Diagnosis and Differential Diagnosis

7

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Abstract

Knee osteoarthritis is a disease that causes structural and functional disorders of the joint due to damage to normal tissues; early diagnosis is difficult because it has various causes and vague symptoms. Even if it is detected early, the disease still needs further examination because of the lack of effective diagnostic tools for early diagnosis. To diagnose osteoarthritis, clinicians must systematically perform diagnostic procedures from detailed history taking to meticulous and thorough examination. Detailed history taking is important and should also include patient information such as ethnic information, age, sex, height, weight, and symptoms. Physical examination including inspection, palpation, and basic function examination is also performed. Plain radiographs are the basic imaging examination, and computed tomography and magnetic resonance imaging can be considered as necessary. Blood examination including white blood cell count, C-reactive protein level, erythrocyte sedimentation rate, rheumatoid factor level, uric acid level, and cartilage oligomeric matrix protein level; joint fluid analysis; and bone scan can be helpful for diagnosis and differential diagnosis. If other diseases causing arthritis are misdiagnosed as osteoarthritis, omitted or unnecessary treatment may adversely affect the patient, so the differential diagnosis should be considered. Therefore, prior to diagnosis of osteoarthritis, the possibility of rheumatoid arthritis, seronegative spondyloarthropathies, infectious arthritis, crystal-induced inflammatory arthropathy, spontaneous and secondary osteonecrosis, and other diseases should be considered.

Keywords

Knee osteoarthritis · Diagnosis · Physical examination · Alignment · Rheumatoid arthritis · Infectious arthritis · Arthropathy Osteonecrosis

7.1 Diagnosis

Knee osteoarthritis (OA) is known to be the clinical and pathological outcome of various disorders that induce structural and functional failure of the synovial joint [1]. The various causes of OA include disorders of the articular cartilage, ligaments, and joint capsule, synovial membrane inflammation, and subchondral bone calcification

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Table 7.1 The American College of Rheumatology criteria for the diagnosis of knee OA

Using medical history and clinical examination
Pain in the knee and three of the following
1. Age > 50 years
2. Morning stiffness <30 min
3. Crepitus on active motions
4. Bony tenderness
5. Bony enlargement
6. No palpable warmth of synovium
Using medical history, clinical examination, and radiographic findings
Pain in the knee and one of the following
1. Age > 50 years
2. Morning stiffness <30 minutes
3. Crepitus on active motions and osteophyte
Using medical history, clinical examination, and laboratory findings
Pain in the knee and five of the following
1. Age > 50 years
2. Morning stiffness <30 min
3. Crepitus on active motions
4. Bony enlargement
5. No palpable warmth of synovium
6. ESR <40 mm/h
7. Rheumatoid factor < 1/40
8. Synovial fluid signs of osteoarthritis

ESR erythrocyte sedimentation rate

[2], and it occurs when the dynamic equilibrium between joint tissues break down and the self-repair system is overwhelmed [3]. Progression of OA may cause pain, physical disability, and psychological distress [4, 5].

Knee OA diagnosis is based on the history of the condition and clinical features (Table 7.1) [6]. Radiological testing such as X-ray and MRI is essential for the degree of involvement and diagnosis of the disease when evaluating patients with suspected osteoarthritis in the knee joint. Clinical findings and physical examination are important. Information about patient's ethnics, age, sex, body mass index (BMI), traumatic onset, difficulty in descending the stairs, and effusion should be also collected. Furthermore, radiologic findings and clinical features such as fixed flexion deformity, restricted flexion range of motion, and crepitus are known to be vital in predicting knee OA, with a sensitivity and specificity of 94% and 93%, respectively [7].

Knee OA can be diagnosed clinically and radiologically as well as based on diagnostic criteria such as the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) diagnostic criteria [8]. The EULAR diagnostic criteria present three symptoms (persistent knee pain, limited morning stiffness, and reduced function) and three signs (crepitus, restricted movement, and bony enlargement), and patients showing all six symptoms and signs can be 99% accurately diagnosed with knee OA.

Knee OA can be classified as primary or secondary depending on the etiology. It may be induced by secondary factors such as obesity, fracture around the knee, ligament injury, and inflammatory or genetic factors; when these factors stimulate the progression of OA, such cases are considered secondary OA [9].

