# Adult onset immunodeficiency syndrome: A case report

**Sutsarun Prunglumpoo MD,**
**Poonawis Sudtikoonaseth MD,**
**Pinnaree Kattipathanapong MD.**

**ABSTRACT:**

**PRUNGLUMPOO S, SUDTIKOONASETH P, KATTIPATHANAPONG P. ADULT ONSET IMMUNODEFICIENCY SYNDROME: A CASE REPORT. THAI J DERMATOL 2018; 34: 279-285.**

*INSTITUTE OF DERMATOLOGY, MINISTRY OF PUBLIC HEALTH, BANGKOK, THAILAND.*

Adult onset immunodeficiency syndrome was first recognized in 2004 as a syndrome associated with high-titer neutralizing antibodies to interferon-gamma. According to clinical manifestation, this syndrome can be divided into 2 categories; disseminated infections and reactive dermatosis. We report two cases; presented with recurrent or disseminated infections together with reactive dermatosis. Both patients were diagnosed with adult onset immunodeficiency syndrome which was confirmed by blood test for anti-interferon-gamma autoantibody.

**Key words:** Adult onset immunodeficiency syndrome, antibodies to interferon-gamma

From: Institute of Dermatology, Ministry of Public Health, Bangkok, Thailand.

Corresponding author: Sutsarun Prunglumpoo, M.D. E-mail: siriraj155@hotmail.com

Received: 3 September 2018 Revised: 24 September 2018 Accepted: 6 November 2018

**บทคัดย่อ :**

**สุตศรัญย์ พรึงลำภู, ปุณวิศ สุทธิกุลณเศรษฐ์, ปิ่นนรี ขัตติพัฒนาพงษ์ รายงานผู้ป่วยโรค ADULT ONSET IMMUNODEFICIENCY SYNDROME วารสารโรคผิวหนัง 2561; 34: 279-285.**

*สถาบันโรคผิวหนัง กรมการแพทย์ กระทรวงสาธารณสุข*

Adult onset immunodeficiency syndrome เป็นโรคที่สัมพันธ์กับแอนติบอดี้ปริมาณมากต่อ interferon gamma ซึ่งถูกรายงานครั้งแรกในช่วงปี ค.ศ. 2004 สามารถแบ่งโรคตามลักษณะทางคลินิกออกเป็น 2 ชนิดคือ ชนิดแรก ผู้ป่วยจะมีการติดเชื้อซ้ำซ้อน ซึ่งอาจเป็นการติดเชื้อฉวยโอกาส และชนิดที่ 2 เกิดผื่นอักเสบจากปฏิกิริยากระตุ้น ในรายงานนี้ได้นำเสนอผู้ป่วย 2 ราย ซึ่งมาด้วยอาการติดเชื้อซ้ำซ้อน ร่วมกับผื่นที่เกิดจากปฏิกิริยากระตุ้น ลักษณะเป็นตุ่มหนองกระจายทั่วตัว ผู้ป่วยทั้ง 2 รายได้รับการวินิจฉัยว่าเป็นโรค adult onset immunodeficiency syndrome และได้รับการตรวจยืนยันโดยการตรวจพบแอนติบอดี้ต่อ interferon gamma

**คำสำคัญ:** กลุ่มอาการโรคภูมิคุ้มกันบกพร่องในวัยผู้ใหญ่, แอนติบอดี้ต่ออินเตอร์เฟอรอน แกมมา

**Case 1**

A 50-year-old Thai man presented with generalized pustules on both legs for 2 months. Since January 2016, he developed recurrent multiple pustules on trunk and extremities. Skin biopsy was compatible with Sweet's syndrome. After hospital admission and treatment for Sweet's syndrome, the lesions resolved. Six months later, he developed an eruption of pustulosis with erythroderma and was treated with topical steroid.

Two months prior to this visit, multiple pustules appeared on both lower legs, together with acute fever. At that time, Salmonella septicemia with disseminated mycobacterium abscessus was diagnosed. Intravenous imipenem was injected for 2 months. After that, oral clarithromycin and levofloxacin were prescribed. One month later, he developed recurrent multiple pustules on both lower legs again. Consequently, he was referred to the Institute of Dermatology.

