INTRODUCTION

Information on the epidemiology of cytomegalovirus (CMV) infections in burn patients is limited. Moreover, most published cases involved non-severely ill patients, with few consequences as regards vital prognosis. CMV may thus be underestimated in burns and misdiagnosed.

We report two cases of seriously burned patients admitted to the burn unit of Cochin Hospital, Paris, who developed symptomatic primary CMV infection, confirmed by evidence of CMV seroconversion. These cases are a reminder that severe CMV infections may develop in patients with serious burns. While the clinical background of these patients predisposed them to contracting CMV, the delayed diagnosis possibly contributed to the fatal outcome. Prevention of transmission of CMV to these vulnerable patients is essential, as highlighted in these cases.

FIRST CASE

The first patient was a 32-yr-old man with serious electrical third-degree burns in 28% of the body surface. Bilateral mid-thigh amputations were performed on day 1 of hospitalization, followed by right femoroiliac disarticulation on day 26. After amputation, the burned surface represented 8% of the body surface.

By day 5 in hospital, the patient had experienced several bacterial and fungal systemic infections, treated with various anti-infective drugs. On day 54, fever of more than 39 °C was noted, without any obvious effect on standard microbiological cultures and radiological investigations, including a magnetic resonance imaging investigation of the amputation stump. Despite pre-emptive antibiotherapy based on colonization, the fever persisted. Development of the fever was associated with moderate lymphocytosis (4.97 x 10⁹/l; 4 x 10⁹/l), cholestasis with rapid elevation of bilirubin (230 µmol/l; 3-17 µmol/l), and elevated procalcitonin (2.7 ng/l; 0.5 ng/l). A real-time quantitative CMV Taq Man-based PCR assay (ABI) was performed on serum drawn on hospital day 96, using an in-house assay adapted from Leruez-Ville et al. The CMV viral load was 500,000 copies/ml, consistent with a highly active CMV infection. CMV serology was then retrospectively performed on stored serum samples, and this evidenced seroconversion between hospital days 88 and 96. The results of hepatitis A, B, and C, of HIV 1 and 2, and of EBV serologies were negative. A fundus autofluorescence found no retinal localization and lung radiography was normal. The multiple blood transfusions required by the patient during hospitalization (in all, 53 red blood cell concentrates) were the only possible source of the infection that was identified.

Ganciclovir treatment was initiated. Despite antiviral medication, the patient rapidly deteriorated and died on hospital day 104.

SECOND CASE

A 52-yr-old woman was admitted after she sustained an 80% total body surface burn, including 37% third-degree, during a house fire. Several skin grafts were performed, including allografts (from 14 donors, including
five CMV-positive donors) and multiple blood transfusions (a total of 35 red blood cell concentrates). On hospital day 61, only 7% of the body surface remained uncovered.

From hospital day 5, several bacterial infections were identified, but none was associated with haemodynamic deterioration and they all responded well to antibiotics.

On hospital day 62, a persistent fever of more than 39 °C developed, and again no focus of infection could be located. This fever was preceded by digestive symptoms such as vomiting, mild blood-stained diarrhoea, and abdominal meteorism. Hepatic biology showed a moderate cholestasis. On hospital day 65, an abdomen ultrasound scan was performed and dilated intra- and extrahepatic biliary tracts were noted, a picture compatible with CMV infection and a “thick sigmoid tract”. An endoscopic retrograde cholangiopancreatography was quickly performed and extensive antibiotherapy was started. At the same time, quantitative Taq Man-based (ABI) CMV PCR showed more than 1,000,000 copies/ml in the patient’s serum. Serology confirmed CMV seroconversion. Other viral serologies (hepatitis A, B, C; HIV 1 and 2) were negative. A fundus autofluorescence found no retinal inflammation due to CMV and a fibrocolonoscopy found no CMV colitis in the left part of the colon.

Forty-eight hours after initiation of Ganciclovir medication, the fever decreased and the digestive symptoms improved. However, after a few days, the patient suddenly died from a massive pulmonary embolism.

**Discussion and conclusion**

The presence of CMV infection in burn patients is considered rare, but according to some trials, the rate would appear to be nearly 20%. This type of infection may be underestimated in burn patients as it is paucisymptomatic. Because of the severe outcome of CMV infection in these patients, it is important to bear in mind the need to consider this infection as part of a systematic approach to the management of burn patients with persistent fever, especially if associated with digestive or hepatic symptoms or a general status of deterioration.

Among published trials, only a few have studied the mode of CMV transmission in seronegative patients. The use of CMV-positive allograft represents a risk. Blood products also constitute a contamination mode, even if the frequency has considerably decreased with leukocyte filtration. Our two patients - both CMV-negative when they entered the ward - were both transfused but only one received a skin allograft. Even if a link cannot be firmly proved in the first case, there is a high probability of an infection due to blood transfusion. In the second case, the two contamination modes are possible. This addresses the issue of the use of blood products and CMV-seropositive skin grafts in CMV-negative burn patients.

