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LETTER TO THE EDITOR

A patient with acquired factor X deficiency and metastatic transitional cell carcinoma of the bladder: is there a link between metastasis and factor deficiency in solid tumors?

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Dear Editor,

Acquired deficiency of factor X (FX) is commonly found during antivitamin K therapy in prevention of thrombosis or as a consequence of liver disease [1]. Less frequently, it has been observed as an isolated deficiency in a number of disease states. It has been associated with amyloidosis and hematologic malignancies [2], and few non amyloid-related cases have been reported. Association with solid tumors is rare [3–5]. We would like to present a patient with a transitional cell carcinoma who developed a FX deficiency.

A 67-year-old man was diagnosed with a localized transitional cell carcinoma of the bladder. He was first admitted to our hospital in January 2014 for a second-opinion consultation. Transurethral resection of the bladder took place and neoadjuvant chemotherapy was administered at our hospital, followed by a cystectomy. During follow-up, suspicious lesions were noticed on medical imaging and a lung biopsy was carried out. Pathological examination revealed a metastasis of the transitional cell carcinoma. The patient subsequently received stereotactic body radiotherapy to all lung lesions yet had progressive disease 6 months later. He was then enrolled in a clinical trial (NCT02826564) in which he received pembrolizumab (Keytruda) and stereotactic body radiation therapy to one lung lesion according to the study protocol [6].

During follow-up, prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen concentration were measured to assess his blood's clotting status. First measurements were within reference ranges, but after the lung metastases were noticed and prior to administration of pembrolizumab, a prolongation of the PT (20s; reference ranges 11.5–14.5 s) and aPTT (51 s; reference ranges 28.9–38.1 s) was detected (Fig. 1).

In the laboratory diagnostic workup, mixing patient's plasma with normal pooled plasma showed correction of aPTT (37.6 s) and PT (14.2 s). Clotting factor activities for the extrinsic factors were determined by a one-stage clotting assay in a 1:10 sample predilution. Factor II, V, and VII levels were within normal ranges with 105, 71, and 98% activity but FX activity was 21% (factor reference ranges 70–120%). Testing was repeated in higher predilutions of 1:40 and 1:100, without increase of FX activity (20%). These findings were confirmed 3 weeks later.

In FX deficiencies, FX activity correlates relatively well with bleeding and may be provoked by levels lower than 10% [1, 7]. If no active bleeding is diagnosed, as in our patient, careful monitoring and treatment of the underlying disease are sufficient. If bleeding occurs, it can be treated with prothrombin complex concentrate or plasma, keeping the target FX level above 20% of the normal reference population [7].

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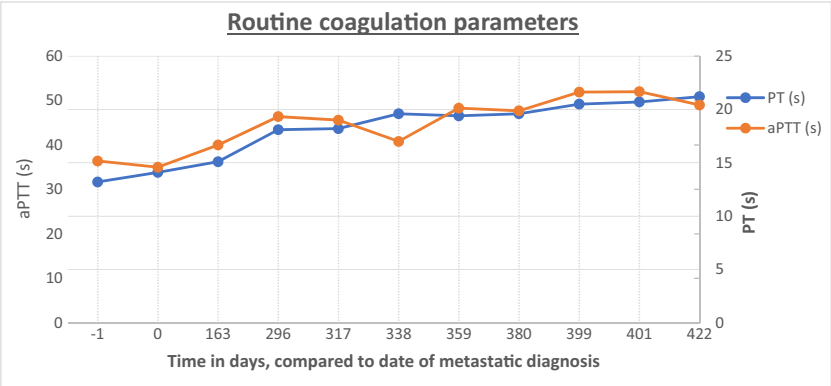

Fig. 1 aPTT and PT results

This is, to our knowledge, the first case of an acquired deficiency of FX associated with an urothelial carcinoma. We suggest that there might be a link with metastasis of solid tumors [4, 5], as the FX deficiency occurred simultaneously with the presence of metastases, in accordance with the previously published articles discussing this deficiency in solid tumors with metastasis. This theory is consistent with the status quo of the lab results and progressive lesions on medical imaging.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Uprichard J, Perry DJ (2002) Factor X deficiency. Blood Rev 16(2): 97–110 Review
2. Furie B, Greene E, Furie B (1977) Syndrome of acquired factor X deficiency and systemic amyloidosis in vivo studies of the metabolic fate of factor X. N Engl J Med 297(2):81–85
3. Coucke L, Trenson S, Deeren D, Van haute I, Devreese K (2013) Life-threatening bleeding tendency provoked by an acquired isolated factor X deficiency associated with respiratory infection. Ann Hematol 92(10):1437–1438
4. Korte W, Flury R (1992) Acquired factor X deficiency and disseminated intravascular coagulation in a case of metastasizing carcinoma of the stomach and its course under chemotherapy. Ann Hematol 64: 152–154
5. Stefanini M, Wiggishoff CC (1966) Stuart factor (factor X) deficiency associated with renal and adrenal cortical insufficiency. Ann Intern Med 64:1285–1291
6. Sundahl N, De Wolf K, Rottey S, Decaestecker K, De Maeseneer D, Meireson A et al (2017) A phase I/II trial of fixed-dose stereotactic body radiotherapy with sequential or concurrent pembrolizumab in metastatic urothelial carcinoma: evaluation of safety and clinical and immunologic response. J Transl Med 15(1):150
7. Henson K, Files J, Morrison F (1989) Transient acquired factor X deficiency: report of the use of activated clotting concentrate to control a life-threatening hemorrhage. Am J Med 87(5):583–585