Audit results of testing for latent TB in the HIV cohort presenting to Sheffield Teaching Hospitals NHS Foundation Trust

Fotinie Ntziora¹, Thushan de Silva¹, Karen Rogstad², Anne Tunbridge¹

¹Infectious Diseases and Tropical Medicine, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Trust, UK,
²Genito-Urinary Medicine, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Trust, UK

Introduction

Worldwide, it is estimated that 14.8% of all new tuberculosis (TB) cases in adults are attributable to HIV infection. HIV-infected individuals with latent TB infection are more likely to progress to active TB than HIV-uninfected people. The British HIV Association (BHIVA) guidelines for TB and HIV co-infection highlight the need to detect and treat latent TB infection in high risk groups within an HIV positive cohort. The aim of this study was to evaluate the proportion of HIV-infected patients that were eligible for latent TB screening at Sheffield Teaching Hospitals NHS Foundation Trust according to BHIVA guidelines. We also evaluated how many eligible patients have had an IGRA test performed, what proportion have positive tests and of these, how many were given chemoprophylaxis for latent TB.

Scientific findings

Eligible patients were identified via criteria recorded on a clinical database of HIV patients attending our services. Retrospective review of case notes was used for further data collection from 01/01/2007 until 31/12/2013. In total 109 out of 844 HIV patients attending the Infectious Diseases (ID) and Genitourinary Medicine (GUM) HIV clinics were identified as fulfilling the eligibility criteria for latent TB testing. QuantiFERON®-TB Gold In-Tube (QFT-G) tests were performed in 8/109 (7.4%) of eligible patients. QFT-G was positive on 2 out of 8 (25%) occasions. Treatment for latent TB was offered to both patients but only one accepted and completed treatment.

Discussion

Several studies suggest the treatment of latent TB infection reduces the risk of active TB in HIV positive individuals, especially in those with a positive tuberculin skin test. BHIVA recommendations on screening for latent TB in HIV-infected individuals takes into account factors such as the risk of exposure to TB and the risk of reactivation according to CD4 count and use of ART. Recent data from England, Wales and Northern Ireland confirms that TB incidence in HIV-infected individuals is higher than background HIV-uninfected population rates and that this risk declines with time on ART.

Conclusions

We find that in our cohorts, latent TB screening has not been routine practice with only 7.4% of eligible patients tested. We are currently drafting robust pathways for systematic testing of all eligible patients, as well as follow up and treatment of those with positive results. Our plan is to re-audit following the implementation of new local guidelines.
Highly sensitive C-reactive protein and CD4/CD8 ratio are independently associated with reduced bone mineral density in people living with HIV infection

Rebecca Marlor¹, David Dockrell¹², Benjamin Stone¹²

¹Academic Unit of Immunology and Infectious Diseases, University of Sheffield, UK
²Department of Infection and Tropical Medicine, Sheffield Teaching Hospitals, Sheffield, UK

Introduction

In the post-HAART era, the screening and management of non-AIDS co-morbidities is an increasing focus of HIV outpatient care. These co-morbidities, including reduced bone mineral density (BMD), are more prevalent in HIV-positive individuals compared with age and sex-matched HIV-negative controls. Studies have shown that immune dysfunction (inflammation and coagulation) and reduced CD4/CD8 ratio (CD4:CD8) predicts development of these non-AIDS co-morbidities. Few studies have assessed these measures in relation to BMD. We hypothesised that in a HIV-infected cohort, markers of inflammation (interleukin-6 (IL-6) and highly-sensitive CRP (hsCRP)), coagulopathy (D-dimer) and CD4:CD8 are related to BMD.

Basic demographics and both HIV-independent and HIV-specific risk factors for osteoporosis were collected in HIV-positive patients attending outpatient clinics over an eight month period. Lumbar spine BMD was measured by dual-energy x-ray absorptiometry (DXA). Hospital laboratories measured D-dimer, hsCRP and T-lymphocyte subsets. Chemiluminescent sandwich ELISA quantified IL-6. Multiple-adjusted linear regression analysis evaluated the relationship between variables.

