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A rare case of infant eosinophilia induced by oral vancomycin: a case report and literature review

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Abstract

Oral vancomycin is mainly used to treat and prevent active *Clostridium difficile* infection. Because it is widely believed that there is a very low absorption rate via the gastrointestinal tract, reports of adverse reactions following oral vancomycin administration are rare. This case report describes for the first time a case of antibiotic-associated diarrhoea in a 2-month-old infant treated with oral vancomycin. After oral vancomycin treatment, the number of eosinophils increased significantly and the levels gradually recovered after drug withdrawal. A review and analysis of the previously reported adverse reactions caused by oral vancomycin and eosinophilia caused by vancomycin confirm the need for physicians to pay close attention to vancomycin-related adverse reactions, to monitor the required concentration and to measure eosinophil counts in patients with rash-related adverse reactions. Patients with concomitant diseases and children should be monitored for adverse events as it is possible that they have increased gastrointestinal absorption of vancomycin following oral administration. When vancomycin causes eosinophilia, fever and rash, physicians should be alert to the possibility of organ damage.

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Introduction

Vancomycin is a glycopeptide antibiotic that is widely used to treat infections caused by severe gram positive and other antibiotic-resistant bacteria, especially methicillin-resistant *Staphylococcus aureus* infection. The common adverse reactions of vancomycin include nephrotoxicity, ototoxicity, fever, vancomycin flushing reaction and other symptoms,[1] but there are a growing number of reports of eosinophilia associated with vancomycin use.[2–8] Oral vancomycin is mainly used to treat and prevent active *Clostridium difficile* infection.[9,10] Because its absorption rate in the intestinal tract is generally considered to be extremely low, adverse drug events associated with intestinal administration are infrequently reported.[11–13] Eosinophilia caused by oral vancomycin in infants with *C. difficile* infection has not been reported previously. This current case report is the first to describe this adverse event in an infant that received oral vancomycin. In addition, this article summarized the clinical characteristics of the adverse reactions of oral vancomycin and the related cases of vancomycin-induced eosinophil elevation. The aim of the current report was to highlight the possible clinical presentations of this condition in order to facilitate early diagnosis and treatment.

Case report

In March 2019, a 2-month-old female was admitted to the Department of Gastroenterology, Wuhan Maternal and Child Healthcare Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, Hubei Province, China presenting with diarrhoea for 15 days and bloody stools for 1 week. In the later stage, the child had yellow watery stools, approximately 20 times/day, accompanied by low fever, with the highest temperature of 37.7°C. The stools became bloody 1 week ago. Montmorillonite powder, probiotics and oral rehydration salts were ineffective. When she was admitted to hospital, her condition was slightly poor, her diet was approximately 500 ml per day, her sleep was not stable and her urine output was 25 ml/kg per day.

There was no family history. In January 2019, she was hospitalized in the Department of Paediatric Surgery of Tongji Hospital, Wuhan, Hubei Province China and underwent intestinal resection and anastomosis due to small intestinal atresia in the neonatal period. After the operation, her surgical incision was infected and she was successively administered the following drugs: 80 mg cefoperazone sodium and 20 mg tazobactam sodium intravenous (i.v.) every 12 h for 10 days; 55 mg meropenem i.v. every 8 h for 7 days; 28 mg teicoplanin i.v. once a day for 7 days; 85 mg amoxicillin clavulanate potassium i.v. every 8 h for 6 days; and 20 mg metronidazole i.v. every 8 h for 21 days. She was discharged from hospital in good condition. Diarrhoea occurred on the 4th day after stopping antibiotic treatment.

A physical examination recorded the following: temperature, 37 °C; pulse rate, 132 beats/min; respiration rate, 32 breaths/min; blood pressure, 85/54 mmHg; conscious mind; decreased skin elasticity; no rash was found; abdominal examination showed no muscle tension; active bowel sounds; no anal fissure; and all other physical

examinations were negative. Routine blood tests recorded the following: white blood cells (WBC), 17.00×10^9/l; neutrophil %, 60.2%; eosinophil %, 1.2%; haemoglobin (Hb), 107 g/l; C-reactive protein (CRP), 17 mg/l; alanine aminotransferase (ALT), 32 U/l; aspartate aminotransferase (AST), 28 U/l. Analysis of renal function, myocardial enzymes and electrolytes showed the following: no obvious abnormalities were found. Ultrasonography showed gas accumulation in the intestine, but there was no evidence of necrotizing enterocolitis and intussusception. Routine stool tests showed the following: occult blood +, but other indices were negative; no abnormalities were found on stool culture.