7.1.1 Evaluation and History Taking

The most basic aspect of diagnosing knee OA is detailed history taking. Because not all radiologic tests can be performed on all patients, knee OA cannot be diagnosed via radiologic assessment alone. It is also possible that clinical and radiological findings might be inconsistent; therefore, the cause of the symptoms should be determined, and differential diagnosis should be performed based on detailed history taking and clinical findings.

7.1.1.1 Patient Information

The first process involves obtaining patient information. Identifying the patient by confirming whether the patient's name, age, and ID number match the records is the most basic step in ensuring patient safety. Once the patient is identified, the patient's job, ethnics, and lifestyle should be additionally examined. Patients who engage in high-intensity manual labor for an extended period would be at an elevated risk for premature joint degenerative changes. Furthermore, kneeling and squatting with heavy lifting can accelerate the progression of OA.

7.1.1.2 Chief Complaint

It is important to obtain information on the specific site of pain: whether it is medial or lateral, the onset of the pain: gradual or sudden, the nature of the pain: focal or radiating, when the symptom exacerbates: whether the symptom improves with rest, whether it is exacerbated when walking, and the presence of swelling or instability. Chronic joint effusion may be observed in meniscus tear or knee OA, and inflammatory arthritis such as rheumatoid arthritis or goutic arthritis should be suspected when knee joints are repeatedly swollen.

7.1.1.3 History Taking

The main symptom of knee OA is pain. Pain on the knee occurs after a weight-bearing activity, and in the early stages, it improves with rest. This characteristic differentiates it from inflammatory arthritis, in which pain usually occurs early during an activity, and once arthritis progresses, pain does not easily improve with rest [10]. There may be persistent pain even at rest and at night with severe joint destruction or with acute inflammation.

The site of OA can be in the tibiofemoral or patellofemoral joint [11]. Patients with OA involving only the patellofemoral joint complain of pain around the patella, and the pain is typically exacerbated when climbing up and down the stairs. Arthritis affecting the tibiofemoral joint is more symptomatic and often causes walking dysfunction. Crepitus and swelling can be observed in the knee as arthritis progresses. When meniscus tear or loose body in the joint is also present, motor restriction or joint locking can also be observed. Disuse atrophy of the quadriceps femoris muscle can be developed with prolonged OA. Weakened quadriceps femoris, pain, and joint degeneration may cause the knee to give way. Substantial cartilage lost in one tibiofemoral compartment may also show progressive changes in the joint axis, such as genu valgum or genu varum (Fig. 7.1).

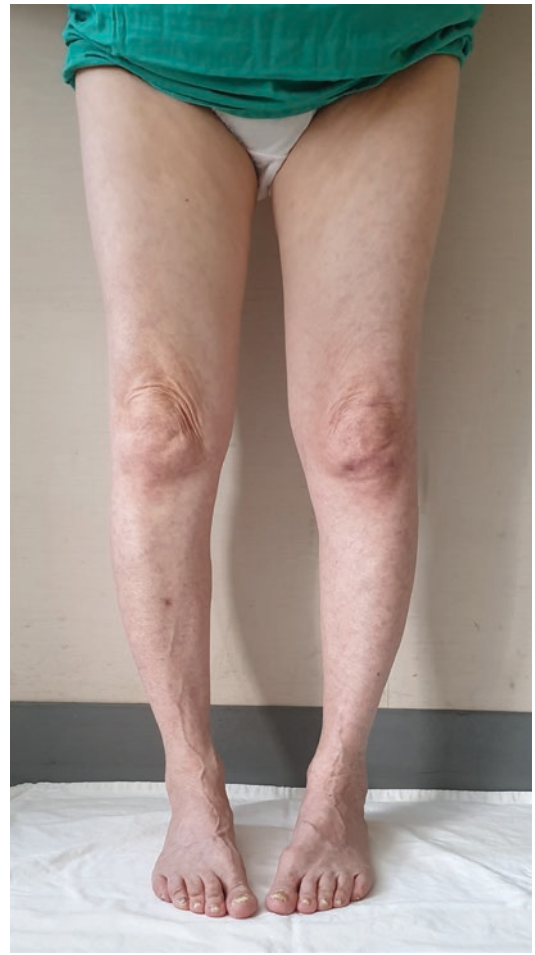

Fig. 7.1 Varus alignment shown in a patient with medial compartment osteoarthritis

