Polyarticular Form of Pigmented Villonodular Synovitis. Radiation and Surgical Therapy: Long Term Follow-up

Polyartikulární formy pigmentové vilonodulární synovitidy – radiační a chirurgická léčba (dlouhodobé výsledky)

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SUMMARY

We describe a case of 30-year old male followed-up since the age of 6 for severe type of rare combination of polyarticular form of pigmented villonodular synovitis with hereditary malformation constellation consistent with Noonan-like syndrome. Within 20 years, the patient underwent repeated synovectomies of large joints with temporary effect only. Radiation therapy with the dose of 30 Gy in 15 sessions has been applied for active aggressive synovitis of both knees associated with pain and progressive joint destruction. Favorable effect lasted for 3 years. Progressive destruction with range-of-motion limitation required successive total joint replacement of both knee joints. Left knee prosthesis has been revised for aseptic loosening after 3.5 years. It is now 5 years since the right knee primoimplantation and 3 years since the left knee reimplantation without signs of component loosening or recurrence, with satisfactory clinical and functional outcome.

Key words: pigmented villonodular syndrome, Noonan-like syndrome, radiotherapy, total knee replacement.

INTRODUCTION

Pigmented villonodular synovitis (PVS) was first described in 1941 (6). PVS occurs most commonly between the ages of 30–50 years as localized monoarticular or diffuse form. Etiology of this disease is unknown. An inflammatory process is considered to play a part in the pathogenesis of PVS, an influence of trauma or repeated bleeding is possible. PVS is considered to be a benign neoplastic process by some authors. Proliferation of synovial cells and fibroblasts associated with collagen production is characteristic. Hemosiderin and lipids accumulate in the cells, giant multinuclear cells are present.

Polyarticular form of pigmented villonodular synovitis (PPVS) affecting children younger than ten years, associated with various congenital malformations, is very rare (14).

DESCRIPTION OF THE CASE

30 year old patient has been treated since the age of six for resilient reccurent synovitis of ankles, knees and both elbows. Typical phenotypic features of Noonan syndrome are also present in our patient. Striking are the findings of brachycephaly with ptosis of right eyelid, low-set ears, short webbed neck with low hairline, slim shoulders, broad deformed chest (pectus carinatum), short lower extremities and multiple nevi on the back (Fig.1). Patient has been followed since birth for pulmonary stenosis. Growth retardation is present, the height in adult age is 157 cm with weight of 51 kg.

Multiple synovectomies of affected joints by standard arthrotomy approach were performed during the last 20 years. Despite meticulous technique, the surgeries had only short term effect. Histology of removed synovial tissue repeatedly revealed large numbers of macrophages and typical pigment-containing giant-cells, massive chronic inflammatory infiltration with lymfocytic predominance, vessel dilatation and proliferation with numerous foci of fresh and old hemorrhages. Structures typical of hemangioma or malignant proliferation were not observed. Systemic therapy was also attempted to halt progression of joint involvement. Administration of low dose glucocorticoids and methotrexate was entirely inefficient.

Progressive joint destruction, mainly knees, has led to a significant worsening of physical functioning. There was marked swelling of both elbows, ankles, knees and left wrist joint present at the age of 22 years. All involved joints were very painful and had various degree of motion limitation. Patient was mobile using forearm crutches with difficulty. X-ray of the knees revealed narrowing of the joint space bilaterally, there were polycystic translucencies and destructions in tibial epifyses and metafyses and epifyses of both femurs. Similar fin-

