## OLGU SUNUMU / *CASE REPORT*

# Varicella Infection Treated with Acyclovir in an Elderly Patient with Rheumatoid Arthritis: Case Report

# ROMATOİD ARTRİTLİ YAŞLI HASTADA ASİKLOVİR İLE TEDAVİ EDİLEN SU ÇİÇEĞİ ENFEKSİYONU

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#### Abstract

Varicella is a common and extremely contagious disease in childhood. The course of infection is usually mild to moderate in children but it may cause serious complications especially in immunosupressed adults and children. We presented a case with nosocomial varicella zoster virus infection in the form of chickenpox in a 67-yearold woman with rheumatoid arthritis (RA) for 15 years who was on treatment of methotrexate and prednisolon. The patient was treated with acyclovir and not only varicella infection but also physical findings and symptoms of RA improved.

Key Words: Arthritis, rheumatoid, chickenpox, methotrexate, acyclovir

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aricella is a common and extremely contagious disease in childhood but it is rare in adults especially in the elderly. It tends to be more severe, even fatal in adults.<sup>1-5</sup> Both RA and the disease-modifying anti-rheumatic drugs such as methotrexate, anti-tumor necrosis factor- $\alpha$ (TNF- $\alpha$ ) and corticosteroids are responsible for increased infection risk in patients with RA.<sup>4-7</sup> It is reported that patients treated with methotrexate and corticosteroids are more susceptible for disseminated varicella.<sup>2,5,7,8</sup> Therefore, early treatment with antiviral agents can prevent this life-threatening

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# Özet -

Su çiçeği enfeksiyonu, çocukluk çağında sık görülen ve oldukça bulaşıcı bir hastalıktır. Çocuklarda hastalığın seyri genellikle hafiforta şiddettedir fakat immünsupresif çocuklarda ve erişkinlerde ciddi komplikasyonlara yol açabilir. Bu yazıda metotreksat ve prednisolon tedavisi alırken nozokomiyal su çiçeği enfeksiyonu gelişen 67 yaşında, 15 yıllık romatoid artrit olgusunu sunulmaktadır. Hasta su çiçeği enfeksiyonuna yönelik asiklovir tedavisi almış, tedavi ile enfeksiyon bulguları yanında romatoid artrite ait aktivasyon bulgularında da gerileme gözlenmistir.

Anahtar Kelimeler: Romatoid artrit, su çiçeği, metotreksat, asiklovir

disease. We presented a case of nosocomial varicella zoster virus (VZV) infection in the form of chickenpox in a 67 years old woman who had RA for 15 years.

#### **Case Report**

A 67-year-old woman was admitted to our outpatient clinic of physical medicine and rehabilitation with the complaints of persistent arthralgia and morning stiffness. She had a 15-year diagnosis of RA and she was on treatment with methotrexate 7.5 mg weekly for 5 years and prednisolone 5 mg daily for 2 months. On the day of admission physical examination revealed swelling, pain and warmth on shoulders, wrists, metacarphophalangeal joints, knees, and ankles. She had typical swan-neck deformity and Zdeformity at the the thumb and ulnar deviation (Figure 1).

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Figure 1. Hand deformities of the patient.

Laboratory results were as follows: Erythrocyte sedimentation rate (ESR) 91 mm/h (0-20 mm/h), C-reactive protein (CRP) 79 mg/L (0-5 mg/L), rheumatoid factor 612 IU/mL (normal <9.6 IU/mL), hemoglobin 10.0 g/dL (12-18 g/dL) and hematocrit 30.3% (37%-52%). Twenty days after her admission, an eruption developed characterized by friable vesicles with an erythematous base covering the abdomen and the upper and lower extremities spreading up to her face and scalp (Figure 2). The vesicles quickly became pustular and they crusted in a few days. Erosions and excoriations were present on some lesions. The lesions were polymorphic, ranging from red macules to vesicles on an erythematous base and from eroded to crusted. The patient was consulted with the Department of Infectious Diseases and Clinical Microbiology and the Department of The diagnosis Dermatology. was primary varicella infection. Multinucleate giant cells were observed in the Tzanck smear, which was obtained from an intact blister. Serologic tests were positive for anti-varicella IgM antibodies. The patient was informed about primary varicella infection, its complications and acyclovir therapy. Written informed consent was taken from the patient. Acyclovir iv 10 mg/kg tid was initiated and after the 6<sup>th</sup> dose, the lesions regressed. After the 5<sup>th</sup> day of acyclovir therapy, physical findings and symptoms related with RA improved significantly. In addition, CRP and ESR levels decreased to 50 mg/L and 50 mm/h, respectively. Methotrexate (7.5 mg/week) and low-dose corticosteroid (5 mg/d) therapy was reinstituted. Patient's remission persisted for three months and afterwards the activity of the disease gradually increased.

Although varicella is a frequently encountered and highly contagious viral infection of childhood, it is also reported in susceptible adults.<sup>1-3,9</sup> The primary form of VZV infection is chickenpox in susceptible individuals. Secondary infection of VZV occurs as zona zoster. However, several investigators suggested that immunucompromised patients might be at risk for exogenous reinfection with VZV, either in the form of chickenpox or zona zoster (lit). Currently, most authorities believe that primary varicella infection generally produces lifetime protection against exogenous reinfections.<sup>10</sup> As varicella is a disease of childhood, the age of our patient was quite old for pri-



Figure 2. Papular and vesicular eruptions on the abdomen.

