

6-1-2002

Severe combined immunodeficiency: a casereport and review of literatures

P. Chatchatee

P. Vanichsetakul

U. Tantibhaedhyangkul

S. Sirivichayakul

P. Kupatawintu

See next page for additional authors

Follow this and additional works at: <https://digital.car.chula.ac.th/clmjjournal>



Part of the [Medicine and Health Sciences Commons](#)

Recommended Citation

Chatchatee, P.; Vanichsetakul, P.; Tantibhaedhyangkul, U.; Sirivichayakul, S.; Kupatawintu, P.; and Ngamphaiboon, J. (2002) "Severe combined immunodeficiency: a casereport and review of literatures," *Chulalongkorn Medical Journal*: Vol. 46: Iss. 6, Article 6.

Available at: <https://digital.car.chula.ac.th/clmjjournal/vol46/iss6/6>

This Case Report is brought to you for free and open access by the Chulalongkorn Journal Online (CUJO) at Chula Digital Collections. It has been accepted for inclusion in Chulalongkorn Medical Journal by an authorized editor of Chula Digital Collections. For more information, please contact ChulaDC@car.chula.ac.th.

Severe combined immunodeficiency: a casereport and review of literatures

Authors

P. Chatchatee, P. Vanichsetakul, U. Tantibhaedhyangkul, S. Sirivichayakul, P. Kupatawintu, and J. Ngamphaiboon

Severe combined immunodeficiency: a case report and review of literatures

Pantipa Chatchatee* Preeda Vanichsetakul*
Usa Tantibhaedhyangkul* Sunee Sirivichayakul***
Pawinee Kupatawintu** Jarungjit Ngamphaiboon*

Chatchatee P, Vanichsetakul P, Tantibhaedhyangkul U, Sirivichayakul S, Kupatawintu P, Ngamphaiboon J. Severe combined immunodeficiency: a case report and review of literatures. Chula Med J 2002 Jun; 46(6): 495 - 500

Severe combined immunodeficiency (SCID) is a rare and fatal primary immunodeficiency syndrome with profoundly impaired cellular and humoral immune function. Without early diagnosis and immunoreconstitution, affected patients suffer from severe infections and generally die in infancy.

We report the clinical presentations, immunologic abnormalities and course of disease of a case of SCID. Since similar presentations may be found in pediatric HIV infection, physicians need high index of suspicion to detect SCID patients. Early recognition of SCID is a pediatric emergency since prompt diagnosis is critical to the treatment outcome which leads to a cure for this otherwise fatal disease.

Key words: *Severe combined immunodeficiency, SCID, Primary immunodeficiency, Manifestation.*

Reprint request : Chatchatee P, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University , Bangkok 10330, Thailand.

Received for publication. March 15, 2002.

* Department of Pediatrics, Faculty of Medicine, Chulalongkorn University

** National Blood Center, The Thai Red Cross

***Department of Medicine, Faculty of Medicine, Chulalongkorn University

พรรณทิพา ฉัตรชาติรี, ปรีดา วาณิชยศเรษฐกุล, อุษา ตันติแพทยางกูร, ภาวินี คุปตวิณฑุ, สุนี ศิริวิชัยกุล, จรุงจิตร งามไพบูลย์. Severe combined immunodeficiency: รายงานผู้ป่วย 1 รายและทบทวนวรรณกรรมที่เกี่ยวข้อง. จุฬาลงกรณ์เวชสาร 2545 มิ.ย; 46(6): 495 - 500

Severe combined immunodeficiency (SCID) เป็นโรคภูมิคุ้มกันบกพร่องแต่กำเนิดที่รุนแรงถึงชีวิต ผู้ป่วยโรคนี้มีความบกพร่องอย่างมากของภูมิคุ้มกันทั้ง cellular และ humoral immune response ผู้ป่วยจะมีการติดเชื้อต่าง ๆ ได้ง่าย ถ้าไม่ได้รับการวินิจฉัยและการรักษาที่ถูกต้อง ผู้ป่วยเกือบทุกรายจะเสียชีวิตในวัยทารก