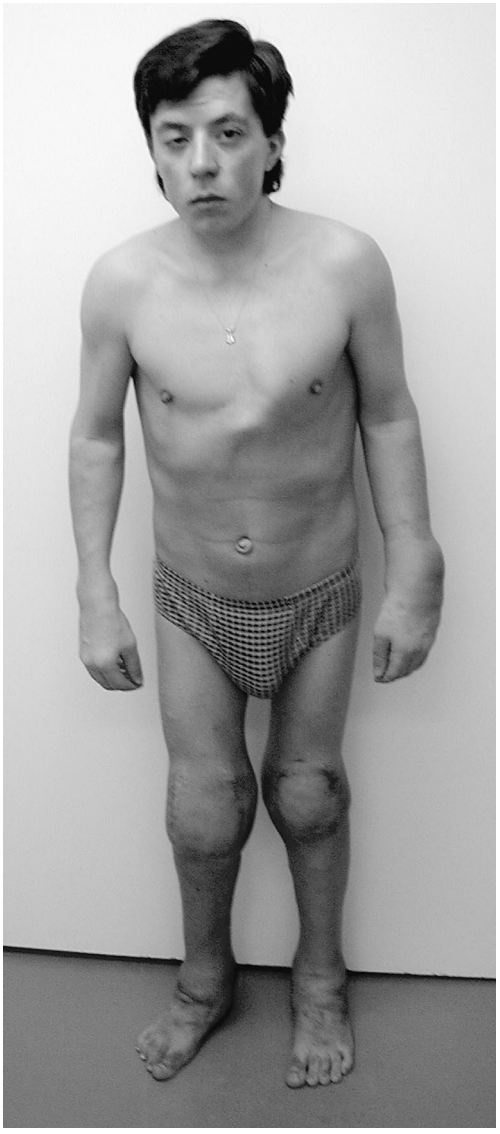

Fig. 1. Typical habitus of Noonan syndrome

dings were seen also on X-rays of other involved joints. Villous hyperplasia in joint spaces of hypointense character with widening of periarticular soft tissue and subchondral osteodystrophic foci was seen on MRI of both knees. Results of standard laboratory tests were within normal limits. Densitometry confirmed presence of severe osteoporosis.

The main problem was enormous painful swelling of the joints with rapidly progressive destructions and flection contractures of both knees.

Given the fact that repeated synovectomies in the past did not lead to a significant improvement, we had attempted to influence the unfavourable condition by radiotherapy.

We have used cesium irradiation of total dose 30 Gy divided into 15 fractions to both knee joints. The treament was very well tolerated by the patient.

Results of a follow-up visit at six months were very satisfactory. The knee joints pain has subsided, volume of both knees decreased and follow-up MRI demonstrated significant regression of pseudotumorous changes and decrease of fluid volume. Findings on the other joints were unchanged. This improvement lasted for 3 years.

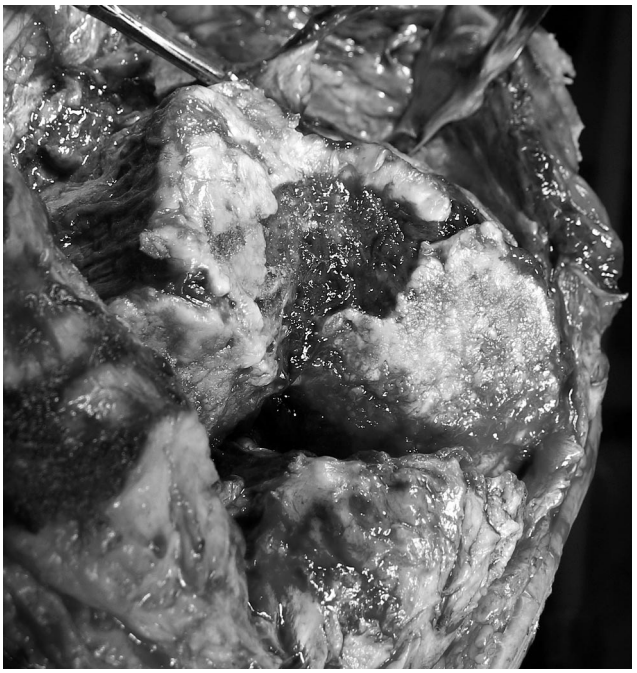

Fig. 2. Severe destruction of femoral condyles (right knee)

After temporary improvement, the clinical findings on the knee joints started to worsen again. Despite significant risks involved, we decided to perform total joint replacement due to severe synovitis of the left knee joint associated with severe pain and worsening of flection contracture.

Peroperative findings confirmed massive hypertrophic synovitis with numerous hemorrhagic foci and complete destruction of joint surfaces (Fig. 2). Surgery has been complicated by diffuse, difficult to control bleeding from minor vessels due to coagulation disorder, which despite detailed hematological testing could not be specified. Careful pre- and per-operative treatement did not prevent this problem, which repeated again during implantation of the right knee joint 1,5 year after the replacement of the left knee joint.

