Osteoid Osteoma
Synopsis of clinical, radiological, and therapeutical relevance of this rare entity

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Abstract

Characteristic of the osteoid osteoma is the so-called nidus enclosed in the tumor and produces a typical picture on X-ray. Since most physicians have little experience with the clinical picture of osteoid osteoma, this is an important reason for the often-long anamnesis time for osteoid osteoma (OO). The period of formation of OO includes the phase of strongest bone growth in childhood and adolescence. The most characteristic clinical symptom is nocturnal attacks of pain around the tumor, which occur independently of preceding physical activity and respond strikingly well to non-steroidal anti-inflammatory drugs (aspirin test). OO most frequently affects the long tubular bones of the lower extremities. Fifty percent of OO are found in the femur and tibia preferentially occurring in the corticalis of metaphysis and diaphysis. This is followed by the long tubular bones of the upper extremity and the short tubular bones. However, any other bone can also be affected. Differentially, osteoblastoma or osteosarcoma must be considered first and foremost. Most widely accepted therapy options are open surgery with en-bloc resection of the tumor, excochleation, minimally invasive percutaneous CT-guided radio or laser ablation. A conservative management by pharmaceutical pain therapy should be reserved for cases in which surgery must be refused either because of the precarious position of the nidus or because the patient's general condition does not permit it, or the patient does not consent to surgical interventions.
Keywords: osteoid osteoma, radio frequency ablation, stereotactic navigation with CT-guidance, benign osseous tumor, excochleation, imaging of nidus.

Clinical picture of osteoid osteoma

In 1935, Jaffé (1) described for the first time 5 cases of a benign, osteoblastic tumor consisting of osteoid and atypical bone, which he then called osteoid osteoma. Characteristic of the osteoid osteoma is the so-called nidus enclosed in the tumor, up to two to three centimeters in size, a sharply delimited zone of osteolysis, which is often surrounded by a sclerosed rim and produces a typical picture on X-ray.

Incidence

Based on larger numbers of cases collected and evaluated at pathological institutes all over the world a proportion of osteoid osteomas of 10% of all benign bone tumors or of 4% of bone tumors in total has been described (2-4). Osteoid osteoma can thus be counted among the rare tumors. Since most physicians have little experience with the clinical picture of osteoid osteoma, this is an important reason for the often-long anamnesis time for osteoid osteoma. Some authors describe an average case history of 14 months (6) and even come to an average of 2 years with a smaller number of cases of 14 patients who were treated within 12 years at the University Hospital Essen (4). In the literature, there are also individual cases with extremely long anamnesis periods of up to 18 years (7).

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Age and gender distribution

Depending on the statistics, men are two (6) to four times (8) as likely to develop osteoid osteoma as women. The age distribution shows a peak in the second decade of life, in which about 50% of all cases are diagnosed. 90% of patients are between 6 and 30 years old (9). Osteoid osteomas are hardly ever seen in infancy and early childhood (5). The period of formation therefore includes the phase of strongest bone growth in childhood and adolescence. Therefore, it can be assumed that the rare osteoid osteomas discovered at a later age also develop during the phase of adolescent bone growth but are discovered later (5).

Localization

The tumor most frequently affects the long tubular bones of the lower extremities. Thus, 50% of osteoid osteomas are found in the femur and tibia (8), where they in turn preferentially occur in the corticalis of the metaphysis and diaphysis (5). This is followed