There is at present no recommendation about the detection and follow-up of CMV-seronegative patients. There is also no consensus on preventing CMV seroconversion in such potentially immunodeficient patients. Considering the possibility of seroconversion due to blood transfusion or skin graft, and the potential morbidity of this infection, the management of seriously burned CMV-negative patient needs to be discussed. First, a CMV serology should be systematically performed in the most serious patients entering the burns ward. In initially seronegative patients, a serological follow-up should be performed regularly during hospitalization. If a septic syndrome occurs without any obvious bacterial aetiology, CMV viraemia should be carried out. The use of CMV-negative blood products should prevent seroconversion - their use should be privileged after advice from the local blood product authorities and according to availability. In the same way, allografts from CMV-negative donors should be specifically requested when their use is indicated. The systematic search for CMV in grafts is not in fact currently a reliable enough method, while it should be preferentially performed with the virology laboratory’s collaboration. Lastly, besides seroconversion in initially seronegative patients, there is also the possibility of reactivation of the virus in primarily CMV-seropositive patients. It would appear logical to ask for CMV viraemia by PCR in every seriously burned patient developing a septic status of unexplained origin.

In conclusion, considering the lack of precise data on CMV infection in burn patients, we suggest that CMV serology should be part of the initial investigation on admission, and that CMV PCR in blood should be performed in the presence of any unexplained serious septic syndrome. Guidelines in the screening and follow-up of CMV-negative patients and in the use of blood products and skin allografts should be established in such patients.

RÉSUMÉ. Deux cas sont présentés de primoinfection sévère par cytomegalovirus (CMV) chez des patients atteints de graves brûlures. Il est possible que cette infection ait joué un certain rôle dans leur décès, ce qui souligne l’importance de la recherche dans le secteur de l’étiologie virale, en particulier pour ce qui concerne le CMV, quand les patients immunodéficients, comme par exemple les patients brûlés, présentent une fièvre non expliquée. Les Auteurs proposent un monitorage et une stratégie de prévention du CMV chez les grands brûlés. Cette stratégie de prévention nécessite l’emploi d’allogreffes cutanées et de produits hématiques chez les patients séronégatifs. Il ne faut pas sous-estimer l’infection par CMV chez les patients atteints de brûlures sévères.
**BIBLIOGRAPHY**


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**AWARD OF THE G. WHITAKER INTERNATIONAL BURNS PRIZE, PALERMO, ITALY, FOR 2007**

At a meeting held on March 26, 2007, at the seat of the G. Whitaker Foundation, Palermo, after examining the scientific activity in the fields of research, teaching, clinical organization, prevention and cooperation presented by various candidates and in consideration of the high level of the candidates, the Adjudicating Committee unanimously decided to award the prize for 2007 to Professor NAOKI AIKAWA, General Director Emergency, Critical Care & Trauma/Burn Services, Keio University Hospital, Tokyo, Japan.

The prize is awarded with the following motivation:

“Professor Naoki Aikawa was born in Kanagawa, in Japan. Within a very few years of taking his medical degree in 1968, he began to develop an interest in the burn disease and from 1973 to 1976 he attended the Clinical and Metabolic Research Laboratories and the Harvard Medical School Clinical Surgical Service of Burn Trauma at Massachusetts Hospital, directed by Professor J.E. Burke, who defined him one of the best Research Fellows. He later completed his training at Keio University Hospital, Tokyo, holding the position of Resident and Chief Resident in General Surgery. From 1988 to 2003 he held the posts of Associate Director and Director, Emergency, Critical Care & Trauma/Burn Services, Keio University Hospital.

“Professor Aikawa’s university teaching career began in 1988, first as Associate Professor and subsequently, in 1992, as Professor, Department of Emergency & Critical Medicine, School of Medicine, Keio University, the position he holds today.

“His training stimulated his interest in study and research in various aspects of the burn disease: initially in the treatment of burn wounds, diagnosis, and the treatment of infection in extensively burned patients and later in the humoral immune response, which he called ‘a cytokine storm’, the shock and reanimation phase in extensively burned patients, and the prevention of renal damage, damage due to inhalation, and multi-organ failure, as a complication of sepsis.

“His findings, published in more than 400 papers in the leading scientific journals and presented at top-level international congresses, have become points of reference for our knowledge of the basic physiopathological variations that occur in the course of the burn disease. In view of his scientific activity he was elected to the Board of Direction of the International Burn Foundation and to the Editorial Board of the most prestigious national and international scientific journals.

“As Director of Emergency, Critical Care & Trauma/Burn Services, his outstanding clinical skills were expressed on the occasion, among others, of the dramatic Kobe earthquake, when together with his team he treated large numbers of burned and polytraumatized patients in difficult and dramatic circumstances.

“As Professor of the Department of Emergency & Critical Care Medicine, School of Medicine, Keio University, he has carried out teaching and training activities at the highest level for numerous young students and doctors; he has also been appointed to the position of member of the Ministry of Education Doctor’s Thesis Approval Committee and member of the Medical Profession Advisory Committee.


“The official prize-giving will take place in Palermo at the G. Whitaker Foundation on 4th October 2007 in the presence of authorities and representatives of the academic, scientific and cultural world.”