Scientific findings

38 participants were assessed, median (IQR) age 46 (16) years, 63.2% male, 63.2% non-black ethnicity, 92.1% on antiretroviral therapy (ART) and 78.9% with undetectable HIV viral load. The mean (SD) CD4+ count was 610 (230) cells/mm³.

Reduced CD4+ T-lymphocyte count (r=0.463, p=0.003) and reduced CD4:CD8 (r=0.472, p=0.003) was significantly associated with reduced lumbar spine BMD; hsCRP was borderline associated (r=-0.307, p=0.061). IL-6 and D-dimer were not associated with lumbar spine BMD.

In multivariate analysis, reduced lumbar spine BMD was significantly related to increased hsCRP (B=-0.021, p=0.004), reduced CD4:CD8 (B=0.121, p=0.027) and increased time since HIV diagnosis (B=-0.001, p=0.048).

Discussion

Increased hsCRP and reduced CD4:CD8 were related to reduced BMD, independent of both age and CD4+ T-lymphocyte count. Alterations in these markers have been observed in the elderly HIV-negative population and are part of the immunosenescent phenotype. Our findings suggest that immunosenescent-like changes may contribute to the development of reduced BMD in HIV-positive individuals; similar observations have been made in relation to other non-AIDS conditions. HsCRP and CD4:CD8 could be incorporated into screening tools to better predict HIV-positive patients at increased risk of reduced BMD, enabling timely investigations and intervention to prevent future fractures and associated morbidity.

Conclusions

Given the relationships observed between these immunological parameters and lumbar spine BMD, we suggest that optimal treatment of HIV-infection should include recovery of CD4+ T-lymphocyte count and normalisation of CD4:CD8; there may also be some benefit in monitoring hsCRP. Optimisation of these parameters may be protective against reduced BMD and therefore fragility fracture.
parameters could also be used to augment existing screening tools for fragility fracture and reduced BMD for people living with HIV.
HIV Testing in Acute Medicine - missed opportunities.

Elen Vink
NHS Lothian, Edinburgh, UK

Introduction

Approximately a third of HIV patients in the UK are undiagnosed and late diagnosis is implicated in 24% of deaths in HIV patients. The 2008 UK HIV Testing Guidelines recommended considering testing of all medical admissions where the local HIV prevalence exceeds 0.2% as well as detailing specific indicator conditions which should trigger targeted HIV testing.

Our local HIV prevalence is >0.2% however targeted HIV testing is the current method of screening. This audit was devised to investigate the proportion of patients admitted to the Acute Medical Unit (AMU) with an HIV indicator condition, and the rate of HIV testing amongst these patients. An educational session for all grades of medical staff in the AMU was carried out, along with distribution of posters identifying HIV Indicator Conditions in relevant clinical areas. A repeat audit was then carried out to test whether this was an effective intervention to increase HIV testing.

Scientific findings

In both audits patient records and laboratory results were reviewed for all admissions via the AMU in a large teaching hospital over a 7 day period. The presence of an indicator condition was recorded along with evidence of HIV testing.

In the initial audit 26% (65/253) of patients admitted had an HIV indicator condition with chronic lymphopaenia and pneumonia being the most common. In these patients 3% were tested. In the second cycle of the audit 20% (68/348) had an indicator condition with 9% receiving an HIV test. This threefold increase in testing did not reach significance but suggests a trend towards increased testing with medical staff education.

Discussion

Both audits indicate that there are many opportunities to test for HIV and that HIV testing targeted at patients with indicator diseases is currently inadequate in this setting. There was some improvement following teaching suggesting that lack of awareness among medical staff of the indications for testing is at least partly to blame for the lack of testing. Given medical staff rotation and shift patterns, regularly repeated teaching sessions would be required to reach all relevant staff and to have a lasting effect. The teaching session also revealed ongoing anxiety among all grades of doctor towards consenting patients for testing.

A limitation of this audit was that, in those patients with indicator conditions who were not tested for HIV, it was usually not possible to distinguish from the patient record between those where HIV testing was not considered, those where HIV testing was considered, offered and refused, or those where HIV testing was considered but decided against. It has to be presumed that in the vast majority of cases HIV testing was not considered.

