

Pelvic tumors with deep venous thromboses as the main symptom: 4 cases reports and literature review

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Summary. *Objective:* To probe into reasons for misdiagnosing pelvic tumor as deep venous thrombosis, as well as diagnostic methods and effective treatments for pelvic tumor. *Methods:* 4 case reports on misdiagnosing pelvic tumor as deep venous thrombosis and further analysis of the causes of misdiagnosis, diagnosis, and treatment, with study of the literature. *Results:* The 4 cases misdiagnosed as pelvic tumor were actually fibroneuroma, myxo-fluidity Liposarcoma, moderately differentiated squamous cell carcinoma, and synovial sarcoma respectively. The tumor in the first case was completely removed, and in the other 3 cases the malignant tumors were resected when the tumors shrank with clear boundary and less blood supply after application of 3 cycles of intra-arterial chemotherapy via an implanted pump. *Conclusion:* Pelvic tumor usually shows up or is misdiagnosed as deep venous thrombosis because of its untypical clinical manifestation, so one should be on the alert for pelvic tumor when deep venous thrombosis occurs. Tumor resection is preferred for benign tumor, and intra-arterial intervention chemotherapy should first be applied for malignant tumor, followed by surgery.

Key words: pelvic tumor, deep venous thromboses (DVTs), misdiagnosis, intra-arterial intervention chemotherapy

«TUMORI PELVICI ASSOCIATI A TROMBOSI VENOSA PROFONDA COME SINTOMO PRINCIPALE: 4 CASI CLINICI E REVISIONE DELLA LETTERATURA»

Riassunto. *Obiettivo:* Comprendere le ragioni di una diagnosi errata di tumore pelvico scambiato per trombosi venosa profonda, così come comprendere i metodi diagnostici ed i trattamenti effettivi per il tumore pelvico. *Metodi:* 4 casi clinici di diagnosi errata di tumore pelvico scambiato per trombosi venosa profonda e successiva analisi delle cause della mal interpretazione della diagnosi e del trattamento con revisione della letteratura. *Risultati:* In realtà i 4 casi mal interpretati di tumore pelvico erano rispettivamente un fibroneuroma, un liposarcoma mixoide-fluido, un carcinoma squamocellulare moderatamente differenziato e un sarcoma sinoviale. Nel primo caso, il tumore è stato rimosso completamente, mentre negli altri tre casi i tumori maligni sono stati rimossi solo dopo riduzione delle dimensioni con margini liberi e un minor apporto sanguigno in seguito a somministrazione di tre cicli di chemioterapia intra-arteriosa attraverso pompa impiantata. *Conclusioni:* Frequentemente il tumore pelvico si manifesta o è mal interpretato come trombosi venosa profonda a causa della sua manifestazione clinica atipica, per cui è necessario prendere in considerazione la presenza di tumore pelvico quando si riscontra una trombosi venosa profonda. La resezione del tumore è preferibile in caso di tumore benigno e un intervento di chemioterapia intra-arteriosa dovrebbe essere la prima scelta per il tumore maligno, seguito da chirurgia.

Parole chiave: tumore pelvico, trombosi venosa profonda (DVTs), mal interpretazione, intervento di chemioterapia intra-arteriosa

Introduction

Pelvic tumors complicated by deep vein thrombosis are rare in clinical practice; sometimes the clinicians only focus on the diagnosis and treatment of deep vein thrombosis and thereby delay the diagnosis and treatment of pelvic tumors because of untypical clinical manifestations. Four cases of pelvic tumors misdiagnosed as deep venous thrombosis were hospitalized in our department from March 2006 to December 2011. The details of the cases are reported and discussed below.

