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Case report

Escherichia coli ST1193 O75 H5: A rare cause of native valve endocarditis with multifocal emboli to brain and spleen

Diana M. Villanueva [a], John R. Lonks [a], Sara Geffert [a,b,c], Sophia Panaccione [a], Jerome Larkin [a], Swapna Charla [b], Jennifer Li [b], Tao Hong [b,c,*]

[a] *Division of Infectious Diseases, The Warren Alpert Medical School of Brown University, Providence, RI 02903, USA*
[b] *Microbiology Laboratory, Department of Pathology and Laboratory Medicine, Rhode Island Hospital, Providence, RI 02903, USA*
[c] *Department of Pathology and Laboratory Medicine, The Warren Alpert Medical School of Brown University, Providence, RI 02903, USA*

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ABSTRACT

Escherichia coli (E. coli) is a facultative anaerobic gram-negative rod bacterium, which can acquire pathogenicity through the acquisition of additional genetic material. We present a case of *E. coli* ST1193, an emerging global multidrug-resistant (MDR) high-risk clone, causing native valve endocarditis and septic brain and splenic emboli in a 67-year-old woman.

Introduction

E. coli is a facultative anaerobic gram-negative rod bacterium found in the flora of the human gastrointestinal tract; however, certain *E. coli* strains can be pathogenic causing diseases such as gastroenteritis, urinary tract infection, abdominal and pelvic infection, pneumonia, bacteremia, and less frequently, meningitis. These pathogenic strains are characterized by possessing additional genetic material, acquired through plasmids, bacteriophages, transposons and/or pathogenicity islands [1]. We present a rare case of *E. coli ST1193*, an emerging global multidrug-resistant (MDR) high-risk clone, causing native valve endocarditis and septic emboli to the brain and spleen.

Case presentation

A 67-year-old female with type II diabetes mellitus, stage III chronic kidney disease, duplicated right renal collecting system, and moderate valvular mitral regurgitation, presented to our institution with right-sided weakness. Of note, the patient had two recent hospitalizations for sepsis secondary to *E. coli* bacteremia (confirmed with two sets of blood cultures collected on each admission) associated with a urinary tract infection in the first admission only asymptomatic bacteriuria with *E. coli* on the second admission. The initial admission had occurred five weeks prior. At that time, the patient was treated with eight days of intravenous antibiotics (one day of piperacillin-tazobactam, followed by seven days of ceftriaxone upon identification of the organism). Two weeks after the last dose of ceftriaxone and thirteen days prior to the most recent admission, she was readmitted and retreated for *E. coli* bacteremia for three days. A transthoracic echocardiogram (TTE) was obtained during the second admission; however, it was non-diagnostic due to motion artifacts. No repeat blood cultures were obtained after the initial positive blood cultures on either admission (not indicated as per current guidelines).

On presentation during the current admission, the patient was noted to have a fever (T 38.1 °C), hypotension (BP 80/41 mmHg), which required transient vasopressor support and intravenous fluid resuscitation, tachycardia (HR 100 beats per minute), and tachypnea (respiratory rate 23). Because of her right-sided weakness, a computed tomography angiography (CTA) emergent large vessel occlusion (ELVO) of the head was obtained, which did not demonstrate a cerebrovascular accident (CVA) or any other acute intracranial abnormality. Computed tomography (CT) of the abdomen and pelvis with intravenous contrast showed a duplicated right collecting system and a new splenic infarct (Fig. 1). On examination, the patient was lethargic and tachycardic, with no

* Correspondence to: 593 Eddy Street, Providence, RI 02903, USA.
E-mail address: thong1@lifespan.org (T. Hong).

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cardiac murmurs auscultated. She had decreased lung sounds at the bilateral lung bases, altered mental status (alert to self and place only), and right-sided weakness.

