

# Upper Limb DVT in an Oncological Patient with a PICC Treated with Edoxaban: A Case Report

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## Abstract

Upper extremities deep venous thrombosis (UEDVT) is less frequent than lower limb DVT but the incidence of UEDVT may be increased in patients affected by malignancies and bearing central venous catheters (CVC) or other devices as peripherally inserted central catheters (PICC). The standard of care for the treatment of cancer-related venous thromboembolism has been low molecular weight heparin (LMWH) for several years. But treatment with direct oral anticoagulants (DOACs) may represent an alternative to LMWH in patients with cancer related VTE. In the present article, we report a case of a 49 year old man with colorectal cancer in treatment with chemotherapy who presented DVT of the upper left limb with involvement of subclavian-axillar venous axis. Patient was treated with edoxaban 60 mg following a few days of LMWH (i.e., 100 u/kg twice daily). After three months, a vascular ultrasound scan showed the disappearance of DVT with a full recanalization of the vessel.

**Keywords:** Deep venous thrombosis; VTE; Antithrombotic treatment; Edoxaban; Chemotherapy

## Background

The two-way clinical association between cancer and venous thromboembolism (VTE) is well known since 19<sup>th</sup> century [1]; deep vein thrombosis (DVT) of lower limbs is the most common clinical manifestation of VTE during malignant diseases but also other sites of venous thrombosis have been reported in epidemiological studies. The appearance of upper extremities deep venous thrombosis (UEDVT), in fact, is less frequent than lower limb DVT but the incidence of UEDVT may be increased in patients affected by malignancies and bearing central venous catheters (CVC) or other devices as peripherally inserted central catheters (PICC) [2-4].

Oncological therapies may influence the risk of PICC-DVT because of infusion of chemotherapy drugs. Such chemotherapeutic regimen in fact is also associated to further thrombotic risk per se [5,6] and this action usually is added to the other thrombotic risk factors already present as prolonged bedrest, recent surgery, prothrombotic actions of other drugs as growth colony stimulating factors and so on [1].

The standard of care for the treatment of cancer-related venous thromboembolism has been LMWH for several years [7]. But treatment with direct oral anticoagulants (DOACs) may represent an alternative to LMWH in patients with cancer related VTE [8,9].

However, large series of patients with UEDVT treated with DOACs are lacking in the literature and specific guidelines too.

## Case History

A 49 year old man with colorectal cancer in treatment with chemotherapy was referred to our hospital describing a sudden pain of the upper left limb, local oedema and difficulty in moving the arm. The pain was localized above PICC insertion site which was placed nearly 1 month ago. He referred neither chest pain nor fever or dyspnea. The last chemotherapy treatment was performed nearly 2 weeks ago and was based also on the administration of bevacizumab.

After a physical examination, blood tests and ultrasonography were carried out. Blood tests were normal except for mild leukocytosis (i.e.,

13.400/*mmcube*), moderate thrombocytosis (i.e., 560.000/*mmcube*) and increased d-dimer (1210 mcg/dL) (Table 1).

Ultrasonography revealed a DVT of upper left limb with involvement of subclavian-axillar venous axis and without involvement of internal jugular vein and superior vena cava (SVC).

Test	Normal value	Patient's value
Red Blood Cells mm cube	3.000.000-5.000.000	3.100.000
Haemoglobin g/dl	11-15	11.0
White Blood cells mm cube	4000-10000	12.300
Platelets mmcube	100.000-400.000	201.000
PT INR	0.8-1.2	0.9
aPTT sec	23-38	33
Fibrinogen mg/dl	200-400	243
d-Dimer mcg/dl	< 500	
MTHFR c677t gene variants	Genotype CC	Genotype CC
PTHRA201210G gene variant	Genotype AA	Genotype AA
Factor V Leiden gene variant	Genotype AA	Genotype AA
Protein S %	60-120	62
Protein C %	60-120	64
AT III %	80-120	86
LAC	absent	Absent
IgG anticardiolipin U\GPL	<20	<20
IgM anticardiolipin U\MPL	<20	<20