7.1.2 Physical Examinations

7.1.2.1 Inspection

Clinicians should not solely rely on radiologic findings when examining a patient. Similar to history taking, physical examination is crucial in the diagnosis of knee OA [12, 13]. When performing physical examination, the entire knee should be exposed, and the anterior, medial, lateral, and posterior aspects of the knee should be visually inspected. The patient should be in an upright position with the patella facing forward

and should be 2 feet apart with the toes pointing forward. While standing, the alignment of the patient's legs should be examined. The patient should be asked to walk to examine the presence of an antalgic or abnormal gait caused by neuropathy as well as lesions in any other parts, such as the spine, hip, and ankle. A gait cycle is broadly divided into the stance and swing phases, and most abnormal findings are observed in the stance phase, from the contact of the heel on the ground to the lifting of the tip of the toe off the ground.

Varus thrust refers to a lateral knee joint motion caused by increased varus in the stance phase, and OA with associated medial compartment erosion is known to be the most common cause [14]. Valgus thrust, the opposite of varus thrust, refers to a medial knee motion during weight-bearing; when valgus thrust occurs in both knee joints, individuals walk with their legs curved outward to prevent the knee joints from clashing into each other. Valgus thrust rarely occurs compared to varus thrust, and it contributes to the onset or progression of lateral OA by increasing the load transmitted onto the lateral tibiofemoral compartment of the knee [15].

To measure the range of motion of the knee joint, the patient should be asked to lie down on an examination bed, and the lateral angle between the thigh and lower leg is measured using a goniometer. An approximately 5-degree hyperextension is normal, but restrictions in extension or flexion compared to the healthy knee may indicate internal joint abnormalities such as meniscus tear or OA.

7.1.2.2 Palpation

Because the knee joint has thin soft tissue except on its posterior aspect, abnormalities can be palpated unless in cases of severe obesity. During palpation, a clinician should screen for bony tenderness around the joint line, examine whether a crackling or grinding sound (crepitus) is heard when the knee is flexed or extended or during weight-bearing, and screen for any bony enlargement in the joint line [5]. Particularly, tenderness and osteophyte in the joint line are serious indications of OA diagnosis. Patellofemoral joint line tenderness is usually observed in patients with patellofemoral pain. Joint effusion refers to increased joint fluid within the joint, and it indicates a problem within the joint such as synovitis. Though a joint effusion is commonly observed in meniscal tear or OA, it may be also caused by inflammatory arthritis, hemarthrosis, or abscess due to infection.

7.1.2.3 Basic Function Examination

Muscle power or joint balance and stability should be performed to assess muscle strength and proprioception. In particular, quadriceps weakness is a characteristic feature of knee OA. Reduced quadriceps strength is one of the initial clinical findings observed before the patient experiences symptoms or disability from knee OA, and it plays an important role in disease development [5].

7.1.2.4 Image Finding

Radiological findings are used to confirm OA and examine the involved compartments and degree of progression. However, the severity of the pain and joint injury on radiological findings are not always consistent. Plain radiographs for evaluating the knee OA include a supine knee anterior-posterior, lateral view, and merchant view which visualize patellofemoral joint. Rosenberg view which is posterior-anterior radiograph with weight-bearing and 45 degrees of knee flexion is helpful for detecting an early chondral loss in the medial and lateral femoral condyle. Standing whole leg radiographs should be taken to assess alignment abnormalities of the lower limbs. For OA, plain radiographs in the weight-bearing position may be more beneficial, and the findings show typical joint space narrowing in the medial, lateral, and patellofemoral compartments, subchondral bone sclerosis, subchondral bone cyst, osteophyte in the joint edges, and irregular joint surface [9, 16]. The Kellgren–Lawrence classification system, which classifies the severity of arthritis based on radiographic findings, is widely used. MRI can detect early arthritic changes as well as abnormalities of the articular cartilage, subchondral bone, meniscus, and other soft tissues. Detailed radiologic assessment and radio-

logic staging were described in the previous chapter.

