Article published online: 2023-07-13

Edwardsiella tarda Causing Fishbone Injury Cellulitis Leading to Sepsis in a Case of Hematological Malignancy—A Rare Report and Review of Literature

Sushree Sarathi[1] Anupam Brahma[2] Prabodha Kumar Das[2] Ashoka Mahapatra[3] Bijayini Behera[3]

[1] Department of Microbiology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
[2] Department of Hematooncology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India
[3] Department of Microbiology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Address for correspondence Ashoka Mahapatra, MD (Microbiology), Additional Professor, Department of Microbiology, All India Institute of Medical Sciences, Bhubaneswar, Odisha 751019, India (e-mail: meetasoka@yahoo.co.in).

J Lab Physicians 2023;15:602–607.

Abstract

Edwardsiella tarda (*E. tarda*), a gram-negative bacillus, a member of order *Enterobacterales*, is typically a fish pathogen frequently isolated from fresh and brackish water environments. It is very rarely implicated in human infections such as gastroenteritis (most common), cellulitis, gas gangrene, hepatobiliary infections, peritonitis, empyema, and meningitis. Bacteremia/sepsis caused by *E. tarda* can be fatal in humans, although very rare (<5%). To date, very few cases of *E. tarda* sepsis have been reported worldwide including India. We report a rare case of cellulitis caused by *E. tarda* following fishbone injury in a patient with underlying hematological malignancy leading to sepsis.

Keywords
- *Edwardsiella tarda*
- cellulitis
- fishbone injury
- hematological malignancy
- sepsis

Key Message

Appropriate supplemented media and a reliable detection system should be used to identify these fastidious organisms. Clinicians should be aware of the pathogenic potential of *Edwardsiella tarda* to initiate appropriate therapy in time to prevent fatal extraintestinal manifestations.

Introduction

The genus *Edwardsiella* first described by Ewing et al in 1965 is a member of the family *Enterobacterales* consisting of three species such as *Edwardsiella hoshinae, E. ictaluri, and E. tarda.* Their usual habitat is freshwater and marine environments thus commonly pathogenic to cold-blooded vertebrates such as reptiles, amphibians, and fish especially those who are associated with these ecological niches.[1] Among the three, *E. tarda* is the only species known to cause human infections. Among them, more than 80% are gastroenteritis presenting as acute watery diarrhea resembling that produced by other toxigenic enteropathogens. Extraintestinal and systemic infections like wound infections meningitis, osteomyelitis, cholecystitis, and septicemia are rarely caused and can lead to potentially life-threatening conditions with a 50% risk of mortality.[2] Exposure to aquatic environments/exotic animals, people with underlying illnesses, including liver disease, and

received
March 27, 2023
accepted after revision
May 18, 2023
article published online
July 13, 2023

DOI https://doi.org/10.1055/s-0043-1770930.
ISSN 0974-2727.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

the ingestion of raw fish are the major risk factors associated with *E. tarda*. Other factors that increase the risk of getting *E. tarda* infection are prolonged contact with water, high iron concentration, and very young or old age.[3]

Case Report

A 71-year-old male with a known case of diffuse large B cell lymphoma (activated B cell type, stage IIIB with national comprehensive cancer network-international prognostic index prognostic score 4) presented to the outpatient department of medical oncology and hematology for the fifth cycle of intravenous rituximab, cyclophosphamide, doxorubicin, vincristine, and oral prednisolone (R-CHOP) chemotherapy. Chemotherapy was started after reviewing the physical and laboratory parameters (serum creatinine, renal function, liver function, complete blood count) to be completely normal. On the next day, he complained of pain and swelling of the right hand that extended moderately up to the lower forearm over the next 4 to 6 hours and developed a fever.

