Management of blood donors whose donations are repeatedly falsely positive by the HIV antibody screening test

H I Atrah, J V Parry, D Gough, J Toswill, F A Ala

Abstract
Since 1985, over 1 800 000 donations have been screened by the West Midlands Regional Blood Transfusion Service for antibody to HIV. Twelve regular donors gave three or more donations that were alternatingly positive and negative in the screening test, but not confirmed to be HIV positive by supplementary testing. Extensive investigation of six of these donors, including the polymerase chain reaction (PCR), failed to confirm HIV infection. The donors were reassured but, nevertheless, retired to comply with the guidelines of the National Blood Transfusion Service. These findings indicate that, for UK donors, ambiguous serological findings are unlikely to reflect HIV infection. On the rare occasions where serological results are particularly ambiguous, PCR testing of donors’ blood may be helpful.

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Keywords: HIV, ELISA, PCR, blood donors.

According to the policy of the United Kingdom Blood Transfusion Service for screening for HIV, a donation that tests repeatedly positive by the screening test should be discarded after an aliquot has been sent to a HIV Reference Centre.1 If the confirmatory tests prove to be positive, the donor is counselled and retired from the panel. However, should the confirmatory tests yield a negative or equivocal result, the donor’s record at the Regional Blood Transfusion Centre is to be “flagged” so that, although the subsequent donation is also discarded, it is retested by the screening and confirmatory tests. The following outcomes of these tests are possible: if both tests are negative, the donor is reinstated; if the confirmatory test is positive, the donor is counselled and retired; if the screening test remains positive with an equivocal or negative confirmatory test, the donor is retired. The last possibility is the least satisfactory outcome. When a donor is retired, it is incumbent upon the Transfusion Centre to offer an easily comprehensible explanation especially as the reason for retirement is related to the possibility of HIV infection. Donors with equivocal supplementary tests may, after initial counselling, legitimately be referred for further investigation in an appropriate outpatient clinic. However, those with repeatedly positive screening tests and persistently negative confirmatory tests for the infection represent a special group of donors who are not well catered for by the present procedures.

Methods and Results
Since HIV screening was introduced in October 1985, over 1 800 000 donations have been tested at the West Midlands Regional Blood Transfusion Centre by several generations of Wellcozyme anti-HIV kits. Repeatedly positive samples are tested at the centre using the SeroDia particle agglutination test for antibodies to HIV. During this period, 12 blood donors were identified with a minimum of three donations, each of which were repeatedly positive by the HIV screening tests but negative by confirmatory tests. These donors shared an unusual feature: their HIV antibody positive donations were interspersed by at least one HIV negative donation in the screening test. The first six of these donors were retired by letter. Some telephoned to seek further information and were reassured. The other six donors, one man and five women (age range 21 to 50 years) were asked to give further blood samples to investigate an inconsistent test result on their last donation. None suspected the possibility of HIV infection although two donors thought that we had invited them for further tests because we had found that they had leukaemia. Clotted and EDTA blood samples were obtained from each donor. Both samples were sent to the Hepatitis and Retrovirus Laboratory of the Virus Reference Division of the Central Public Health Laboratory, London.

At the Hepatitis and Retrovirus Laboratory, the serum samples were tested in several enzyme immunoassays (EIAs) including the assay used by the Transfusion Centre (Wellcozyme HIV 1+2, VK55, Murex Diagnostics, Dartford, UK), Enzygnost HIV 1/2 EIA (OWRP 24/25, Behring Diagnostics, Hounslow, UK)
Summary of serological findings on the repeatedly reactive donors

