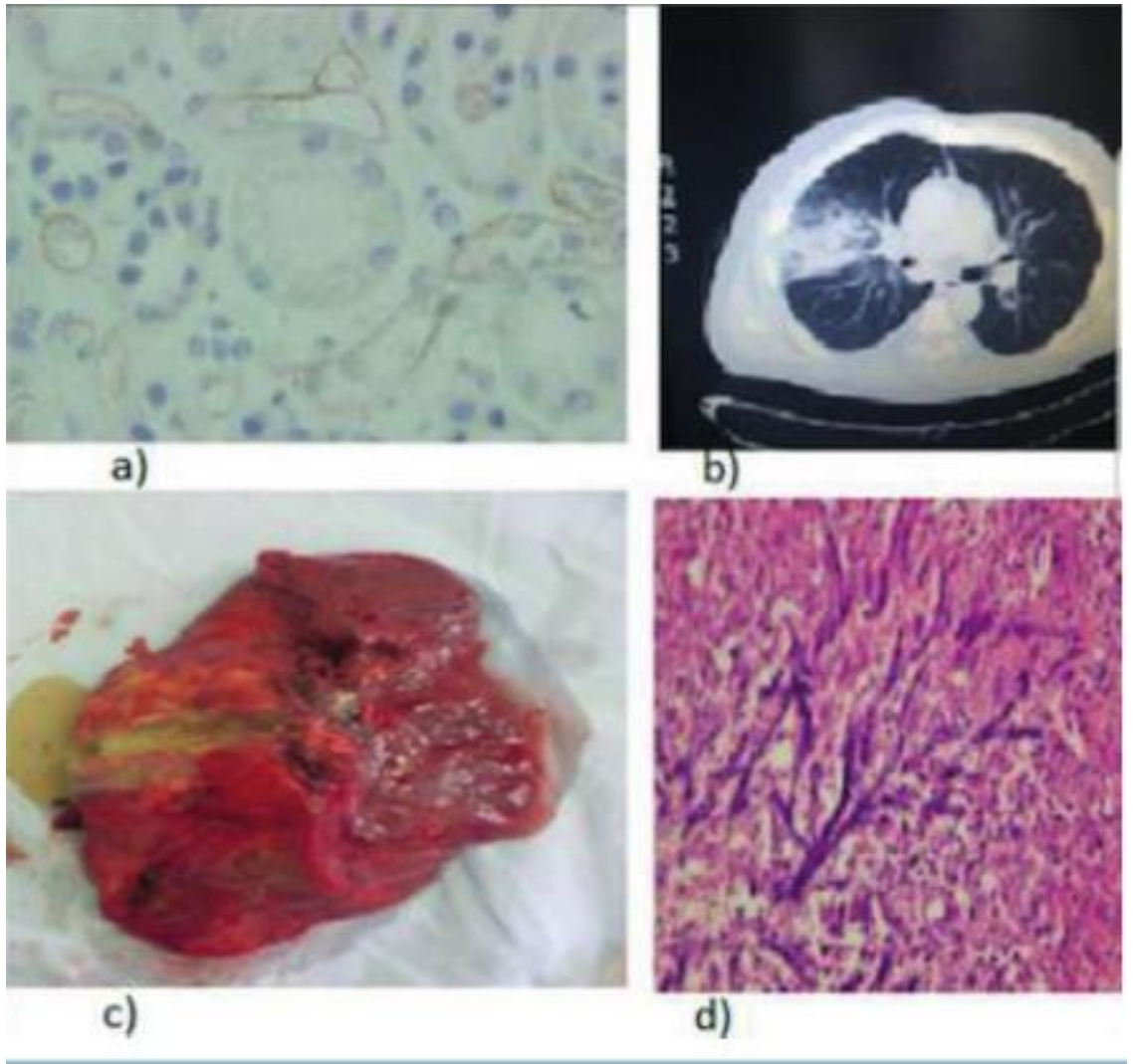
Risk factors for development and mortality of invasive pulmonary Aspergillosis in kidney transplantation recipients

Induction			
Antithymocyte globulin	10 (71.4%)	1 (8.3%)	0.001
Basiliximab	2 (14.3%)	8 (66.7%)	0.014
Any lymphocyte-depleting antibody	13 (92.9%)	9 (75.0%)	0.230
Maintenance			
Mycophenolate	12 (85.7%)	10 (83.3%)	1.000
Cyclosporine	1 (7.1%)	3 (25.0%)	0.306
Tacrolimus	11 (78.6%)	7 (58.3%)	0.401

Published online: 11 April 2020

Pulmonary invasive aspergillosis

- Figure 1. Diagnostic findings in patient a) fine needle biopsy showed positive CD4 antibodies (humoral rejection), b) CT showed cavernous finding, c) pyogenic macroscopic finding after lobectomy d) pathognomonic microscopic Aspergillus finding.



