Differential Diagnosis in Internal Medicine

From Symptom to Diagnosis

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Pain in Joint Diseases
General Differential Considerations in Joint Pain

The symptom “joint pain” has to be clinically substantiated. In not all cases does the joint itself represent the origin of the disorder. Affections of soft tissue may also give rise to joint symptoms. Joint disorders usually are associated with the following symptoms:
- swelling (sometimes with effusion)
- warmth
- pain upon pressure
- functional deficit.

Acute monoarthritis needs immediate evaluation: an infectious disorder must be considered. Other forms of acute joint inflammation include arthritis in gout and pseudogout (calcium pyrophosphate arthropathy). These affections are often associated with severe redness of the skin and tenderness. Other joint disorders usually take a chronic course from the very beginning, such as rheumatoid arthritis, connective tissue diseases, and osteoarthritis. Joint disorders of the spondylarthropathy group usually show intermittent acute to chronic courses.

10.1 Inflammatory Rheumatic Joint Disorders

Rheumatoid Arthritis

Epidemiology. Rheumatoid arthritis is the most frequent inflammatory rheumatic joint disease. Women are affected about three times more often than men.

Clinical Findings. Symmetric distribution of the joint disorder is characteristic. In the early phase of the disease hand, metacarpophalangeal and interphalangeal joints (Fig. 10.1), as well as knee and metatarsophalangeal joints, are affected. Involvement of the distal interphalangeal joints is rare and points to differential diagnoses, such as psoriatic arthritis or reactive arthritis. Usual symptoms of rheumatoid arthritis include joint pain and swelling, often associated with severe and long-standing morning stiffness, as well as loss of strength, particularly in the hands. Fatigue and general malaise, and at times slightly elevated temperatures, are often the first indications of the ongoing disease process.

Without effective medication, rheumatoid arthritis is characterized by functional deficit due to progressive joint destruction. Late stages are characterized by deformities, rheumatic nodules, as well as postinflammatory changes of bones, joints, and soft tissue.

In later stages of the disease extra-articular manifestations may occur. This includes pleuropericarditis, rheumatic nodules, eye involvement, and more rarely, vasculitis with sensorimotor disturbances or amyloidosis.

Diagnosis. Already in the early course of the disease radiologic changes may be detected in the hands and feet. In the early stage changes include periarticular soft tissue swelling and demineralization of the periarticular bones. In later stages they include joint space narrowing along with erosions and subluxations (Fig. 10.2). It is rare for ankylosis to be a feature. Involvement of the cervical

Fig. 10.1 Rheumatoid arthritis with joint swelling and moderate ulnar deviation of the fingers.
spine however is frequent. Rheumatoid arthritis may lead to spondylarthritis, instability, or rarely ankylosis, but also to destruction of the atlantal dentate ligaments through inflammatory pannus resulting in atlantoaxial subluxation or even compression of the spinal cord.

**Laboratory examination** often reveals elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), normochromic and normocytic anemia, thrombocytosis, and low serum iron. Rheumatoid factors tend to be positive at later stages.

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**Differential Diagnosis.** In the differential diagnosis the following disorders have to be considered:
- connective tissue diseases (particularly systemic lupus erythematosus and systemic sclerosis)
- polymyalgia rheumatica (patients over 60 years of age)
- Parvovirus-induced arthritis (usually self-healing)
- osteoarthritis of the fingers.

Rarely, difficulties in the delineation of reactive arthritis are encountered. Most often this disorder shows asymmetric oligoarticular joint involvement along with enthesiopathies.

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**Felty Syndrome**

Felty syndrome is a rare, systemic manifestation of rheumatoid arthritis. Its hallmarks are hepatosplenomegaly, leukopenia, and frequently treatment resistant skin ulceration of the lower extremities. The majority of patients show rheumatoid nodules, lymphadenopathy, high titer rheumatoid factors, as well as antinuclear antibodies. A genetic disposition is characterized by the association with HLA-DR4, which is encountered in over 90% of patients.

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**Adult Still Disease**

**Clinical Findings.** Still disease is a rare form of rheumatoid arthritis. Men and women less than 40 years of age are equally effected. Acute episodes of this inflammatory disorder are characterized by high fever spikes (usually over 39 °C). Arthralgias or even oligoarthritis (especially wrists), phalangetis, weight loss, and transient, salmon-colored exanthema of the trunk and the proximal extremities are characteristic manifestations.

