Differential diagnosis of non-traumatic knee hemarthrosis (case report)

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Hemarthrosis (HA) of the knee of non-traumatic origin is rarely encountered in the practice of a traumatologist-orthopedic surgeon. The differential diagnosis of this pathology requires a thorough medical history tacking and clinical examination of the patient, and a knee joint aspiration can only confirm the presence of blood in the joint. A diagnostic arthroscopy with a synovial biopsy helps to clarify the diagnosis. The most common causes of non-traumatic HA are tumors of vascular or synovial origin, tumor metastases and the use of high-dose anticoagulants in combination with a vascular malformation.

A clinical observation of the development of symptoms of non-traumatic HA on the background of anticoagulant use is presented, where the task of the orthopedic surgeon was to identify the true cause of the disease.

Keywords: *hemarthrosis; knee joint; pigmented villonodular synovitis.*
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Knee hemarthrosis (HA) is a pathology characterized by the accumulation of blood in the joint, which can have various causes. There are three forms of hemarthrosis: posttraumatic, nontraumatic and postoperative; each form includes a wide range of pathologies [1].

The most common cause of posttraumatic knee HA in adults is a rupture of the anterior cruciate ligament (70%), less frequent causes include a dislocation of the patella (15%), meniscus tears (10%), intra-articular fractures (2–5%), and other injuries (5%). However, in adolescence, the most common cause of knee HA is a dislocation of the patella [2, 3].

Nontraumatic hemarthrosis may be associated with a coagulopathy (genetic diseases, taking anticoagulants) or with synovial tumors. The most common cause of nontraumatic HA is hemophilia, and HA is often the first manifestation of this disease. Synovial hemangioma, a benign vascular malformation, is another cause of HA. In rare cases HA may be caused by metastases of nearby tumors. Pigmented villonodular synovitis (PVNS) is a benign neoplasm of the synovial membrane and is manifested by HA. Recurrent HA can also be associated with liver or kidney disease, vitamin K deficiency, anticoagulant therapy or pseudoaneurysm of the vessels around the knee [4, 5].

Postoperative HA is rare complication after knee arthroplasty or after arthroscopic surgery (about 2% of cases) [6].

Clinical case

Patient N.*, a 53-year-old woman, visited the outpatient clinic of V.A. Nasonova Research Institute of Rheumatology in December 2019 with complaints of effusion and limited range of motion in the right knee joint. She first noticed the symptoms in September 2019 without a prior joint injury. She sought medical aid in a local trauma care center where a puncture of the knee joint was performed with aspiration of 80 ml of hemorrhagic fluid. Several subsequent punctures gave the same result. The patient was referred to hospital for diagnostics and treatment of knee hemarthrosis. She underwent a standard clinical examination in the hospital, but the cause was not found. The treatment included immobilizing the lower limb in a plaster cast for 3 weeks, which did not lead to improvement, and the patient contacted the outpatient clinic of V.A. Nasonova Research Institute of Rheumatology in December 2019.*

From the patient's history it is known that she was examined by a cardiologist in March 2019, when atrial fibrillation was detected, and the patient was prescribed anticoagulant therapy. Since March 2019, she has been constantly receiving warfarin at a dose of 10 mg/day.

During the examination at the outpatient clinic we found that the area of the right knee was enlarged due to effusion. The skin had normal color and moisture. There was no local hyperemia and hyperthermia. Palpation of the knee was painless. Active and passive movements in the knee joint were moderately painful, flexion 90є, extension 0є. The ballottement patella test was positive, and effusion was detected in the suprapatellar bursa. Hyperpression of the patella was painful. Symptoms of meniscus tears were negative. There was no lateral and anteroposterior instability. Neurocirculatory and trophic disorders in the feet were not detected. Magnetic resonance imaging (MRI) of the knee joint revealed hypertrophy of the synovial membrane, fluid in the joint cavity (Fig. 1).

We performed a puncture of the knee joint and evacuated 80 ml of hemorrhagic fluid. Cytological examination revealed the presence of hemosiderin.

Due to the absence of a prior trauma, the diagnosis of nontraumatic hemarthrosis of various etiologies was considered. The list of differentiated diagnoses included tumors of the synovial membrane and vascular malformations, which could become a source of bleeding against the background of taking anticoagulants. In order to exclude vascular pathology in the popliteal region, computed tomography (CT) with angiography of the lower limb vessels was performed which detected no vascular anomaly (Fig. 2).