CASE REPORT | MED ARCH. 2018 DEC; 72(6): 456-458

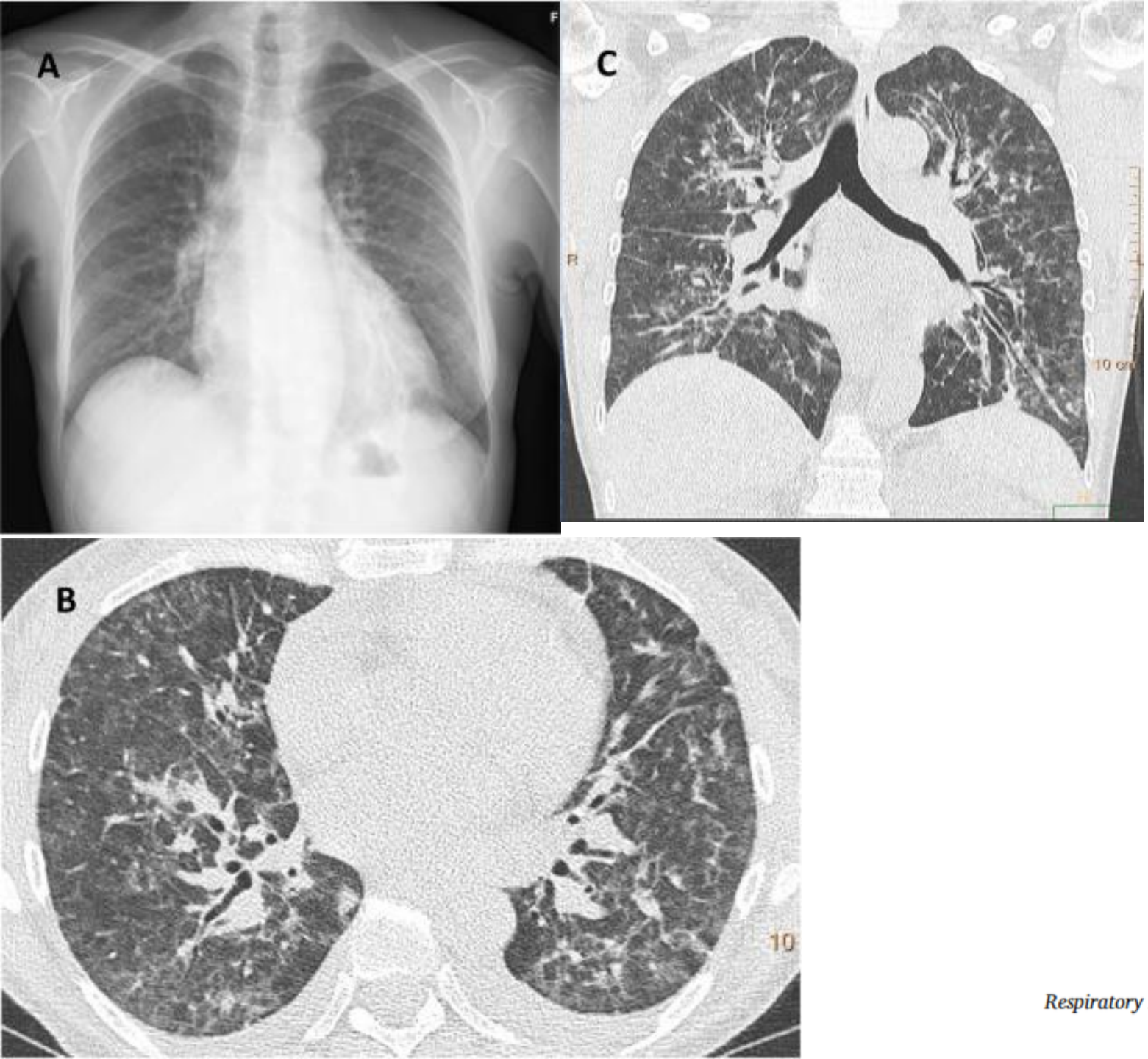


Fig. 1. A 54-year-old woman transplanted with a kidney 3 years ago, presented with dry cough, dyspnea and mild fever for 4 days. **A.** Poster-oanterior chest X-ray performed at day 0 revealed no significant parenchymal abnormalities. A slightly enlarged heart and increased pulmonary vasculature is noted. **B**. CT performed at Day 3. Axial view displayed at the level of the middle lung zones revealed extensive areas of ground glass opacities with discreet increase of interlobular