Septic arthritis and reactive arthritis comparison

Septic infectious arthritis and reactive arthritis are two arthritic disorders that result from an infection. Though they both are related in their etiology and in their characteristic of causing arthritic joints, each of them are actually different in the way the infection triggers the condition. The main difference between the two conditions may be further clarified with the examination of the terminology used for each.

Origin of Terminology

Septic arthritis derives its name from the term sepsis which pertains to the systemic compromise due to the spread of infection[1]; this is the reason why the term is at times used interchangeably with infectious arthritis. Reactive arthritis was previously known as " Reiter's Syndrome" named after the late German physician Hans Conrad Julius Reiter who was instrumental in the identification and description of the condition.[2]The term " Reiter's syndrome" has lost popularity due to the exposure of Reiter's history as a Nazi party member during his prosecution in the Nuremberg trials as a war criminal because of his alleged participation in the forced human experimentations in the Buchenwald concentration camp; this urged a group of doctors to campaign for the renaming of term " Reiter's syndrome" into " reactive arthritis" back in 1977.[3]The condition may also be known as arthritis urethritica, polyarteritis enterica, or venereal arthritis. (1) The term arthritis urethritica was coined due to its tendency to occur after a genitourinary infection, (2) the term polyarteritis enterica was coined due to its tendency to affect multiple joints and its tendency to occur after a gastrointestinal infection, and (3) the term venereal arthritis was coined due to the tendency of the condition to occur after a known venereal disease infection. The main difference between reactive arthritis from septic arthritis

is that septic arthritis caused by the infection of the joint. However, reactive arthritis is not caused by an infection to the joint itself, but is rather an autoimmune response in reaction to an infection on another part of the body. Each disorder will be discussed further in depth in this chapter.

Overviews, Microbiology, and Prevalence

Septic Arthritis

Septic arthritis is an infection resulting in an arthritis characterized by purulent invasion and intense pain at the infected joint.[4]Aside from being interchangeable with the term “ infectious arthritis,” this condition may also be known as suppurative arthritis due to its characteristic of producing purulent substances or pus, and may also be known as “ bacterial arthritis,” even though the condition may at times be of fungal or viral origin instead of the commonly bacterial origin. The causative infectious agent in septic arthritis can spread to the joint from other previously infected areas of the body. The infection may sometimes only affect a single joint without affecting other parts of the body, but the infection may still spread to other body parts. Septic arthritis commonly affects the knee or wrist, and may also affect other joints such as the ankle, hip, elbow, shoulder, and shoulder. The infection infiltrates and damages the joint causing severe pain, suppuration, heat, and swelling. This severe form of arthritis also develops along with the sudden onset of fever, chills, and joint pain.[5]On the occasion that the sufferer of some forms of septic arthritis do not seek rapid medical attention for diagnosis and treatment, the joint may incur irreversible and permanent damage and in a period of days. Therefore, the situation should be regarded as a medical emergency.

Gonococcal arthritis is the most prevalent form of septic arthritis in the United States[6]. This class of septic arthritis is less prevalent in other areas of the world such as Western Europe where it is presently uncommon. The causative organism behind this form of the condition is the gram-negative diplococcus bacteria called Neisseria gonorrhoeae which was most likely spread to the joint systematically due to disseminated gonococcal infection (DGI). This specific condition can be manifested as either arthritis-dermatitis syndrome which is a bacteremic infection accounting for sixty percent of gonococcal arthritis cases, or it can be manifested as an arthritic infection localized to a single joint which accounts for the remaining forty percent of cases.[7]

Reactive Arthritis

Reactive arthritis is an autoimmune condition caused by the body’s immune response to an infection. The causative infection is not located at the affected joint itself (cross-reactivity).[8]The triggering infection is usually or often already in remission by the time the patient presents with arthritic symptoms, thus making it difficult to ascertain the initial cause. Cultures taken from the synovial fluid of the joints affected by reactive arthritis will characteristically yield negative results indicating the cause is not a direct infection to the joint, but instead may be plausibly due to the over-stimulation of the autoimmune response or by the depositing of bacterial antigens in the joints by an unknown manner. Though the mechanism of reaction from the infection is still unknown, it is said that reactive arthritis often manifests within one to three weeks after a known infection.