7.1.2.5 Alignment of the Knee Joint

The alignment of the knee joint can be evaluated in the coronal and sagittal planes, and whole leg weight-bearing radiographs are generally used for this purpose. In the standing position, a neutral alignment of the knee joint in the coronal plane places the weight-bearing axis on the center of the knee joint, but deviation of the center of the knee joint from the weight-bearing axis leads to a malalignment on the coronal plane. Varus alignment shows a lateral displacement of the center of the knee joint from the weight-bearing axis, while valgus alignment shows a medial displacement of the center of the knee joint from the weight-bearing axis. In varus, there is increased weight placed on the medial compartment; therefore, the risk for medial compartment arthritis is increased, while in valgus, there is increased weight placed on the lateral compartment and thus the risk of lateral compartment arthritis is elevated [17, 18]. Many patients with OA who complain of pain show varus alignment. The alignment angle can be deviated from the normal without symptoms in young adults, but increasing degree of misalignment facilitates joint subluxation and may accelerate arthritis due to abnormal increase of loading.

In a normal alignment of the knee joint in the sagittal plane, the center of the knee joint is immediately behind the weight-bearing axis. Flexion contracture occurs when the center of the knee joint is anterior to the weight-bearing axis, while recurvatum occurs when the center of the knee joint is posterior to the weight-bearing axis. In such misalignment, the posterior joint capsule and ligament cannot act to support the body weight, which would cause difficulty in maintaining posture and cause a dysfunction of normal kinematics.

7.1.2.6 Laboratory Findings

Blood test results are generally normal in knee OA and they are mostly used to exclude other conditions, such as infection, gout, and rheumatoid arthritis, as opposed to diagnosing knee OA itself. Parameters such as white blood cell (WBC) count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and rheumatoid factor (RF) may be conducive to differential diagnosis. Joint fluid analysis examines the joint fluid in the knee joint via aspiration. In knee OA, results generally indicate no inflammation, with a WBC (mostly monocytes) count of below 200 mm^3. A recent study has reported the potential utility of cartilage oligomeric matrix protein (COMP) as a diagnostic and prognostic biomarker of knee OA. The median serum COMP levels were significantly higher in the knee OA group than in the control group, and had positive correlations with age, BMI, and pain scores, suggesting their usefulness in the diagnosis of knee OA. However, COMP levels were not significantly correlated with the radiological grade and were high during the first 3 years of the disease, suggesting a limitation [19, 20]. Matrix metalloproteinases suppress chondrocyte synthesis of type II collagen and aggrecan, which is required to restore the extracellular matrix. It is also found during the turnover of osteoarthritic joints, fragments of extracellular matrix molecules, and other degradation products of cartilage metabolism and the cartilage matrix that are released into the synovial fluid and thereafter into the blood serum. However, it seems that further research on this topic is needed [21–23].

7.1.2.7 Bone Scintigraphy

Bone scintigraphy generates functional images that reflect metabolic activities of the bones. It is easily accessible in the clinical settings and is useful in differentiating the type of bone trauma including bone metastases, stress fracture, plantar fasciitis, Paget's disease, and osteomyelitis [24]. Bone scintigraphy uses ^{99m}Technetium labeled methylene diphosphonate (99mTc-MDP), a compound that relatively binds less to the organic phase, and is absorbed by and quickly accumulated in the mineral phase of the bone [24]. OA also includes bone reactivity such as osteophyte formation around the joint and subchondral sclerosis. Progressive OA is characterized by high bone turnover and release of bone miner-

als, which increases the likelihood of bonding with 99mTc-MDP; therefore, the technique can be useful for diagnosis [25].

7.2 Differential Diagnosis

The key aspects of differential diagnosis for degenerative knee OA are medical history and physical examination. First, clinicians should determine whether it is monoarthritis or polyarthritis and whether the onset is acute or chronic. Acute onset within several hours to 1 week typically indicates inflammatory arthritis, particularly bacterial infection, while slow onset suggests degenerative arthritis. Septic arthritis can be suspected in the presence of fever, chills, and infection in other parts of the body. Rheumatoid arthritis can initially be suspected if there are symmetrical polyarthritis symptoms that persist for more than 1 month. Ankylosing spondylitis or Reiter's syndrome can be suspected in the presence of repeated low back pain and lumbar stiffness in addition to knee pain. Psoriatic arthritis, which is related to psoriasis, is characterized by scaly skin rashes and a small number of involved joints. In gouty arthritis, the characteristic monosodium urate monohydrate crystals can be observed in the joint fluid using a polarizing microscope. Tuberculous arthritis and pigmented villonodular synovitis can be differentiated from other oncologic disorders using tissue biopsy. Additionally, knee joint fluid analysis can be helpful for differential diagnosis of inflammatory, septic arthritis, among others (Table 7.2).