Laboratory studies showed marked leukocytosis (white blood count 34.4 $\times$ 10^9/L; reference range 3.5–11.0 $\times$ 10^9/L) with left shift (bands 19 %; reference range 0–5 %), anemia (hemoglobin 9.0 g/dL; reference range 11.0–15.0 g/dL), thrombocytopenia (platelets 50 $\times$ 10^9/L; reference range 150–400 $\times$ 10^9/L), acute kidney injury (AKI) reflected by an elevated creatinine (1.70 mg/dL; reference range 0.44–1.03 with baseline creatinine of 0.98 mg/dL), an elevated blood urea nitrogen (27 mg/dL; reference range 6–24 mg/dL), elevated alkaline phosphatase (157 IU/L; reference range 34–104 IU/L), and marked hypoalbuminemia (1.9 g/dL; reference range 3.5–5.0 g/dL). Urinalysis showed a specific gravity greater than 1.050 (reference range 1.010–1.030), pH of 5.0 (reference range 5.0–8.0), proteinuria (30 mg/dL; reference range $<$ 10 mg/dL), hematuria (red blood cells 12/high power field; reference range 0–5/high power field), absence of pyuria (white blood cells 1/high power field; reference range 0–6/high power field), negative leukocyte esterase, no bacteria/high power field was detected, and there were no squamous epithelial cells/low power field reported. Two sets of blood cultures collected on admission grew *E. coli* and urine culture had no growth.

Transthoracic echocardiogram (TTE) showed a 1.8 $\times$ 1.1 cm mobile echodensity on the atrial surface of the posterior leaflet of the mitral valve with likely attachment at the mitral annulus in an area of moderate mitral annular calcification, resulting in moderate mitral regurgitation (Fig. 2). Subsequent transesophageal echocardiogram (TEE) showed an irregular large mobile echodensity (1.0 cm $\times$ 2.0 cm) located on the atrial surface of the posterior leaflet of the mitral valve, leading to moderate to severe mitral regurgitation. As per both TTE and TEE interpretations, the findings likely reflected perforation of the base of the posterior leaflet. Cardiothoracic Surgery was consulted but the patient was deemed to not be a surgical candidate.

A total of six positive blood cultures of *E. coli* were identified. Time-to-positivity for these cultures ranges from 9 to 14 h (average 10.75 h). Susceptibility testing of all *E. coli* isolates showed identical susceptibilities, with susceptibility to all beta-lactam antibiotics, including Ampicillin. Resistance to ciprofloxacin, levofloxacin, tetracycline, and trimethoprim/sulfamethoxazole was detected.

Whole genome sequencing was performed on the *E. coli* isolate from the blood culture using the Illumina iSeq 100 platform and Illumina DNA library preparation kit. Data analysis included Multi-Locus Sequence Typing (MLST) determination using MLST 2.0.4. SeroTypeFinder was utilized for serotyping. Virulence genes were identified using VirulenceFinder and antimicrobial resistance (AMR) genes and potential resistance markers were identified for the strain. The *E. coli* isolate was identified as *E. coli* ST1193, serotype O75H5. It had resistant genes for sulfamethoxazole (sul2), quinolones (gyrA), tetracycline (tetB), and trimethoprim (dfrA17) consistent with culture susceptibility data (Table 1).

The patient's hospital course was further complicated by the development of emboli to the brain associated with clinical decline in neurologic status. CT of the brain without intravenous contrast obtained six days after admission showed a new hypoattenuation within the left occipital lobe suspicious for non-hemorrhagic infarction. Magnetic resonance imaging (MRI) of the brain with intravenous contrast showed multifocal cerebral infarctions without hemorrhage involving the left thalamus, occipital lobe, and inferior parietal lobule, as well as punctate areas of reduced diffusivity in bilateral centrum semiovale, right caudate head and right occipital lobe, consistent with cerebral embolism (Fig. 3).

The decision was made to treat the patient with six weeks of intravenous ceftriaxone 2 g daily, followed by lifetime suppressive therapy with amoxicillin-clavulanate 875–125 milligrams twice daily, with serial echocardiogram for close monitoring for valvular dysfunction. On subsequent follow-up, the patient's encephalopathy did not improve, and her functional status significantly declined, which prompted her family to place her in a skilled nursing facility for more dedicated care.