Microbiology of Arthritis

The etiology of septic arthritis is commonly bacterial in nature– mycobacterial, viral, and fungal arthritis occur in rare cases.[9]The pathogen responsible for septic arthritis must reach the synovial membrane of the joint. The micro-organisms are usually carried to the joint by the bloodstream from an infectious source such as wound infections and abscesses located elsewhere on the body, introduced by skin lesions or trauma that penetrates into the joint, or by extension of the infection from adjacent body tissue such adjacent soft tissue infections or bones suffering from an osteomyelitic condition. Being the most common cause of septic arthritis, there are various strains of bacteria that may be the culprit behind this condition. Staphylococcus aureus is the common causative pathogen in adults, while streptococci is the second-most likely causative pathogen in adults. [10]Neisseria gonorrhoea is the most prevalent causative microorganism in young adults, although this is now thought to be rare in Western Europe. [11]Moreover, Haemophilus influenzae was the most prevalent causative pathogen in children but is now declining in areas where haemophilus vaccinations have been introduced.[12]Escherichia coli (E. coli) are the most likely causative micro-organism among the elderly, the seriously ill, and users of intravenous drugs. Salmonella, brucella, and tuberculosis are the causative pathogens behind septic spinal arthritis.[13]Pseudomonas aeruginosa, which is the bacterium responsible for endocarditis, has also been identified as a causative pathogen for septic arthritis in children who have suffered a penetrating wound directly to the joint’s.[14]

Reactive arthritis may also be caused by bacterial infection. It is triggered by a recent preceding infection; the most common culprit in the United States would be the genital infection Chlamydia trachomatis. The bacterium known as Ureaplasma urealytium, which is a pathogen of the urinary tract, is also known to trigger the condition. The condition may also be triggered by bouts of gastrointestinal infection or food poisoning from Salmonella, Shigella, Yersinia, and Campylobacter, which are all enteric bacteria genera.[15]The infection is not located in the ailing joint, and may no longer present elsewhere on the body by the time the reactive arthritis develops. Other microorganisms may still be behind a case reactive arthritis but the evidence indicating them to be the actual cause is still circumstantial.[16]

Prevalence of Septic Arthritis and Reactive Arthritis

Young children, older adults, and individuals with artificial joints are at greater risk than the general population to develop septic arthritis. Those with artificial joints may be infected with different organisms in comparison with the general population, and may present with slightly different symptoms.[17]In general, if an individual affected by septic arthritis seeks medical attention and treatment within a week after the first symptoms appear, they will most likely make a full recovery. On the other hand, individuals aged twenty to forty years of age are more likely to be affected by reactive arthritis. Men are more likely to be affected by the condition than women. Caucasian people are more likely to be affected than individuals of African-American descent; this is due to the frequent occurrence of the HLA-B27 gene within the white population.[18]Patients infected with the Human Immunodeficiency Virus (HIV) also have an increased risk of developing this

condition. Arthritis makes it extremely difficult for affected individuals to remain physically active as many individuals become bound to their homes. These individuals will increase their risk for obesity, depression, and heart disease due to their inactivity and anxiety from worsening disability.[19]

The Immune System's Role in Arthritis

Septic arthritis and reactive arthritis are both conditions that involve the immune system's autoimmune response. However, septic arthritis is the result of the body's normal immune response to an actual infection present at the ailing joint. On the other hand, reactive arthritis is the result of the immune system's abnormal immune response to what it believes is a present infection at the joint but is, however, absent or is an infection on a part of the body aside from the joint; this mistaken response which may be due to misinterpretation or oversensitivity is considered abnormal and is classified as an autoimmune disease. An overview of the human body's immune system can better explain the mechanism by which these two conditions come into fruition.