Further findings include hepatosplenomegaly, lymphadenopathy, elevated ESR, marked leukocytosis, and very high values for serum ferritin. Rheumatoid factors and antinuclear antibodies are negative.

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**Sjögren Syndrome**

**Definition and Epidemiology.** Sjögren syndrome is characterized by inflammatory involvement of tear, salivary, and mucosal glands (in the intestinal and the pulmonary airways) resulting in sicca symptoms. The syndrome may evolve as a primary syndrome or as an accompanying disorder in association with rheumatoid arthritis or another connective tissue disease (Tab. 10.1). Women over 50 years of age constitute more than 90% of patients.

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**Table 10.1 Sjögren syndrome**

<table>
<thead>
<tr>
<th>Sicca complex and connective tissue disease</th>
<th>Rheumatoid arthritis</th>
<th>Systemic sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerophthalmia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xerostomia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periarteritis nodosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical Findings. Dryness leads to the characteristic manifestations, which are:

- xerophthalmia (keratoconjunctivitis sicca with sensation of foreign bodies, burning, and redness)
- xerostomia (Fig. 10.3) with impaired swallowing, hoarseness, coughing, and development of severe caries.

Characteristic are recurrent, symmetrical, painful, enlarged salivary glands, particularly the parotid glands (Fig. 10.4). Further symptoms include fatigue, fever, arthritis similar to rheumatoid or pillar arthralgias, lymphadenopathy, vasculitic ulcerations, particularly of the legs, as well as neuropathies. Renal involvement is more rare (interstitial nephritis, tubular acidosis). Transitions to malignant lymphomas may occur.

Diagnosis. ESR is often highly elevated. Further typical findings include hypergammaglobulinemia, rheumatoid factors, and anti-SS-A (Ro), as well as anti-SS-B (La) antibodies.

Differential Diagnosis. Treatment with antidepressants (dry mouth), sarcoidosis, and HIV infection have to be considered in the differential diagnosis. The diagnosis of Sjögren syndrome is strongly supported with the positive Schirmer test (measurement of tear flow), as well as biopsy of the lips.

Juvenile Chronic Arthritis

Classification. Juvenile chronic arthritis (JCA) is classified according to its presentation at the onset of disease. There are three forms:

- The systemic form (Still disease) is characterized by episodes of fever with salmon-colored rash, hepatosplenomegaly, and lymphadenopathy. Often arthritic complaints will follow.
- In the polyarticular form, distal finger joints are often involved, in contrast to rheumatoid arthritis in adults. In this form, rheumatoid factor usually is negative.
- The oligoarticular form shows two special aspects: under the age of four years destructive iridocyclitis may occur; children with positive antinuclear antibodies should undergo regular ophthalmologic examination since iridocyclitis may be asymptomatic. Oligoarthritis after the age of eight years usually displays features similar to ankylosing spondylitis.

Differential Diagnosis. The following disorders have to be considered: acute rheumatic fever, bacterial polyarthritis, tuberculosis, and sarcoidosis. In the differential diagnosis puncture or synovial biopsy of the involved joint are helpful.
Spondylarthropathies

Common Features. Tab. 10.2 lists all disorders within the family of spondylarthropathies. These inflammatory, mostly chronic, musculoskeletal diseases share clinical, radiologic, histopathologic, and genetic features:
➤ peripheral, usually oligoarticular arthritis involvement of the spine and sacroiliac joints
➤ involvement of tendons and tendon insertions (enthesiopathy)
➤ extra-articular features (eyes, skin, mucosa, more rarely heart and lungs)
➤ familiar aggregation and association with HLA-B27.

Often these diseases are called seronegative due to the fact that rheumatoid factors and autoantibodies are usually not found.

Ankylosing Spondylitis (Bekhterev Disease)

Clinical Findings. Ankylosing spondylitis represents the classical spondylarthropathy. This chronic inflammatory disorder affects sacroiliacal, costovertebral, and facet joints leading to progressive ankylosis. Hips and shoulders are most commonly affected whereas other joints are less often involved. Systemic manifestations are rare (uveitis anterior, aortitis with aortic insufficiency, pulmonary fibrosis).

Men are affected more often and more severely than women. First symptoms usually develop between the ages of 20–40. Typical symptoms include low back and buttock pain at night, radiating towards the dorsal aspects of the knees. Motion is followed by decreased pain. Stressing the sacroiliacal joints is painful due to inflammation (Mennel or Patrick sign). Axial involvement often leads to early ankylosis with typical deformities: hyperkyphosis of the thoracic spine, flattening of the lower spine (Fig. 10.5). Plantar and achilles enthesiopathies are frequent origins of heel pain. Hip involvement leads to a tendency towards contracture.