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>No. of referred specimens</th>
<th>Date of first reactive specimen</th>
<th>Date of PCR specimen</th>
<th>Wellcozyme® HIV 1+2 ODICO</th>
<th>Peptide HIV 1/2 ODICO</th>
<th>Recombinant HIV 1/2 ODICO</th>
<th>Western blot Diagnostic HIV Blot 2-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>5</td>
<td>May 1991</td>
<td>Oct 1992</td>
<td>&gt;0.00</td>
<td>0.11</td>
<td>8.07</td>
<td>gp120 (trace), gp160 (1+)</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>5</td>
<td>Dec 1990</td>
<td>Nov 1992</td>
<td>0.68</td>
<td>0.09</td>
<td>0.17</td>
<td>p24 (3+), p55 (trace)</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>5</td>
<td>Oct 1990</td>
<td>Jan 1993</td>
<td>1.02</td>
<td>0.10</td>
<td>0.10</td>
<td>No bands seen</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>5</td>
<td>May 1991</td>
<td>Feb 1993</td>
<td>4.47</td>
<td>0.09</td>
<td>0.02</td>
<td>No bands seen</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>5</td>
<td>Jul 1991</td>
<td>Feb 1993</td>
<td>0.50</td>
<td>0.47</td>
<td>2.22</td>
<td>No bands seen</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>3</td>
<td>Apr 1991</td>
<td>Mar 1993</td>
<td>1.47</td>
<td>0.37</td>
<td>2.22</td>
<td>No bands seen</td>
</tr>
</tbody>
</table>

*Wellcozyme HIV-1+2 EIA is the screening test used by Birmingham BTC.

1 Optical density/cut off.
2 Peptide assay, Behring HIV 1/2 EIA.
3 Recombinant assay, Biotest HIV 1/2 EIA.

based on synthetic peptide antigens, and an EIA based on "recombinant" antigens, the Bio-
test Anti-HIV 1/2 Recombinant (807005, Bio-
test, Solihull, UK). The serum samples were also tested using a western blot (HIV blot 2-2,
Diagnostic Biotechnology, Singapore) which incorporates antigens purified from HIV in-
fected cell culture and a synthetic HIV-2 ant-
gen.

The EDTA blood specimen was divided into
two aliquots: one aliquot was processed using a
commercial polymerase chain reaction (PCR) kit for the detection of HIV proviral DNA
(Amplicor HIV 1, Roche Diagnostics, Welwyn
Garden City, UK); from the second aliquot,
CD4 positive cells were purified by mixing the blood with anti-CD4 coated particles with
ferrous cores (Dynabeads M-450, Dynal, Oslo,
Norway). This permitted purification of CD4
positive cells by magnetic separation. DNA was
extracted from the purified cells and subjected
to nested PCR using SK68/SK69 primers with
an appropriate pair of outer primers.

All but one of the serum samples collected
at the time the EDTA specimen was taken (for
PCR) were reactive in the recombinant based
screening EIA used by the Transfusion Centre
table). Two were reactive in the Biotest HIV
1/2 EIA, which is also based on antigens pro-
duced by expression of rDNA. All were un-
reactive, however, when tested by the Behring
HIV 1/2 EIA which uses synthetic oligopeptide
antigens. Western blotting revealed that three
serum samples were anti-HIV negative—that
is, no bands were present, and two were anti-
HIV indeterminate, giving reactions with gag
derived proteins only. One serum gave a re-
action on western blotting that would be
classified indeterminate by more stringent in-
terpretive criteria but, according to the World
Health Organisation criteria, which call for
reactivity with two *env* gene products, the
pattern could be considered positive.

However, HIV proviral DNA was not de-
tected by either method in any of the donors' 
EDTA blood specimens. This and the lack of a
persisting, confirmed anti-HIV seroconversion
during lengthy follow up lead us to conclude
that these six donors were not infected with
HIV. We invited the donors to attend in-
dividually so that it was possible to "explain
the nature of the tests we carried out, the results
obtained and their implications". Three donors
attended for counselling, the others preferred
that we inform their general practitioners di-
eectly. After the donors' permission had been
obtained, the general practitioners of those who
attended the centre were also informed.

All six donors were retired from the panel.
They (or their general practitioners) were told
that this decision was taken only to comply
with National Blood Transfusion Service codes
of practice. The negative PCR results gave us
the confidence to reassure the donors (and
their general practitioners) that they do not
have the infection according to "state-of-the-
art" tests. One donor who attended for coun-
selling and who appeared to have understood
what was said to her, requested at a later date
for her own general practitioner to be informed
about everything we had done, so that he could
explain it again to her. The general practitioners
of the six donors were informed that, should
their patients require an HIV antibody test in
the future for any reason (for example, for
insurance purposes), the test might produce a
false positive result. General practitioners were
advised that such a result should be verified by
confirmatory tests.

