

Symptoms associated with parvovirus B19 infection in adults:  
A Pilot Study

Key Words: Parvovirus B19, Adults, Primary Care, Erythema Infectiosum, Symptom,  
Prospective Study.

### Abstract

#### Background and Objectives

The clinical features of parvovirus B19 infection in primary care adult patients have not been well described. The aim of this study was to clarify the clinical features of adult patients with parvovirus B19 so that more accurate diagnosis can be made in primary care clinic.

#### Methods

Of adult outpatients over 18 years of age who visited one primary care clinic over a period of one year, subjects were those who could have had contact history with children with erythema infectiosum and had at least two of the following three symptoms: edema, joint pain, and rash. The clinical features of subjects who satisfied the inclusion criteria were investigated prospectively.

#### Results

Twenty patients met the inclusion criteria, and 14 patients were diagnosed with parvovirus B19 infection. There were two groups of patients: in one group, primary and secondary symptoms appeared near each other, and in the other group, primary and secondary symptoms were clearly separated.

#### Conclusions

Parvovirus B19 infection in adults can be efficiently diagnosed in primary care settings by observing such clinical symptoms as, edema, joint pain, and rash, and by questioning patients about their contact with children with erythema infectiosum.

コメント [K11]: primary と secondary の意味が不明

## Introduction

Parvovirus B19 infection is generally known as childhood erythema infectiosum, which causes facial rash. With regard to parvovirus B19 infection in adults, one study retrospectively reviewed the charts of consecutive patients and reported the incidence of major symptoms such as edema, joint pain, and rash.<sup>1)</sup> While symptom severity greatly varies from asymptomatic to severe<sup>2)</sup>, unlike parvovirus B19 infection in children, edema and joint pain are considered characteristic findings for parvovirus B19 infection in adults, but the severity of rash is believed to be mild<sup>3)4)</sup>. However, the clinical features of parvovirus B19 infection in adult outpatients treated in primary care has not been fully explained<sup>3)</sup>. Children with parvovirus B19 infection are thought to be mostly treated by pediatricians. Accordingly, primary care physicians who mainly treat adult patients are not necessarily aware of the clinical features of parvovirus B19 infection. Thus, adult patients with parvovirus B19 infection may not be accurately diagnosed.

The present study was designed to identify the symptoms associated with adults with parvovirus B19 infection treated in outpatient clinics and to clarify the clinical features so that a more accurate diagnosis can be made. ~~In addition, the study was conducted to identify the incidence of parvovirus B19 infection, the clinical features of parvovirus B19 infection and the diagnosis made at the onset of parvovirus B19 infection by one family practice physician in a private clinic in suburban Tokyo.~~

## Methods

Subjects were adult outpatients older than 18 years of age who visited the solo family practice clinic from December 1, 2005 to November 30, 2006 and met the following 2 inclusion criteria.

First criteria; patients who had either one of the following clinical categories as a risk of contact with parvovirus B19:

Category A; patients, who had children living at home, diagnosed with erythema infectiosum within the past month.

Category B; patients who worked at schools (nursery, preschool, grammar school, etc.) where an outbreak of erythema infectiosum had occurred within the past month.

Category C; patients who had children living at home who attended schools (nursery, preschool, grammar school, etc.) where an outbreak of erythema infectiosum had occurred within the past month.

コメント [K12]: 現時点でもそうか、確認ください。

コメント [K13]: 引用番号の位置が不統一です。投稿予定雑誌のスタイルに統一してください。

コメント [K14]: 全ての PC 医が HPV を知らないのではなく (私や和座先生は知っているように)、成人しか診療しない PC 医は、となると思います。

コメント [K15]: 言いたいことの論理的ステップはこうじゃないですか？

コメント [K16]: この文章は余計で不要です (むしろやぶ蛇)。まず、真の発症率はわかりません。次は前の文章と同じです。最後は、大多数の患者で発症時の診断がわかっているわけでもなく、誇張になります。

コメント [K17]: こうではないですか？

Second criteria; patients with at least two of the following three symptoms: edema, joint pain, and rash, which are clinical signs of parvovirus B19 infection.