The patient's physical and systemic examinations were unremarkable except he was febrile(38°C). On further interrogation, he gave the history of prick by a raw fishbone over the left thumb 4 days back. Local examination revealed erythema, swelling, tenderness, and local rise of temperature of left hand and forearm including wrist sparing the elbow. There was no loss of movement, sensation, and vascularity. A scanty amount of serosanguinous collection could be aspirated from the swollen area and sent for gram stain and culture. Gram stain revealed few epithelial cells, 10 to 15 polymorphonuclear cells/low power field, fibrinous debris, and few gram-negative bacilli. Initial blood investigations revealed an absolute neutrophil count of 12,510/cu.mm, a high white blood cell count (14. $3_8 \times 10^3$/µL) with polymorphic predominance (87.8%), platelet count: 2,45,000/mm^3, hemoglobin: 8.5 g/dL, C-reactive protein: 178.4 mg/L. There was no remaining fishbone on the affected finger as confirmed by radiographic imaging. Left upper limb venous Doppler also showed no abnormality. Blood was sent for automated culture and sensitivity before starting empirical therapy of intravenous meropenem 1 g three times daily + linezolid 600 mg twice daily along with local conservative management of the swelling. Prophylactic acyclovir and cotrimoxazole were also continued with the R-CHOP regimen. Automated blood culture came positive on day 2 (gram-negative bacilli), and yielded pure growth of small non-lactose fermenting colonies (0.5–1 mm) on MacConkey agar (►**Fig. 1**). Phenotypic identification was done by putting up a panel of biochemical tests. The isolate was gram-negative motile bacilli, catalase positive, oxidase negative, fermenting only glucose and maltose, negative for nitrate reduction, citrate utilization, Voges Proskauer, phenylpyruvic acid, and urease test. Methyl red, indole, ornithine, and lysine decarboxylase were positive, triple sugar iron-alkaline/acid with H2S and arginine dihydrolase was negative—provisionally identified to be *Edwardsiella spp*. and further identified to be *E. tarda* by VITEK 2 compact system. Antimicrobial susceptibility test was performed on Muller Hinton agar by disc diffusion method using Amikacin (30 µg), Gentamicin (10 µg), Trimethoprim/Sulfamethoxazole (25µg), Ampicillin (10µg), Chloramphenicol (30µg), Ciprofloxacin (5µg), Cefotaxime (30 µg), Meropenem (10µg) and polymyxin (300 µg) for identification purpose and interpreted according to Clinical and Laboratory Standards Institute (CLSI, 2021). ATCC *Escherichia coli* 25922 was used as the control strain. The isolate was susceptible to all the agents tested except ampicillin, cefotaxime, and polymyxin. The same organism with a similar antibiogram was isolated from the aspirate of cellulitis as well. By the time antibiogram was available, the patient had already received the upgraded antibiotic intravenous (IV) meropenem for 48 hours, hence allowed to continue; however, linezolid was deescalated. On day 5, cellulitis was resolved and the complete blood count showed normal parameters. IV meropenem was stopped and the patient was discharged on day 6 with the advice of oral faropenem (200 mg) 1T BD for 10 days. This case of sepsis could be successfully treated by prompt initiation of meropenem.

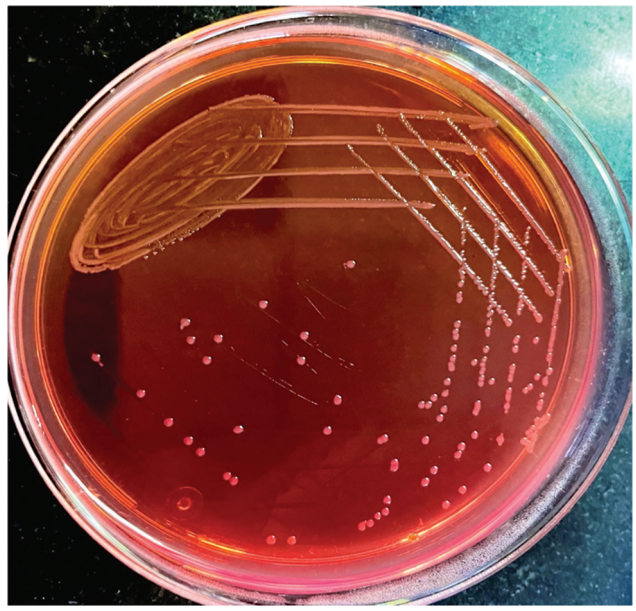

Fig. 1 Small nonlactose fermenting translucent colonies of *E. tarda* on MacConkey agar.