Overview of the Human Immune System

The human immune system is an intricate defense system designed to specifically defend against the many different types of pathogens. Pathogens are any organism, usually a live organism, which can cause disease. Pathogens include bacteria which are single celled organisms capable of living outside the body, protozoa which are single celled organisms that live and are spread through water, pathogenic proteins which are multi-celled organisms that can only reproduce in another more complex living organism, fungi which are plant-like multi-celled organisms that take nutrition from

other living organism such as plants and animals, viruses which are actually multi-celled organisms that invade and reproduce inside another microbial organism, and parasites which are full complex organisms which feed off the nutrients of another complex organisms and which tend to live in the intestinal tract or bloodstream of the human body. In theory any one of these organisms can cause septic arthritis or reactive arthritis, but parasites are very unlikely to cause these conditions and bacteria are the most prevalent culprit. In the event that a pathogen passes through the body's outer physical barriers, such as mucus and the skin, and penetrates into the internal structures of the human body, the immune system kicks in.[20]

The human body's immune system response is composed of the non-specific response and the specific response. Non-specific response consists of the complement response, the interferon response, fever response, and the inflammatory response. The complement response is conducted by the activation of complement proteins which bind with pathogens with lipid layers, such as bacteria, to destroy their lipid layers allowing water to shift into the pathogen to drown them, or by the activation of macrophages which engulf the invading pathogen. Interferon response is conducted by a cell that has been infected with a virus. The infected cell produces a chemical protein known as interferon which will bind to uninfected cells preventing the virus from readily infecting them. The fever is conducted in response to toxin present in the body which may or may not be produced by bacteria; pyrogen, which is a chemical also known as Interleukin 1, is responsible for resetting and increasing the body's temperature and may cause gradual joint degeneration. Inflammatory response is the result of the release of

histamines in response to tissue damage or infection; histamine is capable of causing capillary dilation which allows for greater capillary permeability, which in turn allows for white blood cells to gather at an infected site, for fluid to create inflammation and swelling at the site to create cushioning, and for an increase in temperature at the affected site. The inflammatory response and fever response are the main responses responsible for the signs and symptoms present during both septic arthritis and reactive arthritis. The human body’s specific immune response is mostly managed by the different types of leukocytes which are better known as white blood cells (WBCs). White blood cells can be classified as eosinophils, macrophages, and lymphocytes. Eosinophils serve to produce interleukins which are chemicals that serve a vital role as immune system neurotransmitters that relay messages between the many different white blood cells to ensure that they work together and cooperate as an effective system against pathogens and to ensure that the immune system does not attack the body’s own cells.

Macrophages are also known as phagocytes, meaning they are capable of conducting phagocytosis which is the process of engulfing, killing, and digesting of pathogens and cellular debris; after digestion, the degraded pathogen is turned in peptides which can act as antigens. The antigens produced by the macrophages are then carried by the macrophages into the lymph nodes where the helper T-cells utilize them to signal the B-cells to create antibodies. The last type of white blood cell is collectively called lymphocytes. The lymphocytes can be further subdivided into B-cells, NK cells, and T-cells. B-cells are responsible for creating immunoglobulin, or antibodies, that are specific to a certain pathogen as identified by their

antigen. Antigens are protein peptides that exist on the outer surface of pathogens; these antigens are used to differentiate and identify cells and pathogens that are foreign to the host body. The helper T-cells who receive the antigen produced by the macrophage produce lymphokines which instruct the B-cells on the production of the specific antibody. When the B-cells produce the specific antibody, B plasma cells begin to create more copies of its own self to create more antibodies. These antibodies, when released into the bloodstream, will then proceed to bind with the antigens on the actual pathogens to signal the killer T-cells to attack these foreign organisms. The B-cells will also produce B memory cells, which are inactive B plasma cells. These inactive B memory cells last longer than their active B plasma cell counterparts, which last for about five to seven days; the presence of the B memory cells in the bloodstream allows them to respond faster to secondary exposures to the same pathogens in the future.