thickening. The distribution of lung abnormalities was heterogenous with a mosaïc appearance. **C.** Coronal CT reformatted image on a plane passing through the division of the main bronchi illustrates well the symmetrical and heterogeneous distribu-tion of the lung abnormalities.

Brief Report Annals of Dermatology 2022;34(3) • https://doi.org/10.5021/ad.2022.34.3.233

Check for updates

Cutaneous Aspergillosis As a First Manifestation of Systemic Infection in Patient After Kidney Transplantation

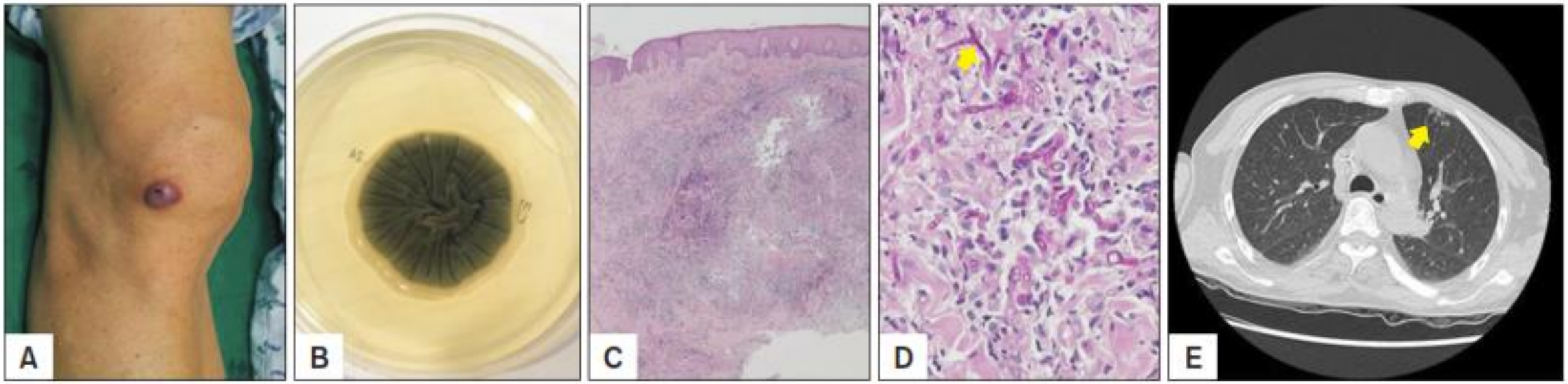
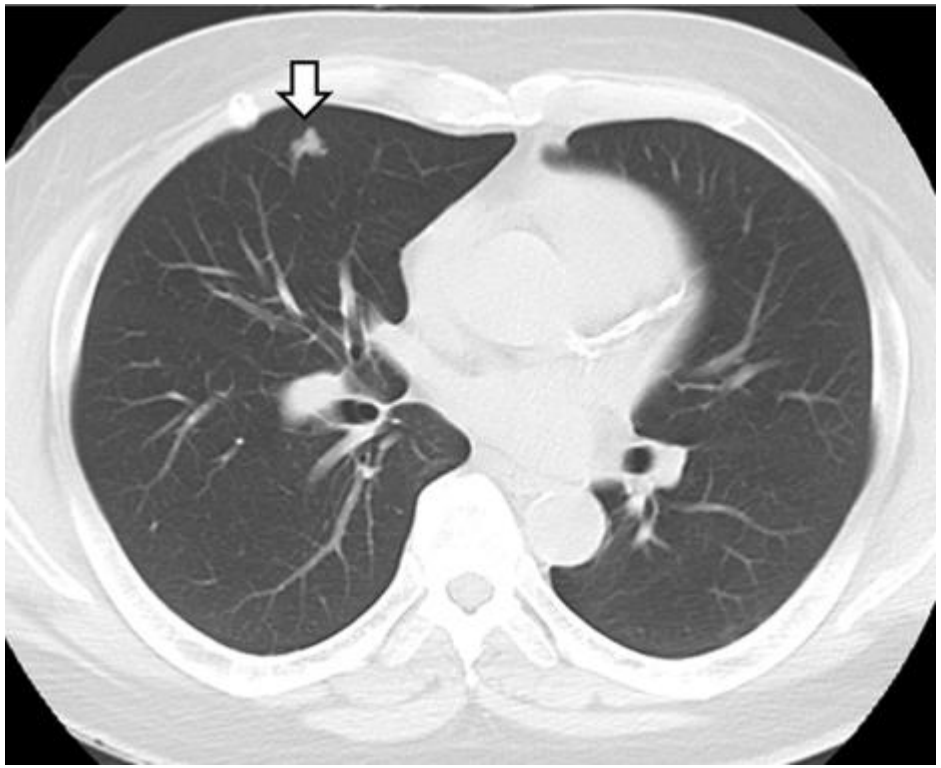


