Advances in Life Science and Technology
ISSN 2224-7181 (Paper) ISSN 2225-062X (Online)
Vol.69, 2018

Gonococcal Acute Septic Arthritis in Immunocompetent Patients

T. Kalo[1] R. Celami[2] E. Puca[3] E. Muça[3] N. Gjermeni[3] Sh. Kurti[3] E. Qyra[3]
Dh. Kraja[3] E. Rapushi[4] M. Hoxha[5] S. Damo[6] M. Eqimi[7]

1Profesor of Infectious Disease, Service of Infectious Diseases, University Hospital Center "Mother Theresa", Tirana, Albania

2Profesor of Obstetrics and Gynecology, Chief of Gynecology Service, Elbasan Regional Hospital, Hospital privileges as Obstetrician and Gynecologist at American Hospital of Tirana, Professor and Chief of TM-I Department at Faculty of Medical Techical Sciences, University of Aldent, Tirana, Albania

3 Physician at Service of Infectious Diseases, University Hospital Center "Mother Theresa", Tirana, Albania

4Physician at Service of Rheumatology, University Hospital Center "Mother Theresa", Tirana, Albania

5Physician at Service of Allergology and Immunology, University Hospital Center "Mother Theresa", Tirana, Albania

6 Physician at Service of Neonatology, Qeen Geraldine University Hospital of Obstetrics Gynecology, Tirana, Albania

7 Physician at American Hospital, Tirana, Albania

Corresponding author Rustem Celami, MD, PhD, Associated Profesor

Abstract

The objective of this study is to estimate the clinical evolution and the biological values and of three cases suffering from Gonococcal acute septic arthritis (GASA).Our study is based in a thoroughfully screening of 18 patients hospitalized in our service during the period of time of March 2011 – July 2016. Among those 18 cases, 12 of them (66.7%) were diagnosed with Acute Septic Arthritis (ASA) due to *Staphylococcus aureus*, 3 cases (16.65%) were diagnosed with ASA due to *Neisseria gonorrhoeae*, and 3 other cases (16.65%) were diagnosed with ASA due to *Streptococcus pneumoniae, Escherichia coli* and *Echinella corrodens*. Two sexually active women at the seventh and tenth day of an untreated suppurative cervico-vaginitis and one man at the eighth day of an untreated suppurative urethritis were consulted at the Service of Infectious Diseases of University Hospital Center "Mother Theresa", because of: severe pains in left wrist, in the left elbow and in the right knee, swollen of those articulation, difficulties in their movements, shivering and a high fever of 38-39.2ºC. *Neisseria gonorrhea* was insolated in three cases in blood cultures and cervical/urethral samples and they were sensitive towards Cyclines, Cephalosporins and Fluoroquinolones. All three patients were immunocompetent.

Keywords: Neisseria gonorrhea, Acute Septic Arthritis, Biological values.

Introduction

Neisseria gonorrhoeae is the most common sexually transmitted bacteria causing infective arthritis. In nowadays the Gonococcal infection may be poised to become more troublesome because of Fluoroquinolones, Ceftriaxone and other antibiotics resistance is increasing, and many contemporary physicians are unfamiliar with musculoskeletal manifestations of Neisseria gonorrhoeae infections. Gonococcal arthritis represents the most common cause of inflammatory monoarthritis in young adults. If it is left untreated a disseminated gonococcal infection (DGI), which occurs in up to 3% of cases, it may results in several complications, such as: *Gonorrheal endocarditis*, *Gonorrheal meningitis* and *Gonorrheal arthritis* (GA), which is caused by the growth of the gonococcus in joints' fluids, most commonly wrists, knees and ankles, and this occurs hopefully in only 1% of cases.). The elapsed time between the initial gonococcal infection and the DGI may vary from 1 day until 3 months. GA manifests as either a bacteremic infection (arthritis-dermatitis syndrome, 60% of cases), or as a localized septic arthritis (remaining 40%). (1, 4, 5, 6, 8, 9)

Methodology and Results:

Our study is based in a thoroughfully screening of 18 patients hospitalized in our Service of Infectious Diseases of University Hospital Center "Mother Theresa", during the period of time of March 2011 – July 2016. Among those 18 cases, 12 of them (66.7%) were diagnosed with Acute Septic Arthritis (ASA) due to *Staphylococcus aureus*, 3 cases (16.65%) were diagnosed with ASA due to *Neisseria gonorrhoeae*, and 3 other cases (16.65%) were diagnosed with ASA due to *Streptococcus pneumoniae, Escherichia coli* and *Echinella corrodens* Two sexually active women at the seventh and tenth day of an untreated suppurative cervico-vaginitis and one man at the eighth day of an untreated suppurative urethritis were consulted at the because of: severe pains in left wrist, in the left elbow and in the right knee, swollen of those articulation, difficulties in their movements, shivering and a high fever of 38-39.2ºC. Septic arthritis was localized in the left wrist and in the left elbow (1st and 2nd case in female persons), as well as in the right knee (3rd case in a male person). We observed an inflammatory painful edema; fluctuation in palpation of the above-mentioned articulations, as well as a purulent liquid was

aspirated from them. All those three elements were compatible of an acute suppurative arthritis (ASA). Plain radiography findings of the affected joints were normal.

