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# Identification of Internationally Disseminated Ceftriaxone-Resistant Neisseria gonorrhoeae Strain FC428, China

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DOI: https://doi.org/10.3201/eid2507.190172

In 2016, we identified a ceftriaxone-resistant *Neisseria gon-orrhoeae* isolate in China. The strain genotype was identical to the resistant clone FC428 that originated in Japan. Enhanced international collaborative surveillance programs are crucial to track the transmission of the ceftriaxone-resistant clones.

Ceftriaxone has been used to treat gonorrhea in China and most other countries for >1 decade, but the level of decreased susceptibility or clinical resistance to ceftriaxone has increased (1). Moreover, the international spread of ceftriaxone-resistant clones has been recognized as a threat to effective control of gonorrhea (2). We describe an imported ceftriaxone-resistant N. gonorrhoeae strain isolated in China in 2016.

The patient was a heterosexual man in his late twenties. He reported unprotected 1-night heterosexual sex in Beijing in July 2016. Urethral discharge with dysuria occurred 3 days after the sexual activity. He was prescribed oral cephalosporin when he visited a private clinic in July. Because the urethral discharge did not resolve, he visited the sexually transmitted diseases clinic in Beijing Ditan Hospital (Beijing, China) in August.

Laboratory analysis of a urethral swab sample found gram-negative diplococci within leukocytes. Culture and nucleic acid amplification test were positive for *N. gonor-rhoeae*. Screening for other sexually transmitted infections by nucleic acid amplification test was negative for *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and *Mycoplasma hominis*.

The patient was treated with a 1-g intravenous dose of ceftriaxone once per day for 3 days. His symptoms improved after 3 days, and a test-of-cure by culture showed

Table. Antimicrobial susceptibility and molecular characteristics of ceftriaxone-resistant Neisseria gonorrhoeae, China\*

		Country	Sexual contact	MIC, mg/L									NG-		NG-
Strains	Year	(reference)	history	TET	SPT	CRO	CIP	AZI	CEF	MLST	porB	tbpB	MAST	penA	STAR
Japan-	2015	Japan (6)	NA	0.5	8	0.5	>32	0.25	1	1903	1053	21	3435	60	233
FC428															
Japan-	2015	Japan (6)	NA	0.5	8	0.5	>32	0.25	1	1903	1053	21	3435	60	233
FC460															
China-	2016	China (this	China	4	16	0.5	>32	0.25	1	1903	1053	21	3435	60	233
BJ16148	Aug	study)													
Denmark-	2017	Denmark	Denmark, China,	NA	8	0.5	>32	0.5	1	1903	1053	33	1614	60	233
GK124	Jan	(7)	Australia												
Canada-	2017	Canada	China, Thailand	4	16	1	>32	0.5	2	1903	1053	33	1614	60	233
47707	Jan	(8)													
Australia-	2017	Australia	Cambodia,	2	8	0.5	>32	0.25	NA	1903	1053	33	1614	60	233
A7846	Apr	(9)	Philippines												
Australia-	2017	Australia	China	4	8	0.5	>32	0.25	NA	1903	9300	21	15925	60	233
A7536	Aua	(9)													

\*AZI, azithromycin; CEF, cefixime; CIP, ciprofloxacin; CRO, ceftriaxone; MLST, multilocus sequence typing; NA, not available; NG-MAST, *N. gonorrhoeae* multiantigen sequence typing; NG-STAR, *N. gonorrhoeae* sequence typing for antimicrobial resistance; SPT, spectinomycin; TET, tetracycline.

the treatment was successful. A telephone follow-up after 1 month indicated a lack of urethral discharge, and the patient provided information that his female sexual partner worked in a nightclub and had sexual contact with men from foreign countries.

The bacterial isolate was transferred to the reference laboratory at the National Center for Sexually Transmitted Disease Control, Chinese Center for Disease Control and Prevention (Nanjing, China). Gram staining and a carbohydrate utilization test confirmed *N. gonorrhoeae*. We confirmed antimicrobial susceptibilities to ceftriaxone, cefixime, spectinomycin, azithromycin, ciprofloxacin, and tetracycline for this isolate by using the agar dilution method. The strain was resistant to ceftriaxone (MIC 0.5 mg/L), cefixime (MIC 1 mg/L), tetracycline (4 mg/L), and ciprofloxacin (>32 mg/L) and susceptible to azithromycin (MIC 0.25 mg/L) and spectinomycin (MIC 16 mg/L) in accordance with the European Committee on Antimicrobial Susceptibility Testing protocol (http://www.eucast.org/clinical breakpoints).