Discussion

We did the literature search over the past 10 years (2013-2022) by the search engines PubMed using Medical Subjects Headings (MeSH) terms "*E. tarda*," "bacteremia," "catfish injury," and "underlying malignancy." Only monomicrobial infections due to *E. tarda* were included in the review. All articles published in English were included in this analysis. We reviewed 519 kinds of literature on the subject (*E. tarda*) over the past 10 years (2013–2022) out of which 25 were found relevant and included in the review. Clinical details of all published kinds of literature are compiled in ►**Table 1**.[2,4–26] As per the review, *E. tarda* was found to be the cause of various infections such as sepsis, cholangitis,

Table 1 Details of infections caused by *Edwardsiella tarda* around the globe in the last 10 years

Infections caused by *Edwardsiella tarda*	Year	Geographical location	Age (years)/ sex	Case	Underlying diseases/Past history	Clinical samples	Possible source	References
Bacteremia	2018	Japan	65/F	Psoas abscess, spinal epidural abscess	Total gastrectomy for advanced gastric cancer	Blood (Pus: no growth)	Consumption of sashimi (sliced raw fish) and grilled eel	Suzuki et al[4]
	2018	Aurora, Colorado, US	58/M	Septic shock with multiple organ dysfunction and bone marrow suppression	COPD, untreated hepatitis C, remote history of lung cancer	Blood, surgical wound	Suspected catfish sting or stick with a contaminated fish hook	Morrisette et al[5]
	2019	Japan	76/M	Bacteremia	Chemotherapy for ALL	Blood	Couldn't access article	Manabe et al[6]
	2019	Tennessee, US	58/M	Sepsis, soft-tissue swelling	Lung cancer, diabetes, tuberculosis, alcohol abuse	Blood, knee aspirate	Catfish bite	LeBlond[7]
	2020	Tokyo	93/F	Acute cholecystitis, sepsis and DIC	Resection of breast cancer and total hysterectomy for uterine fibroids	Blood	Not described	Tonosaki et al[8]
	2021	Florida, USA	59/F	Colitis, septic shock	Advanced lung cancer, cirrhosis of the liver, hepatitis C positivity	Blood	Consumption of raw oysters	Healey et al[9]
Intrauterine infections	2017	Japan	34/F	Septic shock, DIC, postcesarean wound hematoma with abscess	None	Blood, cesarean wound swab	None	Miyazawa et al[10]
	2020	Japan	0 days/F	Mimicked respiratory distress syndrome at Bomsel's stage III	Threatened premature labor	Umbilical cord blood, amniotic fluid and maternal venous blood	None	Egashira et al[11]
Skin infections	2021	Memphis, Tennessee (USA)	58/M	Bullae with desquamation	Hepatitis C and polysubstance abuse	Bullae fluid	Catfish sting	Peravali and Muddassir[12]
Mycotic aneurysm	2018	Japan	65/F	Ruptured aneurysm	Cirrhosis, hepatocellular carcinoma and diabetes mellitus	Blood	None	Ebisawa et al[13]
Liver abscess	2014	Japan	77/M	Hepatic cyst	Diabetes mellitus and CML	Cyst fluid	Not described	Taguchi et al[14]
	2020	Saudi Arabia	37/F	Fulminant septic shock, multiple liver abscess	Laparoscopic cholecystectomy	Blood	None	Bakirova et al[1]
	2021	USA	85/M	Perihepatic abscess, chronic cholecystitis	Chronic kidney disease receiving hemodialysis, myelodysplastic syndrome	Pus	None	Pham et al[15]

Table 1 (*Continued*)

