

**Background:** *Pneumocystis jirovecii* pneumonia is an uncommon and life-threatening disease that can occur following hematopoietic stem cell transplantation (HSCT). Trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis greatly reduces the incidence of PJP. We aim to determine what factors contribute to the development of PJP following HSCT where TMP-SMX prophylaxis is widely used.

**Methods:** We performed a single-center, retrospective case series of HSCT recipients from January 1, 2012 to December 31, 2018. Subjects had clinical symptoms and radiographic evidence for PJP along with at least one positive *Pneumocystis* test obtained from bronchoalveolar lavage (BAL) including direct fluorescence antibody (DFA), quantitative polymerase chain reaction (qPCR), cytology, and pathology.

**Results:** 1111 subjects underwent HSCT; of whom, 25 (2.2%) met inclusion criteria and were treated for PJP. 6 were autologous and 19 were allogeneic HSCT recipients (1.23% and 3.05% of total autologous and allogeneic HSCT, respectively). All allogeneic HSCT recipients received *in-vivo* T-cell depletion. Median duration from autologous and allogeneic HSCT to PJP diagnosis were 138 days (range 20 to 348) and 346 days (range 41 to 771), respectively. PJP qPCR was positive in all samples tested ( $n = 20$ , range < 84 to 14900). DFA was positive in 6 (28%). Death from pneumonia occurred in 2 subjects; 11 (44%) required ICU stay, and 7 (27%) required intubation. At diagnosis, 3 subjects had relapse of underlying disease and 10 were on immunosuppression. 12 were on PJP prophylaxis (autologous HSCT  $n = 3$ ), the most common of which was atovaquone ( $n = 5$ ); only 2 subjects were on TMP-SMX. *Cytomegalovirus* (CMV) viremia was detected in 9 subjects (36%) prior to PJP diagnosis; 4 had pulmonary CMV coinfection. In total, 17 subjects (68%) had one of the above risk factors for PJP. Median total lymphocyte count and % lymphocytes were  $5.1 \times 10^3$  cells/ $\mu$ L (range 1.4 to  $38.5 \times 10^3$  cells/ $\mu$ L) and 9.6% (range 1.1 to 29.5%), respectively.

**Conclusion:** PJP is an uncommon (2.2% of the study population) complication of HSCT while receiving PJP prophylaxis and in the absence of disease relapse, CMV reactivation, or ongoing immunosuppression. Presentation is often delayed in this population; a high degree of clinical suspicion should prompt diagnostic evaluation using a combination of laboratory tests on BAL fluid.

**Additional Figures**

Table 1

|                     | Number (% Total) |
|---------------------|------------------|
| Male                | 22 (88%)         |
| Underlying disease  |                  |
| AML                 | 10               |
| MDS/MPD             | 4                |
| NHL                 | 5                |
| HL                  | 3                |
| Plasma cell myeloma | 2                |
| Aplastic anemia     | 1                |
| Autologous          | 6 (24%)          |
| Allogeneic          | 19 (76%)         |
| MRD                 | 7                |
| MUD                 | 7                |
| Haploidentical/cord | 2                |
| Double cord         | 2                |
| Single cord         | 1                |

AML, acute myeloid leukemia. MDS/MPD, myelodysplastic syndrome/myeloproliferative disease. MRD, matched related donor. MUD, matched unrelated donor.

Table 2

|                              | Number |
|------------------------------|--------|
| Ongoing immunosuppression    | 10     |
| GVHD prophylaxis             | 2      |
| GVHD                         | 4      |
| AIH                          | 3      |
| Relapsed disease             | 1      |
| Prophylaxis at PJP diagnosis | 12     |
| TMP-SMX                      | 2      |
| Atovaquone                   | 5      |
| Pentamidine IV               | 3      |
| Dapsone                      | 2      |

GVHD, graft versus host disease. AIH, autoimmune hemolytic anemia. IV, intravenous. TMP-SMX, Trimethoprim-sulfamethoxazole

Table 3

| Diagnostic test | % Positive results (number tested) |
|-----------------|------------------------------------|
| qPCR            | 100 (20)                           |
| DFA             | 23 (6)                             |
| Cytology        | 13 (3)                             |
| Pathology       | 39 (5)                             |

qPCR, quantitative polymerase chain reaction. DFA, direct fluorescent antigen.

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**2696. Breakthrough Toxoplasmosis While on Atovaquone Prophylaxis Following Allogeneic Hematologic Stem Cell Transplantation**

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**Background:** The opportunistic parasite *Toxoplasma* causes life-threatening complications in immunocompromised hosts such as hematopoietic cell transplantation (HCT) recipients. Trimethoprim-sulfamethoxazole (TMP-SMX) is the agent of choice in preventing *Pneumocystis jirovecii* pneumonia and *Toxoplasma*, but bone marrow suppression often precludes its use. Broad-spectrum atovaquone also targets protozoan

tachyzoite and cyst forms, but few studies examine its efficacy in prophylaxis among this vulnerable population. We present two HCT patients experiencing breakthrough toxoplasmosis despite compliance with atovaquone prophylaxis.