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mary infection. She describes neither chickenpox nor secondary varicella infection during her lifetime. Indeed, adults from rural areas where the incidence of VZV infection is lower than in urban regions may remain susceptible to VZV. However, our patient reported urban residence since her childhood and varicella is a common communicable disease in Turkey.<sup>11</sup>

The course of this infection is usually mild to moderate in children but it may cause serious complications especially in immunosupressed adults and children.<sup>1,2,5</sup> The disease-modifying antirheumatic drugs such as methotrexate may lead to life-threatening adverse effects in patients with RA.<sup>5</sup> Kinder et al reported the incidence of lifethreatening side-effects of methotrexate used for the treatment of inflammatory arthritis as 1.8%.<sup>5</sup> They identified only one patient (0.18%) with disseminated varicella zoster in their study population (673 patients) and that patient died. They suggested that not only methotrexate but also RA itself and corticosteroids might contribute to deaths due to infections.<sup>5</sup> Although our patient had RA and received methotrexate and corticosteroid, none of the systemic complications of varicella infection was observed. Possibly, early diagnosis and acyclovir therapy provided rapid improvement and prevented the patient from severe complications. Hosts with impaired cellular immunity are more susceptible for disseminated varicella. Therefore acyclovir treatment is recommended for immunocompromised children, adolescents and adults.<sup>10,12</sup>

In our patient, the rash of varicella infection occurred on the 20<sup>th</sup> day of hospitalization. Since the incubation period of the disease is 10 to 20 days, we considered this a nosocomial infection. Unfortunately, the source of the infection could not be detected. In hospitalized patients, prior to any immunosuppressive treatment, history of varicella immunization should be clarified. It must be kept in mind that patient who do not remember their immune status, might be prone to nosocomial primary varicella infection during their stay in hospital. It must always be remembered that early and appropriate treatment may be life saving in immunocompromised adult patients who have varicella infection.

An interesting fact about our patient was the remission of RA signs and symptoms after the 5<sup>th</sup> day of the varicella treatment. We could not explain this rapid improvement of symptoms that persisted for three months in our patient. Remission of RA signs and symptoms after primary varicella infection treated with acyclovir were also reported by Saulsbury et al and Aihara et al.<sup>13,14</sup> All reported cases (3 cases) were juvenile RA and post-infectious remission periods lasted for 3 to 6 months. The authors also could not explain the reason for this improvement. Aihara et al suggested that a shift of Th cell subsets might be responsible for the remission of RA after VZV infection. A transient suppression of cell-mediated immunity, which is controlled by Th1 cells results with a relative and transient predominance of Th2 cells. As a result, the inflammation of the joints was suppressed for a couple of weeks.<sup>13,14</sup>

In conclusion, remission of RA after varicella infection may be a coincidence or there may be a relation between RA and varicella or acyclovir. The mechanism of this unusual remission in RA may provide new horizons in the treatment of RA.

#### - REFERENCES -

- 1. Morice AH, Lai WK. Fatal varicella zoster infection in a severe steroid dependent asthmatic patient receiving methotrexate. Thorax 1995;50:1221-2.
- 2. Ching DW. Severe, disseminated, life threatening herpes zoster infection in a patient with rheumatoid arthritis treated with methotrexate. Ann Rheum Dis 1995;54:155.
- 3. Gatnash AA, Connolly CK. Fatal chickenpox pneumonia in an asthmatic patient on oral steroids and methotrexate. Thorax 1995;50:422-3.
- Vonkeman H, ten Napel C, Rasker H, van de Laar M. Disseminated primary varicella infection during infliximab treatment. J Rheumatol 2004;31:2517-8.
- Kinder AJ, Hassell AB, Brand J, Brownfield A, Grove M, Shadforth MF. The treatment of inflammatory arthritis with methotrexate in clinical practice: Treatment duration and incidence of adverse drug reactions. Rheumatology (Oxford) 2005;44:61-6.
- Symmons DP. Mortality in rheumatoid arthritis. Br J Rheumatol 1988;27(Suppl 1):44-54.

- Stephan JL, Kone-Paut I, Galambrun C, Mouy R, Bader-Meunier B, Prieur AM. Reactive haemophagocytic syndrome in children with inflammatory disorders. A retrospective study of 24 patients. Rheumatology (Oxford) 2001;40:1285-92.
- Dass R, Singh S, Kumar V, et al. Varicella glomerulonephritis mimicking microscopic polyangiitis. Rheumatol Int 2004;24:362-4.
- Conti JA, Karetzky MS. Varicella pneumonia in the adult. N J Med 1989;86:475-8.
- Whitley RJ. Varicella-zoster virus. In: Mandell GL, Bennett JE, Dolin R, Mandell GL, Bennett JE, Dolin R, Mandell GL, Bennett JE, Dolin RS, eds. Principles and Practice of Infectious Disease.

6<sup>th</sup> ed. New York: Churchill Livingstone; 2005. p.1780-8.

- Türkmen M, Buğdaycı R, Sönmez M. 0-12 yaş grubu çocuklarda su çiçeği sıklığı. Çukurova Ünv Tıp Fak Derg 2001;26:137-40.
- Gilbert DN, Moellering RC, M EG, Sande MA. The Sanford Guide to Antimicrobial Therapy. 35<sup>th</sup> ed. Dallas, TX: Antimicrobial Therapy Inc; 2005. p.109-10.
- 13. Saulsbury FT. Remission of juvenile rheumatoid arthritis with varicella infection. J Rheumatol 1999;26:1606-8.
- 14. Aihara Y, Katakura S, Imagawa T, Mitsuda T, Yokota S. Transient remission of intractable systemic-type of juvenile rheumatoid arthritis after chickenpox in a 2-year-old boy. Pediatr Int 2001;43:95-7.