Case report

The role of histopathological examination, therapeutic difficulties and thromboembolism treatment during palliative chemotherapy in patient with antithrombin deficiency, colon cancer and endometrial cancer

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ABSTRACT

Palliative chemotherapy in patients with thrombophilia is a challenge for clinical oncologists. On one hand the optimal treatment should be very safe for patient, on the other hand – as effective as possible. That therapy is also connected with proper thromboprophylaxis. The incidence of multiple cancers is a serious problem of modern oncology. In patients whose medical history includes two or more cancers, it is essential to obtain histopathological diagnosis before the administration of treatment of disseminated disease. It allows to avoid improper therapy which is often toxic. The article presents the case of a patient with antithrombin deficiency and two cancers in medical history: colon cancer and endometrial cancer. The treatment of the patient because of the metastatic cancer was started after the histopathological diagnosis. In metastatic lymph node the endometrial cancer was recognized. The carboplatin and paclitaxel were used in the therapy. The treatment was conducted in four course chemotherapy. It revealed considerable polyneuropathy and hematologic toxicity limiting from further therapy. Treatment allowed to obtain biochemical response, decrease of metastases and the condition of a patient improved. During the systemic therapy thromboprophylaxis with acenocumarol was used. The incidence of venous thromboembolism or bleeding complications were not noticed.

Key words: antithrombin deficiency, multiple cancers, palliative chemotherapy, thromboprophylaxis, colon cancer, endometrial cancer

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INTRODUCTION

Thrombophilia is an abnormality of blood coagulation that increases the risk of thrombosis. That prothrombic state can be congenital or acquired condition that tends to cause venous thromboembolism (VTE) [1]. Based on risk level we can divide it into mild and severe coagulopathy.

One of the severe coagulopathies is antithrombine (AT) deficiency, in which heterozygote's risk is 20–50 times higher. There are two types of antithrombine deficiency:

- type I antithrombin deficiency is characterised by a decrease in both antithrombin activity and antithrombin concentration in the blood of affected individuals
- type II antithrombin deficiency is characterised by normal antithrombin levels but reduced antithrombin activity in the blood of affected individuals.

The diagnosis of hypercoagulability itself is not the indication for a treatment but prophylaxis should be taken into consideration. For example in abdominal surgery or delivery in patients with AT deficiency infusion of antithrombin concentrate may be administered. In patients with thrombophilia and VTE vitamin K antagonists (VKA) are used to treat. In AT deficiency heparins are efficient as well. However, in very low AT level, which we can see in Disseminated Intravascular Syndrome (DIC) the role of heparins is limited. After the first episode of venous thromboembolism patients should be treated with anticoagulants for their whole live [1].

CASE STUDY

In 2014 69-year-old women was admitted to the Oncology Department in Rybnik with the history of treatment in nearby hospital. Capecitabine in monotherapy had been advised because of disseminated cancer – probably disseminated colon cancer.

The history treatment of the patient has been analyzed:

1. In 2007 she underwent the treatment of endometrial cancer. Histerectomy has been performed with additional brachytherapy. In histopathology study *adenocarcinoma endometrioides* G1 (FIGO2009 II) was recognized.
2. In August 2012 positron emission tomography (PET) has been performed, where a lymphadenopathy in retroperitoneal space and changes in transversal colon suggesting primary neoplasm were diagnosed.
3. The patient was qualified to an operation. A left side hemicolectomy was performed. In histopathology examination adenocarcinoma was diagnosed.
4. In 2014 patient was diagnosed with right side hydronephrosis. An additional image diagnostic including CT showed the presence of enlarged lymph nodes (4.5 × 8 cm) in periaortical side at the height of kidneys with infiltrating right ureter. In clinical examinations enlarged lymph node in the neck at the left side was identified, and biopsy was performed. Tissue samples were described as a metastatic cancer cells.

Because of atypical case of colon cancer, endometrial cancer in history, and PET result suggested stage of dissemination in 2012 the previous advice to administer a capecitabine was questioned. Before implementing the therapy the further diagnostic should be performed. Comorbidity of patients was coagulopathy-point mutation of (nt 683G.T), correlated with antithrombin I deficiency [2, 3]. Patient was treated with acenocumarol because of VTE episode in the past. Biopsy of neck lymph node was planned. Before that a switch from acenocumarole to enoxaparin in treatment dose was required [3, 4]. In case of large surgery – such as hemicolectomy – patient received antithrombin concentrate [3]. Histopathological test result presented diagnosis different to the primary one – metastatic endometrial cancer in lymph node.