Neisseria gonorrhea was insolated in three cases in blood cultures and cervical/urethral samples and they were sensitive towards Cyclines, Cephalosporins and Fluoroquinolones. All three patients were immunocompetent. The following phenomena have been noticed on the laboratory data of blood samples during the first week of manifestation of GASA: WBC was 21,400/mcL (normal range 4,500-10,000/mcL, Fibrinogen level was 731mg/d (normal range 200-400 mg/dL), PCR was 61. 7mg/L (normal level is <0.5mg/L), ALP was 198 IU/LT (normal range is 44-147 IU/L).

Patients were also tested also other sexually transmitted infections such as HIV, Hepatitis B, Chlamydia, Syphilis and the results were negative.

The treatment was based in the sensitivity of insolated germs and it was as following: Ciprofloxacin: 200 mg x 3 IV for the first three days plus 1 gr of Azithromycin in single dose, followed by oral Ciprofloxacin 750 mg x 2 for 7 days (the first case), and Cefuroxim: 750 mg x 3 IV for the first three days plus 1 gr of Azithromycin in single dose, followed by oral Cefuroxim of 500 mg x 2 for 7 days.

The outcome of GASA after the intensive anti-gonococcal and supportive therapy was excellent for all of them, and we haven't observed any functional sequele after six months of their ambulatory follow-up.

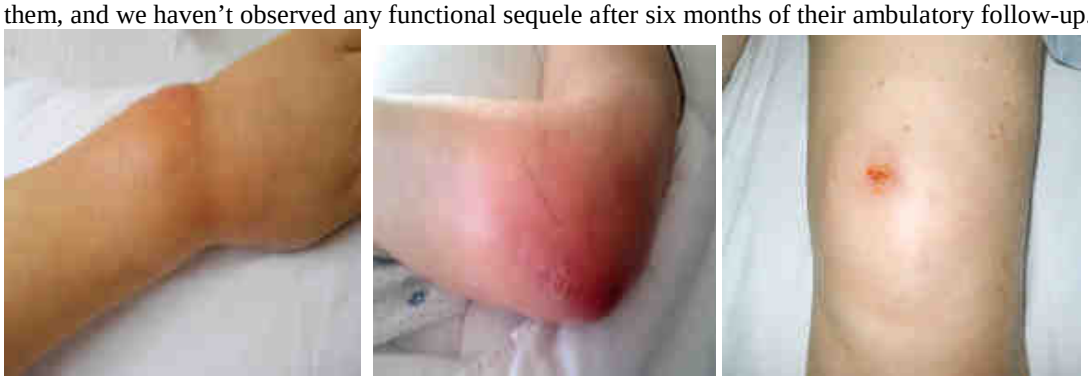

Figure 1, 2 and 3: Left wrist, left elbow and right knee.

Discussion

Gonorrhea is the second most commonly reported notifiable disease in the United States, with 350,062 cases reported in 2014. The sexually transmitted diseases are typically underreported, however the Centers for Disease Control and Prevention (CDC) estimates that approximately 820,000 cases of gonorrhea occur yearly in the US. (2, 3)

The most recent 2008 WHO Report, estimates that they have documented a 21% global increase in the total number of new cases of gonorrhoeae in adults compared with 2005, with an estimated 106 million adults being infected with *N. gonorrhea* in 2008. The incidence of gonococcal infection is lower in Europe than in North America. (13)

Gonococcal arthritis is caused by infection with the gram-negative diplococcus *N gonorrhoeae*, a highly infectious organism capable of colonizing diverse mucosal surfaces. Common sites of infection include the urethra, cervix, pharynx and rectum, but infection may be asymptomatic in some patients. Hematogenous spread of the mucosal infection occurs in 0.5-3% of cases, and disseminated infection is thought to play a major role in the pathogenesis of gonococcal arthritis. Patients with Disseminated Gonococcal Infection (DGI), may present with dermatitis-arthritis syndrome (60% of cases) or with a localized septic arthritis (40%). These presentations may represent different phases of a disease continuum. Unlike *Staphylococcus aureus* septic arthritis, gonococcal arthritis is rarely associated with joint destruction. (1, 4, 5, 6, 8, 9)

Patients may experience pain, redness, and swelling in 1 joint (or sometimes multiple joints), most commonly in a knee, wrist, ankle, or elbow. Joint symptoms begin within days to weeks of gonococcal infection. For patients with septic arthritis resulting from gonococcal infection, proper antibiotic treatment and joint drainage typically leads to full recovery. (4, 9)

Most patients with suspected acute infectious arthritis, including gonococcal arthritis, should be hospitalized to establish a diagnosis and to monitor for improvement or complications. The empiric antibiotics directed against likely pathogens should be used until confirmatory laboratory data are available. Antibiotic coverage in healthy hosts should initially include gram-positive organisms, which account for approximately 80% of non-gonococcal monoarthritis cases (*Staphylococcus aureus*, 60%; non–group A *Streptococcus* species, 15%; *S pneumoniae*, 3%). Gram-negative organisms (18%) should be covered in patients who are immunocompromised, elderly, or otherwise at risk. The transition to oral antibiotics can usually be made 24-48 hours after clinical improvement. (1, 5, 6, 8)

