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LETTER TO THE EDITORS

ANTIPHOSPHOLIPID ANTIBODIES, THROMBOSIS, AND ADENOCARCINOMA

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Antiphospholipid antibodies (APA) are associated with a common thrombotic diathesis of young adults. The antiphospholipid syndrome (APS), and APA have also been observed in patients with infections and cancer[1]. We herein describe the occurrence of APA in two cases of adenocarcinoma, one of them unusual.

The first patient, a 60-year-old man, presented deep vein thrombosis (DVT) of the lower limb followed by pulmonary thromboembolism (PTE) in May 2003. Even though the patient was on an international normalized ratio (INR) for warfarin of 1.99, a new episode of lower limb DVT and PTE developed a month later. An abdominal computed tomography (CT) revealed a thrombus in the aorta. The lupus anticoagulant (LA) factor tested positive, but the anticardiolipin (aCL) IgG, IgM, and IgA antibody tested negative.[1] Antinuclear antibodies (ANA) and rheumatoid factors (RF) were absent. Two months later, he developed DVT of the other lower limb in spite of a INR of 3.7. After 3 weeks, DVT of the upper right limb was noticed. At that time, the INR was 3.6. The LA test was negative. Supraclavicular lymphadenopathy was observed two months later. Biopsy revealed metastatic lung adenocarcinoma. A lung CT, previously inconclusive, showed disseminated nodules. The patient underwent chemotherapy. By April 2004, a lower cava vein filter was successfully introduced to prevent PTE. Oral anticoagulation was maintained until his recent death due to a lung infection.

The second patient, a 73-year-old hypertensive man, was first seen by the rheumatologist in 1996 due to shoulder bursitis. Routine tests disclosed a very high level (77.5 units) of prostate surface antigen (PSA). A biopsy confirmed a prostate adenocarcinoma. The patient was kept on estrogen therapy until 1997. In 1998 a lower limb DVT was diagnosed. The IgA aCL antibody test was positive (26 units; reference value for negative test below 15 units). Tests for LA, ANA, and RF were negative. Oral anticoagulation was introduced. In 1999, the patient suffered a myocardial infarction, irrespective of an INR of 2.5. In October 2003, only IgM aCL antibodies were detected in moderate titers (21 units). Moderate levels of IgM and IgA aCL antibodies (20 and 21 units, respectively) are currently detected. He has been asymptomatic, and the last INR was 4.2.

Probable APS was diagnosed in the first patient.[1] He had a thrombotic diathesis and transient LA. However, the latter LA assays were run after chemotherapy for the lung tumor. In the second patient, APS was confirmed by clinical features and 2 positive IgM aCL assays.[1] Interestingly, "non-classical" IgA aCL was the only isotype detected in the first test. The diagnostic value of IgA aCL antibodies for patients with thrombosis has been a matter of debate.[2,3] Estrogen therapy for prostate carcinoma might have triggered APA and APS in this second patient.

"True" APS has been linked to a variety of malignancies.[4-6] The spectrum of APS-related solid tumors includes renal cell carcinoma,[7] gastric cancer,[8] and cholangiocarcinoma.[9] One patient with breast cancer and another with colorectal carcinoma experienced dramatic exacerbation of APS after surgery. [10]

The association of APS with lung tumors is of interest. A patient with recurrent cerebral ischemia, DVT, and APA was later found to have a lung adenocarcinoma.[11] Similarly to our first patient, thrombosis preceded the lung tumor and occurred in spite of a high INR. Venous gangrene and aCL

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antibodies were described in another case of lung adenocarcinoma.[12] Severe exacerbation of APS was seen in a patient following lung adenocarcinoma biopsy.[13] "Catastrophic" APS was reported in an autopsy case of lung adenocarcinoma.[14] A patient with adrenal insufficiency and APA developed after 6 months a polymetastatic bronchopulmonary tumor.[15] Simultaneous occurrence of thrombocytopenia and LA was described in a patient with primary adenocarcinoma of the bronchus. [16]

Prostate carcinoma has been reported in patients with DVT, but a test for aCL antibodies were not performed in that study.[17] Although APA has been found in cases of lung adenocarcinoma,[11-16] APA has not been clearly linked to prostate carcinoma so far. Owing to the previous estrogen therapy in our patient, an association of prostate carcinoma with APS is only hypothetical. As opposed to the patient with lung adenocarcinoma, our patient with prostate carcinoma presented thrombosis well after the appearence of the tumor. APS might be one of the etiologies for tumor-related thrombosis. However, coincidence of these two entities can not be ruled out in older patients. The presence of APA might eventually be regarded as an epiphenomenon of cancer. Overall, a suspicion of neoplasms in older patients with APS or APA seems appropriate. Lung and prostate adenocarcinoma could be part of this context.

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