Treatment

Clinical condition of a patient before the treatment scored 1 according to ECOG (Eastern Cooperative Oncology Group). There was a concern about soft tissue thickening in scar formation after biopsy of neck lymph nodes. All other lymph nodes were not palpable. Except mild trophic changes of both shanks after episode of deep vein thrombosis (DVT) there were no other clinical findings.

Patient complained most about lower back pain, caused probably by lymph nodes mass effect. The pain was rated with 5–6 points in NRS (Numerical Rating Scale), and affected everyday activity. Transdermal patches of 25 µg/h fentanyl, and 20 mg morphine pills on demand controlled pain sufficiently.

The main comorbidity of patients was arterial hypertension, coagulopathy-AT deficiency. Most relevant issues in the past were pulmonary embolism in her youth and DVT episode in 2012.

Laboratory test revealed II stage anemia according to WHO (World Health Organization). The rest of the results were: Ca125 marker (cancer antigen 125) – 115.7 U/mL, creatinine – 98.9 mmol/L, with relatively good eGFR – 60 mL/min.

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CT scan before the treatment showed a presence of enlarged lymph nodes in retroperitoneal space where right ureter was compressed with subsequent hydronephrosis.

Patient was qualified for palliative chemotherapy with carboplatin and paclitaxel. In 21-day cycles. Because of the increased thrombosis risk during chemotherapy dosage of acenocumarole was based on international normalized ratio (INR). Complications of treatment such as lack of appetite, nausea, vomits were expected and could affect INR and for that reason the test was repeated every week. The total number of 4 cycles was administered. Polyneuropathy and hematologic toxicity prevented from further treatment. After the 4th course of chemotherapy thrombocytopenia (31,000/mm^3) appeared with level 3 according to CTC AE. Polyneuropathy reached level 2 CTC AE. It was decided to end the treatment. It was estimated that no further benefits can be achieved, the continuation of the treatment would aggravate toxicity and possible hemorrhage related complications. Polyneuropathy deteriorates life quality, but hemorrhage complications are life threating.

Performed CT after the treatment showed reduced retroperitoneal lymph nodes that met the criteria of stabile disease (CD) according to RECIST (Response Evaluation Criteria in Solid Tumours). The treatment resulted in better clinical status, lymph nodes reduction, and marker response – total reduction of CA 125 by 50%. Pain was reduced to 2–3 points in NRS scale. There was no thrombotic, no haemorrhagic complications during the treatment.

4 months after the therapy there was an episode of profound anemia. Hemoglobin level was 5.6 g/dL, with upper gastrointestinal tract bleeding. Performed endoscopy showed infiltration in descending part of duodenum. CT confirmed progression of the disease. Palliative surgery by-passing gastro-intestinal junction was performed. There was an attempt of monotherapy with doxorubicin, but after a considerable toxicity and anemia was discontinued after the first course. Best supportive care was recommended.

DISCUSSION

In this case, proper treatment and monitoring of accompanying diseases in palliative treatment was taken into account. Chemotherapy in patients with AT deficiency should be conducted with caution [5, 6]. Chemotherapy, as well as disseminated neoplasm brings higher thrombosis risk, and should be carefully managed in thrombophilia patients [5, 6]. It is suggested that VTE inducing factors may be endothelial cells activations, and pro coagulative agents released during apoptosis [7]. Knowing the reasons of thrombophilia helps proper management, prophylaxis and treatment. Close examinations between the courses can prevent potential complications and drugs interactions with VKA [8]. Malnutrition, diarrhoea, vomits can influence vitamin K1 level [9]. Adequate control of comorbid can prolong palliative treatment by avoiding serious complications (G3–G4 according to CTC AE) [10].

CONCLUSION

Multiple neoplasms (synchronic and metachronic) are becoming more considerable problems of the modern oncology [11]. The presented case with two cancers in history shows how histopathological confirmations of relapsed disease lead to optimal therapy. Every attempt of histopathological test should be undertaken when two cancers are diagnosed before treatment of relapsed disease. It helps to avoid unsuccessful therapy without any benefits but with range of complications.

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