MYOSITIS OSSIFICANS OF THE QUADRICEPS FEMORIS
MIMICKING SARCOMA AS A DIAGNOSTIC AND THERAPEUTIC
PROBLEM – CASE REPORT AND LITERATURE REVIEW

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Myositis ossificans (MO) may be included in the group of lesions described as pseudosarcomas. Its
clinical and histological picture frequently mimics a malignant neoplasm and therefore, ultimate di-
agnosis and implementation of adequate treatment requires the cooperation of interdisciplinary team
of physicians. The paper presents the case of 20-year old female patient suffering from severe pain in
the right thigh. The patient was initially diagnosed with the lower limb overload. Rest and administra-
tion of non-steroidal anti-inflammatory drugs (NSAID) were recommended. Due to the lack of the ef-
cicacy of the recommended conservative treatment and detection of tumorous mass on ultrasound
examination, the patient was referred to the cancer centre. The diagnostic procedures were extended
and an open biopsy of the lesion was performed which revealed the presence of MO. The patient un-
derwent a surgical procedure during which the pathological mass was entirely removed. Follow up
examinations conducted upon the conclusion of the rehabilitation indicate no pathologies in the oper-
ated area.

Key words: myositis ossificans, heterotopic ossification, sarcomas, pseudosarcomas, post-traumatic
lesions

Soft-tissue sarcomas (STS) are rare malig-
nant tumours found in adult patients (mean
incidence in the EU equals 1.0-3.0/100 thou-
sand annually; mortality – 0.6-0.8/100 thou-
sand annually). In Poland, they account for 1%
of malignant neoplasms in adults and 10% in
children (800-1000 episodes per year). They
may form in each mesenchymal tissue, but
they primarily originate from mesoderm and
ectoderm. STS may occur in every age, but the
peak incidence is noted at the age of approxi-
mately 50 (1, 2). They most frequently appear
in the extremities (50%), torso, intra- and ret-

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comas, for example: von Recklinghausen disease (neurofibromatosis), Gardner syndrome, Werner syndrome, tuberous sclerosis, nevoid basal cell carcinoma syndrome (Gorlin syndrome) and Li-Fraumeni syndrome (mutation of the p53 gene). Trauma does not constitute an aetiological factor, but may direct the attention of the patient to the already existing lesion (2).

The most common symptom of STS in the extremities is a slowly growing (from several weeks or months), painless tumour with several centimetres in size, which is localised infrafascially in the region of the muscles and slightly changes the outline of the limb.

Other symptoms – such as pain, constrained mobility of the joint, oedema, neurological or vascular disorders – are rare and most often related to a specific localisation of sarcoma or its histological origin. Systemic symptoms occur even more rarely. They usually comprise paraneoplastic syndrome (subfebrile body temperature, anaemia, arterial hypertension, diabetes) or are related to necrotic processes taking place in larger tumours.

Contemporary imaging diagnosis is based on magnetic resonance imaging (MRI). Ultrasound examination (US), plain X-ray, vascular examinations and computed tomography (CT) are of little importance in determining the diagnosis and treatment, but they are useful in assessing the advancement of the neoplastic process (chest X-ray or CT).

The management depends on the size and histological malignancy of the neoplasm. Prior to the therapy, it is essential to obtain histological diagnosis from the material collected by means of core or open biopsy. The final determination of optimal treatment is based on the cooperation of interdisciplinary team of physicians. In the majority of patients, a combination treatment is applied which consists in combining radical surgical treatment with pre- or post-operative radiotherapy. The role of chemotherapy is not clearly determined and is frequently implemented as part of clinical trials. Well differentiated tumours (G1) may be treated by means of surgical independent procedures. However, sarcomas that are less differentiated (mitotic index calculation, bleeding and necrosis) more frequently result in local recurrence or distant metastases. The mean 5-year survival rates calculated after the resection fluctuate depending on risk factors (30-80%).

The factors that decrease the prognosis include: age above 60 years, tumour with more than 5 cm in diameter and low degree of histological differentiation of the tumour (G3, G4) (2, 3).

The differential diagnosis concerns non-malignant neoplastic lesions (lipomas), post-traumatic changes (haematomas), inflammatory lesions (abscesses) and bone tumours.

