行政院國家科學委員會補助專題研究計畫成果報告

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※台灣地區 PARVOVIRUS B19 感染的研究-著重於其在※
※血液及腫瘤疾病上的意義　　　　　　　　　　　※

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計畫主持人：林亮音

共同主持人：林東燦、鄭安理

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一、中文摘要

研究指出免疫缺陷的病人會增加 parvivovirus B19 感染的機會。本研究主要針對全身性多次化療的病人來做 B19 感染的探討。一共有 59 男與 68 女，平均年齡 49 (18-79)的病人接受評估。她們平均接受 7.1 (4-32)次的全身化療。自接受化療到抽血檢查時間平均約 11 (4-88)個月。我們用 ELISA 方法測定血清中 B19 IgG 與 IGM 的有無、並以 nested PCR 來檢測 B19 DNA 的有無。另有 400 個健康捐血人的血液作為對照組。我們發現，癌症病人與正常對照組之 B19 感染率分別為 61.4%與 25.0%，有顯著差異 ($p<0.01$)。但是，沒有發現有 IgM(+)的病人。我們繼續以年齡分組來探討，發現小於 40 歲的癌症病人有相當高的 B19 感染比率 (19/39 vs 53/310, $p<0.001$)。由病歷記載顯示，感染過 B19 的病人曾有不明原因貧血的機率明顯較高(15% vs 63.2%, $p<0.005$)。這些結果顯示，年輕癌症病患有較高感染 B19 的機率。而前瞻性的研究 B19 感染與臨床症狀之相關性是有其必要性。

關鍵詞：parvovirus B19, anemia, chemotherapy

Abstract

An increased human parvovirus B19 infection rate has previously been observed in immunocompromised hosts. This study sought to determine the prevalence of parvovirus B19 infection in cancer patients receiving multiple courses of systemic chemotherapy. Fifty-nine men and 68 women, with a median age of 49 (18-79) years, were enrolled in this study. They had received an average of 7.1 (4-32) courses of systemic chemotherapy. The median duration from the date of starting chemotherapy to the date of blood sampling was 11 (4-88) months. Serum B19 IgG and IgM levels were examined by enzyme-linked immunosorbent assay and B19 DNA was examined by nested PCR. Another 400 healthy blood donors served as the control group. The overall prevalence of anti-B19 IgG in cancer patients and healthy blood donors was 61.4% and 25.0%, respectively ($P<0.01$). Anti-B19 IgM and B19 DNA were not detectable in these anti-B19 IgG seropositive individuals. Further age–stratified comparison revealed that only patients younger than 40 years had a significantly increased anti-B19 IgG seropositive rate, as compared to the controls (19/39 vs 53/310, $p< 0.001$). The increased incidence of B19 infection in these 39 young patients appeared to be clinically significant since unexplained anemia, a common sequela of B19 infection, was detected in 3 of 20 (15.0%) seronegative and in 12 of 19 (63.2%) seropositive patients ($p< 0.005$). The results of this study suggest that young cancer patients receiving multiple courses of systemic chemotherapy may have a significantly increased risk of B 19 infection. Prospective studies to define the time course and clinical consequence of B19 infection in this group of patients are needed.

Keywords: parvovirus B19, anemia, chemotherapy

二、緣由與目的

Human parvovirus B19, the only known human pathogenic parvovirus, is a small DNA virus with a single-stranded linear genome, which encodes one non-structural protein, NS-1 and two viral capsid proteins, VP1 (83KDa) and VP2 (58KDa) (21, 38).

The virus exhibits a remarkable tropism for erythroid progenitor cells【6】, and is frequently associated with anemia.

