Journal of Turgut Ozal Medical Center 2016;23(4):435-8
OLGU SUNUMU/CASE REPORT DOI: 10.5455/jtomc.2016.01.09

# A rare cause of vertigo: cryoglobulinaemia

## Vertigonun nadir bir sebebi: kriyoglobulinemi

Erkan Karatas[1], Cigdem Firat Koca[2], Sukru Aydin[1], Yuksel Toplu[1], HulyaTaskapan[3]

[1]İnönü University School of Medicine, Department of Otorhinolaryngology, Malatya, Turkey.
[2]Malatya State Hospital, Otolaryngology Depertmant, Malatya, Turkey
[3]İnönü University School of Medicine, Department of Nephrology, Malatya, Turkey

**Abstract**
Cryoglobulinaemia should be taken into consideration as a cause of vertigo. It is the timing of shrewd. An 82-year old man, suffering from peripheral vertigo is evaluated thoroughly. After a long, detailed evaluation the result is cryoglobulinaemia related vertigo. The presence in the serum of one or more immunoglobulins, which precipitate at a temperature below 37-Celsius degrees and redissolve on reheating is called cryoglobulinaemia. Cryoglobulinaemia seems to be responsible for audiovestibular damage probably through an immunologic mechanism. In recent years the audio vestibular manifestations of immun-mediated diseases have been the issue of numerous reports. But there were a few reports about cryoglobulinaemia- related audiovestibular disturbances. The aim of this article is to remind the vestibular manifestations of cryoglobulinaemia; a kind of systemic vasculitis.
**Keywords:** Vertigo; Mixed Cryoglobulinaemia; Hcv Infection.

**Öz**
Kriyoglobulinemi vertigonun bir sebebi olarak akılda tutulmalıdır. Dikkatli olmanın zamanıdır. Feriferik vertigo şikayeti olan 82 yaşındaki erkek hasta ayrıntılı olarak değerlendirildi.. Uzun ve detaylı bir değerlendirmeden sonra sonuç kriyoglobülinemik vertigo idi.Serumda bulunan ve 37 santigrad derecede donan ve ısıtılınca tekrar çözünen immunglobulinler kriyoglobulin olarak adlandırılır. Kriyoglobulineminin işitme ve denge üzerine olan hasarından olası immünolojik bir mekanizmayla sorumlu olduğu görülmektedir. Son yıllarda immün aracılı hastalıkların işitme ve denge sistemi üzerindeki bulguları sayısız makalenin konusu olmuştur. Ancak kriyoglobünemi ilişkili işitme ve denge sistemi bozuklukları hakkında az sayıda makale mevcuttur.Bu makalenin amacı bir çeşit sistemik vaskülit olan kriyoglobülineminin vestibüler bulgularını hatırlatmaktır.
**Anahtar Kelimeler:** Vertigo; Mikst Kriyoglobülinemi; Hcv Infeksiyonu.

Received/Başvuru: 10.01.2016
Accepted/Kabul: 09.03.2016

Correspondence/İletişim
Çigdem Fırat Koca
Malatya Devlet Hastanesi Kulak Burun Boğaz Bölümü,Malatya Turkey
E-mail: cifirat@hotmail.com

How to cite this article/Atıf için
Karatas E, Koca CF, Aydin S, Toplu Y, Taskapan H. A rare cause of vertigo: cryoglobulinaemia. J Turgut Ozal Med Cent 2016;23(4):435-8.

2016;23(4):435-8
DOI:10.5455/jtomc.2016.01.09

## INTRODUCTION

Vertigo is described as an illusion or hallucination of movement, usually rotational, either of oneself or the environment (1). The first step is to evaluate the origin of vertigo; central or peripheral (2). In some cases there may be a rare cause of vertigo such as cryoglobulinemia. Cyroglobulins are immunoglobulins that precipitate in vitro at temperatures below 37-Celsius degrees and redissolve after reheating. The major pathophysiological mechanism of the mixed cryoglobulinemia is immune complex-mediated vasculitis (3).

## CASE REPORT

An 82- year -old man presented to our ENT clinic with acute onset of vertigo. Symptoms typically were lasting more than hours with aural fullness. The patient was feeling cold in every time. A detailed laboratory test including thyroid function test, HBV, HCV were performed. HCV was positive and the patient has been infected with HCV.HCV-RNA was detected by polymerase chain reaction.