Three years after the surgery X-ray signs of loosening of the femoral component of the first implant (i.e. left knee) associated with joint pain were apparent. Laboratory tests, assessment and culture of the joint aspirate and biphasic scintigraphy ruled out low-grade infection as a possible cause of the loosening.(4) After some hesitation, the worsening of X ray findings (Fig. 3) together with increasing clinical symptoms required revision of the left knee joint replacement, which was performed 3,5 years after the initial surgery. Completely loose femoral component with undergrowing pathological synovial tissue which was forming deep cavitations in both femoral condyles was found during the revision. Despite the fact that the tibial component was fully inte-

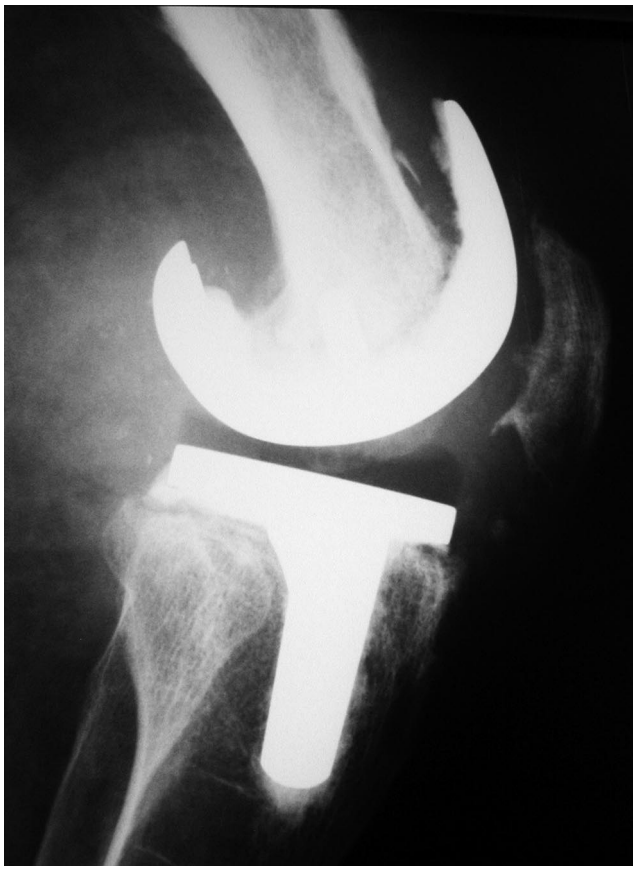

Fig. 3. Aseptic loosening of femoral component – 3,5 years follow-up time

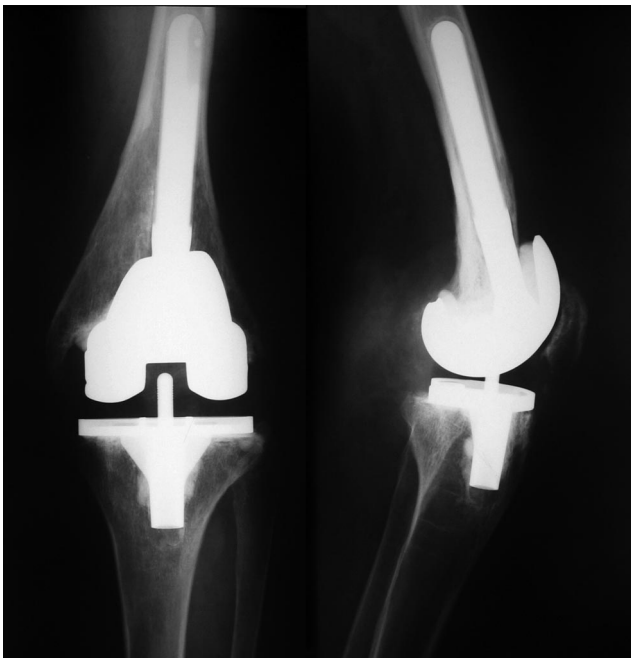

Fig. 4. Revised left knee – 3 years after reimplantation

grated, both components were replaced after careful synovectomy with revision stabilized implant with augmentations and femoral stem.

At the present time; 3 years after the revision arthroplasty of the left knee (Fig. 4) and 5 years after the primoimplantation of the right knee the condition of both knee joints is stabilized (findings are unchanged) without clinical or radiographic signs of loosening. Surgical approaches are well healed. There is only residual thickening of soft tissue around the joints. Both knees are stable, not painful and with satisfactory range of motion (extension- flexion left knee: 5-60 degrees, right knee: 0-80 degrees).

DISCUSSION

An association of PPVS with LEOPARD syndrome (lentiginosis, ECG conduction abnormalities, ocular hypertelorism, pulmonic stenosis, genital abnormalities, growth retardation, sensorineural deafness) was described in two siblings and their father in 1986 (15).A review of 14 cases of association of giant-cell lesions of bones, joints and soft tissue with features of Noonan syndrome was published in 1991 and the designation of Noonan-Like/multiple giant-cell lesion syndrome was suggested (2). Characteristic features of Noonan syndrome are short stature, hypertelorism, ptosis, epicanthus, low set ears, short neck, pterygium, pectus carinatum, kyphosis, scoliosis, cardiovascular malformations (pulmonic stenosis), skin changes (nevi, lentiginosis, depigmentations), osteoporosis, developmental delay and others. Noonan syndrome and Noonan-like syndrome are genetically heterogenous disorders (13). Mutation of PTPN11 gene coding for tyrosine phosphatase SHP-2 is often present (1,8).