Case reports

Case report 1

The 57-year-old male patient underwent tumor resection at another hospital in 1996 when a mass was detected on the left lower abdominal wall, and the pathological report indicated left pelvic neurofibromatosis; postoperative radiation was then performed. Lower extremity vascular ultrasonography was performed due to repeated swelling of the left lower extremity in the spring of 2007 lasting one year, combined with left lower extremity pain for two months. The results suggested: 1. superficial femoral vein thrombosis in the left leg; 2. popliteal artery atherosclerosis in the left leg. The patient visited our hospital for further diagnosis and treatment, after receiving anticoagulation, thrombolysis and expansion treatment with low molecular heparin and warfarin for 20 days without any significant symptom relief. The pelvic CT scan indicated a mass with an irregular shape, uneven density and approximate size of $8 \times 6.5 \times 5 \text{ cm}^3$ located on the left wall of the iliac fossa. The iliac artery was pressed inward, and the bladder compressed and pushed forward to the right side. Physical examinations: a longitudinal surgical scar with a length of 8 cm was observed in the left lower abdominal wall; there was a tough mass of around $9 \times 5 \text{ cm}^2$ in size and palpable deep tenderness. Flexion of the left hip joint was limited, and lower left extremity swelling with slightly lower skin temperature was observed. Left iliac fossa tumor resection was performed under

general anesthesia, and pathological examination indicated neurofibromatosis.

Case report 2

A 38-year-old woman complained of lower left extremity swelling for an unknown reason in March 2006, and deep vein thrombosis in the lower left extremity was indicated by color Doppler ultrasound examination in January 2007 in another hospital. The lower left extremity swelling alleviated after two weeks of anticoagulant therapy with low molecular heparin and thrombolytic therapy, after which warfarin was orally administered for 2 weeks, but the patient experienced progressively worse pain with obvious hypalgia, and self-administration of analgesics proved ineffective. The patient was admitted to our hospital in early March 2007. Physical examinations: the patient suffered from limping, her left hand supporting the left hip. A mass of about $9 \times 6 \times 5 \text{ cm}^3$ in size, moderately hard and obviously tender on palpation, was discernible deep inside the left iliac fossa. Tenderness was obvious in the area along the path of the sciatic nerve in the left hip. The patient suffered from hypoesthesia of the lateral of the lower left extremity and back of the left foot, as well as markedly limited flexion and abduction of the left hip. The thigh perimeter 10 cm above the left knee was 5 cm wider than that of the right leg. Ultrasonography indicated a large hypoechoic solid space-occupying lesion $8.6 \times 5.6 \times 5.7 \text{ cm}^3$ in size, with an unclear boundary, irregular shape, and uneven internal echo. Strong blood flow signals were observed in the area from the lower segment of left iliac blood vessels to the groin as far as the deep pelvic cavity, the left renal pelvis and ureter were expanded, the lower segment of the left ureter was close to the mass, and the uterus, accessories and bladder had shifted to the right. CT scan indicated an unclear enhancement area inside the mass surrounding the left external iliac artery and vein.

Case report 3

A 52 year-old woman reported pain and swelling of her upper right thigh for more than three months in early 2007, and deep vein thrombosis of the low-

er right extremity was indicated by ultrasonography. Anticoagulant and thrombolytic therapies performed with low molecular heparin had no significant effect, so the patient applied to our hospital two months later. Physical examination revealed a mass of about $20 \times 12 \text{ cm}^2$ in size, with poor activity and an unclear boundary in the right iliac fossa and upper right thigh, high skin temperature, red skin, positive tenderness. The right thigh perimeter 5 cm below the femur trochanter was 20 cm wider than on the left thigh. Vascular ultrasound indicated phlebotrombosis in the lower extremity and a mass in the iliac fossa close to the blood vessels.

Case report 4

A 42 year-old man had suffered from swelling and pain in the lower left extremity for unknown reasons since September 2011. The patient had a vascular ultrasound examination at a local hospital when the pain progressively worsened in November 2011, and femoral vein thrombosis in the left leg was indicated. Anticoagulant and thrombolytic therapies as symptomatic treatment were performed with slight symptom relief; however, the patient reported to our hospital after 2 weeks when the symptoms relapsed. Physical examinations: a mass of about $5 \times 6 \text{ cm}^2$ in size with moderate hardness, poor activity, an unclear boundary and deep tenderness in the left iliac fossa near the

groin. The left thigh perimeter 5 cm below the femur trochanter was 20 cm wider than on the right thigh. Pelvic CT scan indicated a soft tissue mass about $7 \times 6 \times 5.5 \text{ cm}^3$ in size in the left pelvic cavity near the groin, which was close to the iliac blood vessels.

