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Acute septic elbow monoarthritis with associated *Neisseria gonorrhoeae* bacteraemia: an uncommon presentation of an old disease

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SUMMARY

Neisseria gonorrhoeae is an uncommon present-day cause of septic arthritis. It is generally seen in the younger patient population and is often difficult to isolate in the lab. Blood cultures performed as routine work are usually negative, and when positive tend to be seen in the classic form of disseminated gonococcal infection. Here we report a case of acute septic monoarthritis, associated with *N. gonorrhoea* bacteraemia, in a 67-year-old male patient with multiple chronic comorbidities, who presented with acute pain and swelling at his left elbow, and no associated skin changes. Arthrocentesis findings were consistent with septic arthritis. Blood cultures drawn on admission grew *N. gonorrhoeae*. Synovial fluid culture was sterile but did exhibit Gram-negative cocci on Gram stain. The patient was started on IV antibiotics, and later underwent incision and drainage with subsequent improvement in symptoms.

We thus present an unusual form of disseminated gonococcal infection in the setting of: epidemiology, physical presentation, as well as microbiologic findings. Although less common, DGI should be considered in the differential for septic join in the older adult population, and a sexual history should be obtained in all patients. This patient ultimately had an excellent outcome given his prompt presentation after symptom onset and immediate initiation of medical therapy.

Keywords: Disseminated gonococcal infection, septic arthritis, gonococcal arthritis, *Neisseria gonorrhoeae.*

INTRODUCTION

Amongst cases of native joint septic arthritis, the most commonly implicated organisms are Gram-positive, with *Staphylococcus aureus* being the number one causative agent [1]. The underlying etiology of septic arthritis is often an occult bacteremia. A rarer etiology is disseminated gonococcal infection (DGI), representing about 1.2% of cases of septic arthritis overall [1]. Approximately 0.5-3% of patients with *N. gonorrhoeae* infection will develop DGI; this will manifest predominantly as polyarthritis with dermatitis, or septic monoarthritis [2]. In terms of epidemiology, gonococcal arthritis is associated with sexually active young adults and represents the predominant form of septic arthritis in that age group [3]. Approximately 50% of patients with diagnosed DGI will have noted positive blood or synovial fluid cultures [2]. Synovial fluid analysis is inflammatory with Gram stain revealing intra- and extracellular Gram-negative diplococci in less than 50% of fluid that is culture positive [3]. We report a case of DGI in a 67-year-old male that manifested as an acute septic monoarthritis, with *N. gonorrhoeae* identified via blood cultures. We highlight the importance of recognizing the pertinent physical exam findings, discuss the different manifestations of DGI as well as the necessary di-

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agnostic work up, and finally discuss the routine management of this infection.

CASE REPORT

A 67-year-old African American man with end-stage renal disease on dialysis, heart failure, diabetes mellitus, and history of prior gout, no longer on allopurinol, presented to the University of Miami Hospital in October of 2019 with acute "sharp" pain and swelling of the left elbow for 2 days. These symptoms were first noticed on waking, and initially attributed to positioning during sleep. He also reported difficulty moving his left upper extremity as well as pain on active range of motion. Acetaminophen was tried at home without much relief. The patient denied any associated fever, chills, skin changes, dysuria, or penile discharge. He was evaluated during a routine outpatient Podiatry visit the day of admission and advised to seek medical attention.

His vital signs on admission were: Temp 98.2°F, pulse 59 bpm, BP 107/47 mmHg, and RR 16. On physical exam he was found to have a tender, and mobile mass along the left medial epicondyle (Figure 1) as well as generalized weakness of the left upper extremity. Significant laboratory studies were noted for: WBCs 12.1k/uL with 83.4% neutrophils, C-reactive protein of 35 mg/dL (0-0.5 mg/dL), erythrocyte sedimentation rate (ESR) of 74 mm/hr (0-10 mm/hr), serum uric acid 4.9 mg/dL (3.4-7.0 mg/dL), blood urea nitrogen (BUN) 67 mg/dL (8-23 mg/dL), creatinine (Cr) 6.78 mg/dL (0.40-1.10 mg/dL), lactic acid of 1.7 mmol/L (0.5-2 mmol/L). An X-ray of the left elbow was performed and noted for mild soft tissue swelling along the medial epicondyle, as well as large elbow joint effusion (Figure 2). While in the Emergency Department (ED) he was evaluated for possible acute stroke in the setting of distal left upper extremity weakness. He was ruled out for ischemic incident in setting of a negative non-contrast CT head, which was only notable for chronic microvascular ischemic changes.