Conclusions

This project demonstrated that only a small proportion of patients admitted to an AMU with an indicator condition for HIV testing were actually tested. A one-off teaching session led to a non-statistically significant increase in HIV testing. Strategies to increase the proportion of patients offered an HIV test may include opt-out testing or the concept of 'notional consent' with HIV testing clearly advertised in the department as being a routine part of hospital admission. Both these strategies deserve consideration in this setting.
Managing HIV in Timor-Leste: cohort review and programmatic challenges

Charlotte Hall, Sally Keat, Thomas Locke

1 Bairo Pite Clinic, Dili, Timor-Leste
2 Castle Hill Hospital, Hull & East Yorkshire NHS Trust, UK
3 Charing Cross Hospital, Imperial College Healthcare Trust, London, UK
4 Newham University Hospital, Barts Healthcare Trust, London, UK

Introduction

Timor-Leste (TL) is a small, low-income country 700km north of Australia. 2010 sentinel surveillance findings estimated prevalence of HIV to be 0.68% in the antenatal population, with higher prevalence in individuals with tuberculosis (1.1%) and sexually transmitted infections (2.6%)\(^1\). An IBBS conducted in five districts in 2011 found HIV prevalence of 1.5% in female sex workers and 1.3% in men who have sex with men, with geographical pockets of higher prevalence (up to 3.6%) demonstrated\(^1\).

Bairo Pite Clinic (BPC) is a non-governmental healthcare facility in Dili, TL's capital city, which cares for approximately 50% of the PLHIV in TL currently accessing health services. We undertook case note review of all patients who had been diagnosed at BPC and audited care against national\(^2\) and WHO\(^3\) guidelines with the aims of generating descriptive data on our cohort of patients, facilitating quality improvement, and highlighting challenging areas of care in the Timorese setting.

Scientific findings

113 cases were identified having had a positive HIV test and having been in contact with the BPC HIV programme (50 female, 63 male). 75/113 patients were registered as receiving antiretroviral therapy, 22/113 were known to have died. 4/113 were newly diagnosed and not yet registered, 2 had been transferred out, and 10/113 did not appear to be under any follow up and outcome was unknown. Among patients who died, mean time from diagnosis to death was 15 months.

Mean patient age was 30.9 years (range 2-82 years). Presenting CD4 was low in the 47 patients who had a laboratory CD4 performed at diagnosis with an average of 159 cells/mm\(^3\) (CD4 <50 N=15, CD4 50-100 N=10, CD4 101-200 N=12, CD4 201-350 N=4, CD4 351-500 N=6, CD4 >500 N=1).

The majority of patients were identified via provider initiated testing. Indication for test was TB in 13 cases. Poor documentation of ongoing care and lack of diagnostic facilities made it difficult to ascertain incidence of opportunistic infections.

Provision of prophylaxis with co-trimoxazole was sub-optimal and no patients had received INH prophylaxis, fluconazole prophylaxis or valganciclovir prophylaxis. Hepatitis B co-infection was noted in 6/60 of those tested and VDRL was positive in 3/57 tested. Other monitoring tests were rarely performed and while all patients were receiving a WHO recommended regime it was not possible to assess for biochemical contraindications in the majority of cases. Evidence of current clinical or immunological failure were noted in 14% of those currently taking ART.

Discussion

Several factors render TL vulnerable to a rapidly increasing incidence of HIV. These include high levels of population movement and socioeconomic displacement, low incidence of condom use, low level of awareness of STIs and HIV, poor access to HIV and STI screening, and presence of risk behaviours within at-risk groups\(^4\). Despite the fact that >400 individuals have tested positive for HIV in TL, fewer than half this number are currently receiving antiretroviral therapy (ART). It is unknown what proportion of those not accessing care have died vs defaulted.
This audit demonstrates low CD4 counts among those newly diagnosed; this is a cause for concern on a population level given the combination of prolonged viraemia with high incidence of risk behaviours and high fertility rate. Contact tracing and six-week PCR for HIV-exposed infants are performed sporadically. On an individual level, high peri-diagnosis mortality can be expected in a low-income setting with limited capacity to diagnose or treat complex opportunistic infections. Co-infection with hepatitis B and/or TB is common but there is no TB culture facility in country, limited microbiology services and the only test available for hepatitis B is HBsAg.

