

Case Report

Disseminated Intravascular Coagulopathy in Cranial Surgery: Case Report and Review of the Literature

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Keywords

Calvarial metastasis · Disseminated intravascular coagulopathy · Prostate cancer · Surgery of metastasis · Stroke

Abstract

We present a rare case with multifocal osseous metastases of prostate cancer and disseminated intravascular coagulopathy (DIC). The patient received systemic tumor therapy, including antiandrogen agents as well as cerebral radiation. Due to rapid clinical deterioration, indication for surgery of the space-occupying calvarial metastasis was made as a salvage therapy procedure. Depleted clotting factors were substituted, and patient underwent tumor embolization prior to surgery. Although his neurological status improved postoperatively, the patient died suffering from multiple supra- and infratentorial infarctions. Our case report elucidates the laboratory results and difficulties of DIC in this case as well as possible treatment strategies.

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Introduction

Disseminated intravascular coagulopathy (DIC), characterized by the intravascular activation of coagulation, is the most common coagulopathy in prostate cancer (PC) patients, reported with an incidence of up to 30% [1], whereas clinical manifestation is rare (0.4–1.65%) but doubles mortality [2]. This case report elucidates the difficulties of treatment and highlights the clinical course of DIC with massive thrombosis causing disseminated cerebral infarction in a patient suffering from a huge calvarial metastasis of PC. Furthermore, reasons for DIC in

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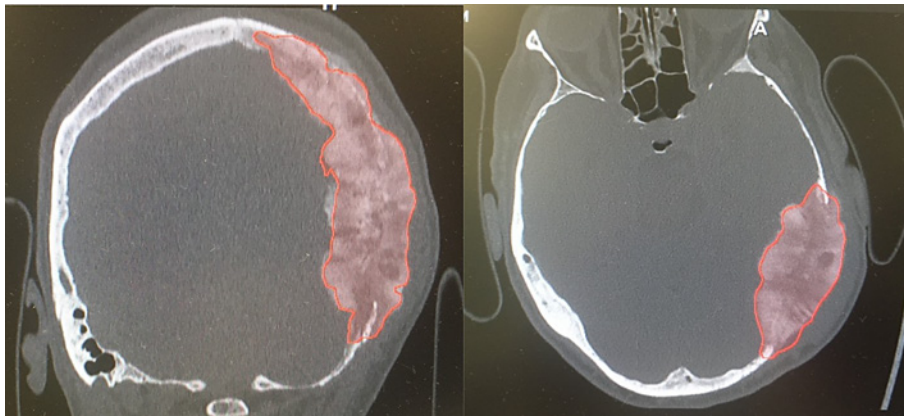


Fig. 1. Extensive osteoblastic calvarial metastasis.

PC patients as well as the typical laboratory parameters, differential diagnosis, and the pitfalls in pre- and perioperative patient care in neurosurgical patients are presented.

Patient Information

In a 61-year-old Caucasian man, PC was diagnosed in 2013. At the time of diagnosis, the patient already suffered from osseous, retroperitoneal as well as para-aortic lymph node metastases. Therapy was initiated with antiandrogen agents in combination with a potent gonadotropin-releasing hormone receptor agonist. Prostate-specific antigen decreased under therapy and was controlled routinely after completing the systemic therapy. In 2017, prostate-specific antigen levels increased; however, the patient denied further tumor treatment or imaging. One year thereafter, he presented with progressive multifocal osseous metastases, involving scapula, ileum, sacrum, and acetabulum. The gonadotropin-releasing hormone receptor agonist was resumed, and nonsteroidal antiandrogen medication was used. At this time, computed tomography (CT) of the neck, chest as well as abdomen excluded further tumor localizations. Cranial imaging was not performed.

During the course of disease in December 2020, the patient presented with disorientation and hypomnesia. Besides the already diagnosed disseminated osseous metastases, the positron emission tomography-CT confirmed an extensive calvarial lesion involving the left-sided temporal, parietal, and occipital bone (Fig. 1). In January 2021, neurosurgical consultation indicated surgical resection to alleviate the mass effect on healthy brain tissue and prevent subfalcine herniation and cerebral infarction. Preoperative MRI excluded intracerebral lesions and confirmed displacement of the healthy brain tissue.