Infections caused by *Edwardsiella tarda*	Year	Geographical location	Age (years)/ sex	Case	Underlying diseases/Past history	Clinical samples	Possible source	References
Cholangitis	2017	Japan	80/F	Lemmel syndrome	Hepatocellular carcinoma and gallbladder cancer	Blood, bile duct fluid	Consumption of contaminated food was suspected as the origin	Miyajima et al[16]
Gastroenteritis	2021	USA	72/F	Diarrhea following, minimal change disease, subacute interstitial nephritis	Hypertension, hyperlipidemia, coronary artery disease, hypothyroidism, and liver cysts	Stool	Consumption of oyster	Bui et al[17]
	2021	Ukraine	22/M	Gastroenteritis	None	Feces	Seafood soup	Sydorchuk et al[18]
Endocarditis	2021	Japan	28/F	Infective endocarditis	Nonimmunocompromised host)	Blood	Couldn't be traced	Koike et al[19]
Deep abscess	2020	Ohio	9/M	Deep leg abscess following trauma by barb of freshwater fish	None	Pus		Sundaram et al[20]
Myonecrosis/ necrotizing fasciitis	2013	Nashville, Tennessee (USA)	57/M	Necrotizing fasciitis	Pulmonary hypertension, hepatitis C, and cirrhosis	Debrided tissue	Puncture injury from a wild catfish	Crosby et al[21]
	2019	Japan	64/F	Necrotizing fasciitis, septicemia with gastroenteritis	None	Blood, debrided tissue (no growth)	None	Yamamuro et al[22]
Gastric submucosal abscess	2020	Japan	74/M	Gastric wall abscess and intra-abdominal abscess around the spleen	Chronic alcohol consumption and hepatobiliary diseases	Blood, pus	None	Ota et al[23]
Osteomyelitis	2019	Singapore	79/M	Chronic osteomyelitis	Atrial fibrillation post-percutaneous coronary intervention	Sinus discharge, debridement tissue	None	Ng et al[24]
Pelvic inflammatory disease	2019	Taiwan	45/F	PID (uterine rupture), splenomegaly	Hepatitis C carrier, with type 2 diabetes mellitus and uterine leiomyoma	Blood	Raw fish/sushi consumption	Tai et al[25]
E. tarda sepsis (5 cases)	2004–2013	Japan	46–88 years	Sepsis	Cholecystitis, end-stage cancer, liver abscess	Blood	One case had dietary history of eating Sushi	Hirai et al[2]
E. tarda Superinfection in relapse of ulcerative colitis	2005–2013	Japan	24–63 years	Ulcerative colitis	3 (33.3%) were steroid-dependent	Stool	All 9 patients were Japanese with dietary habits of eating raw freshwater fish	Koido et al[26]

Abbreviations: ALL, acute lymphoblastic leukemia; CML, chronic myelogenous leukemia; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; PID, pelvic inflammatory disease.

endocarditis, deep abscess, myonecrosis, osteomyelitis, and pelvic inflammatory disease. Out of these, nine were isolated solely from blood, seven from pus/ tissue fluids along with blood, five solely from pus/tissue/fluids, and three from stool. All reports are from abroad, especially from Japan. Out of all, 12 had a history of either consumption/bite of catfish, and five were positive for Hepatitis C. All were adults/elderly except for one case of zero-day neonatal sepsis. There was one report of soft-tissue infection and sepsis following a catfish bite and one case of deep leg abscess following trauma by the barb of freshwater fish from the United States and one report of bacteremia during chemotherapy for acute lymphoblastic leukemia from Japan (►**Table 1**).[2,4–26] So, to the best of our knowledge, the present case is a rare report of *E. tarda* sepsis following fishbone injury cellulitis in an individual with underlying hematological malignancy.

The genus *Edwardsiella,* although belongs to the family *Enterobacterales,* strongly differs in habitats, pathogenic, biochemical, and physiological properties and is weakly related to other members of the family with a genetically distinct taxon. Further, unlike other members, *Edwardsiella* species are susceptible to commonly used antibiotics including penicillin that is very unusual for *Enterobacterales. E. tarda* is a normal gut flora of fish and humans, can cause opportunistic infections, especially in immunocompromised patients, and infection may range from mild gastroenteritis to fatal sepsis.[27]