The number of patients with evidence of clinical or immunological failure is a concern. Until August 2014 no viral load monitoring was available within TL and demonstration of virological failure has not been possible. Given the limited second line regime options available in country, partnership with an overseas institution able to provide resistance testing may be beneficial.

Conclusions

PLHIV in Timor-Leste present at an advanced stage and have frequent co-infection with hepatitis B and/or TB. Facilities to diagnose and treat opportunistic infections are limited, as is access to physicians trained in managing HIV. Treatment failure is a concern; the respective roles of non-adherence and viral resistance in the aetiology of treatment failure in our cohort are not clear, but countrywide a large number of people who have a positive HIV test do not appear to be accessing treatment. TL is at risk of a rapidly increasing incidence of HIV given the factors discussed.
Audit of patients that are inappropriately labelled 'High Risk' with regards to blood borne viruses

Brendan Healy¹, Amber Bryce²
¹Public Health Wales, Cardiff, UK
²Biochemistry Department, UHW, Cardiff, UK

Introduction

Blood borne viruses (BBVs) are transmitted by entry of blood or other bodily fluids containing viruses into the body of a susceptible person. Routes of transmission include skin puncture by blood-contaminated sharp objects. Occupational exposure to BBVs poses a risk to laboratory workers through percutaneous or mucocutaneous transmission [1].

High risk (HR) specimens in UHW should be labelled with a HR yellow sticker in accordance with laboratory standard operating procedures (SOPs) [2]. However there are problems associated with this including; inappropriate labelling whereby samples from patients with BBVs are not labelled with a HR yellow sticker or inappropriate labelling of samples as HR which are not truly HR.

This audit was set up to investigate how many patients are inappropriately labelled HR with regards to BBVs.

Scientific findings

There were 7882 "high risk" entries on the biochemistry database. All duplicate, GUM related and Z numbers were excluded. From the remaining 1235 entries a random selection of 200 patients were chosen for inclusion in the audit. The patients' electronic records were reviewed for evidence of infection with BBVs.

Of 200 patients reviewed, 65% had evidence of BBV infection (truly HR) and 35% had no evidence of BBV infection (potentially inappropriately labelled as HR). 79% of the potentially inappropriately labelled patients had no clear reason as to why their samples had been labelled HR. 72% of these patients had BBV tests carried out, 5% of these as part of a pregnancy screen. It is possible that these specimens were labelled high risk because a BBV screen was being carried out. One patient (2%) was a paed oncology patient. 26% of patients had no clear reason for being labelled HR and had never had a BBV screen carried out. For 17% of patients potentially inappropriately labelled as HR there were possible reasons for mislabelling. These included being positive for MRSA (17%), VDRL (4%), VRE (4%), GAS (4%) having evidence of past Hep B/C (17%), and having a false positive hep C Ab test (4%). The remaining 4% of individuals had no record of any microbiology or virology specimens being sent. Of those that were truly HR, 37% had Hep C, 32% had HIV, 27% had Hep B infection with the remaining 4% having a combination of BBVs.

Discussion

Results show patients are inappropriately identified as high risk. As a consequence of this mislabelling the results from these patients' specimens could be inappropriately delayed during laboratory processing, with possible consequences on patient care.

This audit does not identify how many specimens that aren't labelled as high risk are taken from patients with BBVs and pose a risk of transmission. This is a potential area for further study.

The process for labelling patients as high risk in UHW is unreliable and results in patients being inappropriately labelled as high risk. We recommend that the process for identifying patients as HR is reviewed. We recommend that all specimens are handled as potentially high risk and sensible handling of all specimens is undertaken to prevent a risk of transmission of BBVs. If all specimens were handled
as high risk it would no longer be necessary to label specimens as high risk. This would remove the problem of specimens being inappropriately labelled (as high risk when they shouldn't be and not as high risk when they should).