Natural killer (NK) cells are cells that are activated by interferons, which interfere with virus replication, and chemicals produced by macrophages which have ingested a virus. Natural killer cells engulf virus pathogens to prevent them from reproducing until a killer T-cell is developed to kill the contained virus. T-cells are responsible for identifying and destroying specific pathogens and consist of helper T-cells, killer T-cells, memory T-cells, and suppressor T-cells. Helper T-cells receive antigens from macrophages which have ingested a pathogen and instruct the B-cells to produce antibodies which will in turn signal the killer T-cells. Killer T-cells are responsible for finding and destroying pathogens by injecting them with cytotoxins. Memory T-cells are derivatives of helper T-cells which circulate around the body and

perform the same functions as their parent cells. Suppressor T-cells are responsible for slowing down and deactivating the immune response once the foreign organisms and pathogens have been eliminated.

What Goes Wrong with the Immune Response

Septic arthritis is really the result of the damage caused by the invading organisms and the normal immune response of the body to the infection in that specific joint or set of joints. In septic arthritis, the macrophages ingest a pathogen that has infected a joint. The macrophages then degrade the pathogen into antigens and relay them to the helper T-cells in the lymph nodes. The T-cells then create antibodies specific to the antigens on the pathogens. The inflammatory response also releases histamine which increases the blood flowing into the affected joint to cause swelling, redness, and pain, which in turn causes stiffness and difficulty moving in the joint to cause arthritic symptoms. Meanwhile, the invading organisms cause damage to the joints. Such damage incurred by the joints may be irreparable if medical attention is not immediately sought after. Suppuration which is the result of the white blood cells' fight against the invading microorganisms may also contribute to the arthritic condition. The fever response that triggers the release of pyrogen may also contribute to the degeneration of the joint. Although the exact etiology of the condition is still uncertain, unlike septic arthritis, reactive arthritis is caused by a faulty immune system response. The condition occurs in the absence and aftermath of an actual infection that is located in a part of the body aside from the affected joints.

Two theories exist for the purpose of explanation. The first theory speculates that there are antigens deposited in the affected joint; the second theory

speculates that the immune system has become faulty in detecting the actual presence or absence pathogens and creates an exaggerated immune response in the joints even though there is no infection or the infection is located elsewhere on the body. These theories causes the immune system to believe in a current infection and will release histamine and pyrogen to produce inflammation and fever. The inflammation will again cause the joint(s) to be stiff, painful, and immobile–all of which are arthritic symptoms. The absence of an actual pathogen may mean that the inflammation and fever will last for an uncertain length of time but the absence of an actual pathogen will also mean that there is little to no actual damage to the affected joint.

Distinguishing Characteristics

There are over a hundred forms of arthritis, all of which involve some degree of inflammation, pain, and immobility of an affected joint.[21]The many different types are the result of several different causes and these causes may point towards what distinguishes each form of arthritis from the other. Osteoarthritis is a degenerative joint disease and is the most common presentation of arthritis; it can result from trauma to the joint, direct infection to the joint, daily wear and tear, muscle strain, fatigue, or simply from old age. Other forms of arthritis such as rheumatoid arthritis and psoriatic arthritis are attributed to autoimmune diseases. The main thing that differentiates septic arthritis and reactive arthritis from other types of arthritis is that they are mainly results of infection. This means that they will most likely present with fever. The main difference between reactive arthritis from septic arthritis is that the latter is when infection of the joint itself is the

cause of the suppuration leading to the arthritis. However, reactive arthritis is not caused by an infection to the joint itself, but rather the inflammation is caused by an autoimmune response to an infection located on another part of the body; this is known as cross reactivity.[22]Septic arthritis will most likely affect an individual joint (monoarthritic) if only one joint is infected. Nonetheless, the possible systemic nature of reactive arthritis allows it to most likely affect several joints (polyarthritis). Septic arthritis will also most likely yield positive culture results and present with suppuration, unlike reactive arthritis which may not yield the same results due to the absence of an infection at the actual site of arthritic symptoms.

Techniques and Research

Diagnostic Techniques

The diagnosis of arthritis in general is made through a clinical examination that is conducted by a duly licensed and qualified health professional, who may require other examinations such as blood tests and radiology to create a differential diagnosis for the suspected arthritis. However, radiographs (x-ray) and sonographs (ultrasound) are mostly used only to assess and monitor the severity and progression of the condition. Magnetic resonance imaging (MRI) is also an effective diagnostic tool.