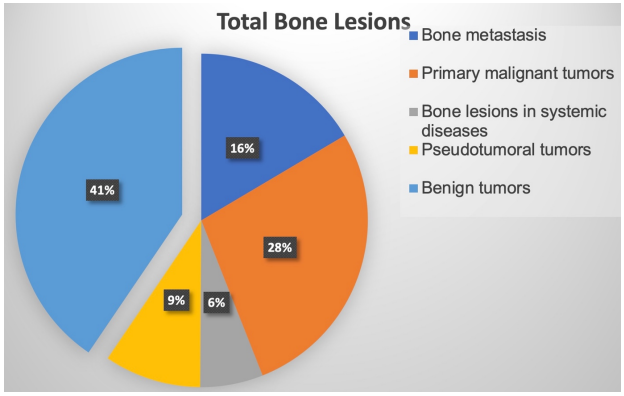

Figure 1: *Frequency distribution of all bone lesions. 41% are benign lesions.*

by the long tubular bones of the upper extremity and the short tubular bones. If the tumor is in the spinal column (13%), the posterior elements such as vertebral arches and vertebral processes are primarily affected (9). However, any other bone can also be affected (5).

Symptoms

Probably the most characteristic clinical symptom is nocturnal attacks of pain around the tumor, which occur independently of preceding physical activity and respond strikingly well to non-steroidal anti-inflammatory drugs (aspirin test) (10). Some authors (8) consider a fluctuating blood filling in the strongly vascularized tumor as a possible cause of the pain, according to which the increasing pressure with increasing blood flow could lead to the irritation of pain receptors (8). Other research saw the cause of pain in the production of prostaglandins by the tumor tissue itself, which excite nerve endings of pain receptors and thus cause vasodilation with a subsequent increase in pressure. Nerve endings were first demonstrated by Schulman (11) and Sherman (12) in the nidus of the osteoid osteoma. These sprouting nerve endings are a special feature of the osteoid osteoma and distinguish it from most other tumors, which remain painless until they grow into the periosteum (13). In the rather rare localization of the tumor in the spine, a typical symptom is scoliosis, which draws attention to the disease. If the tumor is close to the joint or intracapsular, arthritis may be predominant and obscure the diagnosis (14). In addition, muscular atrophies occur due to protective posture of the affected limb; movement restrictions, limping and reflex reductions are also observed. Sometimes the tumor can even be recognized by a palpable swelling with or without pain on pressure. In children, a deformation of the bone section or increased longitudinal growth can also be observed, which is a consequence of the hyperemia caused by the osteoid osteoma (5).

Pathogenesis

The pathogenesis is still largely unclear; the most important theories will be presented here. There is agreement today that osteoid osteoma is a malformation in osteogenesis that occurs for the first-time during bone growth and follows the surrounding bone mass distally towards the metaphysis or diaphysis during further growth. However, the cause of this maldevelopment remains unexplained. Genetic connections could be ruled out. Another approach deals with the idea that the disease could be a chronic inflammatory reaction, to which the thick sclerosis margin and the responsiveness to non-steroidal anti-inflammatory drugs (NSAIDs) could be an indication. However, the pathogen has not yet been identified and the typical signs of inflammation such as increased temperature, increased accelerated blood sedimentation rate or increased leukocyte counts are lacking (15). In addition, cases of post-traumatic osteoid osteomas have been described over time, as Leonhardt shows in 16 cases (16). However, these are exceptions in which a previous trauma usually occurred many years ago, but clearly corresponded to the localization of the osteoid osteoma. Whether all other patients perhaps suffered unnoticed minor injuries in their previous history, which then led to the tumors, is yet unclear.

Diagnostic steps

a) Anamnesis The osteoid osteoma is diagnosed via anamnesis mainly by the typical strong nocturnal pain, which quickly subsides after the administration of aspirin or other NSAIDs. The patients describe regular pain attacks that lead to waking up especially in the early morning hours. The pain may already exist at a time when radiological evidence is still negative because of the small size of the tumor (17).

b) X-ray The X-ray in two planes often confirms the diagnosis by showing the typical image of a nidus. This is a round to oval, well-defined zone of osteolysis consisting of highly vascularized stroma and immature bone tissue, which can be seen as a brightening in the X-ray image. Internally, it may contain a tiny patchy sclerotic core as a shadow. The nidus is surrounded by a sclerotic rim of reactive hyperostotic bone, which also presents as shadowing. Especially tumors located in the cortical bone can form such a strong sclerotic zone that visualization of the nidus itself is no longer possible (5,14,18).