E. tarda has two genomic strains—ATCC23685 strain commonly found in normal human gut flora, while EIB 202 is a virulent strain that causes disease in freshwater/ marine fish.[28] *E. tarda* produces several virulence factors as shown by different studies such as—invasive to HEp-2 cell monolayers, hemolysin, and siderophore production. They have a high affinity for red blood cells due to specific fimbriae and thus have hemagglutination properties.[29] Few studies show that it releases dermato toxins that damage the skin and a high propensity for causing cellulitis. Further, flagellar genes of *E. tarda*—fliC12, fliA, and flhDC—are essential for the length and number of flagellar filaments to facilitate their swimming and swarming ability.[30] Our patient was a known case of diffuse large B cell lymphoma and received the fifth cycle of chemotherapy (R-CHOP). In addition, he had a history of prick by a raw fishbone over his left thumb leading to cellulitis that may have allowed the bacteria to enter the bloodstream more easily. The underlying comorbidity of malignancy and chemotherapy might have facilitated for rapid development of systemic infection (sepsis) following a fishbone injury cellulitis. Thus, clinicians should be aware of the pathogenic potential of this bacteria. As per literature, the majority of *E. tarda* infections have been reported from abroad involving soft tissue and sepsis and had multiple comorbidities with high potential for mortality. To the best of our knowledge, there was only one report of sepsis with multiple liver abscesses associated with Cushing's syndrome because of recreational aquatic exposure from Vellore, India.[31] Thus, early identification and initiation of intravenous broad-spectrum antibiotic treatment are key to saving the patient from fatal systemic illness.

Funding
None.

Conflict of Interest
None declared.

Acknowledgements
We would like to thank Mrs Alakananda Mahapatra Lab Technician for technical help.

References

1 Bakirova GH, Alharthy A, Corcione S, et al. Fulminant septic shock due to Edwardsiella tarda infection associated with multiple liver abscesses: a case report and review of the literature. J Med Case Reports 2020;14(01):144
2 Hirai Y, Asahata-Tago S, Ainoda Y, Fujita T, Kikuchi K. Edwardsiella tarda bacteremia. A rare but fatal water- and foodborne infection: review of the literature and clinical cases from a single centre. Can J Infect Dis Med Microbiol 2015;26(06):313–318
3 Janda JM, Abbott SL, Kroske-Bystrom S, et al. Pathogenic properties of Edwardsiella species. J Clin Microbiol 1991;29(09): 1997–2001
4 Suzuki K, Yanai M, Hayashi Y, Otsuka H, Kato K, Soma M. Edwardsiella tarda bacteremia with psoas and epidural abscess as a food-borne infection: a case report and literature review. Intern Med 2018;57(06):893–897
5 Morrisette T, Hewgley WP, Hewgley H. Edwardsiella tarda bacteremia in untreated hepatitis C: alterations in antimicrobial therapy for a pan-susceptible pathogen in a critically ill patient. Am J Ther 2019;26(04):e530–e533
6 Manabe M, Matsumoto Y, Uchida T, Momose D, Sugano Y, Koh KR. [Bacteremia due to Edwardsiella tarda emerging after chemotherapy for recurrent pH-positive acute lymphoblastic leukemia]. Gan To Kagaku Ryoho 2019;46(12):1903–1905
7 LeBlond L. Catfish bite case report. Wilderness Environ Med 2019; 30(03):291–294
8 Tonosaki K, Yonenaga K, Mikami T, Mizuno T, Oyama S. Acute cholecystitis, sepsis, and disseminated intravascular coagulation caused by *Edwardsiella tarda* in an elderly woman. Tokai J Exp Clin Med 2021;46(01):51–53
9 Healey KD, Rifai SM, Rifai AO, Edmond M, Baker DS, Rifai K. Edwardsiella tarda: a classic presentation of a rare fatal infection, with possible new background risk factors. Am J Case Rep 2021; 22:e934347
10 Miyazawa Y, Murakami K, Kizaki Y, Itaya Y, Takai Y, Seki H. Maternal peripartum septic shock caused by intrauterine infection with Edwardsiella tarda: a case report and review of the literature. J Obstet Gynaecol Res 2018;44(01):171–174
11 Egashira M, Higuchi N, Shichijo A, Egashira T, Takayanagi T. Early-onset Edwardsiella tarda septicemia in an extremely preterm infant. Pediatr Int 2020;62(07):860–861
12 Peravali R, Muddassir K. A rare but fatal waterborne infection. Am J Med 2021;134(05):e329–e330
13 Ebisawa KF, Nishimura S, Yamamoto S, Ohji G, Iwata K. Mycotic aneurysm caused by Edwardsiella tarda successfully treated with stenting and suppressive antibiotic therapy: a case report and systematic review. Ann Clin Microbiol Antimicrob 2018;17(01): 21
14 Taguchi H, Tamai T, Numata M, et al. Endoscopic ultrasonography-guided transmural drainage of an infected hepatic cyst due to Edwardsiella tarda: a case report. Clin J Gastroenterol 2014;7(05): 422–428