This paper presents a case of a patient with myositis ossificans of the quadriceps femoris mimicking sarcoma.

CASE REPORT

The patient aged 20 was admitted to the 1st Clinic of Surgical Oncology and General Surgery of Wielkopolska Cancer Center on 7 April 2012 with a suspicion of sarcoma of the right thigh. In February 2012, she reported to the Emergency Department of one of the hospitals in Poznań due to a sudden, severe pain in the right thigh. On physical examination, the patient presented pain of the adductors, no oedema, symmetrical pulse in both lower extremities and skin with normal colouring. The patient was discharged with the diagnosis of “lower right limb overload.” Rest and NSAIDs were recommended. After 2 weeks, the patient again reported to the Emergency Department of a different hospital in Poznań complaining about pain in the medial surface of the right thigh and no improvement brought about by the previously recommended therapy. On physical examination, a considerable pain and slight thickening were noticed in a half of the anteromedial aspect of the thigh. US examination of this area revealed oval and hypoechoic, 2 cm area of inflammatory infiltration with the dimensions of 20x39 mm with detectable central hyperechoic echo which was suggestive of an abscess. Following the surgical consultation, US-guided puncture of the lesion was conducted (no contents were obtained) and the diagnosis of “the suspicion of haematoma of the right thigh” was established. The patient was discharged. Antibiotic therapy, topical heparin and NSAIDs were recommended. After 4 days, during a control examination, a painful, tumorous lesion was found in the anteromedial surface of the right thigh. The lesion was unmovable with a smooth surface. The patient was referred to the oncological centre for further diagnosis.
On 10 March 2012, the patient presented at the Radiotherapy and Oncology Clinic of Wielkopolska Cancer Centre where painful, spindle-like tumour with the dimensions of 7x5 cm was detected on the medial surface of the right thigh. It was movable against its base and covered by unaltered skin. Additionally, the right inguinal lymph node was palpable with its size of 1.5 cm. The patient was referred to the surgical clinic and US examination was performed: in the medial head of the right quadriceps femoris, an ambiguous focal lesion was imaged with heterogeneous echostructure, calcifications and dimensions of 59x30x37 mm that might correspond to a post-traumatic lesion. A fine-needle biopsy was conducted which revealed mesenchymal cells without features of atypia as well as granulocytes and lymphocytes – histological verification was essential.

On 7 April 2011, the patient was admitted to the 1st Clinic of Surgical Oncology and General Surgery at Wielkopolska Cancer Centre. At the admission, the lesion in the right thigh with the size of 10 cm in the longitudinal axis was painful, poorly movable on palpation and it impaired movement (patient with crutches). Due to the clinical picture, sarcoma was suspected. MRI of the right thigh revealed oval tumorous mass in the medial head of the quadriceps femoris muscle with the dimensions of 75x35 mm which showed strong and heterogeneous enhancement after the administration of a contrast agent from the branch of the femoral artery. In the superior aspect, the infiltration ran through the fascia and penetrated towards the superior trunk of the femoral artery (infiltration suspected). In the muscles adjacent to the tumour the signal was delayed and enhanced after the administration of a contrast agent – again, infiltration was suspected. Conclusion: suspicion of a poorly differentiated rhabdomyosarcoma or neurofibrosarcoma (fig. 1 and 2). Additionally, chest X-ray, abdominal US and inguinal US examinations were performed and revealed no significant irregularities.

On 14 April 2011, an open biopsy of the tumour was performed. The intraoperative examination demonstrated a lesion with uncertain malignancy potential. On 15 April, the analysis of the paraffin specimen was obtained – the presentation may resemble a pseudo-neoplastic lesion of myositis ossificans type. Following the consultation with a pathologist and radiologist, it was decided to supplement the diagnosis with CT and plain thigh X-ray. The X-ray revealed well-calcified and well-defined thickening with the size of 70x35 mm in the half of the thigh (fig. 3). CT revealed a well-calcified mass in the medial head of the right quadriceps femoris with the dimensions of 25x35x70 mm, which caused hypodense oedema in the adjacent muscle fibres. The lesion was vascularised from the femoral artery and infiltrated the neurovascular bundle and cortical layer of the femoral bone. Conclusion: the entire presentation suggests myositis ossificans (fig. 1 and 2). On 20 April 2011, the second surgery was performed – a hard, circumscribed tumour was removed within the limits of unaltered muscles (fig. 4). After the
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Fig. 2. 3D reconstruction of the tumour in MRI (left) and CT (right) scans of the right thigh