Diagnosis. Although elevated ESR is typical, it may also be normal. Typical changes of the sacroiliacal joints in radiographs show narrowing of the joint space along with sclerosing and erosive features (Fig. 10.6), finally leading to ankylosis. Involvement of the spine is characterized by ossification of the ligaments (Fig. 10.7).

Table 10.2 Frequency of HLA-B27 and sacroiliitis in spondylarthropathies

<table>
<thead>
<tr>
<th>Disorder</th>
<th>HLA-B27 (%)</th>
<th>Sacroiliitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td>Reactive arthritis (Reiter syndrome)</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Psoriatic arthropathy</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Enterocolitic arthropathy</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>SAPHO syndrome</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>Undifferentiated spondylarthropathy</td>
<td>50</td>
<td>20</td>
</tr>
</tbody>
</table>

Fig. 10.5 Typical positioning of a patient with Bekhterev disease.
Psoriatic Arthritis

Clinical Findings. The typical pattern of joint involvement in psoriatic arthritis is either characterized by arthritis of all finger joints (DIP, PIP, and MCP joints) resulting in a so-called dactylitis or sausage finger, as well as a transverse involvement of the DIP joints. In contrast to rheumatoid arthritis, the joint swelling is rather tight and the skin often shows a red livid coloration. Arthritis may appear after skin involvement, which is especially the case in children. Radiographically, the hallmark findings consist in both ankylosing ossification and destructive processes at the same time. Given this typical feature, diagnosis is often possible without skin involvement (Fig. 10.8). Nails may show so-called oil spots or onycholysis, particularly when distal joints of fingers or toes are affected. The typical course of psoriatic arthritis is characterized by episodes of highly acute disease and long-standing remissions. Involvement of the spine and the sacroiliac joints (mostly asymmetrical) is less frequent, as compared to ankylosing spondylitis.
**Differential Diagnosis.** Similarities exist with rheumatoid arthritis (symmetrical pattern of joint involvement without affecting the DIP joints), osteoarthritis of the fingers (joint involvement preferentially of DIP and PIP joints), reactive arthritis (manifestation after intestinal or urogenital infection), as well as crystal arthropathies (joint fluid examination).

**Reactive Arthritis (Reiter syndrome)**

**Definition.** Reactive arthritis in its full form is called Reiter syndrome. The syndrome is characterized by arthritis, urethritis, and conjunctivitis, occasionally associated with mucocutaneous lesions. Men between 20 and 40 years of age are most often affected.

**Causes.** Reactive arthritis affects women and men equally after intestinal infections. After urogenital infections most patients are men. Triggering microorganisms includes *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *Brucella*, as well as *Chlamydia* and *Ureaplasma*. In contrast to septic arthritis, these microorganisms can not be cultivated from joint tissue or fluid.

**Clinical Findings.** The first symptoms of a reactive arthritis may evolve only a few weeks after intestinal or urogenital infection. Along with fatigue and occasional fever, several manifestations may occur. Usually, acute asymmetrical oligoarthritis of larger joints of the lower extremities is the first manifestation. Other manifestations include involvement of a single finger or toe with livid skin coloration (so-called dactylitis or sausage finger), spondyloarthropathy with lower back pain in the early morning and stiffness of the spine, frequently along with asymmetric involvement of the sacroiliac joints and inflammatory changes in tendon sheaths, tendons, and ligaments. Extra-articular symptoms are found in the skin and mucosa (keratoderma blennorrhagicum of palms and soles, erythema nodosa, oral ulceration), eyes (often conjunctivitis), and urogenital tract (sterile urethritis, balanitis and cystitis), as well as in the gastrointestinal tract (enteritis). Only very occasionally, nail changes may occur similar to the ones encountered in psoriasis.

**Diagnosis.** The culture of the feces, as well as PCR examination of the serum may detect the enteral infectious agents, as well as *Chlamydia* in the urine in the early stages of the disease. Determination of HLA-B27 does not really contribute to confirming the diagnosis, although 70% of the cases are positive. In the differential diagnosis gonococcal urethritis with septic arthritis should be considered.

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**Rheumatic Fever**

The typical example of a reactive arthritis is rheumatic fever. Currently, this disorder is very rarely encountered in Europe. After infection with beta-hemolytic streptococci group A, fever and polyarthritis, predominantly of the larger joints, carditis, and later chorea minor, transient erythema anulare marginatum of the trunk and thighs, as well as subcutaneous rheumatic nodules, may evolve.