รายงานนี้นำเสนอผู้ป่วย SCID 1 ราย ในด้านของอาการแสดงทางคลินิก ผลการตรวจทางภูมิคุ้มกันวิทยา การดำเนินโรค พร้อมทั้งทบทวนวรรณกรรมที่เกี่ยวข้อง เนื่องจากอาการแสดงของผู้ป่วยโรคนี้คล้ายคลึงกับผู้ป่วยเด็กที่ติดเชื้อ HIV แพทย์ผู้ให้การดูแลรักษาจึงต้องนึกถึง SCID ไว้ในการวินิจฉัยแยกโรคด้วย การให้การวินิจฉัยที่ถูกต้องและทัน่วงที่ จำเป็นอย่างยิ่งเพราะทำให้การรักษาให้ผลดีช่วยให้ผู้ป่วยโรคร้ายแรงนี้สามารถมีชีวิตรอดได้

Severe combined immunodeficiency (SCID) is a rare primary immunodeficiency with profound cellular and humoral immune defects. In this article, we report a case of 10 - month old male infant with recurrent pneumonia and mucocutaneous candidiasis. He was found to have severe combined immunodeficiency (SCID) with a phenotype that was compatible with the X-linked form of this disorder. Clinical presentations and current concepts on immunoreconstitution are reviewed.

Case report

A 10-month-old boy was referred to King Chulalongkorn Memorial Hospital for further evaluation of recurrent infections. He was born by normal delivery with the birth weight of 3400 grams. He received BCG immunization at birth and 2 doses of DTP and OPV at 2 and 4 months old respectively. His family history revealed that his maternal uncle died in early infancy due to infection.

At the age of 7 months, the patient developed oral candidiasis and since the age of 8 months, he had had recurrent pneumonia that required multiple

hospitalizations. No causative organism could be identified. In the last admission prior to the referral, the pneumonia was treated with intravenous cefotaxime with slight improvement. He also developed mucocutaneous candidiasis that was treated with ketoconazole. Two weeks before the referral, the patient had mucous bloody diarrhea and high fever that persisted until the day he was referred to King Chulalongkorn Memorial Hospital.

On admission, the body temperature was 39.8 degree Celcius, heart rate 140/min, respiratory rate 60/min, blood pressure 85/50 mmHg. Physical examination revealed a cachectic child with mildly pale conjunctiva, no icteric sclera. There was no visible tonsillar tissue. Oral thrush was present. There was redness and induration on left shoulder at the site of BCG immunization (Figure 1) and palpable lymph nodes of 0.5-1 centimeter in diameter at left axillary region (Figure 2). Chest auscultation revealed occasional rhonchi at right upper lung field. Liver was palpable 2 centimeters below right costal margin with firm consistency. Spleen was not palpable.



Figure 1. Suppuration of BCG inoculation site on left shoulder.



Figure 2. Enlarged lymph nodes at left axillary region.

Laboratory investigations yielded the following results: Hemoglobin 8.9 g%, hematocrit 28%, MCV 77 fl, MCH 24 pg, MCHC 31.7 g/dl, WBC 15,950/cu.mm. L 17%, Mo 6%, PMN 77% Platelet 388,000/cu.mm. Absolute lymphocyte count was 2,711/cu.mm. Total bilirubin 0.47mg/dl, direct bilirubin 0.14 mg/dl, alkaline phosphatase 80 u/l, SGOT 98 u/l, SGPT 32u/l, albumin 3.3 g/dl, globulin 1.9 g/dl. Anti HIV antibody was negative and chest X-ray showed atelectasis of right upper lung with air bronchogram.

Immunologic evaluations revealed low levels of IgG and IgA, and low normal IgM with IgG 8.9 mg/dl, IgA 5.6 mg/dl, IgM 29.8 mg/dl (normal values for this age are 310-800 mg/dl for IgG, 16-100 mg/dl for IgA, and 26-108 mg/dl for IgM). Lymphocyte phenotyping was performed and demonstrated very low T-cell with increase B-cell (CD3 =2%, CD4 =1%, CD8 =1%, CD16 =1%, CD19 =87%). T-cell response to mitogen using phytohemagglutinin (PHA) stimulation revealed very low response of the patient's T-cells (249 CPM compared to normal control 68,833 CPM) with stimulation index (SI) of 2.00 (control 11.21)

The patient was treated with intravenous cloxacillin and ceftazidime, intravenous immunoglobulin, isoniazid, rifampicin and ethambutol together with trimethoprim-sulfamethoxazole. On day 10th of the admission, right tension pneumothorax developed. He was transferred to intensive care unit and placed on high frequency ventilation. His condition deteriorated. He expired after 3 weeks of hospitalization. No organisms could be identified from lung and liver necropsy.

