Cancer Biol Med 2016. doi: 10.20892/j.issn.2095-3941.2016.0057

ORIGINAL ARTICLE

Implantable port thrombosis in cancer patients: a monocentric experience

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ABSTRACT

Objective: Implantable port thrombosis (IPT) in cancer patients is a relatively rare but severe complication. Several factors are reportedly associated with the occurrence of thrombosis. We aimed to describe the prevalence and the anatomoclinical features of IPT observed in cancer patients who were treated in a medical oncology department in Tunisia.

Methods: A total of 600 cancer patients who had port implantation from January 2013 to December 2015 were retrospectively identified. Cases with symptomatic/incidental IPT (radiologically confirmed) were further identified. Epidemiological and anatomoclinical features were collected from patient records and the department database.

Results: We observed that 33 of the 600 patients had IPT; thus, the prevalence was 5.5%. The median age was 57 years, and the gender ratio was 0.43. Overweight or obesity was observed in 73% of the patients. IPT occurred mainly in patients with breast (36.4%) and colorectal (33.3%) cancers, which were mostly nonmetastatic (79%). At least one identified classical thromboembolic risk factor was found in 13 patients (smoking in 9, tamoxifen in 2). IPT was symptomatic in 93% of the cases, occurring within an average time of 56 days. Implantable ports were removed because of infection in 2 cases and nonfunctionality in 3 cases. IPT treatment was based on low-molecular-weight heparins (94%) and antivitamin K (6%) for an average of 130 days. Four patients had post-therapy complications: one thrombosis recurrence and three infections.

Conclusions: IPT cases in the 600 patients were observed to occur in obese nonmetastatic cancer patients within the first 3 months after IP implantation.

KEYWORDS Implantable port; cancer patients; thrombosis

Introduction

Implantable ports (IP) are extensively used in oncology for many purposes, including chemotherapy administration, blood sampling, parenteral nutrition, and supportive care[1]. Since the 1980s, they have been used as convenient alternatives to avoid venous toxicity and to improve the quality of lives of cancer patients. The IPs are completely implantable without any of its components appearing on the skin. This offers several advantages in contrast to partially implantable systems such as low infection rates and no restrictions on physical activities of the patients[2]. Various catheter materials such as silicone rubber (SiO) or polyurethane (PU) are available. Experimental and clinical investigations have revealed the notable differences among the outer surface properties of intravascular catheters made from different materials. Various degrees of roughness affect the thrombogenicity and susceptibility of patients to catheter-related infections[3]. Different insertion techniques have been commonly known and described, and their associated advantages and risks have been extensively discussed[4].

Implantable port thrombosis (IPT) has been associated with high morbidity and extra health care costs[5]. The manifestations can range from asymptomatic with no clinical significance to serious morbidity related to pulmonary embolism. The incidence of symptomatic IPT reported in the literature is highly inconsistent with 28% of the old studies and 5% of the recent ones. This may be due to the large differences in methods and populations[1]. Several studies has attempted to identify IPT risk factors but no predictive model has been established because of small sample sizes, few catheter associated deep vein thrombosis (DVT) events, variability in the duration of follow-ups, and heterogeneity in

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Received July 7, 2016; accepted August 8, 2016.
Available at www.cancerbiomed.org

the outcome definitions[6]. The aim of this work is to describe the anatomoclinical features of IPT observed in cancer patients who were treated in a medical oncology department in Tunisia.

Patients and methods

From January 2013 to December 2015, 600 cancer patients had port implantation at our medical oncology department. Cases with symptomatic or incidental IPT were retrospectively identified. Epidemiological and anatomoclinical features were collected from the records of the patients and from the department database. We identified classical risk factors of venous thrombosis among our patients, specifically, congenital thrombophilia, prior history of venous thromboembolism (VTE), hormonal therapies, and smoking history. IPT was diagnosed after the appearance of symptoms or after the incidental description on imaging performed for other reasons (e.g. follow-up, evaluation).

All ports were administered to the patients in an operating room by the oncologists of the department. The patients were under local anesthesia and under hemodynamic control, and the oncologists used a blind puncture of the internal jugular vein. Catheter tip placement at the junction of the superior vena cava and the right atrium was confirmed through chest-X ray. IP manipulation and maintenance were conducted by trained nurses. Ports insertion was indicated in case of long duration or continuous chemotherapy infusion, ideally before the start of the therapeutic protocol. Doppler imaging was immediately performed in symptomatic cases of IPT. Diagnosis of IPT was based on at least one of the following criteria observed in imaging: non-compressibility of a venous segment at the upper arm or at the internal jugular vein on venous ultrasonography, absence or reduced flow on doppler imaging with failure to augment upon compression of the arm or lack of respiratory variation, presence of echogenic material compatible with thrombus in the arm or central venous vasculature on real-time imaging, or the presence of an intraluminal filling defect in 2 or more images observed in a venous segment of the arm or central venous vasculature on CT scan.