- Anti-streptolysin titers should always be considered in association with the history and clinical findings, since this titer is not specific for rheumatic fever.

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**Arthropathies Associated with Enterocolitis**

Colitis ulcerosa and Crohn disease may be associated with inflammatory changes of the spine and peripheral joints in about 10%–20% of patients. More rare causes of enterocolitic arthropathies are Whipple disease, arthritis after gastrointestinal bypass operation, as well as gluten-induced enteropathy.

**Clinical Findings.** In *colitis ulcerosa* the arthropathy most often evolves after the enteric symptoms. In contrast, joint involvement is not really a primary manifestation in *Crohn disease*, although inflammatory changes in the gastrointestinal tract may be detected endoscopically in the early stages.

Axial involvement as well as sacroiliitis may precede intestinal symptoms by years. Clinical and radiographic findings often can not be distinguished from classical ankylosing spondylitis. This activity in the peripheral joints often reflects the general intestinal inflammatory activity. Spinal inflammation however appears to take place independently. In contrast to ankylosing spondylitis, arthritis in enterocolitis disorders lasts only from a few days to a few weeks and may change location frequently. Sacroiliitis associated with gastrointestinal diseases often remains asymptomatic and is frequently detected by chance in radiographic examinations.

Systemic manifestations include anterior uveitis (up to 10%, most often along with axial involvement), painful stomatitis ulcerosa, erythema nodosa, and pyoderma gangrenosum.

In *Whipple disease*arthralgias or transient nondestructive arthritis of small and larger joints may precede abdominal manifestations by years. Involvement of the spine and sacroiliac joints, as well as spondylarthritis is rare. Men between 40 and 60 years of age should be examined for *Tropheryma whippelii* if any arthritic condition of unclear origin occurs. The leading clinical symptoms for Whipple disease are abdominal discomfort with diarrhea and weight loss, slightly elevated
temperatures, lymphadenopathy, uveitis, and more rarely eye muscle paresis and encephalopathy.

**Behçet Disease**

Behçet disease belongs to the vasculitides. Most patients are originally from the eastern Mediterranean regions and the Orient. The main rheumatological complaints include chronic synovitis of larger and smaller joints. The diagnosis is based on two main symptoms plus one minor symptom.

**Clinical Findings.**

Main symptoms are:
- mucosal ulcerations in the mouth and/or intestinal tract
- genital ulcerations (vulva, penis, scrotum)
- ocular manifestations (uveitis anterior, hypopyon, retinal vasculitis).

Minor symptoms are:
- skin disease (erythema nodosa, folliculitis)
- arthritis (predominantly knee or ankle joints)
- neurologic symptoms (meningitis, involvement of cranial nerves)
- vessel disease (venous thrombosis, arterial aneurysms).

**SAPHO Syndrome**

**Definition.** SAPHO describes the most frequent manifestations of the syndrome: synovitis, acne, pustulosis, hyperostosis, and osteomyelitis. Men and women are equally affected and the disorder may evolve in patients of any age.

**Clinical Findings.** A hallmark finding of this disorder of unclear origin is an often asymmetrical, painful swelling in the clavicular-costosternal area (Fig. 10.9). The following features are frequent:
- sternoclavicular hyperostosis
- palmoplantar pustulosis
- inflammatory axial involvement
- peripheral oligoarthritis, particularly of large joints.

Manifestations often evolve sequentially; skin and bone symptoms may be found many years apart. Low back pain, axial stiffness, and painful joint swellings are, as with other spondylarthropathies, typical. Palmoplantar pustulosis is characterized by well delineated vesicles or pustules, as well as superficial scaling of the palms and soles. Differentiation from psoriatic skin disease is often not possible. As a complication of clavicular-costal hyperostosis, thrombosis of the subclavian vein or the superior vena cava may occur as a consequence of compression.

**Diagnosis.** Imaging of the strong increase in activity in bones and joints is best done by skeletal scintigraphy. At times, bone changes may simulate infectious osteomyelitis or tumors in radiographs. Such features therefore need more intensive examination.