The patient had ischemic heart disease and hypertension which were well controlled. Physical examination revealed multiple discrete well-defined crusted erythematous plaques and nodules on both legs and ankles. (Figure 1) Hair and nail examinations were both unremarkable.

A 4-mm punch biopsy from left wrist was performed and displayed pseudoepitheliomatous hyperplasia. There was mixed inflammatory cell infiltration in the dermis to subcutaneous fat with fibrosis. The inflammation consisted of lymphocytes, eosinophils, neutrophils, plasma cells and histiocytes. No distinct granulomatous formation was identified. On H&E and special stain sections, no microorganism was seen. (Figure 2-4) The

histopathologic findings suggested chronic infection which might have been partially treated.

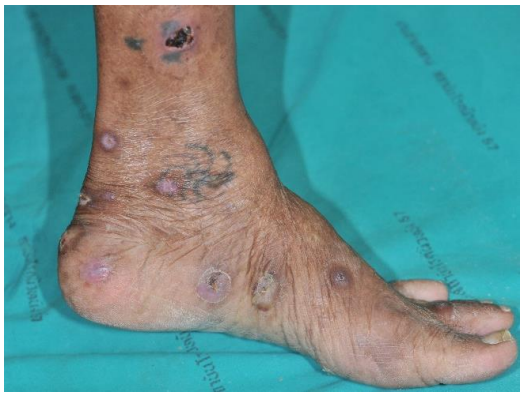


**Figure 1** Multiple discrete well-defined crusted erythematous plaques and nodules on both legs and ankles

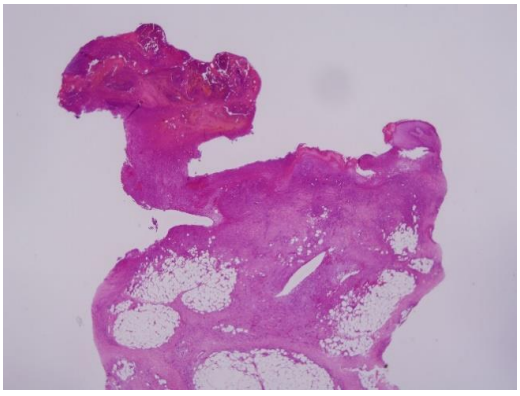


**Figure 2** H&E, original magnification X4
Irregular acanthosis with pseudoepitheliomatous hyperplasia. There is mixed inflammatory cell infiltration in the dermis to subcutaneous fat with fibrosis. The inflammation consists of lymphocytes, eosinophils, neutrophils, plasma cells and histiocytes.

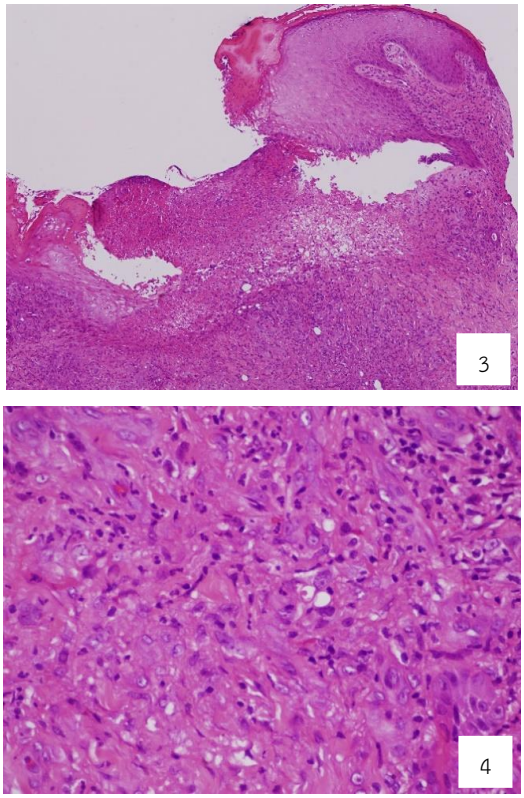



**Figure 3-4** H&E, original magnification X10, X60

Blood test for complete blood count (CBC) and liver function test (LFT) were unremarkable. Serology test for human immunodeficiency virus (HIV), hemoculture, tissue culture for bacteria, tissue culture for fungus and tissue culture for mycobacterium, polymerase chain reaction (PCR) for mycobacterium tuberculosis and non-tuberculous mycobacterium were negative. Blood test for anti-interferon-gamma autoantibody was positive.