Discussion

Within a low incidence population, such as
the United Kingdom blood donors, discordant
serological findings are virtually never as-
associated with HIV infection. We therefore feel
that the appropriate response to the remote
possibility of HIV seroconversion in a reactive,
but unconfirmable, donation is to seek a follow
up specimen for further serological investiga-

However, in view of the low probability of
such reactivity reflecting true HIV infection,
follow up samples are probably best obtained
on the occasion of the next donation (usually
after four to six months) so as not to alarm
donors unnecessarily or put unwarranted extra
burden on the system and this is our usual
practice. Only on the rarest occasion might
this lead to a seroconverting donor not having
access to early support and counselling and to
additional risk to contacts.

For this investigation we asked our donors
to give special samples before the next donation
was due because they had already made three or
more donations with discordant results. While
PCR is not indicated as a routine confirmatory
test for HIV antibody reactive donations, the
selective use of the test is justified for the small
proportion of reactive donors whose serum
samples give rise to results in supplementary

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for J Royal Haematology, Department 21 February

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HIVfalse positive blood to investigate the tests time required. The examples. have the extensively described above, but this should not mean that the donors are left unsure as to whether or not they have the HIV infection with all the difficulties associated with this diagnosis. Donors' tangible expression of concern for others should, if at all possible, not be allowed to become a source of worry for themselves; they deserve reassurance whenever possible.


Osteolytic bone lesions in a patient with idiopathic myelofibrosis and bronchial carcinoma

D J Clutterbuck, A E Morrison, C A Ludlam

Abstract

A 59 year old man with longstanding myelofibrosis and previous splenectomy was incidentally found to have a large lytic lesion in his left femur which required operative fixation. He had undergone right upper lobectomy for squamous carcinoma of the bronchus five years earlier. Histological analysis of bone reamings showed no evidence of metastatic carcinoma. Osteosclerosis is frequently noted in patients with myelofibrosis but osteolytic lesions are uncommon and may be confused with metastatic malignancy.

(J Clin Pathol 1995;48:867-868)

Keywords: Myelofibrosis, bronchial carcinoma, osteolytic lesions.

Case report

A 59 year old man with stable myelofibrosis of 33 years duration presented acutely unwell with bilateral pneumonia, congestive cardiac failure and acute renal failure. He required intensive supportive care including mechanical ventilation, diuretics, inotropes, and intravenous broad spectrum antibiotics. Bronchial washings grew enterococci on culture. Pneumococcal antigen was negative. He made a slow recovery. During his recovery, the patient complained of weakness and paraesthesia in his left leg. He was found to have a flaccid paralysis of the left foot with absent ankle jerk and plantar reflex and sensory loss of all modalities below the knee.

An x ray of the left femur showed a lytic lesion occupying the mid and lower third of the shaft of the bone with extensive endosteal scalloping (figure). A bone scan showed increased uptake of the isotope at the diaphysis of the femur consistent with a metastatic malignancy or primary bone tumour. As there was thought to be significant risk of fracture through this lesion, intramedullary nailing of the bone was performed. Reamings taken from the femur were examined histologically and found to contain macrophages, lymphocytes and haemopoietic cells but there was no evidence of malignancy. Following surgery, the patient made a good recovery. Nerve conduction studies showed changes attributed to critical illness polyneuropathy.

His past medical history included splenectomy at the age of 45 for massive splenomegaly after several painful splenic infarcts, and a right upper lobectomy for squamous carcinoma of the bronchus when aged 55 years. A skeletal survey during this admission showed an abnormality of the bony trabecular pattern in the head of the left humerus, thought to be due to fibrous dysplasia, previously noted in 1960 at which time no abnormality of the left femur was reported. No bone scan was done at the time of lung resection.

Six months later, despite regular post splenectomy prophylaxis with penicillin V, the patient developed a fatal pneumococcal pneumonia and septicaemia. A postmortem examination was not performed.

Discussion

Idiopathic myelofibrosis is a chronic myeloproliferative disorder characterised by marrow
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