A detailed physical examination was performed. Nystagmus was not present, and the neurological examination was normal. Audiological and vestibular evaluations were performed at the ENT Department of Inonu University Malatya, Turkey. After a complete otological examination, audilogical evaluation was performed by pure tone audiometry (0.25, 0.5, 1,2,4 and 6 kHz), impedance audiometry, brainstem response audiometry and video ENG. All tests were normal, except for a bilaterally symmetrical, mild sensorineural hearing loss in the pure tone audiometry. It can be evaluated as presbycusis (Figure 1). Dix-Hallpike test was negative. Against the possibility of central pathology; cranial CT and MRI were performed. They were normal (Figure 2).

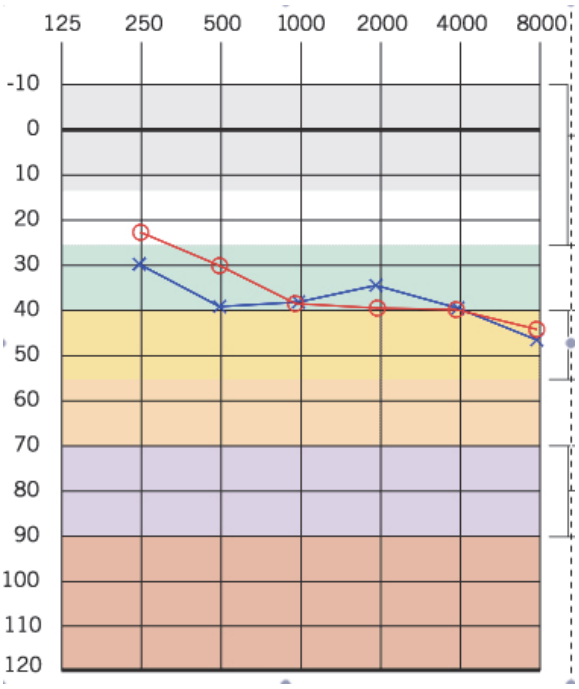


**Figure 1.** A bilaterally symmetrical, mild sensorineural hearing loss found in the pure tone audiometry.

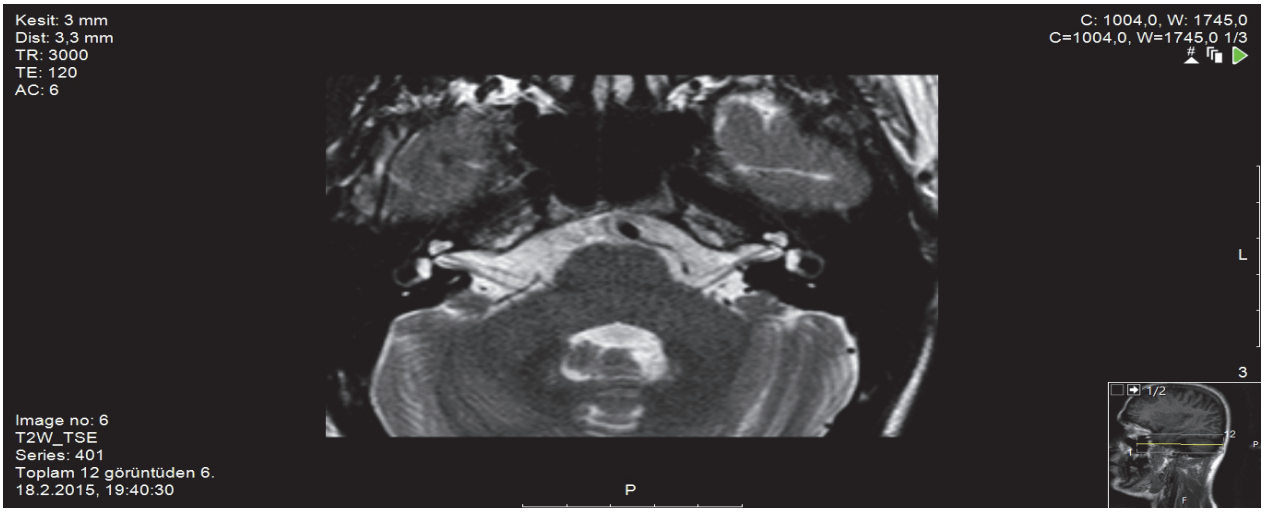


**Figure 2.** Normal temporal and cranial Magnetic Resonance Imaging were detected in the patient.

Carotid and vertebral arterial Doppler's were performed to exclude vertebrobasilar and carotid insufficiency. Electrocardiography and echocardiography were performed. They were normal. According to the strong association between hepatitis C virus (HCV) and mixed cryoglobulinaemia routine blood chemistry was carried out by cold precipitation test. C3-C4, ASO, CRP, RF, was measured. An immunological work-up showed low complement levels (C3 and C4). Serum levels of immunoglobulin were determined by nephelometry using the immunochemistry system. For cryoglobulin identification, two 10 mL red top tubes of sample

2016;23(4):435-8
DOI:10.5455/jtomc.2016.01.09

(without an anticoagulant) were drawn from the patient and transported to the laboratory at 37 Celsius degrees (commonly, this was achieved by submerging the tubes in warm water during transportation to the laboratory). The sample was allowed to clot at 37 Celsius degrees for 1 hr. The clot was separated from the sides of the tube with a Pasteur pipette, and the serum was separated by warm (37 Celsius degrees) centrifugation and aliquoted into three tubes at 37 Celsius degrees. One tube is the Wintrobe tube for quantification of the cryoprecipitate (a Wintrobetube has markings that are used to quantify). The second tube contained a larger quantity of serum, which is used for cryoprecipitate observation and subsequent analysis. The third tube was used to determine the solubility of the cryoprecipitate on rewarming to 37 Celsius degrees. It is important for the sample temperature not to drop below 37 Celsius degrees until serum separation is complete to avoid premature precipitation. The three serum containing tubes are then kept at 4 C and analyzed at 72 hours. A precipitate formed at 72 hours at 4 C. The cryoprecipitate was solubilized at 37 Celsius degrees and analyzed by immunodiffusion and immunofixation. There was 2% cryocit and low complements levels (C3 and C4).

