‘A Rash Diagnosis’- Delayed Diagnosis of Syphilis due to Misinterpretation of CMV IgM Serology: A Case Study

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Abstract

A 46yo man presented with a rash over his trunk, neck and limbs. The rash was initially diagnosed as acute cytomegalovirus (CMV) infection on the basis of a positive CMV IgM result. He subsequently developed visual impairment and was found to have right optic disc swelling. Further investigations revealed positive syphilis serology. He was treated with intravenous benzylpenicillin for 15 days with a diagnosis of tertiary syphilis. Retrospectively, his CMV serology revealed a low positive CMV IgM quantitative value suggesting a likely false positive result. There was no follow serology done in this case to look for IgG seroconversion.

Case Presentation

A 46-year-old man presented with a rash over his trunk, neck and limbs. A viral exanthem was suspected and an initial diagnosis of acute cytomegalovirus (CMV) infection was made on the basis of CMV serology results in which IgM was positive and IgG was negative. However, the rash failed to resolve, he noticed hair loss and he subsequently developed visual impairment which prompted an ophthalmology referral four months after initial presentation. On review by ophthalmology, the patient was found to have decreased visual acuity bilaterally (right eye 6/15, left eye 6/24-2) and right optic disc swelling (figure 1). Syphilis serology was subsequently performed and results (positive Treponema Pallidum Particle Agglutination (TPPA) and RPR reactive 1:32) prompted referral to Infectious Diseases. Clinical examination revealed widespread symmetrical erythematous papulosquamous plaques over his trunk, neck and limbs (figure 2) with several small plaques on the plantar aspect of his left hand and left foot. He also had patchy alopecia (figure 3) and bilateral inguinal lymphadenopathy. The patient reported unprotected intercourse with casual male partners. His HIV test was negative and he had not been tested for syphilis previously. Retrospectively, the earlier serum tested for CMV was retested for syphilis and this test returned with a positive TPPA and RPR reactive 1:64.

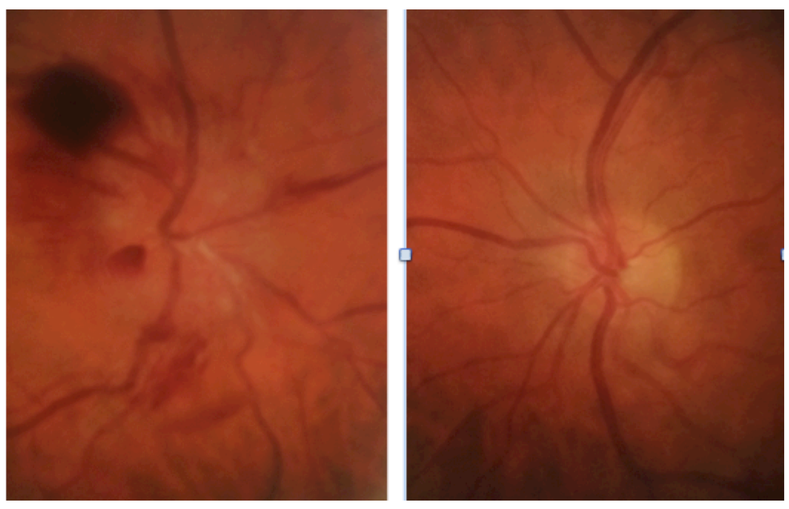

Figure 1

Fundoscopy of right eye showing optic disc swelling

Fundoscopy of left eye- normal

A punch biopsy of the rash showed a plasma cell rich granulomatous process spanning the dermis which supported the diagnosis of syphilis likely consistent with tertiary syphilis. He was treated with a 15 day course of IV benzylpenicillin with concomitant prednisolone in the first 36 hours, given the optic involvement, to reduce the likelihood of a Jarisch-Herxheimer reaction. On follow up 3 months after treatment his alopecia had completely resolved and his rash was significantly improved.