From the medical history, clinical manifestations and imaging analysis, the last three cases were considered to have a high probability of malignant lesions, so puncture biopsies were performed under the guidance of ultrasonography to confirm the nature of the lesions. The pathological results were as follows: the second patient had moderately differentiated squamous cell carcinoma, the third had mucinous liposarcoma, the fourth had synovial sarcoma. A chemotherapy pump was implanted in the common iliac artery through the femoral artery for the above three cases with malignant pelvic masses to administer cisplatin and doxorubicin by way of arterial interventional chemotherapy (1). All 3 patients felt pain relief after 3 cycles of interventional chemotherapy, and the tumor shrank, displaying clear boundaries with the surrounding tissues. A comparison of the images before and after chemotherapy is shown in the attached figure (Fig. 1 and 2). The local vascular compression lessened as the tumors shrank, and the extremity swellings caused by the thrombus were relieved after chemotherapy. Radical naked-eye resection of the tumors was performed after chemotherapy, and subsequent chemotherapy was given to prevent

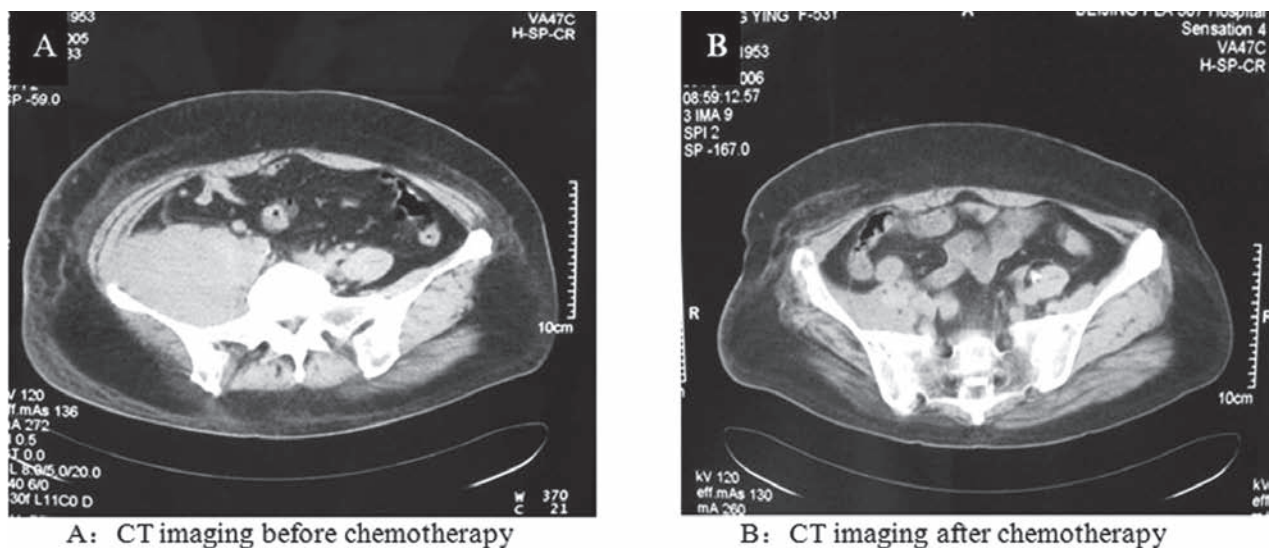


Figure 1. Moderately differentiated squamous cell carcinoma; the tumor shrank apparently after 3 cycles of chemotherapy