Clinicians should note that knee pain may also be caused by a lumbar or an ipsilateral hip joint disorder and should rule out pain originating from periarticular soft tissues, such as tendons or bursa.

7.2.1 Rheumatoid Arthritis

Severity and onset of symptoms and family history are helpful in diagnosing rheumatoid arthritis. In general, rheumatoid arthritis involves multiple joints, and patients complain of pain in several joints. However, rheumatoid arthritis, which only complains of knee symptoms for weeks to months before symptoms begin in other joints, is also not uncommon. Rheumatoid arthritis is characterized by synovial deposition of mononuclear phagocytes, lymphocytes, plasma cells, and polynuclear leukocytes, and as the disease progresses, the synovial tissue swells and enlarges, and the villi protrude into the joint. Rheumatoid arthritis does not show consistent clinical manifestations; some cases end up with synovitis, while other cases may progress aggressively and cause structural injuries of the joint within 2 years of onset [26]. The 2010 ACR and EULAR diagnostic criteria for rheumatoid arthritis are helpful in the diagnosis [27]; According to these criteria, rheumatoid arthritis can be diagnosed with a score of 6 or higher out of 10 for joint involvement (A), RF and anti-citrullinated protein antibody (B), ESR, CRP (C), and symptom duration (D) (Table 7.3). Blood examination includes RF and anti-cyclic citrullinated peptide antibodies.

Table 7.2 Characteristics of joint fluid analysis

	Normal	Non-inflammatory	Inflammatory	Septic arthritis	Hemorrhagic
Viscosity	High	High	Low	Low	Low
Color	Colorless	Straw or yellow	Yellow or white	Various	Blood
Transparency	Transparent	Transparent	Light transmittable	Opaque	Various
White blood cells per mm^3	~200	200–3000	2000–75,000	>100,000, mostly	Various
Polymorphonuclear leukocytes	≤25%	≤25%	>50%	>75%	Various
Glucose	90% of blood	90% of blood	75% of blood	50% of blood	Various
Culture result	Negative	Negative	Bacteria negative	Bacteria positive	Negative

Table 7.3 The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis (Aletaha et al. [27])

	Score
Target population (who should be tested?): Patients who 1. have at least one joint with definite clinical synovitis (swelling)[a] 2. with the synovitis not better explained by another disease[b] Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)[c]	
A. Joint involvement[d]	
1 large joint[e]	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)[f]	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)[g]	5
B. Serology (at least one test result is needed for classification)[h]	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least one test result is needed for classification)[i]	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
D. Duration of symptoms[j]	
<6 weeks	0
≥6 weeks	1

RA rheumatoid arthritis, *RF* rheumatoid factor, *ACPA* anti-citrullinated protein antibody, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

aThe criteria aim at classification of newly presenting patients. In addition, patients with erosive disease typical of RA with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA. Patients with longstanding disease, including those whose disease is inactive (with or without treatment), and who, based on retrospective available data, have previously fulfilled the 2010 criteria should be classified as having RA

[b]Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If the relevant differential diagnoses that need to be considered are unclear, an expert rheumatologist should be consulted

[c]Although patients with a score of 6/10 cannot be classified as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time

(continued)

Table 7.3 (continued)

[d]Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from the assessment. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement

[e]"Large joints" refer to shoulders, elbows, hips, knees, and ankles

[f]"Small joints" refer to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists

[g]In this category, at least one of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, and sternoclavicular)

[h]Negative refers to international unit (IU) values that are less than or equal to the upper limit of normal (ULN) for the laboratory and assay; low-positive refers to IU values that are higher than the ULN but ≤3 times the ULN for the laboratory and assay; high-positive refers to IU values that are >3 times the ULN for the laboratory and assay. Where RF information is only available as positive or negative, a positive result should be scored as low-positive for RF

[i]Normal/abnormal is determined by local laboratory standards

[j]Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status

7.2.2 Seronegative Spondyloarthropathies

Seronegative spondyloarthropathies are a group of disorders related to rheumatoid arthritis that involve joints of the spine and extremities, particularly the knee [28]. The prevalence of the disease is increased among individuals with the human lymphocyte antigen (HLA)-B27 gene. Ankylosing spondylitis, Reiter's syndrome, and psoriatic arthritis fall under this category, and they are characterized by chronic synovitis in the involved joint. The pathology of synovitis is consistent with that of rheumatoid arthritis; therefore, the disease cannot be differentiated based on synovial biopsy; clinical diagnosis is required.