Fig. 3. MO in a plain X-ray of the right thigh
procedure, the Kramer splint was used and cooling dressing was applied to the operated site. Furthermore, the following were administered: antithrombotic medicines, antibiotics, oral magnesium, indomethacin with proton-pump inhibitor and diosmin. One day following the surgery, the drain was removed and rehabilitation began. The patient was discharged on the fifth day after the surgery in good overall condition with recommendation to continue rehabilitation. The final histopathological examination confirmed the diagnosis of myositis ossificans.

When the wound healed, from May to July 2011, the rehabilitation of the leg was continued in the Daily Rehabilitation Unit of Wielkopolska Cancer Centre. At the end of July, the follow up physical examination and CT were conducted and revealed no suspicious masses in the region of the lower extremity. No pathologies were found in CT examination performed in March 2012.

DISCUSSION

In the differential diagnosis of STS, one should consider a heterogeneous group of benign soft-tissue tumours. A particular difficulty is posed by lesions connected with certain recovery processes which clinically and pathologically resemble STS. This group comprises so-called pseudosarcomas—soft-tissue tumours with benign nature, but characterised by rapid growth, hypercellularity, cellular atypia, high mitotic activity, necrosis and infiltration. These features contribute to diagnostic difficulty and may cause erroneous diagnosis. The most common benign lesions consist of fibroblasts and myofibroblasts or osteoblasts and they encompass: nodular fasciitis, proliferative fasciitis and myositis, intravascular fasciitis, postoperative spindle cell tumour, inflammatory pseudotumour or myositis ossificans (4).

MO (myositis ossificans) is a pseudosarcomatous lesion which forms in the recovery process and is characterised by metaplastic bone formation. We distinguish 3 types of myositis ossificans: progressive MO (genetically determined, with severe course), MO that is not genetically determined without the history of trauma which may develop in the course of burns, haemophilia or neurological conditions and post-traumatic MO (5, 6). The last listed type is the most common and usually affects otherwise healthy, active adult population (4). It usually follows injuries to large muscle groups (and constitutes 20% of complications of the quadriceps femoris trauma with a consequential haematoma). MO may also be a complication of a surgical procedure, but is rarely a consequence of overload. It involves the subcutaneous tissue and muscles of the extremities. Seldom does it appear in other places such as in the mesentery or abdomen.

Its most characteristic location is the anterior aspect of the thigh (4, 7, 8). Four conditions must be met for MO to develop i.e.: initiating event (e.g. trauma with a consequential haematoma), sending the signal from the site of injury (inflammatory mediators), presence of mesenchymal cells which may differentiate into osteoblasts and, finally, environment favourable to the formation of a heterotopic bone (9). The key role in the pathogenesis is probably played by prolonged presence of macrophages in the muscle tissue altered by trauma and necrosis, which results in the release of the mediators of osteogenesis (8). MO should be suspected if after 10-14 days follow-
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In the early phase of development, the involved area is painful and swollen. Subsequently, within 6 weeks, it becomes better circumscribed and harder. Finally, it assumes the form of a hard, painless and well-circumscribed mass (4).

