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RENAL TRANSPLANTATION. CLINICAL - 1

FP875 M-TOR INHIBITORS-INDUCED PNEUMONITIS IN RENAL TRANSPLANTED PATIENTS: A SINGLE CENTER EXPERIENCE

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Introduction and Aims: The mTOR inhibitors drugs (mTORi), sirolimus and everolimus, are associated with pulmonary toxicity. Radiological images of mTORi-induced pneumonitis (mTORi P) are characterized either by interstitial damage (NSIP) or by organizing damage (OP). The overall experience about mTORi P incidence, clinical relevance, risk factors and outcomes in renal transplanted patients is limited.
Methods: We performed a retrospective analysis among the mTORi-treated renal transplanted patients in our Center between 01/01/1997-12/31/2011.
Results: In the analyzed period, 434/1052 transplanted patients were m-TORi-treated (in continuous or intermittent protocols), according to indications and clinical tolerance. mTORi P were observed in 17/434 (prevalence 3,9%).
mTORi P population characteristics: 3/17 everolimus-treated and 14/17 sirolimus-treated; 7/17 patients mTORi treated ab-initio; ratio M/F 8/1; median age 58 years (min-max 35-70); risk factors (smoke, a pre-existant pneumopathy, post-transplant CMV infection) in 5/17; "classic" mTORi P symptoms (fever+cough +dyspnoea) in 6/17.
m-TORi P-related characteristics are as it follows. Median time between mTORi initial symptoms and mTORi P radiological demonstration was 716 days (min-max 66-3176); median mTORi serum levels detected respectively 6, 3, 1 months before mTORi P and at diagnosis were 7 ng/mL, 8 ng/mL, 7.6 ng/mL and 7.3 ng/mL (p= NS). Only in 2/17 cases, serum mTORi levels were beyond the prescript target.
Diagnosis was performed with a CT scan in 16/17 patients (10 OP, 6 NSIP); in one case radiological images were inconclusive. All patients presented altered pulmonary functional tests (PFTs) intended as reduction in carbon monoxide diffusing capacity; a lympocytic alveolitis was found in 5/11 patients (bronchoalveolar lavage, BAL).
The mTORi drug was withdrawn at different times after mTORi P onset in all patients; in 3/17 a steroid therapy was associated.
All patients experienced a favorable outcome. Symptoms resolution was observed in 9/17 at ≤3 months, 7/17 at ≤6 months, 1/17 at ≤12 months. No deaths were recorded. Renal function tests remained unchanged after mTORi interruption at a one year f/up.
Conclusions: In the AA's experience mTORi P is not such a rare adverse event as initially reported in literature data. An early diagnosis, a multidisciplinary approach and a well-defined diagnostic pathway (CT scan, PFTs and BAL) are the cornerstones for obtaining a positive outcome. On the basis of this favorable experience the authors suggest: a) to consider an mTORi P diagnosis also without classic symptoms or sovranormal mTORi serum levels b) to withdraw mTORi after a diagnosis of mTORi P if not usually contraindicated (i.e. cancer in the patient) c) to adopt a steroid-based therapeutic regimen in patients with severe pulmonary impairment.