It is recently observed higher rates of infection due to the increase of antimicrobial-resistant gonococci. If

trends continue, researchers say there is a very real possibility that some strains of *Neisseria gonorrhea* may become resistant to all current treatment options. As of right now, the current drug of choice is either Ceftriaxone or Cefixime. Although these two drugs are still very effective they are already showing signs of resistance, especially to Cefixime. If this problem of resistance to medication is not resolved, there is a real possibility that gonorrhea will be a very difficult infection to treat. Gonococcal infection in HIV-positive patients is treated with the same regimen used for the general population. (3, 7, 10, 11, 12)

Ceftriaxone is the drug of choice for disseminated gonococcal infection, pelvic inflammatory disease, and pharyngeal infection. It is the second-line agent for uncomplicated genitourinary infections, but only because of higher cost, along with the discomfort and additional administration expense of injection. Although cephalosporins remain an effective treatment for gonococcal infections, the CDC has reported that resistance to Cefixime increased from 0.2% in 2000 to 1.4% in 2010, and resistance to Ceftriaxone increased from 0.1% to 0.3% in 2010 during that period. (3, 7, 11)

Ten percent to thirty percent of people with gonococcal infection are co-infected with Chlamydia. Thus, routine dual therapy with Doxycycline and Azithromycin has been recommended and shown to be cost effective. Dual therapy also decreases the development of antimicrobial resistance in bacteria. (11)

Because of resistance to oral cephalosporins in the United States, there is only one first-line regimen, which is dual treatment with Ceftriaxone and Azithromycin. In addition, persons infected with *Neisseria gonorrhoeae* frequently are coinfected with *Chlamydia trachomatis*; this finding has led to the longstanding recommendation that persons treated for gonococcal infection also be treated with a regimen that is effective against uncomplicated genital *C trachomatis* infection, further supporting the use of dual therapy that includes Azithromycin. (7, 11)

The 2015 CDC recommendations for disseminated gonococcal infection are:

- Ceftriaxone 1 g IM/IV every 24 h plus a single dose of Azithromycin 1 g PO
- Alternative regimen - Cefotaxime 1 g IV every 8 h plus a single dose of Azithromycin 1 g PO

When treating for the arthritis-dermatitis syndrome, the clinician can switch to an oral agent, with the choice guided by antimicrobial susceptibility testing, 24-48 h after substantial clinical improvement. *The total treatment course should be at least 7 days. (7)*

In conclusion: Early diagnosis and treatment of a disseminated gonococcal infection (DGI) and of a gonococcal acute septic arthritis (GASA), give more chances to the patient for a better outcome of disease. Leukocytosis, Elevated levels of Fibrinogen, PCR and ALP are the common biological features in GASA. They have the same significance for the GASA's outcome as they have for its diagnosis.

References

Bardin T. Gonococcal arthritis. *Best Pract Res Clin Rheumatol*. 2003, 17(2), 201-8.

Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2014*. Atlanta, GA: U.S.Department of Health and Human Services; November 2015.

Centers for Disease Control and Prevention (CDC). Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infections. *MMWR Morb Mortal Wkly Rep*. 2012 Aug 10. 61:590-4.

Cucurull E, Espinoza LR. Gonococcal arthritis. *Rheum Dis Clin N Amer* 1998, 24:305-322.

Dalla Vestra M, Rettore C, Sartore P, Velo E, Sasset L, Chiesa G, et al. Acute septic arthritis: remember gonorrhea. *Rheumatol Int*. 2008 Nov. 29(1):81-5.

Holmes KK, Counts GW, Beaty HN. Disseminated gonococcal infection. *Ann Intern Med*, 1971, 74:979-993.

Lewis, AD. Global Resistance of *Neisseria gonorrhoeae*. When Theory Becomes Reality. Curr Opin Infect Dis. 2014, 27(1), 62-67.

Rice PA. Gonococcal arthritis (disseminated gonococcal infection). *Infect Dis Clin North Am*. 2005 Dec. 19(4):853-61.

Marker-Hermann E. Septic arthritis, osteomyelitis, gonococcal and syphilitic arthritis. Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH. *Rheumatology*. 4th ed. Philadelphia, PA: Mosby Elsevier; 2008. 1013-28.

World Health Organization Fact Sheet Number 110. Available at http://www.who.int/mediacentre/factsheets/fs110/en/index.html. December 2015; Accessed: July 26, 2016.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015 Jun 5. 64 (RR-03):1-137.

Unemo M, Nicholas RA. Emergence of multidrug-resistant, extensively drug-resistant and untreatable gonorrhoea. Future Microbiol 2012; 7:1401–1422.

World Health Organization: Global incidence and prevalence of selectable curable sexually transmitted infections: 2008. 2012, WHO, Geneva, Switzerland.