CASE REPORT

Just another negative DVT?

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devsharm@aol.com**SUMMARY**

A 69-year-old woman presented to the emergency department (ED) with a swollen left thigh and leg. D-dimer test was positive, a radiology department ultrasound showed no direct evidence of a deep venous thrombosis but a lack of respiratory modulation was seen. ED ultrasound showed large groin lymph nodes and this, together with low haemoglobin, prompted a CT scan which led to the diagnosis of metastatic carcinoma.

BACKGROUND

This case shows the importance of pursuing a diagnosis even in those patients without a deep venous thrombosis (DVT). It also shows the utility of the emergency department (ED) ultrasound in helping to focus investigations on relevant patients.

CASE PRESENTATION

A 69-year-old woman, with back pain and increasing swelling of the left leg, was referred by her general practitioner (GP) to the orthopaedics department. She was sent by the orthopaedic clinic to the ED which runs a DVT pathway for the diagnosis and initial management of DVTs. She scored as being very high risk for a DVT on the Wells score. She was started on low-molecular-weight (LMW) heparin, blood tests were taken and an ultrasound examination was organised. She also reported back pain and gave a history of breast cancer with ductal carcinoma in situ for which she had received mastectomy and radiotherapy, followed by tamoxifen for 5 years.

INVESTIGATIONS

The D-dimer test was positive. The ultrasound examination showed no evidence of thrombus in the left lower limb veins. Owing to the absence of respiratory modulation in the common femoral vein and some shadowing causing difficulty in assessment of the common iliac vein, a possible iliac vein thrombus was postulated and a rescans suggested in 1 week with fasting. On clinic review after the ultrasound scan, it was noted that the patient was anaemic with haemoglobin 10.4 g/dL, while the urea and electrolytes and liver function tests were normal. An ED ultrasound was performed which replicated the findings of the vascular ultrasound, but numerous enlarged lymph nodes were found in the groin (figure 1). ED ultrasound of the abdomen also gave an incidental finding of situs inversus. She was aware of her dextrocardia but not the inversion of her abdominal organs. CT scan of the abdomen and pelvis

was performed which showed multiple necrotic appearing lymph nodes in the para-aortic/retroperitoneal distribution. The largest nodal mass lay just proximal to the aortic bifurcation measuring approximately 4 cm in maximum axial dimension. Several other pathological appearing nodes were demonstrated extending along the para-aortic region and along the iliac chains bilaterally. The nodal mass adjacent to the right external iliac vein looked more prominent than that on the left. There appeared to be compression of the inferior vena cava and common iliac veins. Prominence of the endometrial cavity was also commented on, and it was suggested that the transvaginal ultrasound should be performed later.

Following this the patient was admitted, CT of the chest and neck showed no other areas of lymph node enlargement. A tru-cut biopsy was inadequate and a surgical excision biopsy was necessary. This showed that the lymph node was infiltrated by a highly pleomorphic carcinoma. The features were those of undifferentiated metastatic carcinoma but positive staining for PAX-8, oestrogen receptor and progesterone receptor suggested a gynaecological primary rather than an occult breast neoplasm. Further investigation involved admission for hysteroscopy and laparoscopy when examination under anaesthesia showed a normal sized anteverted uterus. It was noted that there was limited mobility due to general induration of the tissues and a short cervix. Hysteroscopy showed obvious thickening of the anterior and left lateral aspects of the uterine cavity. There was clinically malignant tissue which was removed by polyp forceps and general curettage. Laparoscopy revealed a macroscopically normal left tube and ovary, some dilation of the right tube and some adhesions around the ovary which was otherwise normal. There was no evidence of peritoneal disease and no obvious liver metastases.

Histology of the endometrial biopsy revealed tumour formed of solid pleomorphic and highly atypical cells with numerous giant tumour cells and bizarre mitoses. The features were those of a high-grade endometrial carcinoma with anaplastic, serous and clear cell features.

DIFFERENTIAL DIAGNOSIS

Thrombus in external iliac vein and common iliac vein.

OUTCOME AND FOLLOW-UP

The patient received chemotherapy but died 6 months after the ED visit.

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Figure 1 Ultrasound of enlarged lymph node in groin (callipers show size 2.53 cm).

DISCUSSION

Many EDs now provide an outpatient service in the investigation and initial management of DVT. There has been recent advice from the National Institute for Care Excellence (NICE) to standardise diagnosis of this pathology. The old classification into low-risk, moderate-risk and high-risk patients has been replaced by categorisation into DVT 'likely' or 'unlikely' categories using the two level DVT Wells score (table 1).