Due to the concern for septic arthritis, the patient was admitted to the hospital to start empiric antibiotic treatment with vancomycin IV 500 mg x1, and then 1500 mg daily on HD days, and ceftriaxone IV 1g q24. The following day, he was evaluated by Orthopedic Surgery who performed arthrocentesis and removed 15 cc of turbid, cloudy fluid. Synovial fluid analysis revealed 120k WBCs, 97% neutrophils, 54k RBCs and no crystals. The next day the patient underwent surgical incision and drainage (I&D) where approximately 5 cc of purulent fluid was encountered, and a Penrose drain was placed.

Post-operatively the patient was evaluated by the Infectious Disease consult service and escalated from ceftriaxone to IV cefepime 1g daily after HD on dialysis days. Blood cultures drawn on admission were initially read as Gram-positive cocci on Gram stain. They were later finalized as *N. gonorrhoeae*, beta-lactamase negative in 2/2 sets identified via MALDI-TOF (matrix assisted laser desorption ionization-time of flight) mass spectrometry. Antibiotic susceptibilities were

Figure 1 - Gross appearance of left elbow as seen on day of admission.

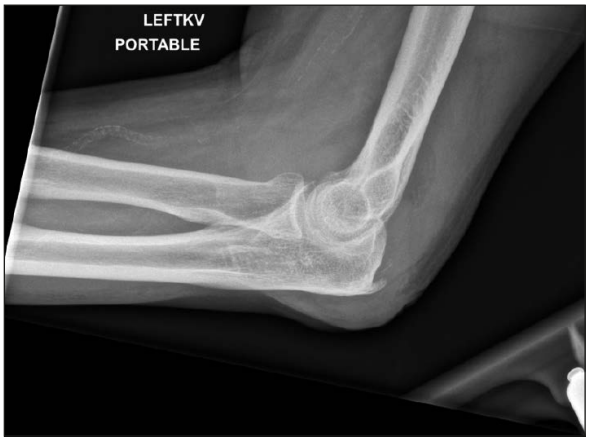

Figure 2 - Lateral X-ray of left elbow with visible effusion.

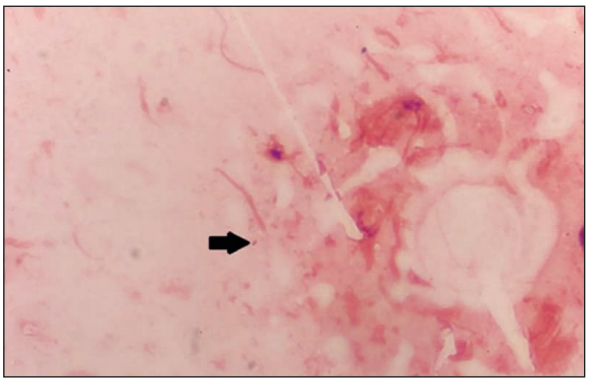

Figure 3 - Gram-stain of synovial fluid with visible Gram-negative diplococci.

not done, as identification was performed at another institution. He was later deescalated to IV ceftriaxone 2g daily (after final speciation) with planned treatment duration of three weeks. He also received a one-time dose of PO azithromycin 1000 mg for both dual gonococcal therapy as well as empiric treatment for chlamydia. He subsequently cleared his blood cultures by hospital day #1. Synovial fluid Gram stain was noted for, "few Gram-negative diplococci", but had no growth at 5 days of culture incubation (Figure 3). Gonococcal cultures of throat and rectum were negative, and serum RPR was unreactive. The patient also tested negative for: HIV by 4th generation testing, as well as hepatitis C antibody. A gonorrhea/chlamydia urine PCR was ordered but was not collected during this admission. The patient was subsequently lost to follow up on discharge. Prior to writing this case report, he was able to confirm via telephone that his pain had completely resolved after finishing his three weeks of IV antibiotics, and that he had regained full range of motion of the left elbow.