**Undifferentiated Spondylarthropathy**

In about 30% of all patients with spondylarthropathies no specific diagnosis is possible. Many manifestations of spondylarthropathies may occur without fulfilling clear criteria for a specific disease, such as isolated peritendinitis of the achilles tendon or severe low back pain in the early morning in a young man. Such, mostly early, forms of spondylarthropathies are classified as undifferentiated.
Arthropathies Associated with Metabolic Diseases

Arthritis Urica (Gout)

Epidemiology and Causes. Primary gout in men occurs about 10 times more often than in women. In men, gout develops most frequently between the ages of 40 and 50 years, but in women usually only after the age of 60 years. Triggering factors include rich meals with high purine intake and/or alcohol consumption.

Clinical Findings. Classical acute gout is always very painful, it occurs during the night, and patients may not be able to walk on the inflamed joints. Typically, the involved joint is red, swollen, and extremely painful. Slightly raised temperatures, elevated ESR, and leucocytosis are the rule. Without treatment the acute attack will subside in about a week, leaving the involved joint slightly painful for longer periods. The first metatarsophalangeal joint is most often involved, however, gout may occur in any joint. In such cases the differential diagnosis of acute septic arthritis or reactive arthritis, as well as psoriatic arthritis has to be considered. Acute onset in rheumatoid arthritis is also possible. In elderly people, pseudogout (chondrocalcinosis) has to be differentiated from gout.

In later stages of the disease deposition of urate occurs in tendons, bursa, and joints, which is known as chronic tophaceous gout (Fig. 10.10). Tophi are located most often in the neighborhood of the involved joints, but may be found at the external ear as well (Fig. 10.11).

Diagnosis. In radiographs, well-delineated erosions at the end of bones are characteristic for gout (Fig. 10.12). The diagnosis of gout is supported by increased serum uric acid levels and proven by the positive finding of uric acid crystals in the joint fluid.

Pathogenesis. The cause of primary gout is multifactorial. About 20% of cases show enzyme defects leading to the overproduction of uric acid. In all other patients uric acid is not excreted sufficiently, probably based on an epithelial insufficiency.

Complications. The most important complication of gout is the so-called gout kidney. Impairment of the kidney is a consequence of hyperuricemia and increased excretion of uric acid. On histological examination, inflammatory interstitial infiltrates as a consequence of deposition with uric acid are found along with an eventual pyelonephritis caused by lithiasis, as well as vascular changes (nephrosclerosis). Many patients with gout develop hypertension. Therefore it may be difficult to differentiate between secondary consequences of hypertension or gout when interpreting renal insufficiency. Gout nephropathy itself may lead to hypertension.

Hyperuricemia and gout are often associated with diabetes mellitus, hyperlipoproteinemia, and hypertension; therefore gout is considered a risk indicator. Whether gout alone or only in combination with other risk factors may lead to coronary sclerosis is controversial.

Secondary Gout. Features of gout may evolve in all diseases associated with increased cell death (e.g., myelo- and lymphoproliferative diseases) or by any treatment leading to decreased excretion of uric acid, such as diuretics. In addition, secondary hyperuricemia may be found in ketosis (fasting, decompensated diabetes mellitus, fat-rich meals), acromegaly, hypo- and hyperparathyroidism, CO intoxication, lead intoxication, myxedema, and with the intravenous application of fructose.

Chondrocalcinosis (Pseudogout)

Deposition of calcium pyrophosphate crystals may lead to joint inflammation. The acute attack may not be differentiated clinically from a gout joint attack. Most often larger joints are involved. Differentiation of crystals is possible by the examination of joint fluid. Radiographically, typical calcifications may be found in...

In elderly patients pseudogout (see Chondrocalcinosis, below) always has to be considered. Serum uric acid levels do not parallel clinical symptoms. However, most patients with increased serum uric acid of over 600 μmol/L will sooner or later be symptomatic.

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Fig. 10.10 Chronic tophaceous gout of the index finger.
menisceal and superficial layers of the joint cartilage (Fig. 10.13).

Chondrocalcinosis has a preference for middle aged and elderly persons, but may occur at any age. Often chondrocalcinosis will be found as an accompanying disorder in damaged joints (osteoarthritis, posttraumatic arthritis) or in metabolic diseases (hyperparathyroidism, hemochromatosis, Wilson disease, gout, ochronosis). Axial involvement is rare and may show calcifications of the intervertebral disks. The course of axial disease is clinically silent with the diagnosis most often resulting from a chance finding in a radiograph of the vertebrae.

