Author's response to reviews

Title: Early invasive vulvar squamous cell carcinoma arising in a woman with vulvar pemphigus vulgaris and systemic lupus erythematosus

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Author's response to reviews: see over
Dear Editor,

We revised our paper entitled "Early invasive vulvar squamous cell carcinoma arising in a woman with vulvar pemphigus vulgaris and systemic lupus erythematosus" according to referee’s suggestions.

Looking forward for your kind reply

Yours sincerely

Vincenzo Dario Mandato
Reviewer: Benjamin Piura

Reviewer's report:

Case presentation section.

“Is the patient had a Pap smear of her cervix?”

**Because she was virgin, she never had a pap smear and we did not perform it.**

“The authors should indicate precisely (in mm) the extent of the SCC vertical invasion of the stoma.”

The SCC vertical invasion of the stroma was less than 1 mm.

“Corticosteroids improved the immunological PV but not the clinical PV”. The authors should provide some details about the immunological improvement of the PV in this patient”.

Current therapy was based on High dose human immunoglobulins (IVIg). IVIg 5% solution were infused intravenously with an electronic pumping device at a total dose of 2 g/kg per cycle divided into three equal doses, administered over 3 consecutive days. The infusion was administered slowly at not more than 50 mg/kg per hour.

The therapy improved the immunological PV but not the clinical PV. The antibody titer showed a progressive decrease (pre-IVIg titer was of 1:1280; during IVIg titer was of 1:640; post IVIg titer was of 1:80).

“Please provide more details about the systemic chemotherapy given to the patient (dosages of cytotoxic drugs per sqm, intervals between cycles of chemotherapy, etc.).”
She received six cycles of cisplatin plus 5-fluorouracil. The doses and schedule was cisplatin 75mg/m2 on day 1 and 5-fluorouracil 800 mg/m2 on day 2 to 5 every three weeks.

The patient did not die, most probably, from her early SCC of the vulva. The author should specify the reason of the patient's death? E.g., renal failure, cardiac arrest, septicemia, etc. Is a post mortem examination was performed? If not, what was the reason?"

The reason of the patient’s death was cardiac arrest but no post mortem examination was performed because her parents refused.

Discussion section.

“I would expect the authors to discuss in their Discussion section a little bit more about the association between chronic inflammation and cancer. The following articles can help the authors with their discussion on the association between infection/inflammation and cancer”

Autoimmune diseases are triggers of chronic inflammation that is a well known risk factor of developing various type of cancer. Since 1863 Virchow noted a connection between inflammation and cancer. He suggested that the “lymphoreticular infiltrate” reflected the origin of cancer at sites of chronic inflammation. The hallmark of cancer related inflammation include the presence of inflammatory cells and inflammatory mediators in tumor tissues, tissue remodelling and angiogenesis similar to that seen in chronic inflammatory responses and tissue repair. There is strong clinical evidence for an association of chronic inflammation with SCC. SCC can arise from a malignant transformation occurred within a chronic inflammatory focus of ulcerative and non healing wounds. This association has been described for LES, epidermolysis bullosa, lichen planus, leg ulcerations. Even areas of healed wounds are more susceptible to development SCC. Moreover, inflammation is not only associated with de novo development of SCC but also play a role in his progression. Probably in our patients both LES and PV played a pivotal role in the SCC development.
“Figure 2 is actually composed of two photos of bad quality that were taken, most probably, with use of the fiber optic of the laparoscopic camera. Although the legend to this figure says, “lesion was extended to perineal and groin area”, it is very difficult to distinguish these areas in the photos. Figure 4 seems to be superfluous and somehow seems to repeat Figure 2. Figure 4, like Figure 2, was taken, most probably, with use of the fiber optic of the laparoscopic camera. In order to improve the identification of the anatomic areas in Figure 2 and Figure 4, I would suggest that the authors should add, build in, within the photos, captions indicating the anatomical areas (clitoris, labium minor, labium major, vaginal orifice, perineum, anus, groin, etc)”.

Anatomical areas are now indicated according to your suggestions.

A new Figure 4 is now reported to show widely groin area.
Reviewer: Neville Hacker

Reviewer's report:

“This article is mainly of interest to medical specialists. From a gynaecological perspective, there does not seem to be rapid progression but the lesion was never adequately treated so it is difficult to draw conclusions. You should explain in more detail why you elected not to excise the VIN, which is not a big surgical procedure”.

A biopsy specimen of the primary tumor revealed a VIN 3 with micro-invasive disease. Vertical invasion of the stroma was less than 1 mm. A wide and deep excision of the primary tumor was required but our patient was classified as ASA IV at preoperative evaluation. She presented a 25 kg weight loss, a worsening of the clinical conditions with a high risk of nonhealing wound and postoperative infection so combined chemotherapy was preferred to surgical approach. She received six cycles of cisplatin plus 5-fluorouracil. The doses and schedule was cisplatin 75mg/m2 on day 1 and 5-fluorouracil 800 mg/m2 on day 2 to 5 every three weeks.