DISCUSSION

N. gonorrhoeae is a non-spore-forming Gram-negative diplococcus with its pair's axis in parallel [2]. It is differentiated from other species of Neisseria by fermentation of glucose and not maltose; certain environmental conditions such as: incubation at 35-37°C, adequate moisture, and an atmosphere of 5-10% CO_2 are required for growth [2, 4, 5]. Isolating the organism from rectal or pharyngeal sites can be difficult without the use of selective media such as Thayer-Martin medium [2, 5]. Within the U.S.A, *N. gonorrhoeae* is the 2nd most common reportable disease, with a peak incidence of 468 cases per 100k in 1975; since then, incidence rates have been on the decline due to public health intervention [2]. Currently the highest rates of gonorrhea are seen in young men and women aged 15 to 24, and by racial or ethnic groups, non-Hispanic blacks [2].

In male patients gonorrhea presents as an acute purulent urethritis within days of unprotected intercourse; only around 5% of males are asymptomatic [4]. Disseminated infection can occur within 3 weeks of genitourinary infection, however oropharyngeal infection has a higher association with bacteremia, and DGI has been found within chronic carriers [6]. Classic DGI represents a majority of cases at 60% and presents with the triad of: papular/pustular dermatitis, asymmetric polyarthralgia, and tenosynovitis known as the arthritis-dermatitis syndrome [3, 7, 8]. The arthritis-dermatitis syndrome may be associated with systemic complaints such as fevers and chills, while the second presentation of a localized purulent septic arthritis often lacks systemic complaints [3, 7].

In terms of presentation, 40% of patients will have a monoarthritis, while the remaining 60% are split evenly between an oligoarthritis or polyarthritis [6]. Risk factors include: HIV infection, C5-C8 complement deficiency, having multiple sexual partners, low socio-economic status, SLE, the female sex, and pregnancy [3]. Any joint can be affected in the purulent monoarthritis and oligoarthritis, but large joints are more commonly involved [9]. A 2019 retrospective review of DGI cases in the Northern Territory of Australia found the following joints involved in decreasing order of prevalence: knee, wrist, ankle, elbow, small joints of the hand, small joints of the foot, hip, sternoclavicular and temporomandibular [10]. A 1974 integrated review of DGI cases within the US found the elbow represented 11% of total involved joints, while Birrell et al. found the elbow affected 16% of the time [6, 10].

A majority of available case reports involve predominantly young females with the arthritis dermatitis syndrome. The following represents a curation of case reports with similar epidemiology. Two cases out of Australia are notable for males over 50 years of age, with prior history of gout,

who developed DGI [11]. They differ from our patient in risk factors (travellers to the Philippines with exposure to commercial sex work, or the local population), as well as the number of joints involved and distribution (polyarticular and distal) [11]. Our patient was married, in a monogamous relationship for over 30 years, with no recent sexual contact nor diagnoses of STI (although on further questioning did recall prior treatment for "the clap" at age 19). While our patient had a normal serum uric acid, as well as arthrocentesis findings negative for crystals, his prior history of gout is significant. Patients with both gout and DGI have been found to have longer hospital stays, as well as more complicated clinical courses [10].

There are similar case reports of a monoarthritis presenting with associated bacteremia. In this example a 41-year-old male with pustular skin lesions over foot, as well as left ankle monoarthritis had positive cultures for *N. gonorrhoeae* in both blood and synovial fluid [12]. While both our patient, and the case exhibited bacteremia, they differed in: the site of arthritis (proximal vs distal respectively), absence or presence of skin findings, as well as the result of synovial culture. A case of purulent wrist arthritis in a 57-year-old male who has sex with men (on pre-exposure prophylaxis) had a similar presentation to our patient. Both had hyperacute onset of symptoms overnight, with similar arthrocentesis findings, >100k WBCs, on cell count [13]. However, that patient also had positive synovial fluid culture results, but negative blood cultures [13].