The child had a history of intestinal surgery and had been treated with many antibiotics for a long period of time. At the same time, she had the following clinical manifestations: severe diarrhoea; low fever; WBC count $>15 \times 10^9$/l; and no other pathogenic bacterial infection was found. Although there was no evidence of *C. difficile*, antibiotic-related diarrhoea was the most likely diagnosis. In addition, it should be noted that the patient was fed with deeply hydrolyzed milk powder and amino acid milk powder after surgery, so it is unlikely that the eosinophil elevation was caused by cow's milk protein allergy. On the same day (in March 2019), she was given 40 mg/kg per day vancomycin orally (actual 34 mg) four times a day (Vianex S.A., Athens, Greece; specification: 500 mg/bottle; batch number: H20140174) and 25 mg metronidazole i.v. twice a day. The diarrhoea improved.

On day 4 of hospitalization, routine blood tests recorded the following: WBC, 23.27×10^9/l, neutrophil %, 29.4%; eosinophil %, 35%; eosinophil count, 8.14×10^9/l; Hb, 101 g/l. On day 7 of hospitalization, routine blood tests recorded the following: WBC, 16.59×10^9/l; neutrophil %, 30%; eosinophil %, 23.9%; eosinophil count, 3.97×10^9/l; Hb, 101 g/l; ALT, 37 U/l; AST, 30 U/l. Renal function indices were normal. After the clinical symptoms were obviously improved, she was discharged from hospital. She continued to be administered 40 mg/kg per day vancomycin and 25 mg metronidazole twice a day orally for 1 week. These drugs were then discontinued. An outpatient examination at 2 weeks after drug withdrawal showed the following: WBC, 9.6×10^9/l; neutrophil %, 42%; eosinophil %, 2.1%; eosinophil count, 0.2×10^9/l; Hb, 97 g/l.

This study was approved by the institutional review board of Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology (no. 2022R053-E02). The reporting of this study conforms to CARE guidelines.[14] The parents of the infant who participated in this case report provided written informed consent for publication.

Discussion

The current case was assessed according to the Naranjo scale as follows:[15] (i) there was a conclusive report before the conclusion of eosinophilia caused by vancomycin (1 point); (ii) the adverse drug reaction (ADR) occurred after oral vancomycin (2 points); (iii) the ADR was relieved after stopping oral vancomycin (1 point); (iv) the child had used metronidazole many times in the past and there was no history of eosinophilia. Presenting after oral vancomycin and considering an ADR caused by oral vancomycin is not another cause that can cause this ADR alone (2 points); (v) the number of eosinophils in routine blood tests before and after medication is the objective evidence to confirm the adverse reaction (1 point). In conclusion, according to the causal evaluation of the ADR, the final score was 6 (i.e. probably related), which suggested that the current case's eosinophilia was probably an adverse reaction caused by oral vancomycin.

The clinical application of oral vancomycin is gradually expanding, but this route of administration has always been considered to be associated with poor intestinal absorption, high intestinal drug concentration and no need to monitor blood drug concentration.[16,17] A previous study confirmed that oral vancomycin is rarely absorbed from the gastrointestinal system even in severe diseases or renal failure.[18] However, some studies have confirmed that vancomycin can be detected in the blood of individuals infected by *C. difficile*, which may be related to the increased absorption of vancomycin by areas of the gastrointestinal tract that have inflammation.[19,20] In published studies, the frequency of detection of serum vancomycin levels in patients receiving oral therapy ranged from 2% to 68%.[18,21,22]

There are few reported cases of adverse reactions related to oral vancomycin worldwide; and the reported cases are mainly skin adverse reactions, such as vancomycin flushing reaction,[23] maculopapule,[24] urticaria[19] and linear immunoglobulin (Ig)A bullous dermatosis.[25] The pathogenesis of different rash types is different. For example, vancomycin flushing reaction is caused by non-IgE-mediated mast cell degranulation and excessive histamine release;[26] and linear IgA bullous dermatosis is type IV delayed type hypersensitivity, with pathological changes characterized by the linear deposition of IgA along the basement membrane zone.[26] The main clinical manifestations of IgE-mediated hypersensitivity induced by oral vancomycin are local or systemic maculopapule and urticaria.[26] Table 1 and Table 2 present a summary and analysis of the case reports (including this current case) of the adverse reactions caused by oral vancomycin,[11,16,19,20,23–25,27–34] which can occur at ages ranging from 2 months to 82 years (median age, 59 years). Skin changes were the most common (13 of 16 patients; 81.3%). In addition, there were two cases with blood dyscrasia, one case with ototoxicity and one case with laryngeal obstruction. This current case is the first report of eosinophilia caused by oral vancomycin in an infant. A previous study reported that the risk factors of the systemic absorption of oral vancomycin included renal insufficiency, severe *C. difficile* infection, high vancomycin dose (>500 mg/day), long-term treatment (>10 days), intensive care unit admission, use of vancomycin retention enema and gastrointestinal inflammation.[32] All 16 patients described in this summary of the published literature had underlying diseases, which was basically consistent with the aforementioned research. Fortunately, except for one patient with serious underlying diseases and a poor prognosis after taking vancomycin orally for a long period of time,[25] all of the other 15 patients achieved good outcomes after stopping vancomycin and/or receiving other treatments.[11,16,19,20,23,24,27–34]