c) Computed tomography (CT) In case of doubt, computed tomography (CT) can ensure imaging in

regions with a high degree of superimposition and in very small tumors, as individual slices can be viewed in this way and the summation effect does not disturb the image. Before computed tomography, which was only made possible by the development of high-performance computers, superimposition could already be reduced by images taken with conventional tomography, which focused on a specific slice depth. CT also shows the osteoid osteoma with the typical signs of nidus and surrounding increased ossification. The slice thickness and the field of view must be chosen small to resolve osteoid osteomas of small size. A slice thickness of 1 mm should allow reliable imaging and three-dimensional reconstructions (17,19,20,21).

d) Skeletal scintigraphy Another method of identifying bone tumors is skeletal scintigraphy. It is used to mark regions of increased metabolism with the help of radioactively enriched substrates - so-called tracers. Often, the skeletal scintigram can show the localization of the tumor at a very early stage due to an over-enrichment in the metabolically active area of the nidus. Since the sclerosis zone does not accumulate due to a lack of blood supply and consequently a zone of reduced accumulation is found there, the so-called "double density sign" typical of osteoid osteomas results (22).

e) Magnetic resonance imaging (MRI) Magnetic resonance imaging (MRI) is a procedure that uses a strong artificial magnetic field to visualize layers of the body by measuring electromagnetic waves coming from the atomic nuclei. Since MRI images the soft tissues with high contrast, it can, for example, show the soft tissue reactions of the tumor-surrounding tissue, such as bone marrow oedema, periostitis or synovitis. Since the bone itself cannot be well demarcated, MRI can lead to misdiagnoses and a not inconsiderable aggravation of findings such as an osteosarcoma (9,23). In particular, the nidus characteristic of osteoid osteoma shows up far less reliably on MRI than on CT, which is why MRI is not normally used in cases of suspected osteoid osteoma and should at least not be one of the early diagnostic measures (24). The radiological diagnosis must always be confirmed postoperatively by histological examination of the excised material. Only the final comparison of the radiological, clinical, and histological findings provides a definite result and prevents possible malignant causes from being overlooked.

Differential diagnosis

Differentially, osteoblastoma or osteosarcoma must be considered first and foremost. Benign osteoblastoma is histologically very similar to osteoid osteoma. However, there are differences in size and growth behavior, which is why the differentiation of the two tumors is relevant for the correct therapy. Osteosarcoma as a common malignant bone tumor is a very important differential diagnosis. If there is any doubt about the radiological diagnosis of osteoid osteoma, which rarely occurs due to the characteristic X-ray image, a biopsy should be performed before surgery to exclude the presence of malignancy. The osteosarcoma appears more diffusely demarcated from the healthy bone on the X-ray, and the sclerotic rim is usually missing due to the rapidly progressing bone destruction caused by its faster growth. Instead, moth-eaten necrosis, periosteal changes in the form of spicules protruding vertically from the shaft, more rarely lamellar onion shells or triangular thickened periosteal shadows (Codman triangles) are characteristic. In advanced stages, the osteosarcoma can even be seen penetrating into the soft tissues in the form of newly formed bone on the X-ray. In the case of osteosarcoma, there are also histologically suspicious cell atypia, which should not occur in osteoid osteoma (5). They must be explicitly excluded by the pathologist. Furthermore, chronic sclerosing osteomyelitis, a chronic inflammation of the bone of various causes, which can also reactively show increased ossification, must be differentiated. In this case, however, a more inhomogeneous sclerosis is noticeable. Brodie's abscess, a bone abscess caused by hematogenous spread of bacteria and leading to chronic osteomyelitis, is usually located centrally in the metaphysis, but the osteoid osteoma is in the cortex. Histology must be consulted in conjunction with radiological findings to exclude eosinophilic granuloma, which may also be conspicuous by osteolysis and nocturnal pain (3,9,15).