We performed diagnostic arthroscopy of the right knee on 19.02.2020. Blood was detected in the joint cavity intraoperatively,

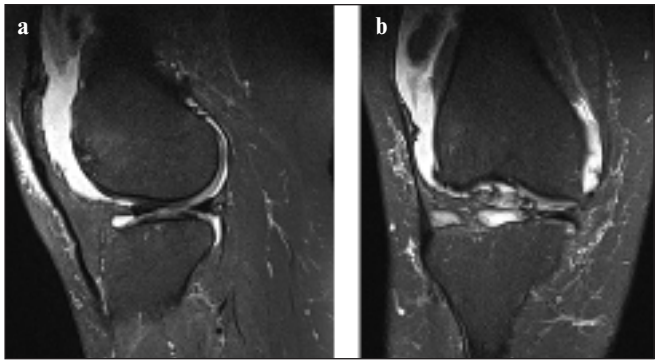

Fig. 1. *Magnetic resonance imaging of the knee (a, b)*

all joint compartments were filled with hypertrophied orange-brown synovial membrane with enlarged villi (Fig. 3). A biopsy of the synovial membrane was performed, followed by histological examination. Microscopic workup revealed proliferation of round polygonal synoviocytes with scanty cytoplasm, which formed finger-shaped outgrowths (villi); nodes containing a cellular infiltrate of fibroblasts, lymphocytes, macrophages with fatty inclusions and hemosiderin, infiltration by multinucleated giant cells (Fig. 4).

It was decided to perform a two-stage synovectomy. The first stage included an open anterolateral synovectomy (Fig. 5). Arthrotomy of the knee joint was performed using Payr's approach. Intra-articular structures were visualized. All sections of the joint were filled with hypertrophied brown synovial membrane. There was a local cartilage defect on the lateral condyle of the femur, which was filled with pannus. Synovial membrane was removed from the suprapatellar recess, lateral canals, intercondylar arch, and above and below the lateral and medial menisci.

The second stage of the operation (posterior synovectomy (Fig. 6) was performed 10 days later. After the isolation of the vascular-nerve bundle, posterior arthrotomy was performed, during which a few nodes of the synovial membrane from the posterior part of the knee joint were removed. At the outpatient stage, the patient underwent 10 sessions of radiation therapy. At the control examination after 3 months, the result was assessed as satisfactory (Fig. 7, a–c).

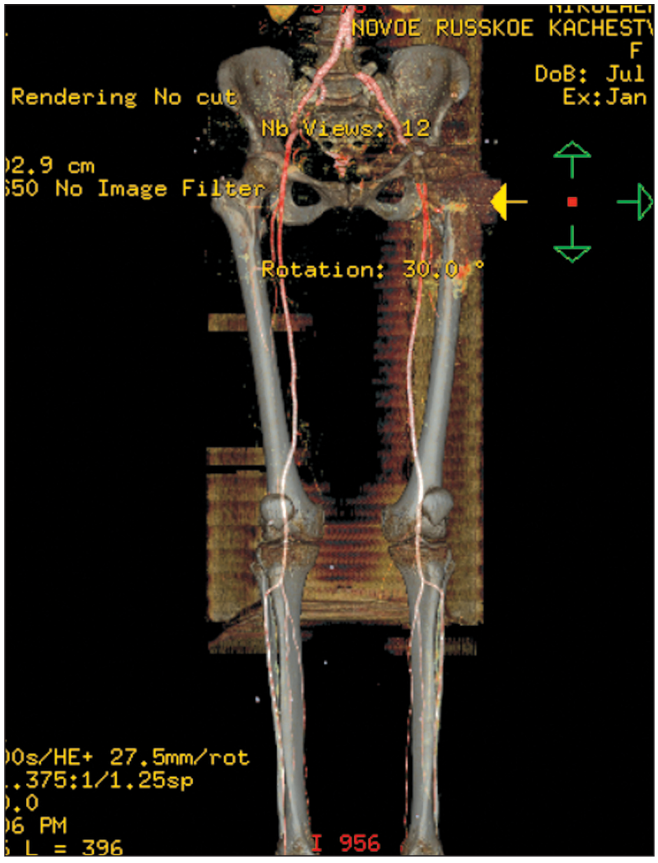

Fig. 2. *CT angiography*

Discussion

PVNS is an intra-articular proliferative disease of the synovial membrane, also described by WHO as a diffuse type of a giant cell tumor [7]. PVNS was first mentioned in 1941 in the article by H.L. Jaffe et al. [8]. The authors characterized the pathology as a proliferative process in the synovial membrane of joints and tendons, which is prone to recurrence after surgical removal. Despite the aggressive growth and spread of pathological tissue to