**Conclusions**

All specimens received in laboratories should be handled with sensible universal precautions that reduces the risk of transmission of infection to a minimum. The process of labelling patients as potentially high risk (which is unreliable) could then be abandoned.
Audit of Junior Doctors understanding of labelling of ‘High Risk’ samples

Brendan Healy1,2, Michelle Noble1, Owen Seddon1,2, Gwennan Jones1,2, Thom Phillips2
1Public Health Wales, Cardiff, UK
2University Hospital of Wales, Cardiff, UK

Introduction

High risk infectious substances are those that are known to or expected to contain high risk pathogens. The Health and Safety at Work Act specifies that the knowledge of known or suspected hazards is passed onto those who need to handle samples. Clinicians submitting samples have a Duty of Care to ensure that any potential risk of infection is communicated to those processing the specimen. In UHW, a ‘High Risk’ or yellow sticker is applied to identify high risk samples. There are a number of problems with this system including a lack of knowledge on what constitutes a high risk sample amongst junior medical staff. This audit investigates the knowledge of junior doctors in UHW Cardiff on the type of samples that should be labelled as High Risk.

Scientific findings

A questionnaire (see figure 1) was sent out to Junior Doctors at the University Hospital of Wales Cardiff asking which samples from a list they would label as being High Risk and which ones they would not.

39 questionnaires from junior doctors working in UHW were collected. Questionnaires were collected from F1, F2 and ST Doctors. All these doctors have responsibility for completing blood forms on the ward. The majority of responses were from F1 and F2 doctors which is appropriate as these are the doctors that most commonly complete the blood forms for ward patients. The results from the questionnaire demonstrate that there is a poor understanding among junior doctors about which samples should be labelled as high risk. As a result samples sent to the laboratory are highly likely to be inappropriately labelled as high risk when they are not and conversely not labelled as high risk when they are. For example samples from patients with MRSA would be incorrectly labelled as high risk by 28% of doctors. Conversely viral haemorrhagic fever would only be labelled as high risk by just over 50% of doctors and HIV by only 87%. This has significant implications for the way samples are currently handled within the laboratory.

Discussion

There is a poor understanding among junior doctors about which samples should be labelled as High Risk resulting in samples being inappropriately labelled as high risk when they are not and not being labelled as high risk when they are. In addition many patients with high risk infections are undiagnosed and samples from these patients will be received in the laboratory without a high risk flag. As a result triaging of samples based on this system is unreliable. All samples should be handled as potentially high risk and the current system of labelling abandoned.

Conclusions

Triaging of samples based on the high risk labelling system currently employed in UHW is unreliable. All samples should be handled as potentially high risk and the current system of labelling abandoned.
The application of guidance regarding the confidentiality of HIV positive patient information by General Practices in Wales

Brendan Healy¹, Stephanie Vincent², Claire Maciver², Anna Jones²

¹Public Health Wales, Cardiff, UK
²Cardiff University, UK

Introduction

An audit of GP practices in the Cardiff area was carried out. The aims of the audit were as follows:

1. To assess how HIV status information is currently stewarded by General Practices within Wales.
2. To compare this current practice to the available guidelines on confidentiality.
3. To identify the areas in which General Practice are performing well in relation to confidentiality guidance.
4. To identify the areas in which GP practices need improvement.
5. To propose suggestions for future work in this area.

Scientific findings

A questionnaire was created to assess adherence to the General Medical Council guidelines 'General Medical Council: Confidentiality: guidelines for doctors (2009). 3 sections of the guidelines were included in our audit (see below). As it is a national guidance required of all practicing doctors, an audit compliance rate of 100% is expected. The questionnaire was e-mailed to every GP in Wales (489 in total). The data collection period was 24/01/12-29/02/12.

Of the 134 practices included in data analysis, 80.6% of practices had HIV positive patients on their register.