Macro morphology and histology

The excised nidus appears as grey-reddish or white yellowish to red tissue, which lies in the sclerosed area of the bone and shows a spongy structure of varying hardness. It is relatively well demarcated and can be peeled out with a sharp spoon (5). The nidus reveals newly formed, meshed, disordered bone under the microscope, lined with active osteoid-producing osteoblasts, but not highly differentiated enough to form ordinary lamellar bone. The osteoid is not fully calcified. Giant osteoclastic cells can lie in between. A cell-dense stroma of fibroblasts and histiocytes lies around it (5). Numerous nerve fiber endings are found in the surrounding fibrous tissue, which are held responsible for the painfulness of the lesion (11). In already long existing tumors, calcifications may have already reached the center of the nidus. The sclerotic zone is composed of lamellar

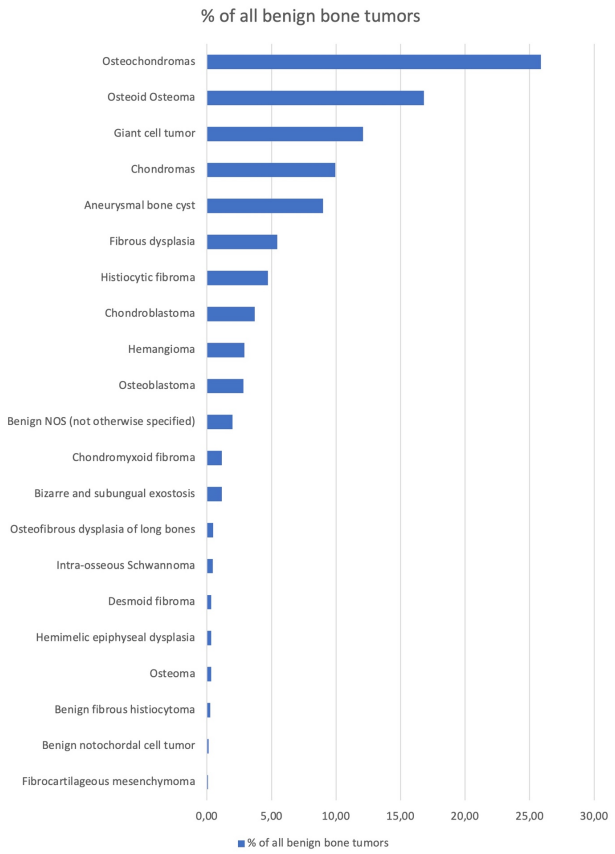

Figure 2: *Frequency distribution of all benign bone tumors. 16.8% of all benign osseous tumors are Osteoid Osteomas.*

bone. In contrast to malignant tumors, cellular or nuclear atypia are not found (8).

Therapy

On the one hand, the therapeutic goal is to surgically remove the nidus as completely as possible to minimize the risk of recurrence. On the other hand, a generous removal always increases the risk of instability of the bone. Therefore, the surgical defect should remain as small as possible. The sclerosis zone does not have to be removed completely because recurrences are only caused by remnants of the nidus tissue (17). To perform the operation as gentle as possible on the bone preserving stability, new minimally invasive surgical techniques have been developed in recent years. If the nidus is successfully removed or destroyed, patients are immediately pain-free after the procedure.

Treatment options

4 treatment options are available.