## DISCUSSION

The presence in the serum of one or more immunoglobulins, which precipitate at a temperature below 37-Celsius degrees and redissolve on rewarming, is called cryoglobulinaemia (4). Cryoglobulins may not be a sign of disease; healthy people may have low concentrations of cryoglobulins. But polyclonal cryoglobulins may be transiently detected during infection (3). The main serological findings of MC are mono- or polyclonal rheumatoid factor (RF) low hemolytic complement activity with a low C4 component (4). Cryoglobulins mediate organ damage by the accumulation of cryoglobulins and auto-immune-mediated vasculitis (3). Pathogenesis of vasculitis, the typical cutaneous and visceral clinical manifestations of MC is generally as a result of the tissue deposition of complement and circulating immune complexes, mainly the cryoglobulins and also due to the haemorheological alterations. There is a strong association between hepatitis C virus (HCV) and MC. Additional, a viral genome has been recently demonstrated in peripheral lymphocytes in MC patients (4).

As mentioned above, in our patient, presented in the case report, the HCV-related markers (anti-HCV antibodies, HCV RNA) were positive. In recent years the immune-mediated audiovestibular manifestations have been the issue of numerous reports. But there were a few reports about cryoglobulinaemia- related audiovestibular disturbances. Probably the first cryoglobulinaemia related audilogical disturbance was presented in 1950. The patient was presented with tinnitus and progressive hearing loss complaints.In the literature a few older studies can be seen after that in the course of cryoglobulinaemia related audiovestibular manifestations (tinnitus, hearing loss and otitis media).Nomura et al, presented an MC patient suffering from tinnitus, vertigo, and progressive bilateral hearing loss (4).

The patient, presented in our case report, was suffering from only vertigo, as an audiovestibular symptom. There was no progressive hearing loss and/or tinnitus, or otitis media. Berretini et al, were studied 32 mixed cryoglobulinemia patients in order to evaluate the nature and prevalence of audiovestibular disturbances in mixed cryoglobulinemia. They found that a rather frequent audiovestibular involvement in MC patients. Sensorineural hearing loss, tinnitus, benign positional paroxysmal vertigo and any other audiovestibular dysfunction may occur according to microvascular inner ear damage caused by immune-complexes. Berretini et al. was observed seven patients with a vestibular disorder that was considered for its clinical and historical features as benign positional paroxysmal vertigo (4).