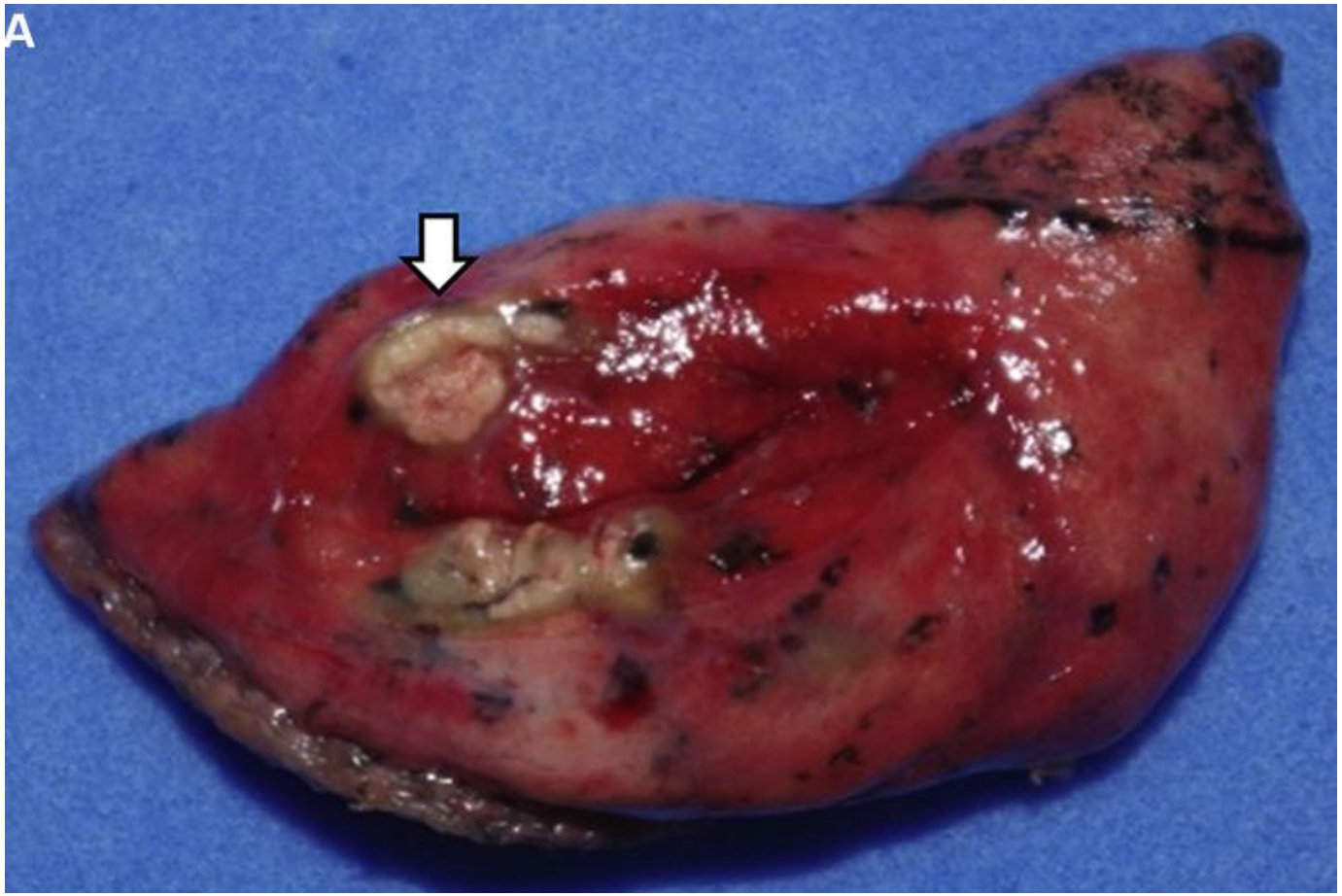
Fig. 1. (A) Purple-colored nodule on the right knee. (B) Spreading yellow-green colony. (C) Skin biopsy revealed dermal neutrophilic and granulomatous infiltration (H&E, original magnification ×20). (D) Numerous septate hyphae with dichotomous branching are visible at 45° angle (D-PAS staining, original magnification ×200; yellow arrow). (E) Fungal balls were observed on chest computed tomography (yellow arrow).