Discussion

Pathogenic *E. coli* include enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enterohaemorrhagic *E. coli* (EHEC), enteroaggregative *E. coli* (EAEC), and extraintestinal pathogenic *E. coli* (ExPEC) [2]. Both ST131 and ST1193 are ExPEC and belong to phylogroup B2 [3,4]. According to time-scaled phylogeny studies, ST131 is thought to have emerged in the mid-1880s while ST1193 is thought to have emerged in the early 1990s [2]. They are reported to have arisen by acquiring quinolone resistance-determining region (QRDR) mutations, incompatibility group F (IncF) plasmids, virulence factors, and type 1 pilus (fimH) recombination [5]. ST131 and ST1193 are the most frequently isolated clones displaying cephalosporin and fluoroquinolone resistance [5], and are thought to have contributed to the spread of MDR *E. coli* due to increased use and overuse of carbapenem antibiotics leading to increased carbapenem resistance [6], which is one of the

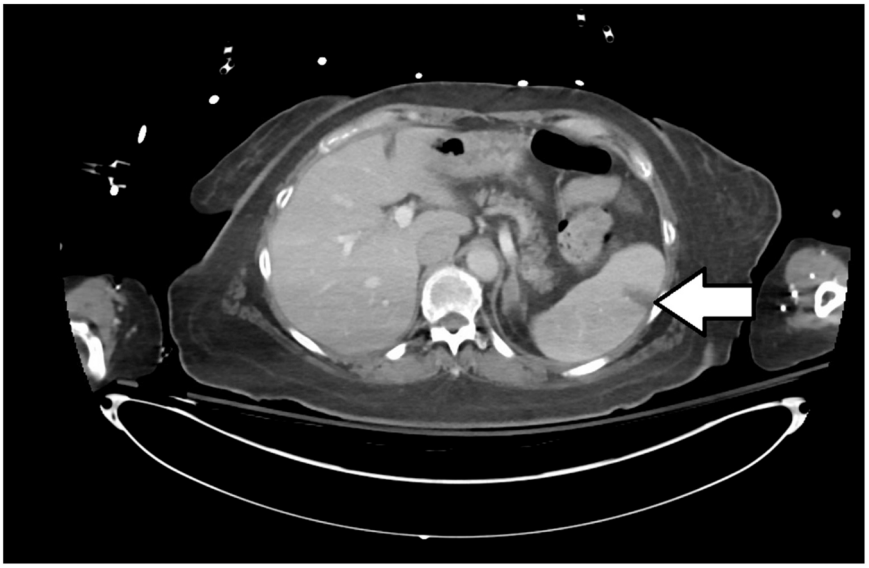

Fig. 1. Abdominal CT, arrow showing splenic infarction.

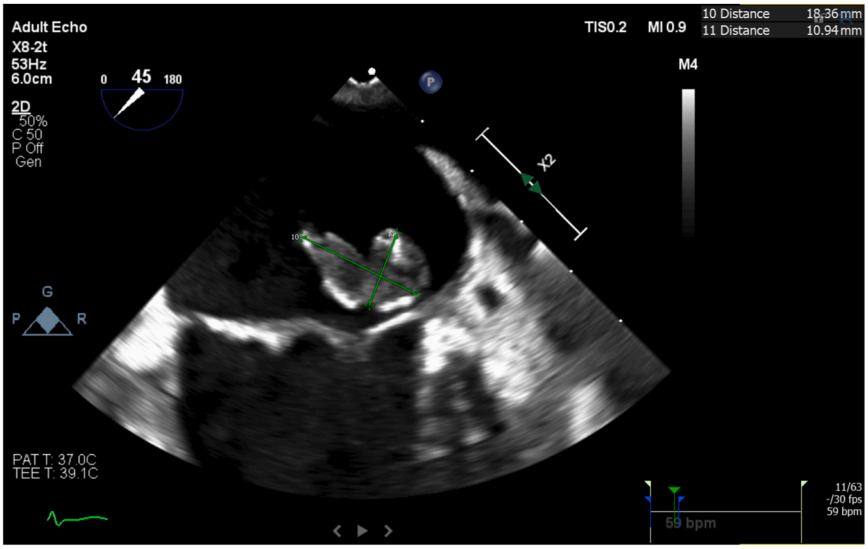

Fig. 2. Transthoracic echocardiogram depicting a 1.8 × 1.1 cm vegetation (thin green arrows) on the atrial surface of the posterior leaflet of the mitral valve.

Table 1
Identified virulence genes and antibiotic resistance genes.