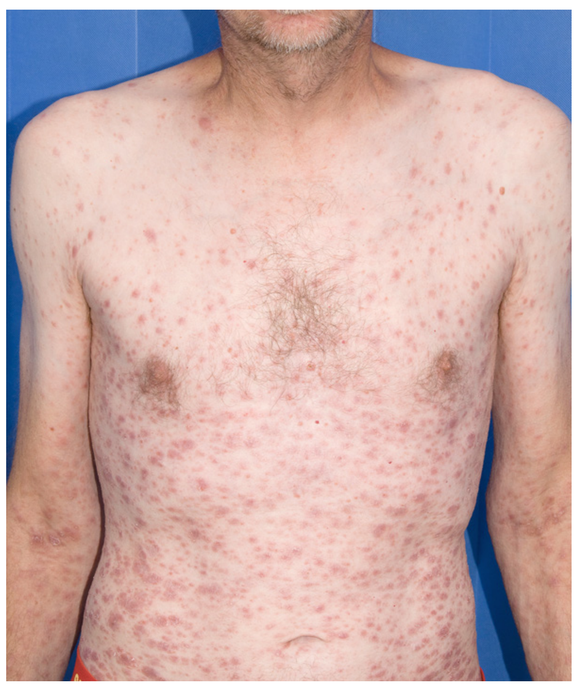

Figure 2- *Erythematous papulosquamous plaques over the trunk and arms of the patient.*

Discussion

This case exemplifies the consequences of misdiagnosis based on performance of a test probably not indicated by the clinical presentation, compounded by a false positive laboratory result. The presentation was not typical of CMV infection. In immunocompetent adults the most common clinical presentation of CMV infection is a self limiting mononucleosis like syndrome[1], characterised by fevers and malaise. Predominant skin manifestations are rare in CMV infection in immunocompetent patients, however, transient rubelliform rashes, generally lasting no longer than a few days[2] and maculopapular eruptions can occur[3]. In this patient, the persistent and atypical rash should have prompted other diagnoses to be considered earlier.

The significance of the CMV IgM serology result is also highly questionable. While the initial laboratory reported CMV serology (Diasorin CLIA assay) as IgM positive and IgG negative, repeat testing in 7 to 14 days to confirm IgG seroconversion is suggested. Unfortunately our patient did not get a follow up test to confirm seroconversion. Upon further clarification from the laboratory, his CMV IgM level was only 23 UmL (normal <17 UmL; equivocal 18-22 UmL). In our experience positive CMV (and indeed other) IgM serology results that are near the defined cut-off values are most commonly false positive results and are rarely confirmed with IgG seroconversion on subsequent testing.

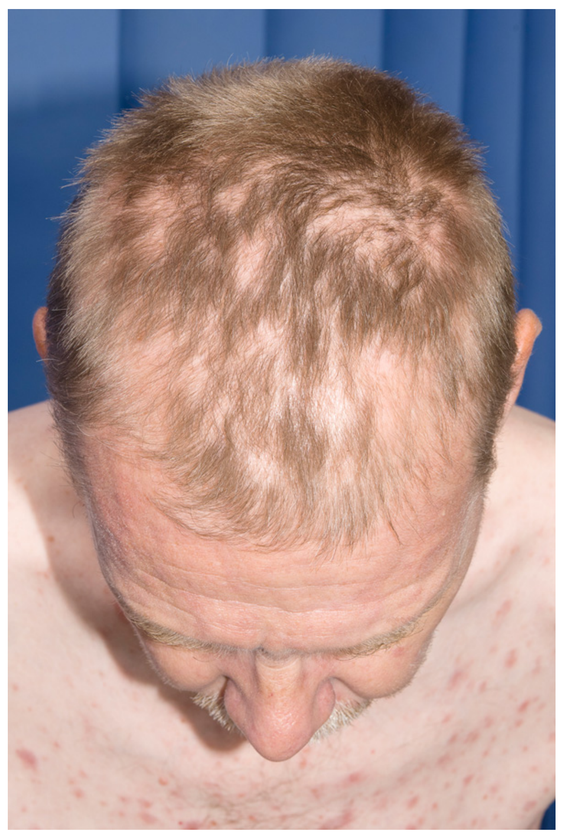

Figure 3- *Patchy alopecia; note the characteristic irregular thinned (“motheaten”) patches of hair loss.*

CMV IgM false positives have also been reported to occur in several situations including patients with rheumatoid factor[3], other infections such as Epstein Barr Virus[4] and in Antiphospholipid syndrome[5], further highlighting the need for paired specimens to confirm seroconversion in suspected cases.

Conclusions

- We would recommend that laboratories add additional cautionary comments for “weakly positive” IgM results.
- To confirm a diagnosis, follow up testing of positive IgM serology results to demonstrate IgG seroconversion is important.
- This case emphasises that positive test results must be cautiously interpreted in the context of the patient’s clinical presentation to avoid a misleading diagnosis.

References:

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