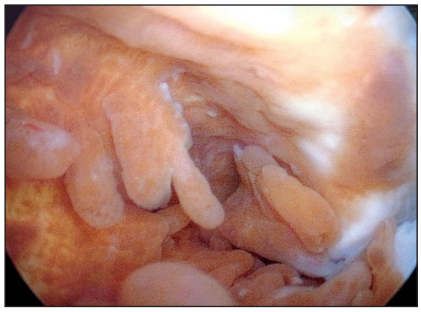

Fig. 3. *View of the synovial membrane of the knee joint during arthroscopy*

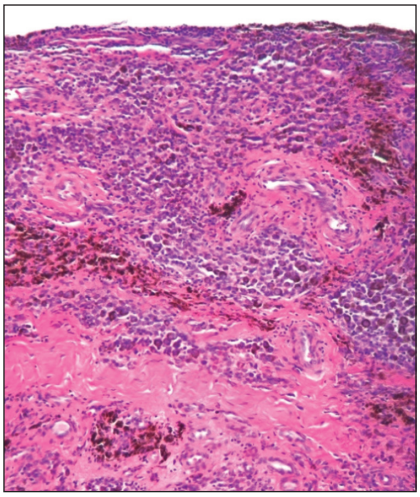

Fig. 4. *The histological picture of the synovial membrane*

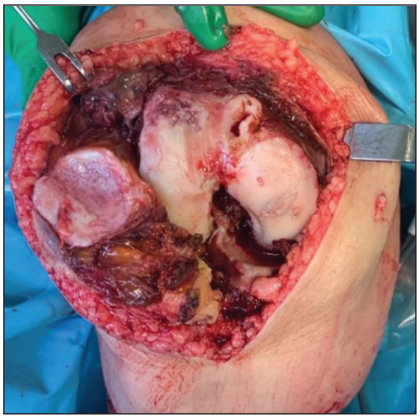

Fig. 5. *The first step of the surgery – anterolateral synovectomy*

the surrounding structures of the joint, PVNS is classified as a benign idiopathic proliferative-dysplastic disease [9, 10]. The etiology of PVNS is still unclear. To date, there are two theories of its origin: some authors regard PVNS as a benign diffuse hyperplastic process in the synovial membrane with vascular proliferation, others – as a chronic inflammatory reaction. The role of genetic factors in the development of the disease is also discussed, in particular, gene translocation in one pair of chromosomes, which leads to hyperexpression of colony-stimulating factor 1. Its excess causes hyperproduction of giant cells, macrophages, and osteoclasts [11–13].

Histologically, the disease is a tenosynovial giant cell tumor. Microscopic examination reveals hypertrophy of the synovial villi, which are formed by mononuclear cells, fibroblasts, histiocytes, and macrophages with a large amount of hemosiderin [14]. PVNS is a rare disease,

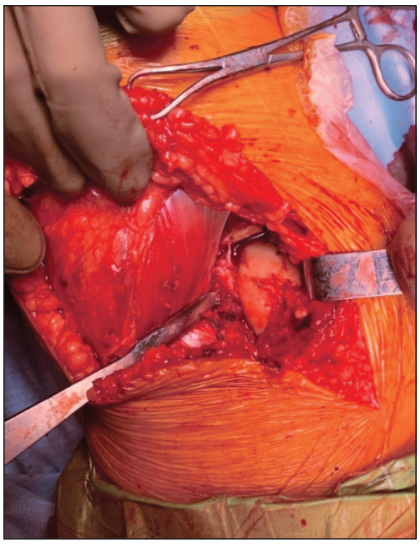

Fig. 6. *The second stage of the surgery – posterior synovectomy*

forms of PVNS, as well as its mild and severe stages [19]. The final diagnosis of PVNS requires histological examination of a sample of synovial tissue [20] removed during arthroscopy [21]. There are no approved treatment protocols for PVNS. Treatment includes surgery and radiation therapy. The localized form of PVNS is successfully treated by removing the pathological tissue. The diffuse form of PVNS is treated using various approaches, including both isolated surgical intervention and its combination with pharmacotherapy [22].

In the pathogenesis of PVNS, a significant role is played by hyperproduction of colony-stimulating factor 1. Thyroxine kinase inhibitors (Nilotinib, Imatinib, Emactuzumab) and Pexidartinib are used for its treatment. These drugs have a cytostatic effect and are also used to treat autoimmune and oncological diseases. According to V. Ravi et al. [23], imatinib led to a decrease in lesions in 50% of patients