IPT therapy was based on the recommendations of the Tunisian National Group of Thrombosis and Cancer, preferring low weigh molecular heparins for at least 3 to 6 months.

Chi-square and Fisher's exact tests were conducted to examine the relationship between IPT and categorical risk factors. In addition, *t*-tests were performed to examine association between IPT and continuous risk factors.

We reported the prevalence, patient's characteristics, and the therapeutic results. This work was approved by the local ethical committee.

Results

We observed 33 cases of IPT among the 600 patients who had port implantation. The prevalence was 5.5%. The patients with IPT have an average age of 57 years (30-74). Approximately 79% (n=26) of the patients were 35-70 years old, 6% were (n=2) less than 35, and 15% (n=5) were more than 70. Sex-ratio was 0.29. Overweight or obesity which was defined by body mass index ≥ 25 was observed in 73% of the patients (n=24). IPT occurred in 36.4% (n=12) of the patients with breast cancer and in 33.3% (n=11) with colorectal cancer. Tumors were nonmetastatic in 79% (n=26) and metastatic in 21% (n=7) of cases. At least one identified classical thromboembolic risk factor was detected in 13 patients, mainly smoking (9/13) and tamoxifen treatment (2/13). IP was inserted in the right side in 63% of the cases (n=21). IPT events were symptomatic in 93% of the cases (n=30). The average time between IP insertion and thrombosis diagnosis was 56 days, and 48% (n=16) were conducted within the first 2 months.

Approximately 78% (n=25) of the IPT diagnosis was based on doppler ultrasound and computed tomography scan which were performed for the remaining 22% of cases (n=7). Thrombosis was located in the jugular vein in 71% of the cases (n=23), 22% (n=7) in the subclavian vein, and 25% (n=8) in the brachiocephalic venous trunk. IP was removed because of infection in 2 cases and nonfunctionality in 3 cases. The characteristics of the patients were described in **Table 1**. Treatment of IPT was based on low weight molecular heparins in 94% (31/33) and antivitamin K in 6% (2/33). The average duration of therapy was 130 days. Four patients had post-therapy complications: 1 thrombosis recurrence and 3 infections. There was no noted case of pulmonary embolism. No statistically significant risk factors for IPT were identified.

Discussion

IPT has been the second major long-term complication of catheter use in cancer patients after infection[4]. Patients with cancer have 5-time higher risk of thrombosis than patients with no cancer. Moreover, catheter placement further increases this risk. Asymptomatic port thrombosis screened through venography occurs at 66% in most cases[7]. However, symptomatic IPT remains relatively rare[8]. In our series, the

Table 1 Patients' characteristics

Characteristics	*n*	%
Thrombosis rate	33/600	5.5
Median age, years	57 (30-74)	
Sex		
Female	23	69.6
Male	10	30.4
Tumor site		
Colorectal	11	33.3
Breast cancer	12	36.4
Others	10	30.3
Stage		
Nonmetastatic	26	78.8
Metastatic	7	21.2
Risk factors (13 cases)		
Smoking	9	-
Tamoxifen	2	-
Thrombosis	2	-
Treatment		
Low weight heparins	31	94
AVK*	2	6

*AVK: antivitamine K

rate of IPT was 5.5 %, which is consistent with data reported in previous studies[9]. The only reported Tunisian series that have IPT rate of 2.9% was in 2001 by Boussen et al.[10], who used different insertion techniques and patient characteristics. Recent studies have reported decreasing incidence, IPT rates between 2.1% and 12.8%[6]. This decrease has been attributed to the improvements in catheter material, insertion techniques, and catheter maintenance.

IPT can have 3 different types. The first type is a fibrin sheath formed around the catheter after insertion, which is a typical blood clotting reaction that cannot be used to predict the subsequent risk of thrombosis. The second type is an intraluminal thrombosis with catheter blockade. It can be lysed by thrombolytic agents in most cases. The third type is a blood vessel thrombosis, which is the most serious complication[10]. IPT occurrence is rarely observed beyond 3 months after port insertion[5].