Cryptococcosis

- Skin lesions
- Pulmonary cryptococcosis
- Cryptococcal meningitis
- Disseminated cryptococcal infection

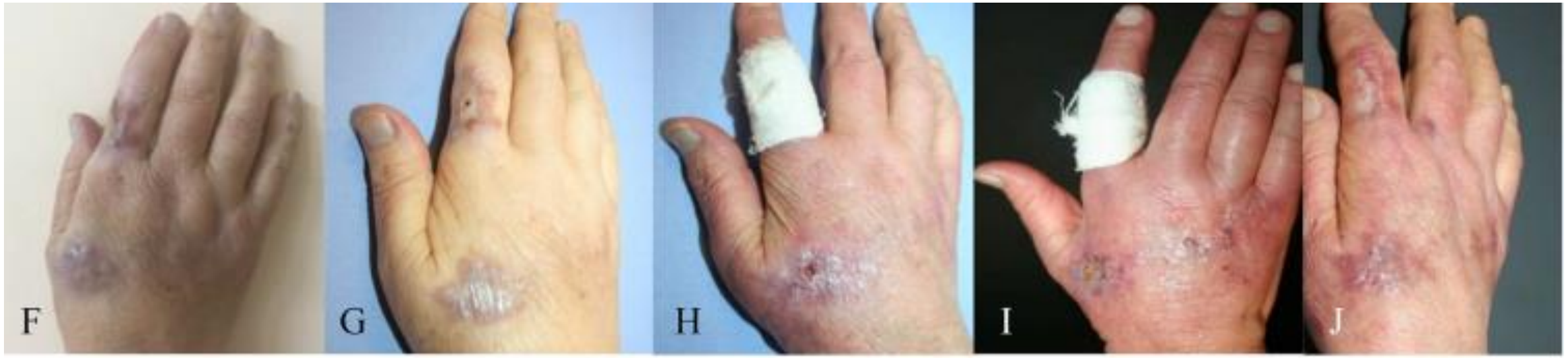
Isolated Pulmonary Cryptococcosis Confused with Lung Tumor 5 Years After Kidney Transplantation: A Case Report





Transplantation Proceedings, 51, 561–564 (2019)

Skin cryptococcosis in an immunocompromised renal-transplant recipient



Gradual clinical improvement in cryptococcal skin lesions from day +579 to day +777. (F) at presentation, and at 1 month (G), 2 months (H), 3 months (I), and 6 months (J) after start antifungal therapy.

Medical Mycology Case Reports 28 (2020) 33–35

Azole antifungal drugs

Antifungal Drug Class	Drug	Mode of Action
Azoles	Fluconazole Voriconazole Posaconazole Itraconazole Ketoconazole Clotrimazole Econazole Miconazole	Inhibitor of lanosterol 14α—demethylase
Echinocandins	Caspofungin Anidulafungin Micafungin	Inhibitor of 1,3–β–glucan synthase
Polyenes	Amphotericin B Nystatin	Binding to ergosterol
Pyrimidine analogue	flucytosine	Inhibitor of DNA/RNA/protein synthesis

