Author's response to reviews

Title: Fever due to cracked mercury dental amalgam: a case report

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

thank you for revising our paper: “Fever due to cracked mercury dental amalgam: a case report”.

Here is our point-by-point response to the referee’s concerns.

1° Reviewer (Joachim Mutter) Thanks for your favourable comments.

2° Reviewer (Pam Factor-Litvak)

According to the reviewer, there is no correlation between fever of unknown origin and damaged mercury dental amalgam, and the patient’s high white-cell count could be due to a viral infection.

Our point-by-point reply:

1) Viral infections relate to a significant increase in percent lymphocytes compared to normal values (the patient’s value was 10.8 percent, much lower than normal). In fact, among white cells, lymphocytes play the most important role in response to viral infection through a specific recognition, by means of their T cell receptor, of viral peptide presented by body cells or by dendritic cells. On the contrary, the patient’s sharp increase in temperature (39.1°C), lasting almost three days, could be related to a possible bacterial infection, considering the percent increase (80.1 percent) in neutrophilic granulocytes (which are aspecifically engaged against bacterial infections). Patients affected by bacterial infections, when not subjected to immunosuppressive therapy, are able to respond to standard antipyretic therapies, which our patient did not respond to. Indeed, viral and bacterial infections cannot account for either the symptoms or our patient’s laboratory data.

A study by Summers et al reports that inorganic mercury, released from dental silver fillings, provokes an increase in mercury- and antibiotic-resistant bacteria in oral and intestinal floras of primates, which could help explain the patient’s increase in temperature. The possible peak in the incidence of resistant bacteria in our patient’s normal floras could
provide an explanation for her fever, which lasted three weeks after removal of mercury amalgam (see reference n° 8 in revised version).

2) The patient’s low haemoglobin concentration (11.4 g/dL) and low hematocrit (34.4%) indicated that she was affected by anemia, whose pathogenesis could be due to the toxic effect of mercury on the bone marrow erythropoiesis. In fact, values normalized three weeks after removal of amalgam.

3) The high erythrocyte sedimentation rate value (66 mm/h)) was possibly due to the production of acute phase proteins by the liver, following the stimulation by some interleukins and TNF alpha released from the activated immune cells. So, an idiosyncratic immuno-toxic reaction caused by mercury could be responsible for the increase in erythrocyte sedimentation rate value.

3° Reviewer (Ulf Lindh)

The responses to the author’s comments are here reported:

1) The amalgam filling was removed before blood samples were drawn. However, the technique of filling removal used by us (see reference n° 3) reduced room mercury vapour levels by $10^{-4}$ (from 0.5-0.7 mg/m$^3$ to 0.00025-0.00045 during cutting) compared to the other previously used techniques.

2) The second set of blood tests reported in the text were performed three weeks after the removal of dental amalgam (see 5 lines before discussion).

3) We have deleted the first and corrected the second sentence of the discussion.

4) The clinical symptoms (palpitations, headache, neurological collapse and sporadic chest pain on the left side) were examined by a cardiologist and a neurologist who did not highlight any organic diseases.

Some modifications of the text have been made, taking into account the referees’ suggestions. We have reported such corrections or additions in bold.
The necessary language corrections have been made, as required.

Sincerely Yours

Maria Elena Ferrero