

## Format for ANSWERING REVIEWERS

August 3, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: Sweet syndrome.doc).

**Title:** Sweet syndrome and differentiation syndrome in a patient with acute promyelocytic leukemia.

**Author:** Solano-López GE; MD, Llamas-Velasco M; MD, Concha-Garzón MJ, Daudén E; MD.

**Name of Journal:** World Journal of Clinical Cases.

**ESPS Manuscript NO:** 11862.

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated.

2. Revision has been made according to the suggestions of the reviewer

(1) The case is interesting, but can be improved on several fronts. Specific suggestions follow: A little more background about his APLM would be nice. In 2-3 sentences mention his presentation, the blood/marrow findings and the molecular/cytogenetic confirmatory result: We have added the following sentences to the clinical case: A 50-year-old man **presented with pancytopenia on a routinal analysis. A bone marrow (BM) aspirate showed 73 % of blasts; homogeneous medium to large cells with visible nucleoli in most cases and clasmotosis. Auer rods were also seen. The red series was decreased without megakaryocytes. The BM biopsy showed that the hematopoietic parenchyma was replaced by a proliferation of myeloid cells showing a monomorphic appearance. The neoplastic cells were positive for myeloperoxidase and CD117 and negative for CD34, TdT and Glycophorin. 30 % of BM cells were positive for PML-RARa by fluorescence in situ hybridization (FISH).**

Did he have any features of DIC? Mention any weight gain, renal dysfunction or rise in TLC at the time of onset of the complications. According to the reviewer we also added: **No features of disseminated vascular coagulation were present. The patient did not gain or lose weight and no renal or hepatic dysfunction was observed.**

Disappearance of the PML-RARa by day +29 is highly unusual. Please document the modality by which this mutation was looked for. Also provide briefly the morphological

status of the bone marrow aspirate. We added the following data to the clinical case:

On day +29, a new BM aspiration **FISH study** did not show the PML-RARa translocation.

As writte above we also added that **“A bone marrow (BM) aspirate showed 73 % of blasts; homogeneous medium to large cells with visible nucleoli in most cases and clasmatosis. Auer rods were also seen. The red series was decreased without megakaryocytes”**.

The discussion is inadequate. It is insufficient to speculate on a connection just because of, “common features such as fever, infiltration of neutrophils and improvement with steroid therapy” as all of these are rather non-specific. The authors must introduce a full new paragraph discussing a shared pathogenesis, deliberating on possible mechanisms, if they want the reader to buy into their hypothesis. Do the prior 2 reports have any clues? In reference 5 it appears that the events were not synchronous but metachronous.

We had to write more about the pathogenesis and possible hypothesis. We added 2 new references and added these new paragraphs to the discussion:

**One of the differences between these two syndromes is that in most cases of SS, the involvement is limited to the skin while the** main difference is the capillary leakage in the DS which is produced by the cytokine storm released by the promyelocytes as they mature. **ATRA induces the differentiation of myelogenous leukemic cells into mature myeloid cells conferring them functional properties with modification of their migratory capability.**

**We know that these two syndromes are caused by ATRA therapy but we cannot rule out the possibility that they can be the sides of the same phenomenon with common mechanisms. For some authors, the SS and the DS are different inflammatory reactions with common mechanisms induced by ATRA therapy <sup>6</sup> while Ueno et al thought that the SS due to ATRA therapy could represent a partial form of the DS.<sup>7</sup>**

Indeed, as the reviewer could read in reference 5, the onset of skin lesions after ATRA therapy was on day 18 and 10 days later the DS appeared.

Figure 2: I am afraid I cannot really appreciate the neutrophils at the magnification provided. Please add an inset with a higher (maybe oil immersion) magnification photograph of the same

We sent another image where neutrophils can be better seen.

3. Two References were added (reference 6 and 7).

Thank you again for publishing our manuscript in the World Journal of Clinical Cases.

Sincerely yours,

Guillermo Enrique Solano-López. MD.  
Department of Dermatology.  
Hospital Universitario de la Princesa.  
Diego de León 62. Madrid.  
Spain.  
Fax: +34-662-193040.  
E-mail: [guitje1@hotmail.com](mailto:guitje1@hotmail.com)