1) Open en-bloc resection of the tumor with parts of the sclerosed marginal zone. In en-bloc resection, the nidus is removed in one piece with large parts of the surrounding sclerosis zone. For this purpose, the surgical area must be prepared free, i.e., the skin and soft tissue over the tumor must be detached. Due to the resulting soft tissue damage, vascular and nerve damage, high blood loss as well as postoperative wound pain and possibly also wound healing disorders and infections must be expected. The area of bone in which the osteoid osteoma is located is then dissected totally out en-bloc. If a large bone defect is created by the operation, it can be filled with the patient's own (autologous) bone or artificial bone substitute to achieve faster healing and thus earlier stabilization. Cancellous bone or cortical bone, for example from the iliac crest, can be used as an autologous substitute, or parts of the fibula can be used as bone fragments. Special hydroxyapatite ceramics have been developed as artificial replacements, which are available in the form of preformed granules or cylinders and are used to fill the resulting bone cavity. In cases where bone stability is in danger due to heavy loading and large defect and an increased risk of fracture is to be expected, a stabilization by means of plate osteosynthesis or even an external fixator may be necessary. Especially for the simultaneous correction of a strong tumor-related bone proliferation (hyperostosis), en-bloc resection is often used (17). A disadvantage of this surgical technique is not least the danger that the nidus is ultimately not contained in the resectate, although it was assumed to be there. Subsequent postoperative fluoroscopy should be performed while the patient is still under anesthesia to visualize the nidus in the resectate and, if it is missing, to proceed with a more extensive resection. To avoid such a case, the nidus can be localized preoperatively by means of fluoroscopy or CT and marked, for example, by drilling at least two Kirschner wires. Alternatively, the nidus can be marked by nuclear medicine using a radioactive metabolic substrate, which is administered before the operation and is increasingly absorbed by the tumor as metabolically active tissue (22). The radioactivity in the resectate and surrounding bone tissue can be determined and provides information about the completeness of the removal. Preoperative labelling with tetracycline is also possible, whereby the patient takes tetracycline orally for 1-2 days preoperatively. This takes advantage of the fact that the nidus particularly accumulates the substance, and it can be found intraoperatively by detecting fluorescence using UV light (25). However, it should be noted that children under 8 years of age should not take tetracycline as it also accumulates in the dentin of the teeth (20). An advantage of the surgical technique is that the pathologist can easily assess the complete resectate and make a statement about the completeness of the

nidus and its dignity (5).

2) Removal of the bone flap and curettage of the bone cavity (excochleation) The approach to the tumor is the same as for en-bloc resection. However, then only the opening of the bone is done by removing a bone flap over the area where the osteoid osteoma is located. As soon as the nidus can be seen macroscopically, it is completely peeled out (curetted) with a sharp spoon. The hyperostotic area surrounding it does not have to be removed, in fact it should be left in place. In this way, less bone mass is removed and sufficient stability in the area can often be maintained. If no remnants are left in the bone, recurrences are not to be expected, whereas incomplete removal is associated with a high risk of recurrence (17). However, since the pathologist only receives fragments of the tumor, he cannot make a statement about the completeness of the removal postoperatively. Particularly at inaccessible sites, a considerable soft tissue defect can also occur during the removal of the nidus, which can result in a high risk of infection, severe pain, and a delay in healing, as has already been described for en-bloc resection. The same applies to the preoperative marking of the nidus as mentioned above.