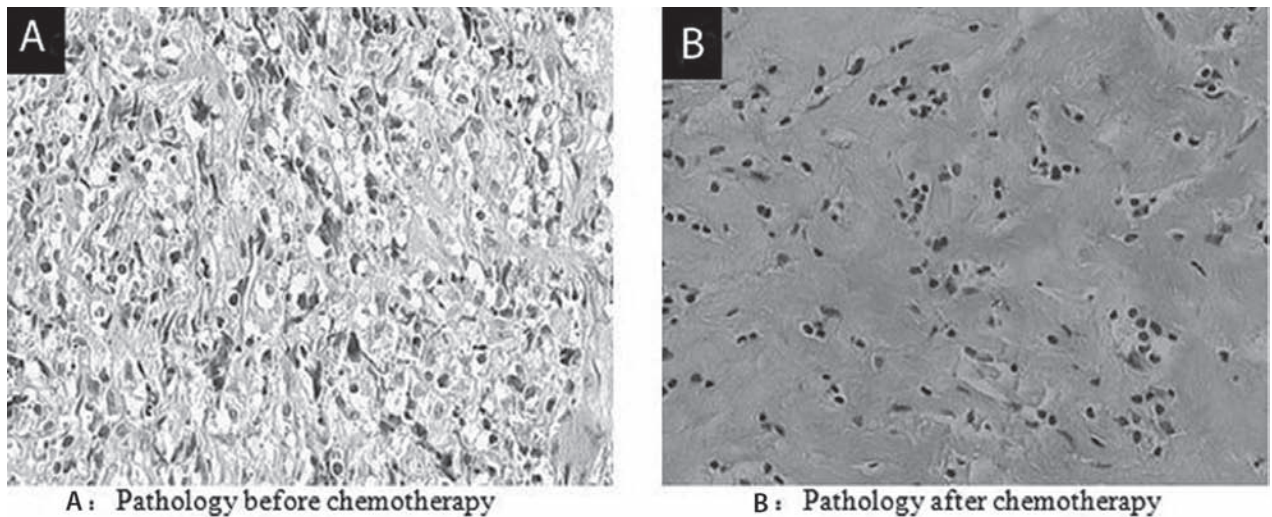


Figure 2. Myxo-fluidity liposarcoma in pelvis, shrunk tumor after chemotherapy, with a clear boundary. Pathological changes: a) a large quantity of atypical cells before chemotherapy; b) obvious necrosis after chemotherapy

any recurrence. The interval between chemotherapies was gradually prolonged until two years after surgery. Up to now, no patients have had any local recurrence or distant metastasis, according to the follow-up.

Discussion

There are various types of pelvic diseases, which can basically be classified under two categories, inflammatory and neoplastic diseases. Neoplastic diseases, especially malignant tumors, are prone to deep vein thrombosis as a complication. It has been reported that the maximum incidence of concomitant deep vein thrombosis (DVT) in patients with malignant tumors may be more than 10%, varying with the tumor type, location, time of diagnosis and individual differences (2). DVT is a major complication and the cause of death connected with malignant tumors. The presence of DVT not only complicates the therapy for malignant tumors and worsens the patient's quality of life, but also indicates poor prognosis (3).

As a soft-tissue malignant tumor in a vulnerable position like the pelvic cavity, especially the iliac fossa, occupies a relatively large space, such tumor patients usually have no obvious symptoms in the early stage, but clinical manifestations appear as the gradually enlarged tumor compresses the surrounding tissues. Pre-

vious studies have indicated that vein wall damage, slow blood flow and hyper-coagulation are the three main factors causing deep vein thrombosis. Pelvic veins are apt to expand and form many curved venous plexuses, ending up in venous stasis as the result of thinner vein walls than the veins in other parts of the body, lack of an outer fascia sheath, no valves, lack of flexibility, and surrounding loose connective tissues in the pelvic cavity. The compression of solid tumors on the pelvic veins further affects the lower extremity venous reflux. On the other hand, exogenous compressions inducing DVT may also be caused by other pelvic diseases such as uterine fibroids, endometriosis, pregnancy and dilated bladder (4).