**Diffuse Idiopathic Skeletal Hyperostosis (DISH)**

Axial hyperostosis is often detected in radiographs by chance. This disorder is characterized by overshooting ossifications with osseous bridge building between single vertebrae without narrowing of the intervertebral spaces. It is based on ossification of the longitudinal ligaments of the spine. The right side of the thoracic spine is preferentially involved, however, ossifications may develop at any site including peripheral joints. Usually hyperostosis is followed by clinical ankylosis, whereas occurrence of pain is rare. In the shoulder area, severe symptoms may be due to hyperostosis at the inferior aspect of the acromion leading to irritation of the subacromial area (impingement). In the pathogenesis,
metabolic disturbances are thought to be the possible cause of the hyperostosis, since metabolic disorders are associated with this disorder, such as impaired glucose tolerance, hyperlipidemia, and hyperuricemia.

**Ochronosis (Alkaptonuria)**

**Definition and Pathogenesis.** Ochronosis is a congenital disorder of metabolism characterized by a deficiency of homogentisic acid oxidase leading to an incomplete metabolism of phenylalanine. This may all take a symptom-free course for years while it is only recognizable in the urine: homogentisic acid is excreted at higher levels and when oxidized the urine will change color to a dark blue.

**Clinical Findings.** Black spots may evolve in many areas and are often recognized as first symptoms of the disease. Homogentisic acid is deposited in cartilage, tendons, and sclerae leading to a darker brown to black discoloration which is called ochronosis (Fig. 10.14). Only many years later does cartilage destruction occur. In this stage, changes in the spine, ossifications of tendon insertion, especially at the pelvis and hips, leading to osteoarthritis of the hips and knees, as well as the elbows occurs. The changes of the spine include severe sclerosis of the horizontal plates of the vertebrae as well as osteophytoselike changes along with severe degeneration of the intervertebral disks. The radiographic hallmarks at the spine are horizontal calcifications of the disks (Fig. 10.15).

**Primary Amyloidosis**

Primary amyloidosis may give rise to amyloid deposits in synovial tissue and hyaline cartilage resulting in pain, stiffness, swelling, and occasionally impaired mobility of the involved joints. In the differential diagnosis, rheumatoid arthritis and other arthritis, which in turn may lead to secondary amyloidosis, must be considered.

**Hemochromatosis**

The first symptoms of the arthropathy in hemochromatosis occur in the inflammatory stage of the disease. In about 20% of all patients, joint symptoms are the first sign of the disease. In later stages of disease about 90% of all patients will have some joint symptoms.

The most characteristic feature of the arthropathy is the involvement of the MCP joints II and III, most often in a symmetrical pattern. In active disease, periarticular tissue swelling with redness and warmth may be found. Cysts, loss of cartilage, and larger osteophytes towards the radial aspects of the finger
are typical radiologic changes. The laboratory diagnostic investigations are described in Chapter 25 (including findings in liver biopsy and determination of mutations in the HFE gene).

**Wilson Disease**

Diffuse osteoporosis is most often found in Wilson disease (hepatolenticular degeneration). Degenerative changes, particularly in the knee joints, periarticular classification, as well as osteochondritis dissecans may be observed.

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### Other Arthropathies

#### Hematologic Disorders

Severe joint destruction may be found in coagulopathies. Hemolytic anemias (thalassemia, sickle cell disease), acute leukemia, and malignant lymphoma may be associated with arthritides as well (see Chapters 13, 14, and 15).

#### Arthrititis Associated with Neoplasms

**Hypertrophic Osteoarthropathy.** The hallmark disorder of paraneoplastic arthritides is the so-called hypertrophic osteoarthropathy often preceding the manifestation of a tumor by a long period of time. This disorder is characterized by:
- clubbed fingers and hourglass nails
- arthralgias and arthritides of hands, elbows, ankles, knees, and MCP joints
- periostial proliferations in radiographs in the area of the diaphyses of long bones
- neurovegetative symptoms (hyperhydrosis, hyperthermia, peripheral vasodilatation)
- possibly gynecomastia.

The full picture of hypertrophic osteoarthropathy is most often found in bronchial carcinoma. However, it may be found in many intrathoracic and extrathoracic disorders as well (see Chapter 3).

#### Arthropathies in Endocrine Disorders

Endocrine disorders such as acromegaly, hyperparathyroidism, and hyperthyroidism/hypothyroidism may be associated with arthropathies. Long-standing cortisone intake may be followed by osteonecrosis of the femur head. Such complications may evolve in systemic lupus erythematosus and progressive sclerosis as well.

**Wilson Disease**

Diffuse osteoporosis is most often found in Wilson disease (hepatolenticular degeneration). Degenerative changes, particularly in the knee joints, periarticular classification, as well as osteochondritis dissecans may be observed.