3) Minimally invasive percutaneous CT-guided technique The minimally invasive technique has been used clinically since the early 1990s and is said to be gentle on tissue, less complicating and, because of the shorter hospital stay, less expensive and more comfortable for the patient. The principle of the surgical technique is that the bone section to be operated on does not have to be prepared free, but the nidus is precisely localized intraoperatively with the help of CT. First, the tissue to be removed is precisely marked with a Kirschner wire, then drilled percutaneously with a hollow drill and retrieved by retraction (14,26-28). The difficulty lies in the fact that the nidus is not advanced into the adjacent soft tissues or deeper bone in the process but is completely grasped by the drill and extracted. For this purpose, a gripping mechanism can be built into the drill. Afterwards, it is sufficient to dress the skin wound with sterile strips and a sterile bandage, the patient is only allowed to put partial weight on the limb for the first few days until the wound has healed, and if there are no complications, even outpatient treatment is possible (26). In some cases, the operation can even be performed under local anesthesia (14). Comparison of invasive treatment: CT-guided vs. surgical approach The CT-guided interventional technique has led to considerably lower morbidity, especially in deep surgical sites, such as tumor sites in the pelvis or femoral neck, where large wounds would occur with the conventional operation technique (17,29). Berning sees an important field of application for transcutaneous CT-guided treatment of osteoid osteomas also in intra-articular localizations, especially of the hip joint, because here it is possible to spare the vascularization zone of the femoral head (14). However, the success rates of recurrence-free healing vary and are highly dependent on the interventionalist and the localization. While some authors (14) report no recurrences or complications, other authors report complications in 24% of the cases (30,31). On the other hand there are opinions (6) that the conventional operation techniques are better than the modern CT-guided ones because of the fact that a histological assessment of the often heavily damaged resectate is only possible in about half of the cases, so that the method should only be used in cases of a confirmed diagnosis of osteoid osteoma (31). The recurrence rate is a little bit higher than with open curettage (recurrence-free rate only 83% versus 100%) (6). However, the minimally invasive techniques tend to be used more and more frequently (16,28). To further minimize the retention of residual tumor with the risk of recurrence, special methods of percutaneous technique have also been developed, whereby residual tissue of the nidus is additionally destroyed using high-percentage ethanol, laser energy or special high-energy radio frequencies after drilling (27,28,32,33). In this procedure, access holes of approximately 5 mm diameter are drilled and the nidus is destroyed or sclerosed by inserting the above-mentioned agents. According to Rosenthal, high-frequency radio ablation is the most effective method as side effects on the surrounding tissue due to the concentrated alcohol or the high temperatures of the laser treatment (up to 240°C) can be ruled out (32).

4) Conservative management by pharmaceutical pain therapy Another method of treating osteoid osteoma is with medication purely (34). Since the tumor itself does not pose a threat to the patient's health, but only the severe pain leads to impairment, taking NSAIDs for several years can be considered as an alternative therapy to surgery. Studies have shown that on average, after 2.75 years, the use of the medication can be stopped, and the patients are pain-free (34). However, gastrointestinal complaints such as nausea, gastric ulcers, and diarrhea as side effects of NSAIDs lead to the discontinuation of therapy in most of the patients (35). Furthermore, taking medication for a long time seems to be more stressful for patients than a quick intervention with immediate pain relief. Thus, drug treatment of osteoid osteoma should be reserved for cases in which surgery must be refused either because of the precarious position of

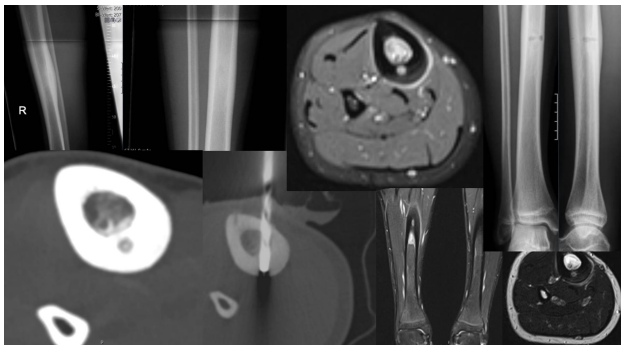

Figure 3: *Bone X-rays, MRI, and CT images before and after treatment of Osteoid Osteoma from our own patients. Please note the typical MRI and CT appearance. In MRI there is a typical contrast enhancing in the nidus located in the cortex of the middle tibial third. 22-year-old male with nocturnal pain attacks in the right tibia. After CT-guided treatment with RFA there was an immediate pain reduction. After three years of follow-up there was no recurrence.*

the nidus or because the patient's general condition does not permit it, or the patient does not consent to invasive procedures (35).

Conclusions and take home messages

Regarding the quite rare entity of osteoid osteoma, the well-informed radiologist should be aware of the following aspects:

1. cardinal symptoms are nocturnal pain in the tumor location and immediate pain reduction after taking aspirin.
2. typical appearance on X-ray and CT images.
3. histologically always benign.
4. well treatable with minimally invasive methods, e.g., CT-guided.

Of course, it must be considered that only the final comparison of the radiological, clinical, and histological findings provides a definite result and prevents possible malignant causes from being overlooked.

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