The patient was diagnosed with adult onset immunodeficiency syndrome due to disseminated infection, history of Sweet's

syndrome in combination with positive anti-interferon gamma autoantibody. The lesions gradually improved after treatment for non-tuberculous mycobacterial infection. These oral agents will be prescribed for one year.

**Case 2**

A 52-year-old Thai man presented with recurrent multiple erythematous pustules on his trunk and extremities since February 2016. At first he was treated with intravenous ceftazidime for 10 days and the lesions subsided. Three months later, he developed small masses on right side of neck and both groins. Tuberculous lymphadenitis was diagnosed by lymph node biopsy which showed granulomatous abscess. Anti-tuberculosis regimen was prescribed from June 2016 to September 2016. At that time, he developed multiple groups of vesicles on forehead which was suspected to be herpes zoster ophthalmicus. He was treated with intravenous acyclovir for 10 days.

Two months prior to the visit, multiple erythematous pustules reappeared on trunk and extremities, together with recurrent multiple lymph node enlargement at right side of neck and both groins. Right cervical lymph node biopsy revealed necrotizing granulomatous lymphadenitis. Skin biopsy from the lesion on his left wrist displayed subcorneal pustules and dense superficial perivascular infiltrate with numerous neutrophils and lymphohistiocytes.

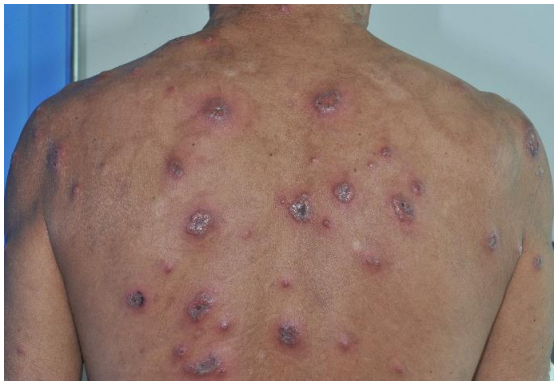


**Figure 5** Multiple discrete erythematous pustules with scaly erythematous hyperkeratotic nodules and plaques on extremities

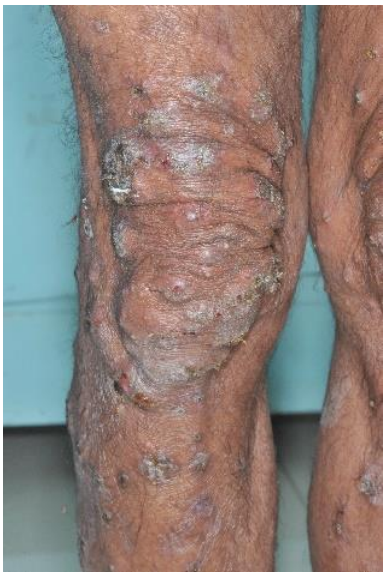
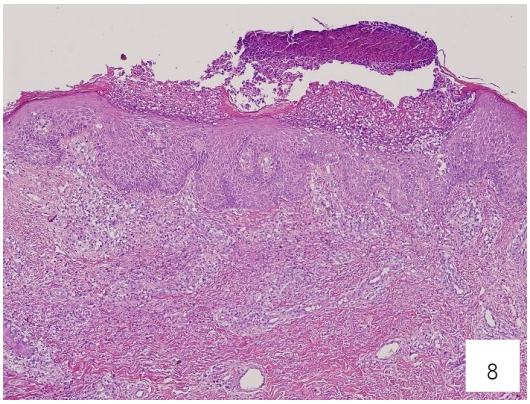


**Figure 6** Multiple discrete erythematous pustules with scaly erythematous hyperkeratotic nodules and plaques on face, back

One month prior to the visit, he had acute fever with recurrent multiple pustules on trunk and extremities. Gram negative septicemia was diagnosed. Intravenous ceftazidime was injected

for 14 days. However, the skin lesions did not improve and the patient was referred to the Institute of Dermatology.