We performed *N. gonorrhoeae* multiantigen sequence typing (NG-MAST) (3) and multilocus sequence typing (MLST) (4) to identify the sequence types (STs). The MLST type was ST1903, and the NG-MAST type was ST3435. We used *N. gonorrhoeae* sequence typing for antimicrobial resistance (NG-STAR) (5) to identify the characteristics of resistance determinants. The NG-STAR type was ST233, which contains a type 60 mosaic *penA* allele (*penA* 60.001), -35A Del in the *mtrR* promoter (*mtrR*1), G120K-A121D in PorB (PorB8), L421P in PonA (PonA1), S91F-D95A in GyrA (GyrA7), S87R in ParC (ParC3), and wild-type 23srRNA (23 srRNA0).

The genotype (MLST1903/NG-MAST3435/NG-STAR233) of this isolate was identical to the 2 ceftriax-one-resistant *N. gonorrhoeae* (FC428 and FC460) isolated in 2015 in Japan (*6*) and similar to other resistant strains isolated in 2017 in Denmark (*7*), Canada (*8*), and Australia (*9*) (Table). Type 60 mosaic PenA (*penA* 60.001), which

contained A311V and T483S alterations, was the key ceftriaxone resistance mutation and typical of this internationally disseminated resistant clone.

The timeline and epidemiologic data of all previous reports of the infections suggest this clone originated in Japan in 2015 and was disseminated to China, Denmark, Canada, and Australia afterward. Moreover, this resistant clone may have a fitness advantage over previously reported "superbug" H041 and has successfully spread worldwide (9). Accordingly, enhancing international collaborative surveillance on the ceftriaxone-resistant clone is crucial.

In conclusion, we identified a ceftriaxone-resistant N. gonorrhoeae strain that has sustainably transmitted in several countries for  $\approx 3$  years. These findings indicate an imported risk and a further transmission of resistant clones in China and demonstrate the need for enhanced local and global gonococcal antimicrobial surveillance to track the emergence and dissemination of resistant strains for timely control of spread (10).

## **Acknowledgments**

We are grateful to Beijing Ditan Hospital, a member of China's Gonococcal Resistance Surveillance Program, for providing the isolate and making the study possible. We thank William Shafer for his valuable comments.

This study was supported by a grant from the Chinese Academy of Medical Sciences Initiative for Innovative Medicine (2016-I2M-3-021) and the Jiangsu Natural Science Foundation (BK20171133).

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# Disseminated Metacestode Versteria Species Infection in Woman, Pennsylvania, USA<sup>1</sup>

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DOI: https://doi.org/10.3201/eid2507.190223

A patient in Pennsylvania, USA, with common variable immunodeficiency sought care for fever, cough, and abdominal pain. Imaging revealed lesions involving multiple organs. Liver resection demonstrated necrotizing granulomas, recognizable tegument, and calcareous corpuscles indicative of an invasive cestode infection. Sequencing revealed 98% identity to a *Versteria* species of cestode found in mink.

In July 2017, a 68-year-old woman in Pennsylvania, USA, sought care for fever, fatigue, cough, and abdominal pain. Her medical history was significant for common variable immunodeficiency and splenic B cell lymphoma that had been treated with R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone); treatment was completed in December 2016.

Imaging showed extensive nodular disease of the lungs and liver and a hepatic abscess. Examination of a fine-needle aspirate of the hepatic lesion detected hepatocytes with focal atypia on a background of marked acute inflammation and necrosis, suggestive of an active infectious process. Subsequent percutaneous needle biopsy samples of the liver, bronchoalveolar lavage and transbronchial biopsy samples, and surgical biopsy samples of the left lower lobe showed necrotizing granulomas and reactive/reparative tissue changes. All histochemically stained slides (Gomorimethenamine silver, Gram, periodic acid Schiff, Warthin-Starry, Ziehl-Neelsen, Fite) yielded negative results for microorganisms. Results of broad-range PCR for bacteria

<sup>&</sup>lt;sup>1</sup>This manuscript was originally presented at the Infectious Disease Society of America IDWeek 2018; October 3–7, 2018; San Francisco, CA, USA.