Protecting confidential information

Phlebotomists (73%) and receptionists (85%) were least likely to have access to patients HIV status. Restriction of access to HIV status was limited in most practices. Whilst most (97%) practices had separate log-ins for each staff member, there was high percentage of practices where log-ins were shared.

23.9% of GP practices took additional measures specifically for HIV positive patients including:

- Restricting access to patient information (8 practices)
- Virtual data cloaking mechanisms (e.g. use of an '0' code for hiding sensitive information) (17 practices)
- Staff HIV specific training (2 practices)

Patients were made aware that information may be shared between staff members in 53% of the General Practices.

Limitations of the audit

- Self reported questionnaire- relies on honest and accurate reporting.
- Tick box nature of response options- limiting, may not encompass all possible situations.
- Sample not randomly selective- self selected by responding to questionnaire.

Discussion

The majority of GP practices have measures in place to protect patients' confidentiality.
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There is considerable variation from practice to practice, with some practices performing very well. However, there is considerable room for improvement for the majority of practices.

**Recommendations**

- Feedback of audit results: circulation of a written report and presentation at GP regional meetings.
- Development of a national guideline to reflect the GMC Duty of Care.
- Implementation of simple measures to ensure confidentiality is maintained: secure storage of records, automatic time-out from electronic record systems etc.
- Repeat audit once above measures have been carried out.

**Conclusions**

The majority of GP practices have measures in place to protect patients' confidentiality.

There is considerable variation from practice to practice, with some practices performing very well. However, there is considerable room for improvement for the majority of practices.
Late diagnoses in HIV - review of cases in a London HIV centre. Are lessons being learnt?

Charles Williams, Alison Barbour, Catherine Cosgrove
St George's Hospital, London, UK

Introduction

It is estimated that around 100,000 people are living with HIV in the UK, of whom 77,610 are diagnosed. A late diagnosis, defined as CD4 <350 cells/ml, is the most important predictor of morbidity and one-year mortality. Although there has been a proportional decline in late diagnosis in recent years, 47% of UK 2012 diagnoses were late stage. The UK National Guidelines for HIV Testing recommend HIV testing for 'clinical indicator conditions', where HIV enters the differential diagnosis, and consideration of testing for general medical admissions and general practice registrants in areas with a seroprevalence exceeding 2 per 1000. Before publication of the guidelines it was shown patients were accessing medical care, but clinicians were missing HIV testing opportunities. Unfortunately a recent systematic review has shown guideline adherence is poor outside of genitourinary and antenatal clinics.

Scientific findings

A database of all HIV positive patients at St George's Hospital, London was interrogated to identify patients diagnosed with CD4 <350 cells/ml in 2012. The electronic patient record and case notes were reviewed to identify patients who were admitted to the hospital, or attended outpatient clinics in the 5 years preceding diagnosis. General practitioners were contacted by letter requesting information regarding presentations to primary care or other hospitals over the same period. Our aim was to characterise so-called 'late presenters' and to identify missed testing opportunities, as recommended by national guidelines.

Demographics: Male 74% Black ethnicity 62%. Mean CD4 count was 157.

Of the 42 patients identified, diagnosis was as follows: 26% GUM clinics, 26% inpatients, 24% outpatient clinics and 19% primary care. 12% had been admitted to hospital during the 12 months preceding diagnosis and 26% were seen in outpatient clinics. Of the admissions, 40% had HIV indicator conditions. Of the outpatients, 38% had indicator conditions. 26% had accessed hospital medical care between 1 and 5 years pre-diagnosis, and in 18% of these cases testing opportunities were missed. For 57% cases, GPs responded to the request for information. Where information was available, there was no record of GP attendance in 42%. Of those who had attended primary care, 1 patient (4.7%) was diagnosed at registration; whilst 36% of patients had indicator conditions and were not offered an HIV test.

Discussion

This retrospective study performed in a tertiary centre with a large HIV cohort continues to demonstrate missed diagnosis opportunities in primary and secondary care despite changed national guidance.