Virulence gene	**Description**
aslA	Arylsulfatase-like gene
chuA	Outer membrane hemin receptor, enables the use of iron
fimH	Type 1 fimbriae, role in extraintestinal colonization and biofilm formation
fyuA	Siderophore receptor
gad	Glutamate decarboxylase
iha	Adherence protein, to iron-regulating genes
irp2	High molecular weight protein 2 non-ribosomal peptide synthetase, siderophore synthesis
iucC	Aerobactin synthetase, for acquiring host iron
iutA	Ferric Aerobactin receptor
kpsE	Capsule polysaccharide export inner-membrane protein
kpsMII_	Polysialic acid transport protein; Group 2 capsule, protection against phagocytosis
neuC	Polysialic acid capsule biosynthesis protein
nlpI	Lipoprotein NlpI precursor
ompT	Outer membrane protease (protein protease 7), Evades host immunity
papA_F43	Major pilin subunit F43
papC	O major pilin subunit F43, facilitates colonization by stimulating T lymphocyte cytokine production
sat	Serine protease autotransporters of Enterobacteriaceae (SPATE), influences on cell vacuolization
terC	Tellurium ion resistance protein
yehA	Outer membrane lipoprotein, YHD fimbriael cluster
yehB	Usher, YHD fimbriael cluster
yehC	Chaperone, YHD fimbriael cluster
yehD	Major pilin subunit, YHD fimbriael cluster
yfcV	Fimbrial protein
Antimicrobial Resistance genes	
Resistance Gene	**Description**
tet(B)	Tetracycline resistance
gyrA	Quinolone resistance
aph(6)-Id (aph(6)-Id_M28829),	Streptomycin resistance
sul2 (sul2_HQ840942)	Sulfamethoxazole resistance
sitABCD	Disinfectant resistance

reasons why MDR *E. coli* has been added to the WHO global MDR watch list [7].

According to *Pitout* et al., *E. coli* ST1193 is "imitating" the most successful and most prevalent MDR *E. coli* clone, *E. coli* ST131. This statement is based on sequencing analysis indicating a rapid expansion of blaCTX-M genes which encode CTX-Ms, extended-spectrum β-lactamases (ESBLs). This expansion was first noted on ST131 in the 2000s,

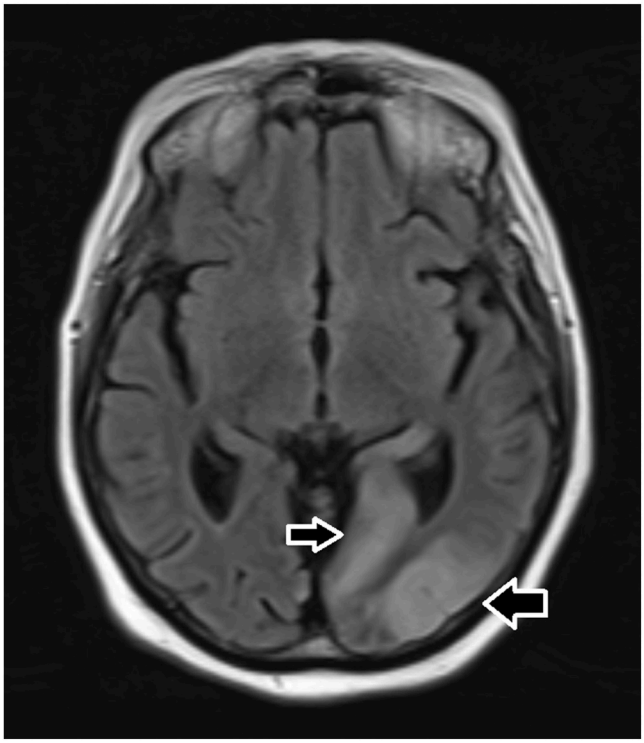

Fig. 3. Brain MRI with IV contrast, FLAIR 16/28**,** arrow showing emboli in the left occipital lobe.

and it is reported that the global prevalence of ST1193 has been increasing since 2012 and in some regions even replacing ST131 as the main ExPEC strain [5].

The estimated incidence of *E. coli* infective endocarditis is only 0.51 % [8]. According to a review of the literature from 1909 to 2022 by Micol et al., urinary tract infection was the most common etiology of infective endocarditis and disproportionally affected elderly females [9]. *E. coli* also appears to prefer native over prosthetic valves, preferentially the mitral valve, often leading to peripheral embolization, congestive heart failure, and valvular abscesses [10].