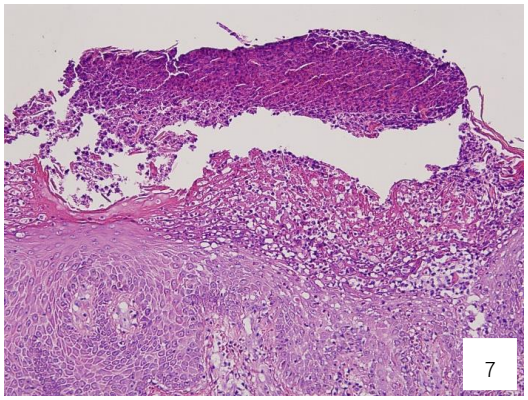




**Figure 7-8** H&E, original magnification X10, X20
Subcorneal collection of neutrophils and irregular acanthosis of the epidermis. There is also collection of neutrophils in upper dermis. Dyskeratotic cells are absent in the epidermis. The dermis show edema of the dermal papillae, dilated capillaries and eosinophils.

The patient had medical history of ischemic heart disease, hypertension, dyslipidemia and chronic kidney disease stage IV. He took these following oral medications: clopidogrel 75 mg/day, metropolol 50 mg/day, simvastatin 40 mg/day, aspirin 81 mg/day and antituberculosis regimens.

Physical examination revealed multiple discrete erythematous pustules with scaly erythematous hyperkeratotic nodules and plaques on face, back and extremities. (Figure 5-6) Eye and nail examinations were both unremarkable.

A 4-mm punch biopsy from left wrist was performed and displayed subcorneal collection of neutrophils and irregular acanthosis of the epidermis. There was also collection of neutrophils in upper dermis. Dyskeratotic cells were absent in the epidermis. The dermis showed edema of the dermal papillae, dilated capillaries and eosinophils. (Figure 7-8) From his clinical and skin biopsy, neutrophilic dermatosis was diagnosed.

CBC and LFT were unremarkable. Serology test for HIV, hemoculture, tissue culture for bacteria, tissue culture for fungus and tissue culture for mycobacterium, PCR for mycobacterium tuberculosis and non-tuberculous mycobacterium were negative. Blood test for anti-interferon-gamma autoantibody was positive.

In conclusion, the patient was diagnosed with adult onset immunodeficiency syndrome due to neutrophilic dermatosis, history of tuberculous lymphadenitis, gram negative bacilli septicemia

and the presence of anti-interferon gamma autoantibody. Oral colchicine was prescribed and the lesions subsided.

## Discussion

Adult onset immunodeficiency syndrome is associated with high-titer neutralizing antibodies to interferon-gamma which was first described in 2004.[1] The patients typically present with AIDS-like illness or reactive dermatosis at the age of 30 to 50.[1,2] All patients have negative result of HIV antibody and never receive any immunosuppressive agents. Most patients do not have any underlying diseases.[3]

IFN-Gamma is a cytokine in the cell-mediated immune cascade secreted in response to the invasion of intracellular infection.[4] This cytokine is primarily produced by T-cells and natural killer cells (NK cells) to stimulate macrophages, which can phagocytose and kill those intracellular pathogens.[5] The depletion of IFN-Gamma may worsen the ability of intracellular organism killing by macrophages.[6]

Clinical presentation of adult onset immunodeficiency syndrome can be divided into two patterns. First is direct invasion of skin by disseminated infection and the other is reactive dermatosis.[7]