Azole antifungals drug interactions

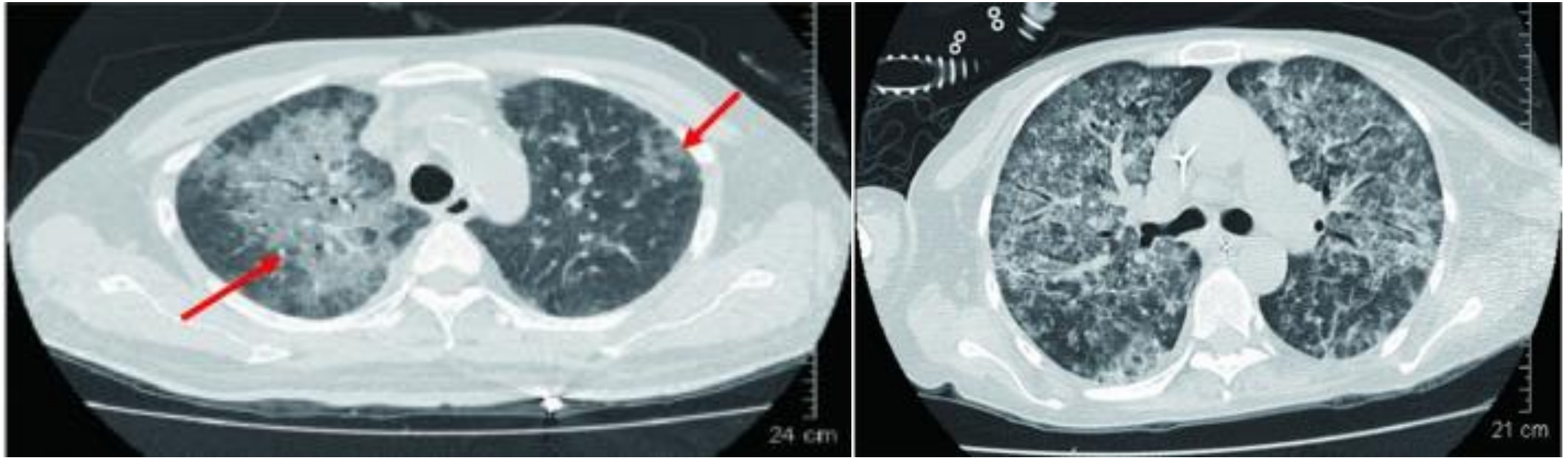
fluconazole	cyclosporine: reduce by 21–50% tacrolimus: reduce by 40% sirolimus: reduce by 50–70%
itraconazole	cyclosporine: reduce by 50–60% tacrolimus: reduce by 50–60% sirolimus dose: reduce by 50-60%
posaconazole	cyclosporine: reduce by 0–30% tacrolimus: reduce by 75–80% sirolimus: coadministration contraindicated
voriconazole	cyclosporine dose: reduce by 50% tacrolimus dose: reduce by 66% sirolimus dose: coadministration contraindicated
isavuconazole	cyclosporine, tacrolimus and sirolimus: no empirical reduction

Antifungal prophylaxis

- **In kidney** and in heart **transplant recipients, administration of antifungal prophylaxis is not routinely recommended**, and should be based on individual risk factors (such as the use of extracorporeal membrane oxygenation (ECMO), or renal replacement therapy(RRT).

VIRULENCE2016, VOL. 7, NO. 3, 329–
340http://dx.doi.org/10.1080/21505594.2016.1139279

Pneumocystis



BIOENGINEERED
2021, VOL. 12, NO. 1, 1264–1272
https://doi.org/10.1080/21655979.2021.1911203

Treatment

Frontline: Trimethoprim/sulfamethoxazole (15–20 mg/kg TMP; 75–100 mg/kg SMX per day) with TMP administered by IV every 6–8 h.
For hypoxemic patients potentially in combination with 40–60 mg of prednisolone (twice daily)
Second line:
IV Pentamidine (Initially 4 mg/kg/day over 1–2 h) Recipients of pancreas/islet transplants should receive an alternative second line therapy.

Prophylaxis

Front line: Trimethoprim/sulfamethoxazole one single-strength (80 mg TMP/400 mg SMX)/day or double strength tablet (160 mg TMP/800 mg SMX)/day or three per week.
Second line:
Dapsone (50–100 mg once a day)
Atovaquone (>1000 mg daily)
Third Line:
Pentamidine aerosols (300 mg every 3–4 weeks)

J. Fungi **2018**, *4*, 127; doi:10.3390/jof4040127

- The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend PJP prophylaxis with daily TMP-SMX for the first 3–6 months after kidney transplantation.

- The American Society of Transplantation recommends prophylaxis for 6–12 months.

- The European Renal Association recommends 12 months of prophylaxis when calcineurin inhibitors are given.