Ankylosing spondylitis involves the sacroiliac joint, joints of the extremities, and knee joint. It generally affects men in their 20s and 30s. It involves the sacroiliac joint at the time of onset; therefore, low back pain and lumbosacral stiffness are characteristic symptoms. If inflammatory arthritis of a single knee joint is accompanied by low back pain, the diagnosis for ankylosing spondylitis may be frequently missed because the symptoms are masked. The disease triggers pain at the tendon and ligament insertion on the bone, and particularly, patients complain of multiple pain sites such as the Achilles tendon insertion. Patients exhibit spastic gait, where they compensate for spinal stiffness with knee flexion to maintain a standing posture and walk. HLA-B27 can be tested for diagnostic purposes, and most patients are diagnosed based on history, physical examination, and radiologic findings.

Reiter's syndrome is a disease that asymmetrical arthritis occurs in a small number of joints following an infection of the urogenital or gastrointestinal tract, and inflammation of the eyes, mucosa, and skin may occur. Asymmetrical arthritis occurs in a small number of joints 1–3 weeks after urethritis or gastrointestinal tract infection, and the knee joint is commonly involved. Inflammation at tendon or ligament insertion of a bone, such as the Achilles tendon, is also common. Radiographs show sacroiliac joint involvement in 70% of the patients, and 80% of the patients are positive for HLA-B27.

The concept of psoriatic arthritis emerged as it had been reported that psoriasis was associated with inflammatory arthritis. Various types of arthritis occur in the extremities or spinal joints, but unlike other spinal arthritis, sacroiliac arthritis is rare. The diagnosis can be made based on psoriasis in the skin or fingernails and toenails with polyarthritis. Synovial findings are similar to those of rheumatoid arthritis.

7.2.3 Infectious Arthritis

Infection of the knee joint can affect individuals of any age; however, it most commonly affects immunocompromised patients with cancer, diabetes mellitus, alcoholism, acquired immunodeficiency syndrome, or corticosteroid therapy. In septic arthritis, sudden pain or swelling often occurs in the knee joint without trauma [29]. During physical examination, the knee is warm and swollen, and the patient experiences intense pain even with slight motion of the knee joint. Septic arthritis that occurs after an invasive procedure is believed to be a common cause. This is because the use of intraarticular injection and acupuncture for degenerative arthritis is increasing in the aged population and the knee joint is vulnerable to microbial infiltration and trauma [30].

When patients present to the hospital, systemic symptoms are not uncommon, with fever, sweat, and chills presented in 34%, 15%, and 6% of cases, respectively; however, fever is not an essential criterion for the diagnosis of septic arthritis [31]. Arthrocentesis is required for the diagnosis, and the joint fluid is turbid. In septic arthritis, the WBC count in the fluid exceeds 50,000 per mm^3 (50×10^9 per L); however, the WBC count may be below 28,000 per mm^3 in immunocompromised individuals. Particularly, more than 90% (0.90) polymorphonuclear cells strongly indicate acute septic arthritis. Although the likelihood is low, it cannot be completely ruled out even in normal patients with a WBC count of below 50,000 per mm^3 [32]. Common pathogens include *Staphylococcus aureus*, Streptococcus species, *Haemophilus influenzae*, and *Neisseria gonorrhoeae*.

7.2.4 Crystal-Induced Inflammatory Arthropathy

Acute inflammation, pain, or sudden swelling that is nontraumatic may indicate septic arthritis as well as crystal-induced inflammatory arthropathy such as gout or pseudogout. The latter commonly affects the knee joint and is characterized by heat sensation and increased WBC count, showing similar symptoms with those of septic arthritis. Crystal arthritis and septic arthritis are differentiated based on synovial analysis, by confirming crystals and positivity on culture test. Acute gout, an inflammatory crystal arthropathy,

is spontaneously resolved within an average of 1–2 weeks [33, 34]. However, if gouty attack occurs more frequently, persists longer, and is not completely resolved, these lead to chronic gouty arthropathy. Gouty arthropathy is characterized by joint space narrowing but not periarticular osteopenia, which contrasts with rheumatoid arthritis. In gout, monosodium urate crystal precipitates can be observed in the knee joint fluid using a polarized microscope, and in pseudogout, calcium pyrophosphate crystals are observed.

