Hematologic Malignancies/Stem Cell Transplantation Program
Clinical Section

UCLA Health System
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CS 6.4 DIAGNOSIS AND MANAGEMENT OF CYTOMEGALOVIRUS (CMV) INFECTION AND DISEASE

Location: Clinical Section *Supersedes/Replaces: B3.422d*
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Purpose and Background

Allogeneic bone marrow transplant patients are at risk for serious CMV infections and diseases which can be fatal. Because CMV infections and disease are very common in allogeneic bone marrow transplant patients without effective prophylaxis, it is critical to prevent or treat these complications.

Objectives

To establish uniform guidelines for prevention, diagnosis, and treatment of CMV infections and disease.

Procedure

1. Prophylaxis:

   All allogeneic transplant patients who are CMV-seronegative pretransplant as well as CMV-seronegative patients who will be eligible for an allogeneic transplant in the future will receive CMV-negative blood products to prevent CMV infections. This includes patients who are CMV-seronegative and who receive a transplant from a sero-positive donor.

   All allogeneic bone marrow transplant patients who are CMV-seropositive before transplant will receive prophylactic ganciclovir. The prophylactic IV ganciclovir (6 mg/kg IVPB/day) will be started at time of admission (if hospitalized prior to stem cell conditioning, start at least 7 days prior to transplant [day –7]) and continued until day-2 pre-transplant. After transplant, the prophylactic IV ganciclovir (6 mg/kg IVPB/day, Monday thru Friday) will be restarted when the ANC $\geq 1000/mm^3$ and continued until day 100 after transplant

   CMV-negative patients who receive CMV-positive blood for bleeding or platelet refractoriness or are otherwise unable to receive CMV-negative blood products will receive prophylactic ganciclovir following the transplant as discussed above.

2. CMV Testing:

Since development of CMV disease very rarely occurs when patients are receiving prophylactic IV ganciclovir during the initial 100 days after transplantation, routine CMV PCR tests are not needed during the initial 100 days after transplantation. After day 100, when patients are no longer receiving prophylactic ganciclovir, a CMV PCR test should be done every 2 to 4 weeks in patients still on high doses of immunosuppression or have active graft-versus-host disease (GVHD).

3. Diagnosis:

If a patient develops a clinical syndrome suggestive of CMV disease after transplant, CMV PCR will be obtained. Cultures of buffy coat cells, urine, and other suspected sites of infection will also be done. For patients with suspected CMV pneumonia, bronchoscopy with bronchoalveolar lavage will be done when clinically indicated. If the bronchoscopy is nondiagnostic, then an open-lung biopsy should be considered. Similarly, biopsy of the GI tract, liver, or other suspected sites of CMV infection will be done if clinically indicated.

3. Treatment:

For treatment of CMV pneumonia, a combination of treatment doses of ganciclovir (5 mg/kg IV q12h) plus intravenous immunoglobulin (500 mg/kg q.48 hrs) will be used. For other types of CMV infections, intravenous ganciclovir alone will be used. For patients with suspected ganciclovir-resistant CMV disease or unable to tolerate ganciclovir due to myelosuppression, foscarnet can be used. Oral valganciclovir should not be used for initial treatment of symptomatic CMV infection, but can be used as follow-up therapy (900 mg po bid) in a patient who has improved on IV ganciclovir.

After day 100, patients with CMV PCR positivity without clinical signs of CMV infection will receive therapeutic doses of intravenous ganciclovir (5 mg/kg IVPB q12h) for 2 weeks, and then may be restarted on prophylactic doses if still on immunosuppression. Oral valganciclovir (900 mg bid) can be used in selective patients with asymptomatic CMV viremia who are clinically stable but have no IV access.

4. If patients are enrolled on a study protocol for the prevention or treatment of CMV infections, the study protocol takes precedence over the SOP guidelines.

References:

1) Winston, DJ: Prophylaxis And Treatment Of Infection In The Bone Marrow Transplant Recipient. Current Clinical Topics in Infectious Diseases, Vol. 13 (Remington JS, Swartz MN, eds.). Blackwell Scientific Publications, Inc., Boston 1993. p. 293-321.

2) Winston, DJ: Infections in bone marrow transplant recipients. Principles and Practice of Infectious Disease, Fourth Edition, (Mandell GL, Besett JE, Nolin R, eds). Churchill Livingstone, Inc, New York 1995. p.2717-2722.

3) Winston, DJ, et al: Ganciclovir prophylaxis of cytomegalovirus infection and disease in allogeneic bone marrow transplants: results of a placebo-controlled, double-blind trial. Ann Intern Med 1993; 118:179-184.

4) Winston, DJ, et al: Pharmacokinetics of ganciclovir following oral valganciclovir versus intravenous ganciclovir in allogeneic stem-cell transplant patients with graft-versus-host disease of the gastrointestinal tract. Biol Blood Marrow Transplant 2006;12:635-640.

ATTACHMENTS:

Attachment A: Procedure History
Attachment B: New/Revised Procedure Checklist

APPROVAL:

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PROCEDURE HISTORY

Date	Initials	Page	Item and Summary of Changes
8/4/09		1	Changed SOP number
8/4/09			Revised format
8/4/09		2	Added: CMV Testing: Since the development of CMV disease very rarely occurs when patients are receiving prophylactic IV ganciclovir during the initial 100 days after transplantation, routine CMV PCR tests are not needed during the initial 100 days after transplantation. After day 100, when patients are no longer receiving prophylactic ganciclovir, a CMV PCR test should be done every 2 to 4 weeks in patients still on high doses of immunosupression or have active graft-versus-host disease (GVHD)
8/4/09		2	Added under Treatment: Oral valganiclovir should not be used for initial treatment of symptomatic CMV infection but can be used as follow-up therapy (900 mg po bid) in a patient who has improved on IV ganciclovir.
8/4/09		2	Added under treatment: Oral valganciclovir (900 mg bid) can be used in selective patients with asymptomatic CMV viremia who are clinically stable but have no IV access.

Attachment A