There have been thirty-six documented cases of *E. coli* endocarditis that met Duke criteria reported in the literature from 1909 to 2002,

including most recently the case of a 26-year-old patient with native mitral valve endocarditis in the setting of recurrent urinary tract infections [11]. A review of the literature yielded one other *E. coli* ST131 leading to endocarditis; however, the isolate was an ESBL strain, and the patient had undergone a prosthetic ring annuloplasty [12]. Our case highlights the rare case of non-MDR, beta-lactam susceptible *E. coli* ST1193 causing native valve endocarditis, evidence that ST1193 is following the steps of ST131.

According to the 2023 Duke-International Society for Cardiovascular Infectious Disease (ISCVID) criteria for infective endocarditis (IE) [13], which was updated from the 2000 modified Duke criteria, a patient must meet either two major clinical criteria, one major and three minor clinical criteria or five minor clinical criteria for a definitive diagnosis of IE to be given. Our patient met two major criteria: imaging major criteria with evidence of vegetation on echocardiogram, and microbiologic major criteria with the same organism being isolated on three separate blood cultures. *E. coli* is a rare cause of IE and hence not included among the list of typical Gram-negative IE-causing organisms such as the HACEK group microorganisms (*Haemophilus species, Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae*). Additionally, the patient met three minor criteria: presence of valvular regurgitation, fever, and vascular phenomena, therefore meeting definitive IE criteria.

According to Calderón Parra et al., who performed an analysis of a national prospective cohort in Spain of patients with definitive IE diagnosis with focus on gram-negative non-HACEK organisms, 61.6 % of the identified cases were due to *Enterobacterales*, with 38.4 % of those cases being attributed to *E. coli,* with preference for elderly patients [14]. Although the reason why non-HACEK organisms are not currently included in Duke's criteria may be because IE cases with gram-negative non-HACEK organisms are relatively rare (2.6 %) [14].

Despite susceptibility data indicating vulnerability to the chosen antibiotics, *E. coli ST1193* resulted in endocarditis, which was further complicated by valvular dysfunction and multifocal emboli to the spleen and the brain, leading to long-term sequelae. Our patient had two risk factors which may have made her prone to the development of IE: age $>$ 60 years and the presence of valvular heart disease (an echocardiogram done approximately 9 months earlier showed sclerodegenerative mitral valve disease without evidence of stenosis, regurgitation, or vegetation). In view of the persistence of this pathogen, it may be advisable to ensure clearance of blood cultures prior to determining the final therapy duration. Given the recurrence of bacteremia, it is suspected that endocarditis may have been present at least during the second admission. Hence, it may be prudent to pursue further confirmatory testing such as a transesophageal echocardiogram when there is a suspicion of endocarditis, especially in the setting of limited imaging data.

Conclusion

Escherichia coli ST1193 is following in the footsteps of the most successful and most prevalent MDR clone, *E. coli* ST131, potentially adding to public health burden and antimicrobial resistance. We presented the rare case of ST1193 causing native valve endocarditis with septic brain and splenic emboli, which should be kept in the differential, especially in cases of appropriately treated bacteremia, to avoid long-term sequelae.

Ethical approval

NA.

Consent

NA.

Author contribution

Clinical and microbiologic workup: DMV, JRL, SP, JL, SG, TH. Whole genome sequencing analysis: TH, SC, JL. Manuscript writeup: DMV, JRL, SP, SG, TH.

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Author statement

All authors have seen and approved the manuscript, and they contribute significantly to this work. I confirm that this work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere.

CRediT authorship contribution statement

Jennifer Li: Investigation, Data curation. **Tao Hong:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Data curation. **Diana M Villanueva:** Writing – review & editing, Writing – original draft, Investigation. **John R Lonks:** Writing – review & editing, Investigation. **Sophia Panaccione:** Writing – review & editing, Investigation. **Jerome Larkin:** Writing – review & editing, Supervision, Investigation. **Sara Geffert:** Writing – review & editing, Investigation. **Swapna Charla:** Investigation, Data curation.

Declaration of Competing Interest

We have no conflicts of interest to disclose.

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Conflict of Interest

No potential conflict of interest was reported by the authors.

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