Our patient's symptoms did not show the characteristics features of the most common causes of peripheral vertigo such as Benign Paroxysmal Positional Vertigo (BPPV), Vestibular neuritis and Meniere's disease. Our patient's symptoms typically were lasting more than hours with aural fullness. Dix-Hallpike test was negative. There was no progressive hearing loss and/or tinnitus, or otitis media. There was no nausea and/or vomiting and he was asked for any upper respiratory infection for vestibular neuritis. According to the strong association between hepatitis C virus (HCV) and mixed cryoglobulinaemia, we had remembered the inner ear involvement in mixed cryoglobulinaemia. Routine blood chemistry was carried out by cold precipitation test. C3-C4, ASO, CRP, RF, was measured. An immunological work-up showed low complement levels (C3 and C4). Serum levels of immunoglobulines were determined by nephelometry using the immunochemistry system as mentioned in case report.

The common pathophysiological mechanism of systemic vasculitis is inflammation of the lining of blood vessels, causing occluding of the lumens, tissue necrosis and ischemia. According to the size number and type of affected vessels and organs involved, clinical symptoms may differ.in some cases patients are consulted to otolaryngology clinics with the initial symptoms. The ENT specialists should be familiar with these diseases (5).

Systemic lupus erythematous (SLE) can be determined as a prototype of the autoimmune diseases. Pathogenic immune complexes and autoantibodies are the main causes of organ damage. Karataset al, reported audiovestibular disturbance in patients with SLE (6). Except SLE; polychondritis, Cogan syndrome, rheumatoid arthritis, Behcet's Disease, systemic sclerosis, Panarteritisnudosa, Kawasaki disease, Scleroderma should be taken into consideration as an auto-immune diseases responsible for ear damage (5,7).

Mixed cryoglobulinaemia seems to be responsible for audiovestibular damage probably through an immunologic mechanism The circulating

2016;23(4):435-8
DOI:10.5455/jtomc.2016.01.09

immunocomplexes, predominantly cryoglobulins, can precipitate in the labyrinthine vessels and this causes vasculitis. Also an increased blood viscosity and reduced blood filterability can be related with the vascular damage (4).

In conclusion; the inner ear may be involved in organ specific autoimmune diseases such as cryoglobulinemia. This subject is not a well-known issue among otolaryngologists. With this case report, we wanted to underline the audiovestibular system involvement in mixed cryoglobulinaemia.

## REFERENCES

1. Hanley K, O'Dowd T. Symptoms of vertigo in general practice: a prospectivestudy of diagnosis. Br J Gen Pract 2002;52(483):809-12.
2. Hanley K, O'Dowd T, Considine N. A systematicreview of vertigo in primary care. Br J Gen Pract 2001;51(469):666-71.
3. Retamozo S, Brito-Zerón P, Bosch X, Stone JH, Ramos-Casals M. Cryoglobulinemic disease. Oncology (Williston Park) 2013;27(11):1098-1105, 1110-6.
4. Berrettini S, Ferri C, La Civita L, Segnini G, Lombardini F, Bruschini P, Longombardo G, et al. Sellari-Franceschini S-Inner ear involvement in mixed cryoglobulinaemia patients. Br J Rheumatol 1995;34(4):370-4.
5. Parra-García GD, Callejas-Rubio JL, Ríos-Fernández R, Sainz-Quevedo M, Ortego-Centeno N. Otolaryngologic manifestations of systemic vasculitis. Acta Otorrinolaringol Esp 2012;63(4):303-10.
6. Karatas E, Onat AM, Durucu C, Baglam T, Kanlikama M, Altunoren O, Buyukhatipoglu H. et al. Audiovestibular disturbance in patients with systemic lupus erythematosus. Otolaryngol Head Neck Surg 2007;136(1):82-6.
7. Amor Dorado JC, Barreira Fernández Mdel P, RegueiroVillarin S, González-Gay MA [Audiovestibular manifestations in systemic vasculitis]. Acta Otorrinolaringol Esp 2009;60(6):432-42.