コメント [KI18]: 文献引用

Patients who satisfied one of the three conditions for the first criterion and the second criterion served as subjects. After obtaining informed consent, the following investigations were carried out at initial consultation. First, presence or absence of primary (muscle pain, general malaise, fever, and other symptoms), secondary symptoms (skin rash, edema, joint symptoms, and other symptoms) and familial infection of parvovirus B19 was ascertained and recorded. Familial infection was defined as positive when a child who lived with had erythema infectiosum within the past month. Second, a blood test was performed to measure the followings; antibody titers of immunoglobulin G (IgG), immunoglobulin M (IgM), white blood cell count (WBC), hemoglobin (Hb), platelet (Plt) count, and liver enzymes (aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH)). The serological test of IgM and IgG were defined as positive when the titers were more than a reference range. Informed consent was obtained from all patients who met the above-mentioned inclusion criteria by explaining the study objectives and informing them of the possibility of adulthood erythema infectiosum.

コメント [KI19]: primaryにも secondaryにも other symptomsがあります。混乱しません、明確に区別してください。そして primaryと secondaryの区別の論理的根拠は？

コメント [KI10]: 最初はスペルアウト、基本です。

コメント [KI11]: (これで正確ですか?) もしそうであるなら、基準値を記入してください。

コメント [KI12]: この段落は完全に変えました。キーワードは簡潔さと論理の明確さです。番号やアルファベット記号は、明らかに必要でなければつけないほうがいいです。

## Results

Of patients who visited the clinic over a one-year period from December 1, 2005 to November 30, 2006, a total of 20 patients satisfied the inclusion criteria. The breakdown number of the first inclusion criterion was as follows: 12 patients in category A, 1 in category B, and 1 in category C. Of the 20 patients, 13 (65%) patients were diagnosed as parvovirus B19 infection based on positive parvovirus B19 IgG and IgM tests.

コメント [KI13]: breakdown は一般的ではありません。

Among these, 12 had both positive IgG and IgM test. The rest one had negative IgG but positive IgM test, and was also diagnosed as parvovirus B19 infection.

コメント [KI14]: この表現はMethodsと同じで redundant です。これがベストとは言えませんが、一考ください。それから、これが一番の結果とは言えないのもっと前に移すべきです (そうしました)。

The other six patients had negative IgG and negative IgM tests, who were denied for parvovirus B19 infection. Of these six patients, four had viral infection (details are unspecified), one had drug-induced rash, and one had hemolytic streptococcal infection and the others remained as unknown diseases after the first examination (Table 1).??

コメント [KI15]: With はおかしい

コメント [KI16]: 記載を明確に、時間的關係を再確認してください。

Table 1 shows clinical characteristics of the 14 adult patients diagnosed as parvovirus B19 infection, who were two men and twelve women in ages ranging from 33 to 63 years with a median age of 38 years. These 14 patients could be divided into two groups based on the development of the primary and secondary symptoms. In seven patients, primary and secondary symptoms appeared very closely (secondary symptoms appeared

コメント [KI17]: これは嘘です。Table 1のどこにもそんな記載はありません。20名のうち HPV B16 感染と診断されなかった 6名じゃないですか？

within two days of primary symptoms), and in the other seven patients, secondary symptoms occurred at least seven days after primary symptoms. Furthermore, in two of the seven patients in the latter group, secondary symptoms appeared twice with an interval of about two weeks. The median value of disease duration between the onset and cure was 21 days. Other symptoms included numbness, skin pain and itching. In addition, 5 (35.7%) patients visited other medical institutions prior to the present study clinic and were diagnosed with various illnesses, including collagen disease, rheumatoid arthritis, shingles, viral disease, and muscle pain. The abnormal results of laboratory tests were observed as follows: leukopenia (WBC count less than \*\*\* / ) in four patients (28.6%), thrombocytopenia (Plt count less than \*\*\*) in two patients (14.3%), elevated AST (>= \*\* IU/L) and/or ALT (>= \*\* IU/L) in five patients (35.7%); and elevated LDH (>= \*\* IU/L) in four patients (28.6%).

### Discussion

In adult parvovirus B19 infection, primary symptoms such as malaise, muscle pain and fever, appear 4 to 14 days after infection, and secondary symptoms such as edema, rash and joint pain, occur several days later<sup>5)</sup>. About half of mothers do not have the IgG antibody for parvovirus B19. In addition, among adults with parvovirus B19 infection, primary symptoms appear in about 50% and secondary symptoms appear in about 25%<sup>6,7)</sup>.

