Fulminant thrombotic microangiopathy as a clinical presentation of an occult signet-ring cell carcinoma of the lung and misdiagnosed as idiopathic thrombotic thrombocytopenic purpura

Pasquale Niscola, MD, PhD, Maria B. Palmieri, MD, Laura Scaramucci, MD, Gisella Vischini, MD, Marco Giovannini, MD, Michele Ferrannini, MD, Roberto Palumbo, MD, PhD, Stefano Fratoni, MD.

The initial diagnosis of patients presenting with microangiopathic hemolytic anemia and thrombocytopenia (thrombotic microangiopathy [TMA]) may represent a diagnostic concern, given that these findings may be related to different underlying disorders,[1] including thrombotic thrombocytopenic purpura (TTP).[2,3] As a consequence of an incorrect diagnosis, inappropriate and sometimes risky treatments, such as plasma exchange, may be given. Therefore, the present case is being reported for its rarity and for the diagnostic and clinical concerns related to this rare occurrence.

Cancer related TMA misdiagnosed as TTP has been rarely described in the setting of advanced and disseminated malignancies,[3] and this occurrence as an abrupt presentation and fatal course of an occult and rare neoplasm, such as the signet-ring cell carcinoma (SRCC),[4] represents an exceptionally rare observation. Thereby, we report the case of an otherwise healthy 48-year-old man recently observed by us. He had been well and active until admission to a general hospital because of severe malaise, weakness, and confusion; he presented no clinically apparent signs of neoplastic disease. A routine laboratory evaluation revealed severe anemia and thrombocytopenia; very increased lactate dehydrogenase and creatinine serum values were also found. All hemolytic parameters were altered; the Coombs test was negative. The coagulation profile was only slightly altered. The examination of the peripheral blood smear showed very few platelets and numerous red cell fragments. An x-ray of the chest and a body CT scan revealed pulmonary congestion, but no other abnormalities. A provisional diagnosis of TTP was made. Therefore, he was given steroids and 24 hours after the admission was transferred to our specialized hospital by an equipped ambulance with the assistance of a skilled anesthetist. After the admission, the diagnosis of TTP was confirmed. Despite plasma exchange and supportive and resuscitative measures promptly given in an intensive care setting, he died 24 hours after the admission due to multiorgan failure. At autopsy, pathological findings consistent with TMA were evident in almost all organs; the lungs appeared congested and enlarged. Some autopsy sections were taken from major organs and a microscopic examination was performed. Microvascular and lymphangitic neoplastic dissemination, involving the right lung and the regional lymph nodes, was found. The malignant cells presented morphological features of an SRCC;[4] on immunochemistry, the tumor cells were AE1/AE3 and CK7 positive whereas CK20 and CD68 were not expressed. Other than the right lung, no other organ involvement by neoplastic cells was detected on the examination of other organs, although the origin of the neoplasm from a distant site has not been absolutely excluded.

Signet-ring cell carcinoma is a mucin-producing adenocarcinoma, which may arise from several organs, including the lung;[4] it has very aggressive clinical features and portrays a rapid fatal course. Thrombotic microangiopathy associated malignancy is a well-described specific disorder,[3,5] which may complicate several kinds of disseminated neoplasm; its presenting clinical features are often indistinguishable from those observed in TTP. The detection of malignancy-related findings and the lack of the response to plasma exchange can allow the correct diagnosis.

In conclusion, on literature review, we found no previous reports of TMA-associated SRCC; moreover, this complication is very uncommon in patients whose systemic malignancy is not initially apparent, as in our case, in which there was only the observation of a diffuse microscopic pulmonary involvement by SRCC.

Received 18th January 2010. Accepted 10th March 2010.

From the Hematology Unit (Niscola, Scaramucci, Giovannini), Pathology Unit (Palmieri, Fratoni), and Nephrology Unit (Vischini, Ferrannini, Palumbo), S. Eugenio Hospital, Rome, Italy. Address correspondence and reprints request to: Dr. Pasquale Niscola, Hematology Unit, S. Eugenio Hospital, Piazzale dell'Umanesimo 10, Rome 00144, Italy. Tel. +39 (06) 51002454. Fax. +39 (06) 51002100. E-mail: pniscola@gmail.com

References

1. Coppo P, Veyradier A. Thrombotic microangiopathies: towards a pathophysiology-based classification. ***Cardiovasc Hematol Disord Drug Targets*** 2009; 9: 36-50.
2. George JN. Clinical practice. Thrombotic thrombocytopenic purpura. ***N Engl J Med*** 2006; 354: 1927-1935.
3. Francis KK, Kalyanam N, Terrell DR, Vesely SK, George JN. Disseminated malignancy misdiagnosed as thrombotic thrombocytopenic purpura: A report of 10 patients and a systematic review of published cases. ***Oncologist*** 2007; 12: 11-19.
4. Jin N, Nguyen C, Shuja S, Makary R, Wolfson D. Cytomorphology of primary signet ring-cell carcinoma of the lung. ***Diagn Cytopathol*** 2009; 37: 146-149.
5. Oberic L, Buffet M, Schwarzinger M, Veyradier A, Clabault K, Malot S, et al. Cancer awareness in atypical thrombotic microangiopathies. ***Oncologist*** 2009; 14: 769-779.