Author's response to reviews

Title: Paget's Disease of the Breast in a Male with Lymphomatoid Papulosis.

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Dear Dr. Chiu and Dr. Leung,

Subject: Response to comments. MS: 1400972461356082 - Paget’s Disease of the Breast in a Male with Lymphomatoid Papulosis.

Many thanks for all of your comments and suggestions. I have enclosed a point by point response below and a revised manuscript with all changes tracked.

If there are any further questions or comments I am more than happy to respond.

Yours Sincerely

Dina Fouad
1) “The patient had been having lymphomatoid papulosis for 30 years and was controlled with methotrexate. How was the disease distribution in him?”

On examination on the Breast ward there were visible, faded, scattered pink papules across the upper chest, upper back, lower abdomen and lower legs.

2) How was his disease control recently?

There was no record that the disease control had been poor recently, however the patient stated that he did generally become itchy due to the lymphomatoid papulosis. The patient had suffered from several recorded flare ups; in 1992, 2000, 2003 and 2004 and required several dermatology clinic visits and medication adjustments (e.g. increasing dose of methotrexate). As well as the anterior chest, upper back, lower abdomen and lower limbs the patient also had flare ups affecting the left pre-auricular area and left upper eyelid.

3) Was there any residual disease that made him prone to confusion of the nipple lesion with his original skin lesions?

Yes, the residual faded, pink papules present on the upper chest could have certainly caused confusion in diagnosing Paget’s disease of the nipple as the disease did extend across the chest including the nipples.

4) What was the staging and site of his lymphoma, and did he receive any radiotherapy over the chest area?

The lymphoma was discovered on palpation of two left sided inguinal nodes and one right sided inguinal node. Palpable lumps were also present in the left upper thigh, left lower quadrant of the abdomen and the right hypochondrium. CT scan revealed retroperitoneal lymphadenopathy, bilateral inguinal lymphadenopathy and nodes present in the both iliac chains. It was Stage 2B Mixed Cellularity Hodgkins lymphoma for which the patient received 6 cycles of ABVD chemotherapy (Doxorubicin, Bleomycin, Vincristine and Dacarbazine) with no radiotherapy. The patient received no radiotherapy for any other cause.

5) Is there any association between the breast lesion and his past medical history or drug use?

There may be a link between the long term use of methotrexate and the development of Paget’s disease of the nipple due to the anti-folate effects of methotrexate. Folic acid is essential for DNA synthesis and studies have shown that decreased folic acid can increase the risk of developing malignancy. Notably, the patient did not commence folic acid supplementation until 2006. (1)

6) Pre-operative photograph.

Unfortunately, the patient was seen on the day of operation but there was a photograph taken by the general practitioner who was contacted by telephone, email and writing several times and failed to respond. Moreover, the histology department were contacted to enquire about histological images who replied stating there were none.

References

DNA and chromosome breakage: implications for cancer and neuronal damage. Proc Natl Acad Sci U S A. 1997 Apr 1;94(7):3290-5.