15 Pham K, Wu Y, Turett G, et al. *Edwardsiella tarda*, a rare human pathogen isolated from a perihepatic abscess: implications of transient versus long term colonization of the gastrointestinal tract. IDCases 2021;26:e01283
16 Miyajima S, Yamakawa G, Ohana M. *Edwardsiella tarda*-associated cholangitis associated with Lemmel syndrome. IDCases 2018; 11:94–96
17 Bui A, Cortese C, Libertin CR, Porter IE II. Minimal change disease and subacute interstitial nephritis in association with *Edwardsiella tarda* gastroenteritis following oyster consumption. IDCases 2021;25:e01236
18 Sydorchuk AS, Bogachyk NA, Venhlovska YV. Clinical case of Edwardsiellosis in Ukraine. Wiad Lek 2021;74(01):165–167
19 Koike M, Doi T, Iba Y, Yuda S. Edwardsiella tarda native valve infective endocarditis in a young and non-immunocompromised host: a case report. Am J Case Rep 2021;22:e932387
20 Sundaram K, Ohliger E, Hoban C, Gurd DP. Treatment of an abscess of the leg in a febrile child after incidental trauma from the barb of a freshwater fish: a case report. JBJS Case Connect 2020;10(02): e0464
21 Crosby SN, Snoddy MC, Atkinson CT, Lee DH, Weikert DR. Upper extremity myonecrosis caused by Edwardsiella tarda resulting in transhumeral amputation: case report. J Hand Surg Am 2013;38 (01):129–132
22 Yamamuro T, Fukuhara A, Kang J, Takamatsu J. A case of necrotizing fasciitis following Edwardsiella tarda septicemia with gastroenteritis. J Infect Chemother 2019;25(12): 1053–1056
23 Ota K, Yamanoue H, Aizawa N, Suzuki N, Ota K, Takasu A. Gastric submucosal abscess caused by Edwardsiella tarda infection: a case report. BMC Gastroenterol 2020;20(01):299
24 Ng QX, Seng C, Chan FZY, Yeo WS. Zoonosis: an unusual case of chronic osteomyelitis. Singapore Med J 2019;60(07):379–381
25 Tai CH, Kuo SF, Lee CH. Concurrency of splenomegaly and numerous enlarged mesenteric and retroperitoneal lymph nodes in a patient with pelvic inflammatory disease caused by Edwardsiella tarda: mimicking lymphoma. Kaohsiung J Med Sci 2019;35(07):446–447
26 Koido S, Ohkusa T, Kato K, et al. Edwardsiella tarda superinfection in relapse of ulcerative colitis. J Clin Gastroenterol 2014;48(02): 191–193
27 Verjan N, Hirono I, Aoki T. Genetic loci of major antigenic protein genes of Edwardsiella tarda. Appl Environ Microbiol 2005;71(09): 5654–5658
28 Du M, Chen J, Zhang X, Li A, Li Y, Wang Y. Retention of virulence in a viable but nonculturable Edwardsiella tarda isolate. Appl Environ Microbiol 2007;73(04):1349–1354
29 Sakai T, Kanai K, Osatomi K, Yoshikoshi K. Identification of a 19.3-kDa protein in MRHA-positive Edwardsiella tarda: putative fimbrial major subunit. FEMS Microbiol Lett 2003;226(01):127–133
30 Xu T, Su Y, Xu Y, et al. Mutations of flagellar genes fliC12, fliA and flhDC of Edwardsiella tarda attenuated bacterial motility, biofilm formation and virulence to fish. J Appl Microbiol 2014;116(02): 236–244
31 John AM, Prakash JA, Simon EG, Thomas N. Edwardsiella tarda sepsis with multiple liver abscesses in a patient with Cushing's syndrome. Indian J Med Microbiol 2012;30(03):352–354