In our series, nearly half of the IPT cases occurred within the first 2 months following port insertion[11].

In our series, IPT occurred at a certain rate similar to that observed in patients with cystic fibrosis (CF). Dal Molin et al.[12] reported 3 cases of IPT among 80 CF patients. The average time between the positioning of the device and the onset of thrombosis was 203.6 days (6.7 months). One of the patients had been taking oral contraceptive therapy.

Clinical suspicion of deep vein thrombosis is based on the presence of oedema, pain, and collateral circulation in the limb but none of these signs is specific[13].

The doppler ultrasound has been commonly used to confirm the diagnosis of IPT because of its high sensitivity (78% to 100%) and specificity (82% to 100%) as reported in 6 prospective studies[14]. Much research on IPT risk factors has already been reported, such as smoking, comorbidities, biology and underlying disease, and related catheter/technique[11]. In a retrospective study evaluating the correlation between the underlying disease and the port complications, pancreatic and gastric cancers were significantly associated with thrombosis occurrence[4]. A prospective observational cohort study published by Hohl Moinat et al.[16] identified high Khorana risk score and lung cancer as indicators of venous thrombotic events and catheter-related thrombotic events. Narducci et al.[17] reported that delay of less than 8 days between CVP implantation and first use could highly indicate complications.

In our series, IPT notably occurred in patients with breast and colorectal cancer. This can be explained by a selection bias because these patients were candidates of IP-dependent chemotherapy.

The huge number of associated risk factors has made it difficult to create a predictive score or to characterize a high risk group. The identification of a potential candidate for thromboprophylaxis has not been necessarily associated to thrombotic events reduction and there has been no available data specific to IPT. Bleeding has considerably limited thromboprophylaxis during chemotherapy.

Nevertheless, other methods have been used to avoid IPT, such as flushing using turbulent flush and positive-pressure locking techniques. Heparin flushing has been the most extensively used procedure despite the fact that its efficacy is still unproven[18].

In fact, Goossens et al.[19] reported that normal saline is a safe and effective locking solution for TIVADs in a randomized open trial. Dal Molin et al.[20] conducted a randomized open trial to determine the non-inferiority of normal saline in contrast to heparin solution in maintaining catheter patency. This study failed to demonstrate non-inferiority of normal saline with regard to heparin solution. No significant difference between the two solutions was found.

Data on optimal curative treatment of IPT have been insufficient. A three-month treatment has been advised for

patients with low weight molecular heparin without IP removal. Nonfunctional, infected, or poorly positioned implanted devices must be removed[21]. Warfarin can be an alternative but less preferred because of the difficulty in controlling its dosage caused by interferences from certain chemotherapy drugs, thrombocytopaenia, nutritional status, and liver metastasis. There have been no data on the use of new oral anticoagulants for prevention or for therapy[22].

Probability of recurrent deep vein thrombosis in cancer patients reaches 10% after 3 to 6 months of anticoagulation[23]. Clinical risk factors of recurrence in cancer patients are not well known. Louzada et al.[24] conducted a systematic review including 6 prospective and 5 retrospective studies, and evaluated the clinical characteristics associated to the recurrence of thrombosis during anticoagulant treatment. Younger patients with adenocarcinoma, lung, or gastrointestinal metastatic cancer appear to have the highest risk of recurrence. Ottawa score can be used to predict thrombosis recurrence in cancer patients. It is based on the female sex , lung cancer, breast cancer, TNM stage, prior thrombosis[25].

There has been no data available to identify the clinical risk factors of recurrence after anticoagulation[23]. Secondary prophylaxis must be proposed to be used on cancer patients with high risk of recurrence for its proven effectiveness and safety although its optimal management has not been clear yet (duration after 6 months of treatment, dose)[25].

Conclusions

We reported our experience with IPT in a Tunisian medical oncology department in order to detail the clinical presentation and practice management. More specific studies on insertion techniques are necessary to identify predictive factors. Furthermore, patients with high risk of IPT requiring special monitoring schedules must be selected.

Conflict of interest statement

No potential conflicts of interest are disclosed.

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Cite this article as: Dridi M, Mejri N, Labidi S, Afrit M, Benna HE, Miled KB, et al. Implantable port thrombosis in cancer patients: a monocentric experience. Cancer Biol Med. 2016; 13: 384-8. doi: 10.20892/j.issn.2095-3941.2016.0057