The effects of vancomycin on the haematological system include anaemia, leukopenia, thrombocytopenia and eosinophilia. However, there are few cases of eosinophilia caused by vancomycin in both the clinic and the published literature. With the increasing use of vancomycin in clinical practice, it is particularly important to summarize this type of literature. Table 3 and Table 4 present a summary and analysis of 44 cases of eosinophilia caused by vancomycin.[2–8,35–65] Of these 44 cases, drug reaction with eosinophilia and systemic symptoms (DRESS), also known as drug-induced hypersensitivity syndrome, was found in 35 cases.[2–8,35–57] In other cases, some patients had increased eosinophil counts and involvement of other organs such as kidney, lung and heart function due to intravenous use of vancomycin.[58,62,63] Although the reported cases were been clearly diagnosed as DRESS, they were considered to have this syndrome based on the case data.

Table 1. Clinical characteristics of adverse reactions related to oral vancomycin reported in 16 cases in the published literature.[11,16,19,20,23–25,27–34]

Author	Sex	Age	Adverse reaction	Time of onset	Treatment	Medical history and risk factors	Outcome
Bailey et al.[27]	Male	82 years	Vancomycin flushing reaction	4 days	Drug withdrawal; antihistamine	Acute attack of chronic kidney disease; high dose vancomycin	Improved
Bergeron et al.[23]	Male	23 months	Vancomycin flushing reaction	1 h	Drug withdrawal; diphenhydramine	Previous multiple drug allergy; Down's syndrome; leukaemia	Improved
Killian et al.[28]	Female	67 years	Vancomycin flushing reaction	14 days	Diphenhydramine	High dose vancomycin	Improved
Nallasivan et al.[29]	Male	58 years	Vancomycin flushing reaction	3 days	Drug withdrawal; chlorpheniramine	Acute kidney injury	Improved
Choudhry et al.[25]	Female	60 years	Linear IgA bullous dermatosis	6 days	Drug withdrawal; gamma-globulin	Long medication history; hypertension; type 2 diabetes mellitus	Death
O'Brien et al.[30]	Male	45 years	Linear IgA bullous dermatosis	2 days	Not described	Pneumonia; septicaemia; end-stage renal failure	Improved
Baumgartner et al.[24]	Male	51 years	Maculopapule	3 days	Drug withdrawal; antihistamine	Diverticulitis; severe CDI	Improved
McCullough et al.[16]	Female	82 years	Maculopapule	8 days	Drug withdrawal; diphenhydramine; hormone	Chronic kidney disease	Improved
Mizumura et al.[31]	Male	76 years	Maculopapule	9 days	Drug withdrawal; glucocorticoid; antihistamine	High dose vancomycin; severe CDI	Improved
Osawa et al.[20]	Female	73 years	Maculopapule	1 day	Not described	Vancomycin allergy; perforation of colon	Improved
Barron et al.[32]	Female	66 years	Maculopapule	4 days	Drug withdrawal; chlorpheniramine	End-stage neurodegenerative diseases	Improved
Bossé et al.[19]	Male	35 years	Urticaria, laryngeal obstruction	Immediate	Drug withdrawal; adrenaline; diphenhydramine; methylprednisolone; ranitidine	Cystic fibrosis; multiple hypersensitivity-IV; vancomycin hypersensitivity; severe CDI	Improved
Mahabir et al.[33]	Female	55 years	Urticaria	Immediate	Drug withdrawal; antihistamine; hydrocortisone	Renal dysfunction; intestinal obstruction	Improved
Gomceli et al.[34]	Female	42 years	Hearing impairment	1 day	Drug withdrawal	Hypertension, diabetes mellitus	Improved
Aradhyula et al.[11]	Female	77 years	Leukopaenia	11 days	Untreated	Sigmoid diverticulosis; pancreatitis; lactose intolerance	Improved
This current case	Female	2 months	Eosinophilia	4 days	Untreated	Antibiotic-related diarrhoea after bowel resection	Improved

Ig, immunoglobulin; CDI, *Clostridium difficile* infection.