7.2.5 Spontaneous and Secondary Osteonecrosis

Osteonecrosis of the knee is a disease that causes knee pain, similar to that generated by OA; it can be classified into spontaneous and secondary osteonecrosis. Although the exact etiology of osteonecrosis is still unknown, medical conditions such as blood diseases, steroid use, systemic lupus erythematosus, organ transplantation, Casson's disease, Gaucher's disease, and alcohol overuse are some known causes.

Spontaneous osteonecrosis is three times more common among women, and most patients are 60 years or older. In general, sudden knee joint pain is caused by mild trauma or abnormal behavior, and pain is mostly severe. The disease exacerbates proportionately with activity, and the symptoms tend to be worse at night. While the medial femoral condyle is the typical site affected, it is also relatively common in the tibial condyle and lateral femoral condyle, as well as in the patella. Recently, it has been reported that spontaneous osteonecrosis of the knee (SONK) is a subchondral insufficiency fracture (SIF) that has progressed into collapse with secondary necrosis. Because proven microtraumatic origin of SONK and the histopathologic and MRI features unite it with SIF, this notion is currently accepted [35].

Secondary osteonecrosis mostly affects young patients under 55 years, and most patients have risk factors including trauma, use of corticosteroids, sickle cell anemia, collagen vascular disease, and alcoholism. Multiple joints are affected in many cases, and more than 80% of secondary osteonecrosis cases in the knee joint are bilateral, with a 60–90% probability of involving an additional joint [36]. Radiologic evaluation is important in the diagnosis of knee osteonecrosis. Bone scan is essential for the diagnosis of osteonecrosis, and MRI is crucial for staging and differential diagnosis of osteonecrosis, as it enables a detailed observation of the changes in the subchondral bone related to osteonecrosis.

7.2.6 Other Diseases to Be Diagnosed Differentially

In many cases, it is difficult to differentiate symptoms of meniscal tear in older adults with OA from progressive OA and spontaneous osteonecrosis. Even if a patient complains of severe pain in the knee without trauma, there are many difficulties in determining the cause if the cause of the symptoms such as an additional meniscal tear, exacerbation of an existing disease, and loose body in the joint have not been identified. If the symptoms are not severe, observing clinical progress for an appropriate period of time will help with clinical treatment and prognosis.

One or more bursae are present around the knee joint, and some are connected to the knee joint. Depending on their location, they are called the suprapatellar bursa, prepatellar bursa, infrapatellar bursa, popliteal cyst, pes anserine bursa, medial collateral ligament bursa, and iliotibial bursa. As the medial collateral ligament bursa is commonly shown on an MRI of a normal joint, it must be differentiated from meniscal tear and medial collateral ligament tear. Iliotibial band syndrome causes lateral knee pain that is related to repeated motion. Its etiology is chronic infection of the iliotibial bursa due to friction between the iliotibial band and lateral femoral epicondyle. Patients complain of local pain in the distal iliotibial band between the epicondyle and Gerdy tubercle. Anserine bursitis shows swelling and tenderness on the medial aspect of the knee joint.

Connective tissue diseases, such as lupus, may show inflammatory arthritis of the knee joint. Fortunately, arthritis is rare, and this disease can

be suspected in the presence of systemic joint symptoms.

Lyme disease is a complex multiorgan infection caused by *Borrelia burgdorferi*, a spirochete found in ticks. The pathogen circulates in the blood and causes rash and pain at the infection site, and following a migrating joint pain, unilateral or bilateral knee chronic synovitis ultimately develops.

7.3 Summary

Diagnosis of OA is made by combining patient's detailed medical history and physical examination, radiological examination, and blood test results. Knee OA should not be diagnosed by radiological changes alone, as they are detected after the disease has progressed. Moreover, since most elderly people are accompanied by degenerative changes in their knee joints, differential diagnosis with other diseases that cause degenerative changes in the knee is of great importance, especially in the elderly. Misdiagnosis can be harmful to patients if it does not provide proper treatment. Therefore, differential diagnosis of rheumatoid arthritis, seronegative spondyloarthropathies, infectious arthritis, crystalline inflammatory arthropathy, spontaneous and secondary osteonecrosis, and other diseases should be considered.

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