Because the subjects of the present study had secondary symptoms, the results may be biased towards parvovirus B19 infection resulting in secondary symptoms. While it has been generally accepted that parvovirus B19 infection affects young people<sup>8)</sup>, one 63-year-old patient (case 1) was diagnosed in the present study, thus suggesting that parvovirus B19 infection can occur in older individuals. In 12 of 14 patients, erythema infectiosum occurred between March and August, during epidemics. Furthermore, among patients with secondary symptoms, the median disease duration tended to be long at 21 days.

When compared to parvovirus B19 infection in children, primary care physicians, including clinicians, are not fully aware of parvovirus B19 infection in adults, and only case reports have been available for such patients. Therefore, patients with secondary symptoms may be not treated properly at medical institutions. The present study confirmed that In fact, more than one thirds of the study patients were diagnosed as other diseases than parvovirus B19 infection at other institutions, before being correctly diagnosed as parvovirus B19 infection in the study clinic.

コメント [K118]: これで正しいですか？あるいは初診と終診という意味ですか？

コメント [K119]: 病期は重要なので分布を示すべきです。

コメント [K120]: この other symptom は primary ですか secondary ですか？

コメント [K121]: こども間違いです。例えば、4人の白血球減少症の患者の (median, 4200; range, 2400 to 6600) ではないでしょうか。さして重要な情報とも思えないので、異常値の患者の情報だけでいいんじゃないでしょうか。

コメント [K122]: (数値を入れる、以下同じ)

コメント [K123]: Discussion の冒頭では、まずこの研究の Main finding を述べてください。段落であれセクションであれ、最初の文章を読めば大意がわかるようにする必要があります。

コメント [K124]: ここはどういう意義付けがあるんですか？

コメント [K125]: ここは混乱するので削除しては？あるいは general internist? いずれにせよ英文誌に投稿するので、明確な区別があるべきです。

コメント [K126]: 先行文献引用

コメント [K127]: これは言い過ぎ、わずかな名前の情報です。

In the present study, over a period of one year, 14 adult patients were diagnosed with parvovirus B19 infection at a single clinic, thus suggesting that parvovirus B19 infection in adults is not necessarily few in primary care setting. When presented with joint pain, edema and/or rash, it may be useful to consider parvovirus B19 infection, particularly in adults with children living together who had erythema infectiosum ~~within the past month~~, adults working at nurseries, preschools and grammar schools, or adults with children living together who attended a school with an outbreak of erythema infectiosum ~~within the past month~~.

There are a number of limitations to this study.

1. This is a single-center study, and nothing more than a pilot study.
2. In this study, serodiagnosis was conducted following clinical diagnosis. Therefore, asymptomatic or mild cases of infection may have been overlooked.

However, despite the above limitations, this study can be considered important due to the following:

1. It is a compilation of cases at a primary care clinic
2. It is a prospective study
3. It ensured accurate diagnosis through the use of serodiagnosis
4. Various clinical features were compiled from the symptoms observed in a large number of cases

In the present study, subjects were divided into two groups: in one group, primary and secondary symptoms appeared at almost the same time, and in the other group, primary and secondary symptoms appeared at two distinct periods. Secondary symptoms appeared twice in some patients. While experimental studies have shown that primary and secondary symptoms appear in a biphasic manner<sup>5)</sup>, various patterns may exist in clinical settings. When diagnosing parvovirus B19 infection based on symptoms such as joint pain, edema, and rash, and contact history with erythema infectiosum patients, clarification of sensitivity, specificity, and likelihood should lead to more accurate diagnosis. To further clarify the clinical features of parvovirus B19 infection in adults, further study at multiple primary care institutions is needed.

In conclusion, parvovirus B19 infection in adults can be efficiently diagnosed based on clinical symptoms such as edema, joint pain, and rash, and contact history with children with erythema infectiosum in primary care settings. In addition, parvovirus B19 infection is a common disease in adults, and may be long, up to several weeks. Therefore, it is important for primary care physicians to properly diagnose this disease with clinical history and symptoms in order to avoid unnecessary tests and visits. This study will help to increase physician knowledge about parvovirus and may improve

コメント [K128]: 表現を弱める。今研究だけで確証にはならない。

physicians' ability to accurately diagnosis it in adult patients.

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