Ultimate diagnosis requires the clinical assessment supported with imaging and histological examinations. In the earliest stadium, the lesion, when examined under the microscope, resembles nodular fasciitis. Subsequently, morphological “zonation” is observed — division into zones. In the centre, fibroblasts, mucopolysaccharides and collagen fibres may be found; the intermediate zone holds osteoblasts that produce trabeculae of a woven bone; the peripheral zone holds trabeculae which undergo remodelling and mineralisation and their structure resembles a lamellar bone. After 3 weeks, radiological picture presents heterogeneous, irregular shadowing that corresponds to calcifications which after subsequent 3 weeks, transform into evident, mineralised peripheral bony structure with central radiolucency i.e. the soft tissue (4). CT is a more sensitive modality in detecting early mineralisation than X-ray (11). However, in its early stages, in T2-weighted images of MRI, we observe a heterogeneous mass with highly intensive signal surrounded with extensive diffuse oedema. As the lesion develops, a hypointensive rim appears which corresponds to the mineralisation visible in X-ray pictures. In T1-weighted images, the tumour shows the same signal intensity as the surrounding muscles and after the administration of a contrast agent, the rim may become enhanced (12, 13). In early stadia of MO, MRI scan is nonspecific (4). The division into zones may also be observed on US examination: the central hypoechoic area surrounded by a hyperechoic band, which corresponds to ossification, and the external hypoechoic zone with visible hypervascular area on Doppler US examination (15). A sensitive modality in early stages of the disease is bone scintigraphy where one may observe increased uptake in the region of damaged muscles (5). The serum alkaline phosphatase is elevated.

The differential diagnosis of MO should also encompass malignant lesions including extraskeletal osteosarcoma. This neoplasm usually develops in older patients than those suffering from MO (on average at the age of 50 — in contrast to conventional osteosarcoma which appears at the average age of 26) and has a distinct histological presentation. The proliferating and immature fibroblasts with hyperchromatic nuclei which are present in MO may indeed suggest neoplastic cells. However, the “zonation” — central zone of cells with peripheral layer of osteoid — excludes osteosarcoma. The malignant potential of inflammatory process is a rare possibility. Nevertheless, it should be born in mind (16, 17).

MO treatment, due to the absence of randomised trails, is based on empirical experience. It is disputable whether after the injury to the muscle, MO may be avoided. Surely, in order to stop the bleeding and inhibit the progression of the injury, the RICE-based management should be implemented (rest, ice, compression, elevation) (8, 10). Additionally, the administration of NSAIDs and delicate, passive extending of the damaged muscles are recommended. After severe contusions of the quadriceps muscle, a flexion of 120º should be maintained for 24 h and the patient should rest for 1-2 weeks until the local inflammation subsides completely. There are special rehabilitation programmes which in some cases, enable conservative treatment e.g. West Point Flexion Protocol — a three-phase treatment programme where phase 1 conforms to RICE principle, phase 2 constitutes the restoration of mobility starting from a complete extension and phase 3 is the rehabilitation that encompasses e.g. weight-bearing exercises.

In treating overload MO, 25-50 mg of indomethacin is recommended 2-3 times a day over 7-11 days with proton pump inhibitors (other medicines, such as meloxicam, are ineffective). It was also attempted to apply radiotherapy and the effect of such a treatment was similar to the results obtained by means of indomethacin. There are also single reports on using bisphosphonates, calcitonin or warfarin as well as local injections of magnesium sulphate and oral administration of magnesium lactate over the period of 4-6 months with injections of xylocaine, dexamethasone and hyaluronidase (8). In patients who underwent hip arthroplasty, the risk of heterotopic ossification may be decreased by the administration of indomethacin, diclofenac, naproxen or ibuprofen.
over at least 7 days. In the case of contraindications for using NSAIDs, pre- or postoperative radiotherapy appears to be effective (18).

Surgical treatment is considered when the symptoms do not recede, the process has become circumscribed and does not appear to improve after the conservative treatment as well as when the newly formed bone structure is fully matured (the removal of immature ectopic bone may result in local recurrence) (10, 19). The surgery involves simple excision of the tumorous lesion.

To sum up, it needs to be underlined that MO is a rare disease entity. In the case of the presented patient, the ultimate diagnosis was established after the examination of paraffin specimens obtained in the open biopsy. The imaging examinations which had been performed before, particularly MRI, occurred to be non-specific and indicated poorly-differentiated sarcoma. The correct diagnosis could be established only when the radiological scans capable of visualising calcified structures (X-ray and CT) and histological examination had been performed. The most significant element in MO management is the preventive treatment following muscle trauma (RICE principle). The subsequent diagnostic steps and the therapy require the cooperation of physicians representing various specialities.

REFERENCES


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