In immunologically normal hosts, B19 may cause a number of acute, generally self-limiting diseases, notably fifth disease or erythema infectiosum in children, acute polyarthritis in adults, and aplastic crisis in patients with chronic hemolytic anemia such as sickle cell anemia or hereditary spherocytosis【3, 4】. In pregnant women, B19 infection may result in lysis of nucleated fetal red cells, hydrops fetalis, and subsequent spontaneous abortion and fetal death【2, 7】. B19 was also found to be associated with glomerulonephritis【14】, vasculitis【9】, peripheral neuropathies【5】, myocarditis【13】, and fulminant hepatic failure【12】. In immunocompromised hosts, B19 infection may persist and lead to chronic anemia, red cell aplasia, and, less frequently, thrombocytopenia, neutropenia, and pancytopenia【1】. This study sought to clarify whether B19 infection poses a significant problem in cancer patients receiving multiple courses of chemotherapy. The results indicate that young cancer patients receiving multiple courses of chemotherapy are at an increased risk of B19 infection.

三、結果與討論、

From March 1999 through April 2000, a total of 127 cancer patients were enrolled in this study. There were 59 men and 68 women, with a median age of 49 (18-79) years. They received an average of 7.1 (4-32) courses of systemic chemotherapy. Forty-six patients received only one regimen; 58 patients received two regimens; and 23 patients received three or more regimens of chemotherapy. The median duration from the date of starting chemotherapy to the date of blood sampling was 11 (4-88) months. There were 39 patients with gastrointestinal cancer, 25 with breast cancer, 24 with lung cancer, 10 with head and neck cancer, and 29 with other cancers.

Of the 127 cancer patients examined, parvovirus B19 IgG antibodies were detected in the plasma of 78 patients. In contrast, 100 of 400 healthy blood donors had IgG antibodies to parvovirus B19. The overall B19 seropositive rates in cancer patients and healthy blood donors were 61.4% and 25.0%, respectively ($p < 0.01$). However, B19 IgM and B19 DNA were not detectable in any of these patients. Further age-stratified comparison revealed that the prevalence of B19 IgG infection was significantly increased only in cancer patients younger than 40 years of age. Increased risk of B19 infection was not related to sex, cancer type, or duration, regimen and course of chemotherapy, or to history and frequency of blood transfusion.

Examination of the relationship between B19 infection and pertinent clinicopathologic variables in young cancer patients revealed a significantly higher incidence of unexplained anemia in seropositive patients (Table 3). Unexplained anemia was detected in 3 of 20 seronegative and 12 of 19 seropositive patients ($p < 0.005$). Eight patients presented with unexplained anemia 3 to 4 months following chemotherapy. One patient developed anemia two months after the completion of chemotherapy. Another three patients were found to have unexplained anemia more than 5 months after the completion of chemotherapy. The mean drop of hemoglobin in these twelve patients was 3.71 ± 1.17 mg/dl. The mean duration between the date of diagnosis of unexplained anemia and the date of blood sampling for this study was 6.50 ± 2.65 months. We could not identify other B19 infection-related constitutional symptoms and signs in these seropositive patients.

This study has demonstrated that young patients receiving multiple courses of chemotherapy are at increased risk of parvovirus B19 infection. B19 infection in these patients may cause important sequela, as exemplified in this series by the significantly higher incidence of unexplained anemia, which is a common complication of B19 infection. To date, parvovirus B19 has been recognized as an important cause of

severe anemia in immunocompromised patients, including transplants recipients【1】, patients with congenital and acquired immunodeficiency【8, 11】, and leukemic patients receiving maintenance or consolidation chemotherapy【10】. This is the first report describing an increased incidence of B19 infection in young cancer patients receiving multiple courses of chemotherapy. Since B19 infection usually presents with non-specific symptoms and signs, and is easily overlooked, a high degree of suspicion and careful search for clinical evidence of infection are needed.

In conclusion, the incidence of human parvovirus B19 infection is increased in young cancer patients receiving multiple courses of systemic chemotherapy. The infection may be associated with significant anemia. A high degree of clinical suspicion is the only way to make early diagnosis of this easily overlooked infection. Prospective study is needed to delineate the course of serological and clinical response of the patients.

四、計畫成果自評

如當初研究計畫所期待的，結果顯示年輕癌症病患有較高感染 B19 的機率。而前瞻性的研究 B19 感染與臨床症狀之相關性是有其必要性。

五、參考文獻

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