Discussion

SCID is a rare, fatal syndrome of a profoundly

impaired cellular and humoral immune function.⁽¹⁻³⁾

Without immunoreconstitution, affected patients suffer severe and persistent infections, and generally die in infancy. Diagnosis of SCID is suggested when an affected infant has lymphopenia and severe hypogammaglobulinemia (IgG, <150 mg/dL).⁽⁴⁾ Most SCID patients have peripheral CD3⁺ T-cell counts of 500 cells/mm³ or less (normal range, 3000-6500 cells/mm³) and variable numbers of B and natural killer (NK) lymphocytes, depending on the underlying genetic defect. SCID can be classified according to the presence or absence of B and NK cells into T⁻ B⁺ NK⁺, T⁻ B⁺ NK⁻, T⁻ B⁻ NK⁺, T⁻ B⁻ NK⁻, and atypical T⁺ B⁺ syndromes. Although both X-linked recessive and autosomal forms of SCID are recognized, the X-linked form is the most frequent. Patients with X-linked SCID generally have very low numbers of T cells and NK cells, whereas B cells are often found in relatively high numbers even though specific antibody responses are deficient (T⁻, NK⁻, B⁺ phenotype).⁽⁴⁾ X-linked SCID is caused by mutations of interleukin receptor gamma gene (IL2RG),^(5,6) the gene encoding the common gamma (γ) chain, known as γ c, found in the interleukin-2 (IL-2) receptor and multiple other cytokine receptors, including those for IL-4, IL-7, IL-9, and IL-15. The intracellular portion of γ c is known to interact with Janus kinase 3 (Jak3), a signaling kinase that cooperates with other Jak and STAT proteins in a complex signal transduction pathway.^(7,8)

Our patient presented with recurrent pneumonia and mucocutaneous candidiasis. Even though he did not have profound lymphopenia, he had a low lymphocyte count for his age. (ALC 2711, median value for age is 5990, range 3610-8840).⁽⁹⁾ His low IgG level indicated B-cell defect while a low

lymphocyte proliferative response to PHA indicated T-cell defect. The lymphocyte phenotype in this patient was compatible with X-linked SCID ($T^- NK^- B^+$). This is supported by the family history of the maternal uncle who died of infection in early infancy. Molecular analysis for gene mutation in this family are underway. In a report by Buckley et al, reviewing 108 SCID cases, it was found that the mean age at diagnosis of SCID was 201 days, or 6.59 months. The common presentations were oral candidiasis, respiratory syncytial virus, parainfluenza 3 or *Pneumocystis carinii* pneumonia, adenovirus infection, gram-negative sepsis, persistent diarrhea, and failure to thrive.⁽⁴⁾ In our patient, the causative organisms of recurrent pneumonia and diarrhea could not be identified.

Stem-cell transplantation is considered a life-saving treatment for patients with SCID. It is highly effective in reconstituting T-cell immunity in SCID patients.⁽¹⁰⁾ The most optimal treatment is bone marrow transplantation or peripheral stem-cell transplantation from a histocompatible sibling. In cases where the patients do not have an HLA-identical family donor, T-cell-depleted haploidentical bone marrow transplantation from a parent can be performed and is successful in many patients with SCID.⁽¹¹⁻¹³⁾ If stem cells can be transplanted in the first 3.5 months of life, before infections develop, there is a high (95 percent) probability of success.⁽¹⁰⁾

Early recognition of SCID should be considered a pediatric emergency. Making a diagnosis before the onset of opportunistic infections is critical to successful outcome. If SCID is not detected until the infant is older, death can occur from infection before successful cellular therapy can be achieved. The absolute lymphocyte count is the most

useful initial test, because lymphopenia is present in almost all patients with SCID from the time of birth.⁽¹⁴⁾ Knowledge of the fact that normal ranges for lymphocyte counts are much higher in infancy than in older children is essential to the recognition of this syndrome; for example, the lower limit of normal for an absolute lymphocyte count at 4-8 months of age is $3,600/mm^3$ and the median is $6,000/mm^3$; in contrast the lower limit value is $1,600/mm^3$ in adults.⁽⁹⁾

In our current situation where secondary immunodeficiency especially HIV infection is a much more common cause of immunodeficiency in infants, physicians need to have a high index of suspicion in order to detect patients with primary immunodeficiency. Recurrent severe bacterial infections, prolonged suppuration of BCG vaccination site, persistent oral candidiasis (despite proper oral care) are the presentations that should prompt physicians to work up for immune defect. Low absolute lymphocyte count and low globulin levels especially with a relatively normal albumin level are strongly suggestive of T- and B-cell defects respectively.

