CASE REPORT

Hepatitis A infections in men who have sex with men using HIV PrEP in Paris

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SUMMARY

The current hepatitis A outbreak in Europe is largely involving men having sex with multiple male partners. The objective of the present report was to warn teams dealing against the persistent risk of viral and bacterial sexually transmitted infection (STIs) in patients receiving HIV pre-exposure prophylaxis (PrEP). We have notified and investigated three cases of acute hepatitis A virus (HAV) infection in people receiving HIV PrEP in our clinic between December 2016 and March 2017. The patients were not epidemiologically related, had no recent travel history to HAV endemic areas, reported multiple STIs during this period and had not been vaccinated against HAV. They were all identified as genotype A, strain VRD_521_2016 virus.

Large-scale vaccination against viral hepatitis is recommended in men having sex with men, especially in those using PrEP, as PrEP is used by people who have high-risk sexual behaviour.

BACKGROUND

Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for HIV pre-exposure prophylaxis (PrEP) has proven efficacy in reducing HIV incidence in men having sex with men (MSM) and has been approved for this indication in France from January 2016. Since then, other sexually transmitted infections (STIs) in patients receiving PrEP have been regularly screened for and, where possible, prevented by vaccination. Despite hepatitis A virus (HAV) serology being included in the baseline check-up and vaccination recommended for all non-immune participants in the PrEP programme, three acute hepatitis A infections occurred in our cohort between December 2016 and March 2017.

CASE PRESENTATION

We report three consecutive cases of sexually acquired acute HAV in MSM using PrEP. The three patients presented with symptomatic acute HAV infection between December 2016 and March 2017, without any recent travel history to HAV endemic areas. All three were also diagnosed with multiple STIs during this period, suggesting a low use of condoms and a likely sexual transmission of HAV. In addition, none of them was vaccinated against HAV (table 1).

The first patient was a 28-year-old HIV-negative man who started PrEP in September 2016 and had multiple unprotected anal intercourses,

mainly in gay clubs. He had not travel to HAV endemic areas since August 2016. He had recently been treated for syphilis and had a history of hepatitis B, gonococcal and chlamydial infections. He travelled to Berlin, Germany, from 3 November to 5 November 2016, where he had multiple unprotected oral and sexual intercourses. He developed a flu-like syndrome on 30 November, followed by pruritic jaundice, for which he was hospitalised on 7 December. Liver tests were elevated more than 40-fold above the normal range (serum aminotransferase (ALAT): 1749 IU/L, normal <41, aspartate amino transferase: 454 IU/L, normal <50) with icteric cholestasis (serum bilirubin: 195 µmol/L, normal <17, conjugated bilirubin: 178 µmol/L) with a normal prothrombin time.

The second case was a 29-year-old HIV-negative man, in a stable relationship with a virologically suppressed HIV-positive partner who had been taking PrEP since March 2016 for extra-marital unprotected sexual intercourses. He met his partners through dating apps. He had a history of treatment for anal warts and recent anal chlamydial carriage. On 15 December, he felt feverish with nausea and clinical urethritis. One week later, tests detected urogenital gonococcal infection and a high ALAT level (937 IU/L, n<41). PrEP was discontinued. Twelve days later, he complained of generalised pruritus. He had not travelled abroad recently. On further questioning, he reported to have licked the anus of a casual partner in November 26, who developed hepatitis A in early December.

The third patient was a 21-year-old HIV-negative MSM, on PrEP since September 2016, with multiple unprotected sexual intercourse in a context of drug and alcohol abuse. His medical history was remarkable for multiple STIs in 2016: anal warts, syphilis, anorectal gonococcal infection, lymphogranuloma venereum, two episodes of gonococcal urethritis and oral gonococcal carriage. He had vaccine-induced immunity against hepatitis B. He was admitted to the intensive care unit on 7 March 2017 for vomiting with jaundice due to acute hepatitis: ALAT: 4201 IU/L (n<41), serum bilirubin: 135 µmol/L (n<17) and conjugated bilirubin: 119 µmol/L. He had a normal prothrombin time.

