Primary Sjögren's syndrome as paraneoplastic disorder: a case report

Sirs,

A 57-year-old man was referred for a 4-month history of symmetrical arthritis at wrist and hand small joints with concomitant oral and ocular sicca syndrome. Patient reported heavy cigarette smoking. Excepting a systemic arterial hypertension on calcium channel blocker therapy, his medical history was otherwise unremarkable.

Administration of medications known to cause sicca symptoms as well as the most common causes of sicca syndrome, including hepatitis C virus or HIV infection, diabetes mellitus, thyroid dysfunction and sarcoidosis, were ruled out. Antinuclear antibodies (ANA) were positive at immunofluorescence assay on Hep-2 cells at 1:640 titer with a fine granular pattern of nucleoplasm and weak staining of the nucleoli. Anti-SSA(Ro) 52/60 and anti-SSB (La) antibodies were detected at high titer by enzyme immunoassay. Serum levels of other immunological parameters, including C-reactive protein, rheumatoid factor, C3 and C4, IgG, IgA and IgM and anti-cyclic peptide citrullinated antibodies, were normal. Impaired lacrimal and salivary secretion was confirmed by Schirmer's and unstimulated whole salivary flow tests, respectively. Parotid ultrasonography resulted normal. Finally, minor salivary gland biopsy showed a mild, non-specific, mononuclear cell infiltrate.

A diagnosis of primary SS was made according to the American-European Consensus Group classification criteria (1) and low-dose corticosteroid (CS) treatment was introduced to control articular pain. However, arthritis remission was not achieved despite prednisone doses up to 25 mg daily. Because of the poor response to CS therapy and the atypical late onset of a connective tissue disease in a male subject, screening tests were performed to exclude an occult underlying pathologic condition. Chest radiography, dosage of prostate specific antigen and fecal occult blood resulted negative, whereas upper abdominal US revealed a right kidney mass confirmed by computed tomography scan. One month later, patient underwent right total nephrectomy. Histological examination was consistent with multilocular cystic clear cell carcinoma, Fuhrman grade II, not infiltrating renal capsule. Complete remission of arthritis and sicca symptoms were rapidly obtained following neoplasm removal. Anti-Ro/SSA and anti-La/SSB antibodies slowly decreased and resulted negative three months after surgery. Patient is still asymptomatic at nine months of follow-up.

It is well established that some chronic inflammatory rheumatic diseases (RDs), including rheumatoid arthritis (RA) and SS, are associated with a high long-term risk of developing lymphoproliferative disorders and solid tumors. On the other hand, some RDs may be associated with or precede the clinical manifestations of a variety of solid and haematological cancers. In this setting, inflammatory myopathies, seronegative RA, some atypical vasculitides and scleroderma-like syndromes are the most frequently reported paraneoplastic RDs (2). Their prevalence ranges from 3% to 15% and etiopathogenesis has not been fully clarified (3). Symmetrical small joints polyarthritis is the most common articular paraneoplastic manifestation, together with Raynaud phenomenon (3). Rapid onset of an unusual inflammatory polyarthritis in subjects older than 50 years without family history for RDs, smoking habit and poor response to CS and/or immunosuppressive therapy have been identified as helpful clues to suspect paraneoplastic conditions (3). Of interest, kidney and urogenital tumors have been frequently reported in paraneoplastic RDs (3). In general, immunologic parameters are not helpful to discriminate such conditions and increased incidence of ANA positivity without recognition of extractable nuclear antigen specificity usually characterises these patients (3).

The present clinical case is of particular interest as it is a report of a paraneoplastic SS, a CTD almost exclusively affecting young women, occurring in a male subject and completely resolved after neoplasm removal. From a pathogenic point of view, it is intriguing the finding that some specific cancer-associated antigens display a significant structural homology with Ro/SSA antigen (4). In addition, Ro52 antigen has been shown to interact with a specific deubiquitinating enzyme, UnpEL, commonly detected in cultured human cardiocytes, human renal carcinoma cells and monkey kidney fibroblasts (5). Thus, the induction of a specific humoral and cell-mediated autoimmune response by some cancer-associated antigens may be a possible pathogenic mechanism leading to paraneoplastic syndrome clinical manifestations.

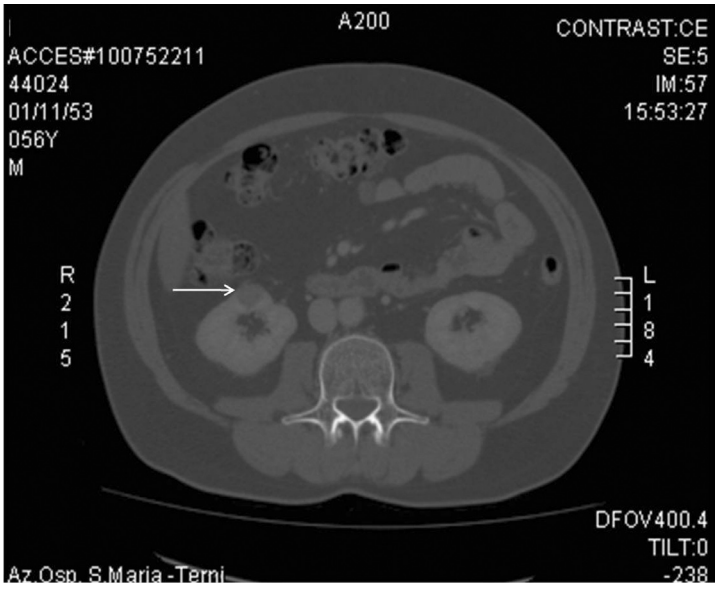

Fig. 1. Abdomen CT scan showing enhancing lesion in lower pole of right kidney (arrow).

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