Conclusion

We reported a case of infant with SCID who presented with recurrent pneumonia, mucocutaneous candidiasis and prolonged suppuration of BCG inoculation site. Early recognition of the disease will allow us to offer a cure to this otherwise fatal disease.

References

1. Bortin MM, Rimm AA. Severe combined immunodeficiency disease. Characterization of the disease and results of transplantation. *JAMA* 1977 Aug 15; 238(7): 591 - 600

2. Buckley RH, Schiff SE, Schiff RI, Roberts JL, Markert ML, Peters W, Williams LW, Ward FE. Haploidentical bone marrow stem cell transplantation in human severe combined immunodeficiency. *Semin Hematol* 1993 Oct; 30(4 Suppl 4): 92- 101
3. Primary immunodeficiency diseases. Report of a WHO Scientific Group. *Clin Exp Immunol* 1995 Jan; 99 Suppl 1: 1 - 24
4. Buckley RH, Schiff RI, Schiff SE, Markert ML, Williams LW, Harville TO, Roberts JL, Puck JM et al. Human severe combined immunodeficiency: genetic, phenotypic, and functional diversity in one hundred eight infants. *J Pediatr* 1997 Mar; 130(3): 378 - 87
5. Puck JM, Deschenes SM, Porter JC, Dutra AS, Brown CJ, Willard HF, et al. The interleukin-2 receptor gamma chain maps to Xq13.1 and is mutated in X-linked severe combined immunodeficiency, SCIDX1. *Hum Mol Genet* 1993 Aug; 2(8): 1099 - 104
6. Noguchi M, Yi H, Rosenblatt HM, Filipovich AH, Adelstein S, Modi WS, et al. Interleukin-2 receptor gamma chain mutation results in X-linked severe combined immunodeficiency in humans. *Cell* 1993 Apr 9; 73 (1): 147 - 57
7. Miyazaki T, Kawahara A, Fujii H, Nakagawa Y, Minami Y, Liu ZJ, Oishi I, Silvennoinen O, Witthuhn BA, Ihle JN. Functional activation of Jak1 and Jak3 by selective association with IL-2 receptor subunits. *Science* 1994 Nov 11; 266(5187): 1045 - 7
8. Russell SM, Johnston JA, Noguchi M, Kawamura M, Bacon CM, Friedmann M, McVicar DW, Witthuhn BA, Silvennoinen O. Interaction of IL-2R beta and gamma chains with Jak1 and Jak3: implications for XSCID and XCID. *Science* 1994 Nov 11; 266(5187): 1042 - 5
9. Conley ME, Stiehm ER. Immunodeficiency disorders: general considerations. In: Stiehm ER, ed. *Immunologic Disorders in Infants & Children*. 4th ed. Philadelphia: W.B. Saunders, 1996 :217
10. Buckley RH, Schiff SE, Schiff RI, Markert L, Williams LW, Roberts JL, et al. Hematopoietic stem-cell transplantation for the treatment of severe combined immunodeficiency. *N Engl J Med* 1999 Feb 18; 340(7): 508 - 16
11. Dror Y, Gallagher R, Wara DW, Colombe BW, Merino A, Benkerrou M, Cowan MJ. Immune reconstitution in severe combined immunodeficiency disease after lectin-treated, T-cell-depleted haplocompatible bone marrow transplantation. *Blood* 1993 Apr 15; 81(8): 2021 - 30
12. Fischer A, Landais P, Friedrich W, Morgan G, Gerritsen B, Fasth A, Porta F, Griscelli G, Goldman SF, Levinsky R. European experience of bone-marrow transplantation for severe combined immunodeficiency. *Lancet* 1990; 336 (8719): 850 - 4
13. Stephan JL, Vlekova V, Le Deist F, Blanche S, Donadieu J, De Saint-Basile G, Durandy A, Griscelli G, Goldman SF, Levinsky R. Severe combined immunodeficiency: a retrospective single-center study of clinical presentation and outcome in 117 patients. *J Pediatr* 1993 Oct; 123(4): 564 - 72
14. Gossage DL, Buckley RH. Prevalence of lymphocytopenia in severe combined immunodeficiency. *N Engl J Med* 1990 Nov 15; 323 (20): 1422 - 3