

## Disappearance of immunoglobulins in acute phase of influenza A infection

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In February, 2005, a 52-year-old previously healthy man was admitted to our hospital intensive care unit with progressive dyspnoea and diminished consciousness. He had been experiencing fatigue, headache, abdominal pain, and nausea for 4 days. During transport to the hospital the patient had a cardiac arrest and needed to be resuscitated. On admission, his temperature was 35.2°C, blood pressure was 80/40 mm Hg, and heart rate was 130 beats per min. The patient was comatose and had respiratory failure; septic shock, acute myocardial infarction, and haemorrhagic shock were considered as possible causes. Treatment with antibiotics (cefotaxime and levofloxacin) was initiated after taking samples of blood, sputum, stool, and urine for culture. Simultaneously, supportive treatment, including fluid resuscitation, mechanical ventilation, and vasopressor support, was instituted. Chest radiography showed some signs of interstitial oedema. ECG was normal. These findings, combined with normal cardiac biomarker levels, made myocardial infarction an unlikely diagnosis. Laboratory test results showed a left-shifted leucocytosis ( $19.6 \times 10^9/L$ ), haemoconcentration (haemoglobin 195 g/L; haematocrit 0.56), and evidence of tissue hypoxaemia (lactic acid 16 mmol/L; arterial pH 6.82).

Despite vasopressors and fluid resuscitation, the patient remained hypotensive. Low colloid osmotic pressure as a result of capillary leak seemed to be partly responsible. Low albumin (16 g/L) and total protein (19 g/L) were indicative for this condition; hypogammaglobulinaemia was present (IgA 0.23 g/L; IgM 0.12 g/L; IgG 1.0 g/L). Both high usage and impairment of liver synthesis function (the latter supported by hypogammaglobulinaemia and an antithrombin of 0.20 U/mL) were possible explanations. Causes of hypogammaglobulinaemia were considered.<sup>1</sup> In this patient, without previous illnesses, medication, or recurring infections, a primary cause was unlikely. A viral

infection as causal factor was considered. Serology for Epstein-Barr virus, cytomegalovirus, HIV, and parvovirus B19 was negative. Influenza A (H3N2) was isolated in sputum samples (2nd and 4th day in hospital). All other cultures remained negative. Although a diagnosis was established, the patient's clinical condition had vastly improved, and, therefore, antiviral therapy was not initiated. Liver synthesis function recovered after a few days. After 9 days the patient was transferred to the ward and was discharged after another 5 days. Until final follow-up in February, 2006, there had been no recurrence of illness and immunoglobulin concentrations remained normal (figure). Because of a remaining monoclonal IgG- $\lambda$  in an otherwise normal protein  $\gamma$ -fraction, a first episode of the rare systemic capillary leak syndrome has to be considered as well, although this is less likely.

Reports of shock caused by viral infections are limited, and, in most cases, associated with underlying disease or occur in immune compromised patients.<sup>2</sup> Although hypogammaglobulinaemia indicated a state of immunodeficiency, we have no reason to believe this was the case before admission because our patient did not have a history of recurrent infections and we could not identify a pre-existing immune deficiency in a plasma sample taken several weeks before admission (figure). Immunoglobulin concentrations returning to normal on recovery gave further evidence to support the hypothesis that the transient hypogammaglobulinaemia was caused by influenza A infection. In mice, depletion of B cells by influenza virus has been demonstrated.<sup>3</sup> Alternatively, since anti-influenza antibodies can promote the resolution of primary influenza infection in animals, the severity of the clinical course in this case could have been caused by the lack of an antibody response.<sup>4</sup> Common flu-like diseases can have serious complications even in healthy persons who are not considered part of a high-risk population. Hypogammaglobulinaemia in a non-immunocompromised patient with sepsis syndrome should prompt the clinician to consider a viral cause and should allow for rapid institution of antiviral therapy.

### References

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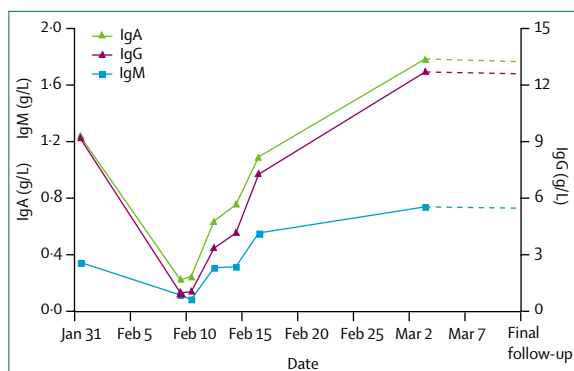


Figure: Dynamics of immunoglobulin levels

The patient was admitted on Feb 9, 2005. IgA=immunoglobulin A. IgM=immunoglobulin M; IgG=immunoglobulin G.