12% of patients with late diagnosis had hospital admission over the preceding year and 26% were seen in outpatients, with similar indicator condition proportions in each. Screening all inpatients for HIV is not cost-effective, but improved guideline awareness and increased offer rate for medical admissions in high prevalence areas is recommended. Clinicians are increasingly proactive in testing patients with the benefits conferred by earlier diagnosis and HIV is being more readily thought of in the differential diagnosis.

As expected, more patients had attended their GP than secondary care, although similar proportions of indicator conditions were missed in both settings. Whilst knowledge of HIV indicator conditions is improving, we continue to diagnose patients late.
In a district general hospital with high prevalence, routine HIV testing was introduced for medical admissions. They showed patients diagnosed through routine screening had significantly higher CD4 counts than targeted testing.

The limitations include reliance on accurate documentation and GP data supply. GP response rate was lower than was hoped, potentially limiting the ability to generalise findings and there may be self-selection bias in those who chose to respond who may represent a more motivated group. If this is the case it is likely that the rate of adherence to the guidelines is likely to be lower than reported.

Conclusions

Adherence to HIV testing guidelines remains suboptimal. Nonetheless, a substantial number of people diagnosed late are seeking medical care without indicator conditions, supporting routine screening as a more effective way to prevent late diagnosis. 42% of patients do not appear to have sought medical care at all prior to diagnosis and initiatives to expand testing such as home testing and community testing are needed. Robust systems will be required to ensure that those diagnosed outside conventional settings are efficiently able to access good quality, integrated care so as to minimise those undiagnosed and subsequent transmissions, morbidity and mortality.
A diagnostic dilemma: HIV ‘elite controller’

Sook Fong Sharon Koo, Nelun Perera, Julian Tang
University Hospital of Leicester NHS Trust, UK

Introduction

The Human Immunodeficiency Virus (HIV) is a lentivirus that belongs to the family of Retroviridae. It causes progressive failure of the immune system leading to acquired immunodeficiency syndrome (AIDS). Patients with AIDS are at risk of opportunistic infections and cancers. Since its discovery in the early 1980s, a small number of patients infected with the virus were found to be able to maintain low levels of plasma HIV RNA with stable CD4 counts in the absence of antiretroviral medication. This group of patients are known to be elite controllers. Here we present a case of an ‘elite controller’ and the challenges encountered during its diagnosis.

Scientific findings

A 30 year old female of UK-born Asian heritage presented to the Genitourinary Medicine (GUM) clinic for screening as part of a sexual contact tracing of a Chlamydia case. She suffers from depression but is otherwise fit and well. She was not forthcoming in her sexual history but did disclose that she has had 2 male sexual partners in the last 5 years, one of which was of Ghanian descent who was not traceable for sexual screening. She was asymptomatic at presentation. Her first serology for HIV 1 and 2 Ab/Ag was found to be positive with 2 assays (Advia Centaur and Siemens Integral II) and this was confirmed on another sample sent 1 week later. Further confirmatory assay using the Western blot showed positive bands to gp120, gp41, p31, p24 consistent with HIV1 antibodies. HIV RNA viral load was undetectable (< 40 copies/mL) on the initial sample and on 2 further samples (11 days and 21 days from initial sample). HIV avidity was low at 0.109 suggesting a recently acquired infection. All her blood markers including total lymphocyte counts were normal. CD4 count was 700. A serum sample was submitted to the reference laboratory for confirmation. The presence of HIV 1 and 2 antibodies were confirmed using the IgG-capture particle-adherence test (GACPAT) and ImmunoComb Ab/Ag assay. Western Blot was positive for HIV1 antibodies (p17, p24, p31, p51, p66, gp120, gp160). HIV-1 proviral DNA was negative. Repeat HIV RNA viral at 5 months load remains at < 40 copies/mL.

Discussion

HIV infected individuals including elite controllers are being identified more frequently nowadays due to expanded HIV screening programmes all over the world. The true definition of an elite controller is someone having "persistently undetectable plasma HIV RNA for 15-20 years, with stable CD4 counts, without therapy". These patients need to be distinguished from the long-term non-progressors (LTNP) who may show variable but low plasma viraemia. Unknown host immune factors are thought to be responsible for controlling and preventing the progression the infection in these patients.