Besides iliac vein compression, pelvic malignancy itself influences DVT. Studies have shown that patients with malignant tumors are prone to DVT mainly for the following reasons: 1) Hemorrhheologic changes: the vast majority of patients with malignant tumors are found to have hemorrhheologic changes. A number of relevant indexes including the whole blood viscosity, plasma viscosity, fibrinogen, hematocrit and erythrocyte sedimentation rate (ESR) in patients with malignant tumors are significantly higher than in healthy adults (5); 2) The hypercoagulable state can activate the body's blood clotting process through various pathways. On the one hand, the tumor cells may secrete clotting factors and activate prothrom-

bin, initiating the blood clotting process through a cascade reaction, which is further promoted by vascular endothelial growth factor being secreted by the tumor cells. On the other hand, the tumor cell produces abundant fibrinolytic system-regulating proteins and thrombin, which may promote red blood cell and platelet aggregation in addition, while necrotic and disintegrated tumor cells also produce abundant thromboplastins. All the above factors contribute to thrombus formation (6). Hence, patients with malignant tumors are high-risk populations for deep vein thrombosis. The thrombosis of our last three patients was associated with these changes. Thus, clinicians of tumor patients should beware of complications with deep venous thrombosis.

Highly malignant soft tissue tumors are characterized by local growth and distant metastasis. It has been reported (7) that lower extremity soft tissue sarcoma sometimes manifests as deep vein thrombosis, so that soft tissue sarcoma should be considered when lower limbs swell with pain, especially recurrent or refractory deep vein thrombosis. Like other orthopedic diseases, bone and soft tissue tumors are likely to be complicated by deep vein thrombosis, and many cases are misdiagnosed as their primary symptoms are thrombosis. Hip tumors, usually anatomically close to iliac blood vessels, may result in deep vein thrombosis in the lower limbs (8).

As deep vein thrombosis is a common disease, the doctors usually concentrate on the treatment instead of probing into the etiology, so that some important diseases may be missed, including cancer. The main reasons for misdiagnosis include: 1) Lack of knowledge about any pelvic tumor. Insufficiently detailed clinical history is acquired because of its low morbidity, which leads to insufficient diagnosis and differential diagnosis of the disease. 2) The pelvic tumor has no obvious symptom in the early stage since the pelvic cavity is a relatively large space. As the gradually enlarged tumor compresses the surrounding tissues, the subsequent clinical manifestations are not specific enough and most laboratory tests and auxiliary examinations lack specificity. 3) The diagnosis and treatment of thrombotic disease are concentrated on, and diagnosis of the primary diseases is ignored.

All three patients in this paper came to hospital

with swelling of the lower extremity, had been diagnosed as deep venous thrombosis and were subsequently identified as pelvic tumors upon further examination, which suggests that deep venous thrombosis of the lower extremities may be the primary symptom of pelvic tumor: in other words, deep vein thrombosis, the complication of pelvic tumor, may occur as the first symptom of pelvic tumor. Pelvic iliac fossa tumor was found by abdominal and pelvic ultrasound and CT examination in all four patients misdiagnosed as DVT in this paper. Thus, we believe that imaging examination is necessary for identifying occult tumors from patients with spontaneous DVT. Especially with aged patients who have no obvious factors leading to DVT formation, a detailed physical examination, routine laboratory tests and X-ray examination should be performed, and then further tests such as ultrasound, CT and MRI should be carried out, depending on the results of these tests.

Radical resection of malignant pelvic tumor is difficult as the anatomical structure of the pelvic cavity is complex, so local recurrence of malignant tumors is relatively high after resection. For these reasons, chemotherapy followed by resection should be applied for confirmed malignant pelvic tumors. Intra-arterial chemotherapy with a subcutaneously implanted pump may be applied for 3 to 4 cycles to maintain a high drug concentration in the blood around the tumor (9). The tumor in our cases shrank, the boundary became clear, and the blood supply was reduced after chemotherapy, to paving the way for radical resection of the tumors. The preoperative chemotherapy effects and postoperative chemotherapy protocol were determined by the tumor necrosis rate in postoperative pathological examination. Postoperative chemotherapy at a gradually prolonged interval was continued till two years after the surgery. Of the four patients reported in this paper, one patient with benign tumor underwent radical resection. The three patients with malignant pelvic tumor underwent radical tumor resection after 3 cycles of intra-arterial chemotherapy. After the chemotherapy, the patients' pains were completely relieved; the tumors significantly shrank, the gaps between tumors and surrounding tissues widened, and the blood supplies were reduced. Up to now, tumor recurrence and metastasis has not been observed in the follow-up.

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Received: 14.10.2014

Accepted: 13.1.2015

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