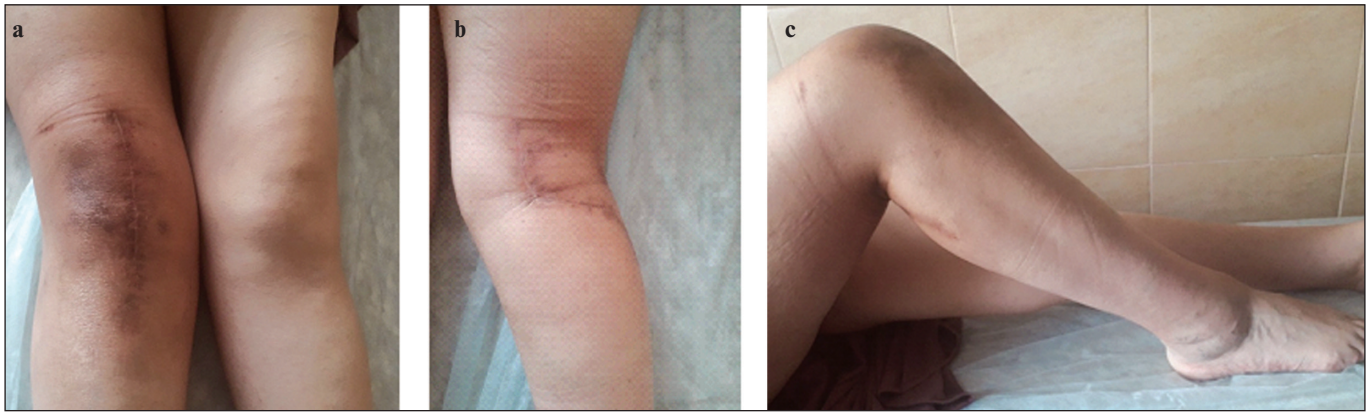

Fig. 7. *Follow-up examination 3 months after the surgery (a–c)*

according to some authors, it occurs in 14 cases per 1 million people. It usually affects adults aged 20 to 50 years, the average age of onset of the disease is 35 years. According to some observations, PVNS more often affects women. The knee joint is the favorite localization of the disease, accounting for about 80% of all cases of this pathology [15, 16].

The main symptom of PVNS is joint effusion. Joint pain is moderate and does not cause suffering to the patient. Despite a significant increase in the size of the joint, full range of motion is usually preserved. The disease is often asymptomatic until joint function is impaired [17].

Diagnosis of PVNS presents certain difficulties due to the lack of characteristic clinical symptoms. Various imaging techniques, including radiography and MRI, are used to diagnose PVNS. However, due to the lack of specific pathognomonic signs, these techniques do not allow distinguishing PVNS from other proliferative diseases of the synovial tissue [18]. Some researchers consider that MRI can clearly show signs of PVNS, but the use of contrast and appropriate qualifications of the radiologist are often required. There is a classification that distinguishes diffuse and localized with PVNS, and stabilization of the disease – in 33%. However, after discontinuation of the drug, the progression of PVNS resumes. Therefore, today surgery is considered the first and main step in the treatment of PVNS [23, 24].

Surgical removal of the pathological focus is the method of choice for both isolated and diffuse forms of the disease. Open synovectomy has long remained the "gold standard" for the treatment of PVNS [25]. However, several publications have appeared comparing the results of open and arthroscopic synovectomy. In a retrospective study by H.F. Gu et al. [26], which included 41 patients, no significant differences were found between the results of open and arthroscopic synovectomy for the diffuse form of PVNS. The data from this study are used to popularize arthroscopy in the treatment of this disease due to its low invasiveness, low blood loss, and a shorter recovery period. A larger retrospective study by M.W. Colman et al. [27] demonstrated a significant advantage of the combined approach in the diffuse form of PVNS (a combination of anterior arthroscopic and posterior open synovectomy), in which the recurrence rate was reduced from 64% to 9% (p=0.008).

M.J.L. Mastboom et al. [28] in a multicenter study showed that recurrences after arthroscopic synovectomy occur more often in both localized and diffuse forms of PVNS.

Currently, the recurrence rate after both open and arthroscopic surgeries remains quite significant – from 8% to 17%, and in diffuse PVNS it can reach 46%. It should be noted that the development of PVNS recurrences after surgical treatment is due to insufficient radicality of resection of the affected synovial membrane, its increased mitotic activity and involvement of bone tissue in the process [29, 30].

Radiation therapy is used as an independent method or in combination with surgical treatment of PVNS. The goal of radiation therapy is to impact the remaining synovial tissue and the transition zones in subtotal synovectomy [29]. Postoperative adjuvant radiation therapy is used in the form of external irradiation of the affected area, as well as in the form of intra-articular injections of radioisotope drugs (yttrium-90, rhenium-186, erbium-169, chromium-32P phosphate). Several studies of the comparative effectiveness of radiation therapy demonstrated conflicting data. However, a meta-analysis of 35 studies indicates that the use of radiation therapy reduces the risk of relapse in the diffuse form of PVNS [31].

Conclusion

Nontraumatic knee hemarthrosis is a rare condition in the practice of an orthopedic surgeon. PVNS is a benign neoplasm of the synovial membrane and manifests itself as hemarthrosis of the knee joint. Its differential diagnosis requires a careful history taking and a clinical examination of the patient. Diagnostic arthroscopy with a biopsy of the synovial membrane helps make a correct diagnosis.

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Conflict of Interest Statement

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