The natural course of an acute HIV infection is characterised by flu-like symptoms, rapid decrease of CD4+ T cells, and high viral loads (acute phase of infection) typically lasting for 2-6 weeks. This is followed by stabilization of the number of CD4+ T cells and viral load (chronic phase of infection) over a number of years. It was surprising to find undetectable HIV viral load in this patient given the fact that this was an early HIV infection. Further testing including negative HIV proviral DNA, CD4 counts and repeated HIV viral loads suggested that this patient might be an elite controller, even though we only have results over a 5 month period.

Conclusions

Serial testing of HIV viral load and CD4 count is the key to the diagnosis of an elite controller. Our patient does not strictly fit the time period criteria as yet but all tests so far are suggesting this. In the meantime,
a new diagnostic classification would be useful for this group of patients who are in the early stage of the infection.
Evaluation of the QIAGEN Artus QS-RGQ assay for HIV-1 RNA quantitation

Paul Grant¹, Stuart Kirk¹, Eleni Nastouli¹, Jeremy Garson², Gavin Wall³, Shelley Wilson¹, Mike Kidd¹

¹UCLH, London, UK  
²UCL, London, UK  
³Qiagen, Hilden, Germany

Introduction

The QIAGEN Artus HIV-1 QS RGQ kit was evaluated and results compared with an in-house developed assay. The Artus assay uses the QIAsymphony instrument for purification of HIV-1 RNA from 1 ml patient plasma samples, and an automated reverse transcriptase PCR (RT-PCR) assay set up. The real time RT-PCR is run on the Rotor-Gene Q thermal cycler.

The evaluation was carried out using International standards and panels. In addition 400 patient samples were compared to the in-house HIV1 real time RT-PCR assay developed at UCLH.

Scientific findings

The analytical sensitivity was determined by testing dilutions of the WHO 3rd International standard for HIV-1 RNA (10/152). Probit analysis showed the 95% level of sensitivity of 60.5 IU/ml which equates to 27 copies/ml. The accuracy of quantification of the International Standard was good with an average IU/ml slightly higher by 0.06 log10 IU/ml.

The Linearity of the assay was assessed by testing a high positive sample from 10⁷ to 10 copies/ml in triplicate. An R² value of 0.96 was obtained.

The analytical specificity of the assay was tested using the 2nd WHO International Reference Panel Preparation for HIV-1 Subtypes for NAT (12/224). All HIV1 group M subtypes were detected with equal efficiency.

Assay precision was tested by diluting a sample to approximately 100,000 and 1000 copies/ml. At the high viral load, the inter assay precision was 0.15 log₁₀ copies/ml (1.41 fold change). At the Low viral load, the inter assay precision was 0.78 log₁₀ copies/ml (6.09 fold change).

400 clinical specimens were tested using the Artus HIV1 viral load assay and the results compared with an in house assay developed and in clinical use at UCLH. Approximately 200 HIV1 positive samples were collected and stored at -80°C before testing using the Artus assay. Another 200 samples were tested concurrently with the in house assay. Linear regression was performed with an R² value of 0.856.

The average difference was 0.198 log₁₀ copies/ml, however Bland Altman analysis showed 6 samples that were under quantified compared to the in house assay.

Discussion

The sensitivity of the Artus assay exceeded the manufacturers' claim and was found to be at a similar level to other commercial assays. The quantitation of samples was in agreement with the International Standard for HIV1 RNA. The assay showed good linearity across a wide range of HIV-1 RNA titres with good inter assay precision at both high and low viral loads.

A wide range of HIV1 group M subtypes including common recombinants were tested using the International reference panel, and good quantification was achieved for the whole panel.
When 400 clinical specimens were tested and compared to an in house real time RT PCR assay, apart from 6 samples, good correlation was found between the two assays with the Artus assay giving just slightly higher viral load results than the inhouse assay.

**Conclusions**

There was good correlation between the assays and the Artus assay showed good sensitivity, specificity, accuracy and precision. The Artus assay is suitable for clinical use.