The history of the current disorder may guide diagnosis; some significant markers include: speed and time of onset, pattern and symmetry of joint involvement, aggravating and relieving factors, quality and severity of pain, and other systemic symptoms. An example of this is the use of pain patterns; for example, rheumatoid arthritis is generally worse in pain and stiffness during mornings, but in comparison, osteoarthritis is usually aggravated

after strenuous activities such as exercise. There is no diagnostic test to completely rule out septic arthritis; however, it should be considered whenever a patient presents with rapid onset of joint pain. Usually it only affects one joint (monoarthritis); however, several joints can be affected simultaneously in cases involving staphylococcus or gonococcus infections. The affected joints may present with pain, swelling, redness, and warmth, often affecting joints in the limbs instead of deep joints such as the hips or shoulders. A fever of above 38. 5 degrees Celsius and history of septic arthritis may also be indicative of the condition.

The Gram stain can rule towards a septic arthritis diagnosis but cannot rule it out.[23]Gram stain and culture of fluid from the joint and blood test serums can also rule towards a positive diagnosis when yielding elevated neutrophils, erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), and WBCs. Being a sort of systemic autoimmune disorder, reactive arthritis can be expected to cause polyarthritis which is a multiple joint arthritic condition. The affected joints may also present with pain, swelling, redness, and warmth. Swabs taken from the urethra, cervix, stool, urine, or the throat can be cultured in an attempt to identify the causative organisms. Blood tests and synovial fluid cultures may also be done to reveal elevated erythrocyte sedimentation rate (ESR), and CRP to support the diagnosis. A blood screening may be done to identify the presence of the gene HLA-B27, which is present in an estimated eighty percent of all patients suffering from reactive arthritis.[24]

Treatment Techniques

Treatment for arthritis in general includes lifestyle changes such as exercise and weight control, physical therapy, orthopedic braces, and medications. The main goal of treatment for both septic and reactive arthritis is to identify and eradicate the causative pathogen with the appropriate antibiotics. In the meantime, the treatment is symptomatic. Medications such as antibiotics, NSAIDS, steroids, and analgesia can help decrease inflammation in the joint resulting in decreased pain and hampered joint damage.[25]Reactive arthritis may require immunosuppressant medications in addition to the above medications to reduce oversensitivity of the immune system. Extreme pain, redness, and swelling may require drainage by needle puncture to alleviate these signs of inflammation. Surgical replacement of the joints may also be needed in eroding types of arthritis such as certain strains of septic arthritis. Surgical debridement or arthrotomy is usually indicated for infections involving prosthetic joints. Individuals for whom surgery is contraindicated will have to undergo long-term trial antibiotic therapy.[26]

Analysis

Septic arthritis and reactive arthritis are two arthritic conditions that result from the human immune systems response to infection. Septic arthritis is the result of an infection on the arthritic joint; if one joint is infected, only one joint shall be suffer arthritic symptoms. Reactive arthritis is the result of an exaggerated immune response to an infection that does not involve the arthritic joint; this condition may be systemic and may affect multiple joints. Septic arthritis and reactive arthritis may both be caused by any pathogen including bacteria, mycobacterium, virus, and fungi; however, bacterial infections are the most prevalent culprit. Since both septic arthritis and

reactive arthritis are the result of an infection, what distinguishes them from most other forms of arthritis is that both of them may present with fever and some degree of suppuration in addition to the usual symptoms of inflammation which include pain, swelling, redness, and warmth at the joint. Septic arthritis will however prove to be the more destructive of the two conditions because it directly infects the joint and may cause permanent and irreversible damage. Since both of the conditions are the result of an infection, both of their treatments include antibiotics, which may usually be given intravenously, and medications that may deal with the symptoms of pain and inflammation may be given. Orthopedic bracing for support and surgical intervention for damaged joints may also be needed in certain cases.