

“Incidence of Occult Malignancy Diagnosed in Patients With Unprovoked Pulmonary Embolism”

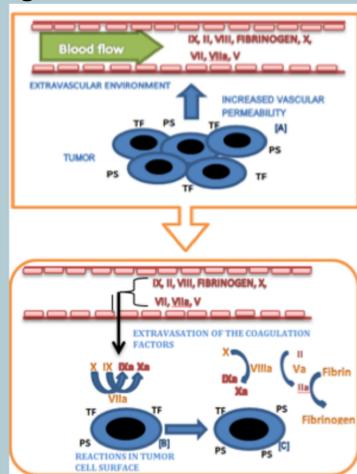
Dr Fatma Eminaga, Dr Reema Akhter, Dr Sridhar Redla
Princess Alexandra Hospital, Harlow

INTRODUCTION

A group of patients with venous thromboembolism (VTE) have no readily identified underlying cause and this type of VTE is referred to as idiopathic or unprovoked.

Patients suffering from an unprovoked VTE episode have a higher incidence of new cancer diagnosis during the following years, compared to the rest of the population. In some cases, a VTE event is the first clinical manifestation of an occult malignancy. This is thought to be through various mechanisms, such as tumour and treatment-associated hypercoagulability, endothelial damage (chemotherapy toxicity and use of venous catheters) or venous stasis due to bed rest or surgical immobilization. During the process of malignant transformation, tumours also secrete tissue factors, which enable the tumour cells to invade and metastasize. Tissue factor also simultaneously triggers the coagulation cascade leading to VTE. (1,2)

Figure 1



(A) Neoplastic cells stimulate vascular permeability in the tumour microenvironment through the generation of proangiogenic factors such as VEGF. In this way, blood coagulation proteins can leave the plasma circulation and reach the extravascular tumour microenvironment, getting in contact with the plasma membrane of tumour cells, which is rich in procoagulant molecules such as (B) TF and (C) PS. The assembly of different blood coagulation complexes thus culminates in the local generation of thrombin and fibrin (4)

As a result of above-mentioned factors, there is a 3-fold increased risk of VTE with cancer, both solid and lympho-proliferative. Diagnosis of such an underlying malignancy plays a pivotal role in optimising the management of the patients as it could have an impact on the patient's mortality and morbidity through the implementation of appropriate VTE treatment, as well as early treatment of the cancer and is cost effective (1,2).

Recently published studies have suggested that approximately 4-5% of patients with newly diagnosed unprovoked VTE will be diagnosed with cancer within 12 months of follow-up. Because of this, it is important for clinicians to maintain a low threshold of suspicion for possible occult cancer in this patient group.(4)

A Swedish population-based study performed with almost 62 000 patients over 18 years demonstrated that apparent unprovoked VTE was associated with significant increase in the risk of cancer within the first 2 years, with a standardised incidence ratio of 4.4%. (3)

National Institute for Health Care Excellence (NICE) clinical practice guidelines recommend that all patients diagnosed with unprovoked VTE should undergo a limited screening that includes a physical examination guided by the patient's medical history, a chest X-ray, blood tests and urinalysis. (3)

Furthermore, for all patients over the age of 40, physicians are suggested to consider a CT abdomen/pelvis (CTAP), as well as mammography for women. (3)

AIM

To the best of our knowledge, there is no previous study investigating the incidence of malignancy found solely by CT AP as a part of the screening following an episode of an unprovoked PE.

The aim of this study is to evaluate the incidence of occult malignancies diagnosed with a CT AP following an episode of an unprovoked pulmonary embolism as part of the cancer screening according to NICE guidelines.

METHODOLOGY

We retrospectively analysed the radiology PACS database of Princess Alexandra Hospital, Harlow and identified all “CT abdomen and pelvis” referrals containing the word “unprovoked” in the clinical information. The data analysis was performed for the period from May 2015 to May 2019.

Two investigators analysed the CT reports of each case to identify eligible cases.

RESULTS

124 eligible cases of unprovoked PE were identified. 56 of these patients were female (45%) and 68 were male (55%). (Table 1)

Ages of the patients ranged from 30 to 96 with a mean of 67.6.

8 out of 124 patients (6.4%) with unprovoked PE were found to have an abnormal CT AP which was diagnostic for an occult malignancy or triggered further investigations which eventually confirmed the diagnosis of a malignancy.

One patient was found to have multiple liver metastases on the CT. The subsequent investigations confirmed diagnosis of colon cancer. Another patient was diagnosed with prostate cancer after the CT report pointed to an irregularly enlarged prostate.

The other types of cancers diagnosed were renal, bladder, endometrial and ovarian.

4 out of 8 positive cases for underlying malignancy were found to have pulmonary emboli within the main pulmonary arteries, 1 patient had PE in the lobar pulmonary artery and 3 had segmental pulmonary emboli. None of the patients which had subsegmental pulmonary emboli only were found to have an underlying malignancy.

The mean age of patients with positive CT AP was 67.9.

Table 1

Gender	Percentage	Age group	Percentage
Male	54% (68)	30-39	3.2% (4)
Female	46% (56)	40-49	8% (10)
Type of PE:		50-59	19.3% (24)
Saddle	8.8% (11)	60-69	17.7% (22)
Main	29% (36)	70-79	28.2% (35)
Lobar	20.9% (26)	80-89	19.3% (24)
Segmental	29.8% (37)	90-99	4% (5)
Subsegmental	8% (10)		
Not specified	3.2% (4)		

CONCLUSION

The results of this study are in line with previous studies which had suggested that approximately 4-5% of patients with new unprovoked VTE will be diagnosed with cancer within 12 months of follow-up.

Mean interval between the diagnosis of the unprovoked PE and CT AP was found to be 7 days, which was within the recommended timeframe (2 weeks). (3)

Taken together, these findings highlight the role of targeted screening for occult malignancy in patients with first presentation of an unprovoked PE.

RECOMMENDATIONS

Unprovoked venous thromboembolism (VTE) could well be one of the first manifestation of an undiagnosed malignancy and clinicians should have a low threshold of suspicion for occult cancer in this group of patients.

Patients should undergo the cancer screening as laid out by NICE guidelines.

Our findings from Princess Alexandra Hospital, Harlow showed that the current screening practice for the occult malignancies in patients with unprovoked PE are satisfactory and in line with the NICE guidelines. We therefore do not think a change is required in our current practice.

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