Systemic disease burden was assessed by an interdisciplinary panel (oncology, urology, neurosurgery, radiology). The laboratory results confirmed the rare case of clinical manifestation of DIC. For this reason, palliative radiochemotherapy was preferred over surgical removal of the calvarial lesion.

During 2 weeks of radiation therapy, the patient deteriorated rapidly. Therefore, radiation therapy of the calvarial was cut short after 15 Gy. After preclusion of other reasons, mass effect caused by the calvarial metastasis was accounted for the ongoing clinical deterioration. Therefore, tumor resection as a salvage therapy procedure was indicated.

During the following weeks, the hematologists performed a detailed coagulation assessment and specific substitution with vitamin K, fibrinogen, and tranexamic acid, according to the

current guidelines in order to minimize intra- and postoperative complications of DIC. To reduce intraoperative tumor bleeding, tumor feeding vessels were embolized 3 days prior to surgery.

The calvarial metastasis was resected on 15 February 2021 without major bleeding, and the patient was transferred postoperatively to the intensive care unit. The thromboelastogram confirmed normal coagulation at that time.

Treatment Options

Systemic tumor treatment was already performed; nevertheless, patient presented with progressive cancer. Possible treatment options for calvarial metastasis were surgical removal or radiation therapy, as well as gamma knife radiosurgery in small lesions. However, the extensive lesion cannot be adequately treated with radiosurgery [3].

Surgical removal, leading to an immediate pressure relief and reduction of tumor mass, seemed to be the first choice. Due to the clinical manifestation of DIC, radiation therapy was preferred over surgical removal, which could be performed independently of DIC. Nevertheless, an immediate tumor cell relief is not possible with this treatment option.

Laboratory Results

The laboratory results at admission confirmed regular kidney and liver function. Our patient suffered from thrombocytopenia (58/nL, normal 140–440/nL), reduced thromboplastin time (48%), and therefore prolonged internal thromboplastin time (1.59; reference: 0.90–1.15). Activated partial thromboplastin time was normal.

D-Dimer, as a fibrin cleavage product, was high (25,467 ng/mL; reference <500 ng/mL), and patient presented with hypofibrinogenemia (<50 mg/dL; reference 210–400 mg/dL). Furthermore, antithrombin 3 (AT3) was elevated (130%, reference 83–118%). All these parameters display a high consumption of clotting factors, confirmed by the elevated percentage of reticulocytes (2.16%; reference 0.5–2.0%). The extended coagulation diagnosis validated this finding with prolonged extrinsic clotting time (332 s; reference: 38–65 s), reduced extrinsic clotting stability (23 mm; reference 53–68 mm), and prolonged extrinsic clot formation time (1,025; reference 42–93%). Reduction of factor V (52%; reference 70–120%) further increased the risk of hemorrhage. Laboratory results confirmed DIC with a high consumption of clotting factors [4].

After 2 weeks, a normal platelet count (148/nL) was measured for the first time. At that day, the thromboplastin time (67%), the internal thromboplastin time (1.25), fibrinogen (79 mg/dL), and AT3 (126%) recovered significantly. The laboratory results directly prior surgery confirmed normal platelet count (142/nL), thromboplastin time (116%), internal thromboplastin time (0.09), and fibrinogen (279 mg/dL). Solely AT3 was still elevated (125%). Extrinsic clotting time (90 s) and fibrinogen clotting time (92, reference 55–87 s) were slightly elevated the day after surgery, whereas the other parameters stayed normal. On the third postoperative day, AT3 increased (145%) and activated partial thromboplastin time (23 s; reference 26–36) decreased. Indicating a progressive consumption, platelet counts were reduced (94/nL) at the seventh postoperative day.

Histopathological Results

Osseous metastasis of the PC, infiltrating the dura mater.