PPVS is a rare chronic condition of unknown etiology and pathogenesis. A genetic factor is presumed to play a role given the association with many various congenital abnormalities. Presence of some of the phenotypic features of the Noonan syndrome together with PVVS joint involvement in our patient is in accordance with the described Noonan-like/multiple giant cell lesion syndrome.

Treatment of joint involvement in cases in which the surgical treatment (synovectomy) failed and in which recurrence of synovitis and progression of painful joint destruction occurs is very problematic. Systemic antiinflamatory therapy, used in the treatment of arthritis, is ineffective. A possibility of influencing the process by therapy blocking the main proinflammatory cytokine tumor necrosis factor alpha (TNF-alpha), which is used in patients with inflammatory diseases, remains a question. Sporadic case reports of patients with monoarticular form of PVS suggest a possible favourable effect of infliximab. In a patient with refractory PVS a year long treatment led to a significant reduction of clinical symptoms, reduction of macrophage number and TNF-alpha expression in the synovial tissue (7).

There are published reports about the use of radiation therapy or aplication of a radiocolloid (3,5) to affected joints. The most comprehensive being a paper on use of a low radiation dose of cobalt (35 Gy in 15 fractions)

in 14 patients with refractory diffuse form of PVS affecting the knee joint (10). According to the authors, this treatment allowed in very advanced cases of impending amputation to preserve acceptable function of the extremity. On the other hand some authors point toward the risk of damage to the limb or the joint after the use of higher radiation doses and to the potential risk of sarcoma development (9). The dose of 35 Gy is considered to be safe and effective. However there are no clear guidelines for this therapy. Our experience has shown that this modality may at least slow down the process for several years.

The decision about joint replacement was also difficult because despite reports about relatively succesful use in basic forms of PVS(11,12) we have not found a case of multiple joint replacement in a patient with PPVS in the literature. Repeated synovectomy probably would not produce long-term improvement and in addition would not improve the already existing advanced destruction of joint surfaces. Another treatment option – arthrodesis, would, in the setting of severe ankle involvement and presumed bilateral indication, critically and permanently limit mobility of the patient. The mind-set of the patient, who refused arthrodesis, has played a role as well. In our case we have accepted this solution as the only possibility which might affect long-term functional state of our patient. This modality is not without risks as demonstrated by the disease course and component loosening may occur due to undergrowth of synovial tissue. Despite the fact that we were not able to identify any specific coagulation disorder, increased bleeding tendency was evident during all surgeries and was confirmed by multiple hemosiderin deposits in collected samples of synovial tissues.

Chronic hemorrhage in the cement-bone or implant-bone interlayer may play a role by mechanism analogous to the one known to affect joint replacements in hemophiliacs. Crucial attention has to be payed to maximally careful synovectomy and controlling per and postoperative bleeding by all available means. Long-term follow up of all coagulation factor levels is also advisable.

ZÁVĚR

Kazuistika popisuje efekty radiační a opakované chirurgické léčby 30letého muže sledovaného od 6 let pro těžký průběh vzácné kombinace polyartikulární formy pigmentové vilonodulární synovitidy s kombinací vrozených vad odpovídajících Noonan like syndromu. Pacient v průběhu 20 let podstoupil opakované synovektomie 8 velkých kloubů, vždy jen s krátkodobým efektem. Pro pokračující agresivní synovialitidu zejména obou kolen, provázenou bolestmi a progredující kloubní destrukcí, bylo provedeno ozáření těchto kloubů dávkou 30 Gy, aplikovanou v 15 sezeních. Příznivý efekt přetrvával 3 roky. Poté došlo k recidivě a pro pokračující destrukci s omezením hybnosti byly postupně implantovány endoprotézy kolenních kloubů. Endoprotéza vlevo byla revidována po 3,5 letech pro aseptické uvolnění femorální komponenty a nahrazena revizním implantátem. V současnosti je pacient 5 let po implantaci vpravo a 3 roky po reimplantaci vlevo, bez známek uvolnění komponent a recidivy s uspokojivým klinickým i funkčním výsledkem.

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