Patients with a likely DVT on the Wells score have blood tests and an outpatient ultrasound. Treatment dose LMW heparin is started if they cannot have a proximal vein ultrasound within 4 h (and a D-dimer test if the proximal vein ultrasound is negative with patients who have a positive D-dimer test having a repeat ultrasound scan 6–8 days later). In patients with a 'DVT unlikely' score a D-dimer test should be performed and if positive then either LMW heparin and ultrasound within 24 h should be given or above knee ultrasound within 4 h should be performed (figure 2). The D-dimer test is used as it generally has a high negative predictive value and is a useful rule-out tests that reduces the need for imaging when used in conjunction with clinical probability, plethysmography or ultrasonography.¹

Table 1 Two level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm more than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	–2
Clinical probability simplified score	
'DVT likely'	2 or more
'DVT unlikely'	Less than 2

DVT, deep venous thrombosis.
Source: Wells *et al.*⁸

In practice, at the weekend in most hospitals it is unlikely that a formal Doppler ultrasound can be performed within 24 h and LMW heparin is given until the formal ultrasound is performed. Following the ultrasound the patient is reviewed. If DVT is found anticoagulation is continued. Generally if no DVT is found the patient is sent back for further management by the GP, although recent NICE guidance² has recommended repeat ultrasound scan in those with a positive D-dimer test who have only received proximal vein ultrasound. NICE has suggested that alternative diagnoses should be taken into consideration in patients with:

- ▶ an *unlikely* two-level DVT Wells score (see table 1) and
 - a negative D-dimer test or
 - a positive D-dimer test and a negative proximal leg vein ultrasound scan.
- ▶ a *likely* two-level DVT Wells score (see table 1) and
 - a negative proximal leg vein ultrasound scan and a negative D-dimer test or
 - a repeat negative proximal leg vein ultrasound scan.

It is recommended that these groups should be advised that it is not likely that they have DVT, and to discuss with them the signs and symptoms of DVT and when and where to seek further medical help.

This patient was felt to be at high risk of DVT based on her Wells score.

Tamoxifen is an antioestrogen (a selective oestrogen receptor modulator) which is used as a chemoprotective agent for breast cancer risk reduction.³ An increase in venous thromboembolic (VTE) events has been found of 1.9-fold (95% CI 1.4-fold–2.6-fold; $p < 0.0001$) in one meta-analysis.⁴ Pulmonary embolus was the most frequent event followed by DVT and retinal vein thrombosis. It was associated with a threefold increase in risk of superficial thrombophlebitis.⁵ It is thought that the risk of VTE is more in the first 2 and 3 years of tamoxifen treatment.⁶

Tamoxifen is, because of the above, not recommended in women with a history of DVT, pulmonary embolus, stroke or transient ischaemic attack.

Despite this additional risk she did not, in fact, have a DVT.

Painful swollen leg is a common clinical presentation. DVT often presents as a painful swollen leg; and prompt management is vital to prevent fatal pulmonary embolism. It can be seen that most of the NICE guideline is devoted to accurate diagnosis and appropriate treatment of DVT.

Patients with no DVT also require appropriate management. The common differential diagnoses include cellulitis and a ruptured Baker's cyst. It should be remembered, however, that although Baker's cyst and cellulitis are the commonest findings, other significant pathologies may occur including soft tissue sarcomas.⁷ Other pathologies causing lymphoedema of the leg include conditions affecting lymph nodes such as metastatic carcinoma as in this case. In this case if vascular department ultrasound had been repeated after 1 week as suggested in the formal ultrasound report, it was quite likely that again no DVT would have been found and the patient could easily have been discharged back to the GP with no definite diagnosis.

It is important that patients with no diagnosis of DVT are investigated as appropriate and underlying important pathology found. Special investigations (CT or MR) should be utilised when necessary. While it is unlikely that this level of investigation would often be used in the UK, focused investigation may find significant pathology when blood results and general ultrasound are used to concentrate attention on appropriate patients as in this case.

Figure 2 The National Institute for Care Excellence guidelines for diagnosis of deep venous thrombosis algorithm.

Learning points

- ▶ Common causes of leg swelling without deep venous thrombosis include Baker's cyst and cellulitis.
- ▶ Other causes, however, include compression of veins by neoplastic lymph nodes.
- ▶ Blood tests must be reviewed.
- ▶ Use general ultrasound in addition to vascular ultrasound to investigate.
- ▶ CT and MRI may be needed in addition.
- ▶ Advise patients to seek review if swelling does not settle and no cause is found for the swelling.

Contributors DS attended and managed the patient clinically as well as performed the emergency department ultrasound. Both authors were involved in discussion, manuscript writing and the literature review.

Competing interests None.

Patient consent Obtained.

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