Postoperative Course

The routinely performed cranial CT prior the transfer to our normal neurosurgical ward exhibits multiple cerebral infarctions involving the areas supplied by the left posterior cerebral artery and the right middle cerebral artery. Transesophageal echocardiography of the following

day excluded cardiac vegetations. One week after surgery, the neurological status of the patient deteriorated. He solely responded to external stimuli aggressive, but somnolent during the course of the day.

On the 10th postoperative day, patient was found comatose. An emergency CCT confirmed disseminated cerebral and cerebellar infarctions encompassing both hemispheres. For this reason, best supportive care was initiated. Patient passed away on February 27, 2021, because of DIC, resulting in multiple supra- and infratentorial infarctions. From the first day after surgery on, patient received prophylactic doses of unfractionated heparin for venous thromboembolism prophylaxis.

Discussion

DIC is an acquired, pathological systemic disorder, often associated with solid or hematological malignancies [5]. Furthermore, it is well known in patients suffering from sepsis, severe trauma, or vascular disorders, being characterized by a widespread cross-activation among coagulation and inflammatory responses [2]. Leading to consumption of pro- and anti-coagulant factors and disrupted homeostasis at the blood vessel wall interface [5], this provokes micro- and macro-thrombosis and, due to consumption coagulopathy, severe bleeding. Being difficult to treat, acute DIC is accompanied by a high mortality rate during the first 4 weeks after onset [6]. Treating the underlying disease and eliminating trigger mechanisms are the most important therapeutic approaches [7].

DIC in PC

Older age, male sex, and advanced tumor stage are identified risk factors for DIC, which were all present in this case [8]. In the presented case, patient suffered from PC for 7 years causing chronic DIC, being triggered by malignant mucin production of tumor cells [9], with the possible introduction of thromboplastic substances into the blood stream during tumor resection [9].

Tumor Treatment Leading to DIC

During the course of disease, the patient already received multiple therapies, including androgen deprivation therapy, being fraught with thromboembolic events [10]. Moreover, radiation therapy harbors an elevated risk of DIC and thromboembolic events, potentially aggravating the post-radiational course [11].

Another tumor treatment being worth to discuss is the preoperative endovascular embolization. In extra axial lesions, embolization is most often used to reduce blood loss in meningioma resection harboring the risk of bleeding/infarction in 0–6.5% [12].

Differential Diagnosis

Nevertheless, there are other factors associated with hematological dysfunction such as massive blood loss, heparin-induced thrombocytopenia, or liver insufficiency which must be ruled out to proceed with the appropriate treatment strategy [2].

Treating DIC

Reducing the systemic tumor burden by radiation and systemic tumor therapy is the most important milestone in treating DIC [13]. Furthermore, the consumption of clotting factors and platelets was compensated with intravenous application of fibrinogen, vitamin K, tranexamic acid, and platelet concentrates. This, especially preoperatively intensified substitution, may have further increased the risk of thromboembolic events and disturbed the sensitive equilibrium,

which subsequently led to the demise of a critically ill patient suffering from metastatic PC. In conclusion, we present a highly unusual case of a huge calvarial metastasis and fatal DIC in PC, illustrating the therapeutical decision-making and the clinical course.

Conclusion

Although DIC is a rare disease, diagnosis and adequate treatment are compulsory to improve patient's outcome and reduce morbidity and mortality.

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Statement of Ethics

The retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. The Human Investigation Committee of Ludwig-Maximilians-University Munich, Germany, approved this study (November 19, 2021/Hb/mbg). Written informed consent was obtained from the legal guardian of patient for the case report and for publication of the details of the medical case and any accompanying images. Legal guardians have consented to the submission of the case report including images to the journal.

Conflict of Interest Statement

The authors have no relevant financial or nonfinancial interests to disclose.

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Author Contributions

Study design and implementation: Christina Wolfert, Björn Sommer, and Ehab Shiban. Data acquisition, analysis, and interpretation: Christina Wolfert and Björn Sommer. Manuscript drafting: Christina Wolfert. Approval of the manuscript: Christina Wolfert, Björn Sommer, and Ehab Shiban.

Data Availability Statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

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