Pathogens associated with immune defects in interleukin-12 dependent interferon gamma pathway, are intracellular organisms, including non-tuberculous mycobacteria, non-typhoid salmonella, *Burkholderia spp*, *Penicillium marneffei*, *Cryptococcus neoformans*, *Histoplasma capsulatum* and varicella zoster virus.[8] According to studies in Thailand and Taiwan in 2012, rapid growing mycobacteria was the most common non-mycobacterial infection, followed by Salmonella septicemia.[1]

Reactive dermatosis of adult onset immunodeficiency includes Sweet's syndrome, generalized pustular eruptions (acute generalized exanthematous pustulosis, pustular psoriasis and subcorneal pustulosis), erythema nodosum and lobular panniculitis.[7,9] Sweet's syndrome is the most common reactive dermatosis found in patients with positive anti-interferon-gamma autoantibody.[7]

Pathogenesis and triggering factors of anti-interferon-gamma autoantibodies remain unclear, but may depend on host genetic factors and environmenal exposure.[1] Asian population is the most affected group.[3]

For diagnosis, apart from the test for besides the result of anti-interferon-gamma autoantibody positive, the normal results of several laboratory test including human immunodeficiency virus status, absolute lymphocyte count, lymphocyte subset profile, lymphocyte proliferation assay and autoimmune marker must be confirmed.[8]

Treatment generally depend on the clinical presentation. For reactive dermatosis, corticosteroids, NSAIDs, colchicine, dapsone,

acitretin and calcitriol have been applied in idiopathic or refractory cases.[7] On the other hand, antimicrobial treatment is markedly effective for infective dermatosis.[7]

Selective anti-mycobacterial and antifungal agents for concomitant opportunistic infection are administered depending on the underlying pathogenesis.[2]

In the previous report, rituximab was used in patients with high-titer anti–interferon-gamma autoantibodies who had progressive refractory non-tuberculous mycobacterial disease despite aggressive anti-infective treatment. The patients had reduction of anti-interferon-gamma autoantibodies and had improvement of clinical disease.[10]

According to our cases, both patients presented with recurrent infections and reactive dermatosis. Both of them were diagnosed as adult onset immunodeficiency syndrome and were confirmed by blood test for anti-interferon-gamma autoantibody.

### *References*


1. Browne SK, Burbele OD, Chetchotisakd P, et al, Adult-onset immunodeficiency in Thailand and Taiwan. N Engl J Med 2012; 367: 725-34.
2. Patel SY, Ding L, Brown MR, et al. Anti-IFN-gamma autoantibodies in dissiminated nontuberlous mycobacterial infections. J Immunol 2005; 175: 4769-76.
3. Kampitak T, Suwanpimonkul G, Browne S, Suankratay C. Anti-interferon-gamma autoantibody and opportunistic infection: case series and review of the literature. Infection 2011; 39: 65-71.
4. Billiau A, Matthys P. Interferon-gamma: a historical perspective. Cytokine Growth factor Rev 2009; 20: 97-113.
5. Günter W, Ulrich E. Macrophage defense mechanisms against intracellular bacteria. Immunol Rev 2015; 264: 182-203.
6. Doffinger R, Patel S, Kumararatne DS. Human immunodeficiencies that predispose to intracellular bacterial infections. Curr Opin Rheumatol 2005; 17: 440-446.
7. Chan JF, Trendell-smith NJ, Chan JC, et al. Reactive and infective deratoses associated with adult-onset immunodeficiency due to anti-interferon-gamma autoantibody: Sweet's syndrome and beyond. Dermatology 2013; 226; 157-66.
8. Wongkulab P, Wipasa J, Chaiwarith R, Supparatpinyo K. Autoantibody to interferon-gamma Associated with Adult-Onset Immunodeficiency in Non-HIV Individuals in Northern Thailand. PLoS One 2013; 8: e76371.
9. Tuchinda C, Puavilai S, Sathapatayavongs B, et al. Sweet's syndrome: a reaction to non-tuberculous mycobacterial infections. J Med Assoc Thai 2004; 87: 567-72
10. Browne SK, Zaman R, Sampaio EP, et al. Anti-CD20 (rituximab) therapy for anti–IFN-gamma autoantibody–associated nontuberculous mycobacterial infection. Blood 2012; 119: 3933-9.