Pseudoleucocytosis and pseudothrombocytosis due to cryoglobulinaemia

Erroneously high blood counts, measured by the Coulter Model S plus phase IV blood counter, may be caused by artefactual particulate matter, such as platelet clumps, epidermal cells, dust or small air bubbles. Cryoglobulins are immunoglobulins of one or more classes that precipitate on cooling below 37°C to form globules. This phenomenon is most prominent at 4°C, though it occurs to a lesser degree at higher temperatures. Pseudoleucocytosis due to cryoglobulinaemia has long been recognised, but the phenomenon of pseudothrombocytosis due to cryoglobulinaemia has not been previously reported.

Case report

A sixty year old West Indian woman presented with menorrhagia in March 1986. A full blood count on a Coulter Counter S plus phase IV showed a haemoglobin concentration of 13·5 g/l, with an increased leucocyte count of 46·9 \times 10^9/l and a platelet count of 646 \times 10^9/l. The red cell count was within normal limits at 5·24 \times 10^{12}/l. Examination of the peripheral blood film and manual white cell and platelet counts did not corroborate the automated results. The peripheral blood film showed small translucent globules dispersed among the red cells. Cryoglobulinaemia was suspected, and the sample was reprocessed at varying temperatures. This showed a progressive increase in the leucocyte and platelet counts when the sample cooled on standing (figure). The plasma viscosity using a Luckham clinical viscometer was 2·9 cps, at 37°C but was greater than 5 cps at 4°C.

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Samples of plasma and serum were processed at similar temperatures. The table gives the results.

**Table**  Comparison of cell counts on plasma and serum with falling temperature

<table>
<thead>
<tr>
<th>Temperature</th>
<th>White cell count (\times 10^9/l)</th>
<th>Platelet count (\times 10^9/l)</th>
<th>Red cell count (\times 10^{12}/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plasma</td>
<td>Serum</td>
<td>Plasma</td>
</tr>
<tr>
<td>37°C</td>
<td>0·2</td>
<td>0·1</td>
<td>90</td>
</tr>
<tr>
<td>30°C</td>
<td>0·3</td>
<td>0·1</td>
<td>90</td>
</tr>
<tr>
<td>20°C</td>
<td>42·7</td>
<td>0·2</td>
<td>776</td>
</tr>
<tr>
<td>4°C</td>
<td>85·6</td>
<td>58·5</td>
<td>1125</td>
</tr>
</tbody>
</table>

**Discussion**

Cryoglobulins form particles of various sizes, ranging from 3–24 μ when they precipitate. The Coulter Counter Model S plus phase IV is an electronic blood counter, which operates on the principle of an impedance change being produced by particles passing through a small aperture. It usually measures particles ranging from 2 μ to 450 μ (Instruction Manual, Coulter Model S, 1983.) Our findings showed interference in whole blood counts in the 2 μ and 35 μ regions, with smaller particles being counted as platelets and the larger ones as leucocytes. As expected, the spurious platelet and leucocyte counts were greater in plasma than in serum. Emori et al. described a case of pseudoleucocytosis due to cryoglobulinaemia, in which they attributed the spuriously increased leucocyte count to the particle formation between cryoglobulin and fibrinogen.

Previous reports of pseudoleucocytosis caused by cryoglobulinaemia have been of counts performed on older models of blood counters without the ability to report platelets. With the advent of the Coulter S series and the additional availability of automated platelet counts, pseudoleucocytosis and pseud thrombocytosis should now also be detected. Leucocytosis and thrombocytosis, unsubstantiated by examination of a peripheral blood film and manual counts, should raise the suspicion of cryoglobulinaemia.

KJ Patel
CG Hughes
LA Parapin
*Department of Haematology, Bradford Royal Infirmary, Bradford BD9 6RJ
†Department of Biomedical Science, Bradford University, Bradford BD7 1DP
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References

Some preliminary studies on low incidence of infant botulism in the United Kingdom

Since the first recognition of infant botulism in 19761 over 500 cases have been reported worldwide, more than 95% of which have occurred in the United States. There has been one reported case in the United Kingdom.2 About one third of all cases occurred in babies known to have eaten honey.3 Several surveys4–6 in the United States on the incidence of Clostridium botulinum in honey have shown that up to 10% of retail samples (principally American produce) were contaminated with the organism. There have also been reports7,8 of the presence of C. botulinum in post mortem faecal specimens from infants who had died suddenly and unexpectedly (sudden infant death syndrome, SIDS).

In view of these findings we felt it worth while to investigate the incidence of C. botulinum in honey, either produced in or imported into this country, and to determine whether any deaths in infants diagnosed as SIDS could be attributed to C. botulinum intoxication.

Honey samples on sale in the United Kingdom from 16 countries, excluding the United States, were examined for C. botulinum using a combination of dilution and centrifugation9 and membrane filtration.10 The technique was validated using a naturally contaminated honey sample provided by Dr SS Arnon, Department of Health Services, California, United States, and could detect one C. botulinum type B spore per 5 g honey. C. botulinum was not detected in a 20 g portion of 122 samples examined.

Specimens of faeces (n = 97), ileocecal contents (n = 34), and heart blood (n = 34) from 97 cases of SIDS, and specimens of faeces (n = 27) and serum (n = 7) from 27 cases of suspected infant botulism were examined by standard procedures.11 Neither C. botulinum toxin nor the organism were found in any of the specimens examined.

C. botulinum has been found in honey only in the United States to date, except for a single case in Canada.3 This may reflect a more common occurrence of the organism in the American environment, although this is difficult to substantiate. Variations in the numbers of spores in the environment have been suggested as a reason why some states in America have a very low incidence of infant botulism.12 It seems unlikely that increased clinical awareness of the disease in the United States would account for the difference in reported international incidence.

One of the many theories concerning some cases of SIDS proposes that the syndrome is a clinical manifestation of infant botulism in its most severe form.12 If this were the case then it is not surprising that none of the specimens examined from the SIDS cases in this study was positive, as infant botulism in this country is extremely rare. The two conditions may not be linked, however, as Swiss workers8 found that 15% of SIDS cases were associated with the presence of C. botulinum or its toxins, yet Switzerland has a very low incidence of infant botulism. We are continuing the investigation of cases of SIDS in this country for the presence of C. botulinum.

Although C. botulinum intoxication is very rare in the United Kingdom, it would seem prudent to avoid potential risk factors, such as feeding honey to infants under 12 months of age13 especially as a good deal of honey is imported into this country.

FR BERRY*
RJ GILBERT*
RWA OLIVERT†
AAM GIBSON‡
*Food Hygiene Laboratory, Central Public Health Laboratory, London NW9 5HT
†Biological Materials Analysis Research Unit, University of Salford, Salford M5 4WT
‡Pathology Department, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ, Scotland

References

Bios = life

Alas, I had on two occasions to write to one of your predecessors to remind him that a biopsy after death is, by definition, an impossibility. I note in the paper by Cairns et al14 that three references to the impossible have escaped the present editorial eye.

HG PENMAN
Department of Pathology, Crawley Hospital, West Green Drive, Crawley, Sussex RH11 7DH

Reference

Professor Slavin replies:

Dr Penman is correct—and the editor nodded. This is particularly reprehensible for he (GS) performed the necropsy.