Blood cultures are only positive in less than 1/3 of cases of gonococcal arthritis; when blood culture is positive, it is usually seen in the arthritis-dermatitis syndrome [7]. The Belkacem et al. retrospective analysis found positive blood cultures in 4/21 (19%) patients, while Birrell et al. found blood cultures positive in 25/106 (23.6%) patients [10,14]. Unfortunately, there is no modern data in regard to prevalence of positive blood cultures in patients with monoarthritis. Keiser et al., in a retrospective analysis of 30 patients with gonococcal arthritis from 1963-1967, found only 6 to have monoarthritis; none of which had documented bacteremia, but all of which were found to have gonococci demonstrated in joint effusion (Group A) [15]. Similar retrospective analysis such as Brogadir et al., from 1967-1977, found 29/41 (70.7%) patients with monoarthritis to be culture positive; however, they did not distinguish between those who had positive blood, mucosal, or synovial fluid cultures [16]. The number of patients with monoarthritis and bacteremia from that study can be generalized to be very low, if not zero, as only 2/63 (3.2%) of patients with arthritis (Groups II + III), regardless of joint number, had positive blood cultures [16].

Given the fastidious nature of *N. gonorrhoeae*, in cases of negative culture data, it is recommended to proceed with testing of additional sites such as: rectum, throat, synovial fluid or skin lesions [14]. Up to 80% of DGI cases can have *N. gonorrhoea*e isolated from such sites despite being asymptomatic [9,17]. Such additional testing may be necessary in certain patients. A 2014 case report involving a 24-year-old HIV + patient with gonococcal arthritis of wrists and ankle, only identified the organism on pharyngeal swab; this was also true for one patient in Belkacem et al. [14, 18]. The value of PCR cannot be understated. Without PCR testing of mucosal sites, Birrell et al. would have been unable to identify 25 out of their 76 proven cases of DGI [10].

The treatment duration of DGI has not been well studied. The 2015 CDC STI Treatment Guidelines recommend a minimum duration of 7 days for the arthritis-dermatitis spectrum; first-line treatment is dual therapy with ceftriaxone 1 g IM/IV q24 + PO azithromycin 1g as a single dose [19]. The rational being empiric treatment for chlamydial coinfection, and to help prevent cephalosporin resistance [19]. Once the patient has improved, and susceptibilities have returned, this can be changed to an oral regimen in 24-48 hours [19]. However, final antibiotic duration varies on a case-by-case basis. Belkacem et al. found the median treatment duration of DGI to be 14 days, and the final ceftriaxone dosage to vary according to the treating physician, as well as patient complications [14]. Some case reports, such as Vidaurrazaga et al., with a purulent gonococcal arthritis treated for up to 4 weeks [13]. The decision to treat our patient with a 3-week course of parenteral therapy was made on the basis of his medical comorbidities, as well as the presence of a purulent arthritis, which may require extended treatment durations [3]. In regard to the question of surgical intervention, this is not universally indicated as patients generally have favourable outcomes when started on appropriate antimicrobial therapy [3]. Our

patient was also advised on discharge to inform his wife of his diagnosis. Sex partners are often asymptomatic, and per CDC guidelines any sex partner, within 60 days of symptom onset or diagnosis, should be tested and receive dual treatment. If the last sexual encounter was greater than 60 days ago, then the most recent partner should be treated [19].

In conclusion, DGI represents a less common form of septic arthritis within the United States of America. It is usually associated to the younger, sexually active population, and the bacteria is often hard to culture. The condition manifests in two unique presentations, with a septic monoarthritis not only being less common, but also less likely to be associated with bacteremia. Clinicians must have a high degree of suspicion in patients who present with an acutely, painful and swollen joint for these reasons. Active discussion between the health care provider, as well as the surgeon, and microbiology lab is useful to help increase diagnostic yield. This case of DGI associated with positive bacterial blood cultures, as well as positive synovial fluid Gram stain in an older individual with monoarthritis, was thus a unique presentation in an otherwise old disease process.

Author contributions

M.J.P. was involved in direct patient care and wrote the manuscript. J.A.G.Z edited the manuscript and performed critical revision. All the authors have discussed, read and approved the final manuscript.

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No potential conflict of interest was reported by the authors.

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