LAC: Lupus Anticoagulant

**Table 1:** laboratory tests of patients with PICC-DVT of upper limb.

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An antithrombotic treatment based on therapeutic doses of LMWH (i.e., 100 u/kg twice daily) according to international guidelines was started. However, after few days the patient rejected the idea to perform nearly three months of subcutaneous injections and asked to be treated with other antithrombotic drugs. Based on the large use of DOACs in several setting of patients, the demonstrated efficacy and safety of edoxaban in oncological patients with DVT of lower limbs, and the recent update to NCCN Clinical Practice Guidelines in Oncology, an antithrombotic treatment with edoxaban 60 mg daily was started. Before starting treatment with edoxaban, bun and creatinine levels were analyzed. These blood tests and full blood count were performed every 30-40 days and/or after each chemotherapy cycle.

The choice of edoxaban 60 mg, in according to the SmPC, was based on the good clinical conditions of the patient and the absence of any other contraindication to the treatment.

After 10 days, pain and oedema of the left arm disappeared and an early ultrasound scan revealed a subtotal recanalisation.

From an oncological point of view, the PICC was removed and the patient was planned to other oncological treatments.

There were not any types of intolerances to the antithrombotic treatment with edoxaban.

After three months, a further vascular ultrasound scan confirmed the disappearance of DVT with a full recanalisation. In the screened three months, neither VTE recurrence or any type of bleeding (i.e., Major or minor bleedings) was recorded confirming the good outcome of the episode of VTE.

## Discussion

VTE is a common complication in oncological patients requiring PICCs for chemotherapy. In clinical practice, these devices are considered safe to deliver antibiotics and fluids but they present a trend to develop thrombotic complications [3]. Upper limb DVT are the most common thrombotic complication associated with central venous access devices, but the rate of thrombotic complication varies from study to study [3,10]. On the other hand, also the rate of DVT of upper limbs in presence of PICC varies in all studies [3]; yet, venous thrombosis of upper limbs associated to PICCs are also associated to pulmonary embolism and represent a new interesting topic on prevention of recurrent VTE in this clinical setting. In addition, in the last years, PICCs have been increasingly used to enable delivery of intravenous chemotherapy, and this clinical aspect may increase the rate of thrombotic complications related to the presence of these devices. Moreover, some chemotherapy drugs, seem to have a prothrombotic action stronger than other drugs, such as bevacizumab [6]. Bevacizumab acts as anti-vascular endothelial growth factor and it is added to several chemotherapeutic protocols, in particular for ovarian, brain and colorectal cancer. In murine models it has been reported that its prothrombotic action is due to a specific induced hypofibrinolysis, related an increased release of PAI-1 [11]. In literature, an increased trend to thrombotic disorders in patients treated with bevacizumab has been reported, but a specific thromboprophylaxis in these patients is still matter of discussion [6-7].

International guidelines suggest a treatment with LMWH in oncological patients that develop clinically overt VTE [7]. Results by metanalysis of phase III trials of DOACs in the treatment of VTE that considered only oncological patients, and specific trials focused only on the treatment of VTE in cancer patients with DOACs, open

a new scenario in this clinical setting [8,12]. Several experts in this field recently suggested to take into account the treatment of VTE in oncological patients with DOACs as first choice of treatment [8,9]. Although the treatment of VTE with DOACs in oncological patients has been mainly tested in patients with DVT of lower limbs, this antithrombotic treatment is also used in the real life to treat other clinical types of VTE as upper limb DVT [13].

The case that we have reported shows an antithrombotic treatment with DOACs after first days of full doses of LMWH in a patient with upper limb DVT developed during chemotherapy treatment with bevacizumab through a PICC line. The treatment was confirmed to be safe and efficacy. Complications as recurrent VTE or bleedings were not present. Moreover, the safety of the treatment based on edoxaban was also confirmed by the absence of side effects and anemia that has been frequently reported as a complication of antithrombotic treatment with DOACs [8].

Furthermore, the treatment with edoxaban has been also associated to a fast recanalisation of the DVT of upper limbs and to a fast disappearance of all symptoms associated to the thrombotic event as already showed for lower limbs DVT [14].

## Conclusion

This case report provides a good perspective for patients with PICC-associated UEDVT so that edoxaban may be a good option to the standard of care. Further studies on large based population should be addressed to improve the outcome and quality of life of oncological patients affected by UEDVT.

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