**Methods:** Review of literature and electronic medical records.

**Results:** Case 1. A 68-year-old *Toxoplasma* seropositive woman with myelodysplastic syndrome underwent Flu-Mel-ATG-matched unrelated donor HCT. On day +68 post HCT, she presented with encephalopathy. MRI brain revealed solid and ring-enhancing lesions correlating with positive CSF *T. gondii* PCR. Serum DNA PCR was negative. She received 12 weeks of sulfadiazine, pyrimethamine, and leucovorin with clinical and radiological improvement. Atovaquone prophylaxis was restarted given pancytopenia intolerance of TMP-SMX. Despite compliance, she experienced recurrent central nervous system toxoplasmosis. Her demise followed an unrelated ischemic cerebrovascular accident. Case 2. A 53-year-old *Toxoplasma* seropositive woman with CMV viremia and severe aplastic anemia limiting TMP-SMX use presented with pancytopenia on day +46 after HCT. Diagnosed with graft failure, routine screening revealed positive *Toxoplasma* PCR while on atovaquone prophylaxis. *Toxoplasma* PCR became negative after preemptive therapy. She underwent a second Flu-Cy-ATG-TBI-matched related donor HCT. 2 months later, medication noncompliance led to readmission with CMV viremia and culture-negative sepsis. Blood *Toxoplasma* PCR was positive at the time of death.

**Conclusion:** Toxoplasmosis prophylaxis failure can occur in allogeneic HCT recipients receiving atovaquone. When possible, TMP-SMX should remain first-line agent for this indication. In those unable to tolerate TMP-SMX, close clinical and *Toxoplasma* PCR monitoring may help identify reactivation and facilitate early initiation of therapy.

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**2697. The Impact of Universal Deceased Donor Screening on Donor-Derived Toxoplasmosis in Solid-Organ Transplant: Report of the OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC)**

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**Background:** Donor-derived toxoplasmosis (DDT) is a severe and potentially life-threatening infection after solid-organ transplantation (SOT). Serologic testing for *Toxoplasma gondii* is required for all deceased donors per OPTN policy as of 4/6/17. To assess the impact of universal donor testing and the optimal approach to DDT prevention, we analyzed potential DDT cases reviewed by DTAC.

**Methods:** All potential *Toxoplasma* donor-derived transmission events adjudicated by DTAC from 2008 to 2018 were reviewed. A standardized classification algorithm was used to adjudicate each event as proven, probable, possible, unlikely, excluded or intervention without disease transmission.

**Results:** Twenty-eight potential DDT events were reported between 2008 and 2018. Proven or probable (p/p) DDT developed in 16 organ recipients from 15 donors. In the 9 years prior to the new testing requirement (January 2008–March 2017) 11 organ recipients from 10 donors had p/p DDT (0.13 transmissions per 1,000 donors); in the first 21 months of the new testing requirement 5 recipients from 5 donors had p/p DDT (0.27 transmissions per 1,000 donors), rate ratio 2.15; 95% CI 0.577, 6.90;  $P = 0.18$ . 10.2% of 18,328 donors tested between April 6, 2017 and December 31, 2018 were *Toxoplasma* IgG seropositive. Recipient pre-SOT serostatus was unknown in 4 of 5 and negative in 1 case of p/p DDT. Trimethoprim-sulfamethoxazole prophylaxis was either stopped at < 3 months or not used in all 5 cases. Infection was diagnosed a median of 103 days (range 42–153) post-transplant. Four of the 5 recipients died.

**Conclusion:** DDT remains a morbid infection in both heart and non-heart recipients. Despite an apparent increase in DDT reporting to DTAC, it is unlikely that the actual incidence of this donor-derived event is increasing. Rather, with universal serologic screening of deceased donors and wider access to molecular diagnostics, DDT is increasingly recognized and diagnosed. To decrease risk for illness and death related to DDT, broader pre-transplant recipient serologic testing and use of prophylaxis or monitoring for high-risk serostatus recipients (*Toxoplasma* D+/R-) is critical. The optimal duration of prophylaxis is uncertain at this time and warrants further study.

Table 1. Proven/probable donor-derived toxoplasmosis

|                       | 1/08 – 3/17                     | 4/17 – 12/18           |
|-----------------------|---------------------------------|------------------------|
| Heart recipients      | 6                               | 2                      |
| Non-heart recipients  | 5 (2 livers, 2 kidneys, 1 lung) | 3 (2 kidneys, 1 liver) |
| Post-mortem diagnosis | 3 (27%)                         | 3 (60%)                |
| Death                 | 5 (45%)                         | 4 (80%)                |

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**2698. Timing of Standalone Vaccine Administration in Infants Receiving DTaP-Based Combination Vaccines**

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