Reviewer's report

Title: Severe paraneoplastic hypereosinophilia in metastatic renal cell carcinoma

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Reviewer: Shin-ichi Takeda

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The authors report a 46-year-old patient with renal cell carcinoma who subsequently developed severe hypereosinophilia. The WBC count increased up to 57930/microl with 37.7% of eosinophilic granulocytes, accompanied by multiple fresh embolic lesions in the brain and hypokinesia in inferior wall of the left ventricle. Although they described the present case as paraneoplastic hypereosinophilia, several points need to be clarified from the perspectives of the causality and pathophysiology.

1) Hypereosinophilia is observed in diverse conditions. In fact the authors briefly described as “Several tests were performed to rule out non-cancer causes………., which remained all negative” (Case presentation and management), but this issue is crucial. Physicians often devote much effort but actually have lots of difficulties to identify the underlying disease. Besides, various disorders are likely in such a reduced general conditions (e.g. drugs use, infections). The authors should specify how the differential diagnosis was made. A convincing account will be also informative to readers (physicians). Otherwise the term “paraneoplastic” is not appropriate.

2) The authors should note the past medical history (completely disease-free?). This will be clue for the above differential diagnosis and in clarifying what happened along with the development of hypereosinophilia.

3) How were organ involvements associated with hypereosinophilia other than the brain and heart? In general, lung (except for tumor metastasis) and skin are the sites of predilection.

4) Is the left ventricular asynergy a new event? Was there a temporal change in electrocardiogram (comparison with the admission time)?

5) How was the bone-marrow examination? The results (if available) might be helpful to rule out hematological malignancies and provide a deep insight into the pathomechanism of hypereosinophilia just as the authors documented in Discussion.

6) Conclusions are lengthy. It should be