INVESTIGATIONS

All three cases had significant levels of HAV IgM (Architect HAVA-IgM Technique CMIA, Abbott,

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Table 1 Patient's characteristics

	Patient 1	Patient 2	Patient 3
Previous vaccination against hepatitis A	No	No	No
Previous STIs	Hepatitis B, gonococcal urethritis, chlamydial anorectitis, syphilis	Warts, genital chlamydia	Pharyngeal, genital and anorectal gonococchia, anorectal L2 chlamydia, syphilis, anal warts
STI concomitant of HAV infection	Pharyngeal gonococcal carriage	Gonococcal urethritis	Genital gonococcal carriage
PrEP start	21 September 2016	7 March 2016	20 September 2016
Hepatitis A infection	7 December 2016	22 December 2016	7 March 2017
Travel during VHA incubation period	Berlin: 3–5 November (European gay meeting)	No	No
Drug abuse (chem sex)	Yes	Yes	Yes
Intravenous drug use	No	No	No

HAV, hepatitis A virus; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infections.

index 5.30, threshold 1.2 ; Diasorin LIAISON Assay, index > 10, threshold 1.1; Architect HAVA-IgM Technique CMIA, Abbott, index 7.85, threshold 1.2 , respectively) and positive HAV IgG, whereas HIV and HCV PCR testing were negative. They all had protective levels of antibodies against hepatitis B surface antigen.

All three cases were identified as genotype 1A, strain VRD_521_2016, first reported in the UK in December 2016 and likely imported from Spain several times.¹²

OUTCOME AND FOLLOW-UP

The three patients fully recovered and resumed PrEP after an average of 1-month interruption.

DISCUSSION

Although hepatitis A is most commonly acquired via the faecal–oral route in endemic countries, male-to-male sexual transmission is well described^{3–5} and has led to a multicountry outbreak in Western Europe,^{1 6 7} prompting the European Centre For Disease Prevention and Control to issue a rapid risk assessment in December 2016.² It is likely that our first patient was infected in Berlin during the beginning of the outbreak.⁷ This proves how well connected the MSM sexual networks are and how fast STIs spread through Europe. PrEP-receiving MSM engage in high-risk sexual behaviour more frequently than do MSM that do not receive PrEP.⁸ To our knowledge, this is the first case series of HAV infections reported in a PrEP clinic, reminding us of the persistent risk of viral and bacterial STIs in people using TDF/FTC PrEP for HIV prevention. In France, HAV vaccination is recommended in MSM, but not reimbursed, contrary to PrEP. Data recorded during 2016 in our clinic showed that 47% of the MSM seen in PrEP had no or undocumented HAV IgG at baseline. HAV vaccination was later recorded for 81% of them. During our observation period (1 November 2016 and 1 August 2017), 1142 MSM were seen in PrEP. Imputing the rates from the previous year, we tot up about 102 vulnerable men. During that period, three additional cases of acute hepatitis A were diagnosed in our cohort, resulting in an attack rate of 5.9% among susceptible PrEP users. Furthermore, we faced recurrent shortages in hepatitis A vaccine in France since 2015 that may have lowered the general vaccination coverage in high-risk MSM.

Learning points

- ▶ Hepatitis A virus (HAV) infection can be sexually transmitted, mostly through oral–anal sex but also through hand carriage, which makes condom use imperfectly protective.
- ▶ HIV pre-exposure prophylaxis is an opportunity to extend HAV and hepatitis B virus vaccination coverage in men having sex with men (MSM) with high-risk sexual behaviour.
- ▶ On a broader level, sexually transmitted infection prevention should be reinforced in MSM, through vaccination when available and through safer sex practice in general.

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Competing interests None declared.

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