Table 2. Analysis of adverse reactions related to oral vancomycin use as reported in 16 cases in the published literature.[11,16,19,20,23–25,27–34]

Characteristic	Number of cases/total number	Proportion, %
Sex, female	6/16	37.5%
Median age, years	59	
Age range, years	2 months–82 years	
Adverse reaction manifestation		
Vancomycin flushing reaction	4/16	25.0%
Linear IgA bullous dermatosis	2/16	12.5%
Maculopapule	5/16	31.25%
Urticaria	2/16	12.5%
Blood dyscrasia	2/16	12.5%
Others (laryngeal obstruction, hearing impairment)	2/16	12.5%
Time of vancomycin administration		
$\leq$2 days	6/16	37.5%
Treatment[a]		
Untreated/only drug withdrawal	3/14	21.4%
Drug withdrawal and/or antihistamine	6/14	42.9%
Glucocorticoid	4/14	28.6%
Gamma-globulin	1/14	7.1%
Complicated with underlying diseases	16/16	100.0%
Outcome (remission)	15/16	93.8%

[a]Treatment data only available for 14 patients.
Ig, immunoglobulin.

A comprehensive review all of the 44 published cases with eosinophilia caused by vancomycin demonstrated the following (Table 4):[2–8,35–65] male patients were more often affected (27 of 44 patients; 61.4%); the median age was 46.8 years (range, 2 months to 59 years); the median time to vancomycin-related symptoms was 23.5 days (range, 3–49 days); and the median eosinophil count was 5.22×10^9/l (range, 0.85–37.5 $\times$ 10^9/l). Fever (32 of 44 patients; 72.7%) and/or rash (36 of 44 patients; 81.8%) were the first symptoms of eosinophilia in patients with vancomycin treatment; and another two cases had hypotension or were asymptomatic after intraperitoneal injection of vancomycin.[60,61] Organs and other systems were involved in the 44 cases; including the liver (21 of 44 patients; 47.7%), kidney dysfunction or failure (23 of 44 patients; 52.3%), lung involvement (six of 44 patients; 13.6%), peritonitis (two of 44 patients; 4.5%), neurological system (meningitis; one of 44 patients; 2.3%) and cardiac insufficiency (one of 44 patients; 2.3%). Therefore, when vancomycin causes fever, rash and eosinophilia in the clinic, physicians should be alert to the possibility of organ damage and closely monitor for this complication.

When a patient presents with suspected vancomycin-related adverse reactions, the first treatment is to stop the vancomycin and then give steroids, antihistamines and other treatments according to the condition. Due to the prolonged half-life of vancomycin, the current summary of 44 cases showed that severe refractory cases need renal replacement therapy (three of 44 patients; 6.8%)[47,54,62] or even liver transplantation (one of 44 patients; 2.3%).[40] A total of 41 of 44 patients (93.2%) achieved a good outcome and were considered to have

Table 3. Clinical characteristics of eosinophilia caused by vancomycin reported in 44 cases in the published literature.[2–8,35–65]

Author	Sex	Age	Time of onset	First symptom	Involved organs	Treatment	Eosinophil count, $\times 10^9$/l	Outcome
Drug reaction with eosinophilia and systemic symptoms								
Kim et al.[35]	Male	11 years	10 days	Fever, rash	Kidney injury	Steroids	5.45	Cured
Maxfield et al.[36]	Male	52 years	22 days	Maculopapule	Kidney injury	Methylprednisolone	6.1	Improved
Roy et al.[37]	Female	37 years	22 days	Elevated ALT, maculopapule	Liver function impairment; Renal insufficiency	Steroids	6	Improved
Marik et al.[38]	Male	51 years	28 days	Fever, maculopapule	Interstitial nephritis	Methylprednisolone	5.87	Cured
Yuan et al.[39]	Male	52 years	4 weeks	Diffuse papule	Suspicious lung damage	Prednisone	2.02	Cured
Song et al.[40]	Female	14 years	5 weeks	Fever, erythema and prurigo	Acute liver failure	Methylprednisolone; liver transplantation	3.15	Improved
Maldonado et al.[41]	Male	16 years	4 weeks	Diffuse rash, fever	Impaired liver function	Methylprednisolone	1	Improved
Hewitson et al.[42]	Male	57 years	24 days	Fever, abdominal pain, diarrhoea, rash	Hepatic dysfunction	Prednisone	6.7	Cured
Gangireddy et al.[43]	Female	79 years	6 weeks	Yellow staining of sclera, diffuse maculopapule	Damage of liver and kidney function	Methylprednisolone	1.73	Death
Young et al.[44]	Male	24 years	3 weeks	Fever, maculopapule	Impaired liver function; mucosal lesion	Steroids and antihistamine	2.9	Remission
	Female	48 years	2 weeks	Fever, maculopapule	Hepatic dysfunction	Steroids	2.2	Cured
	Male	59 years	3 weeks	Fever, maculopapule	Hepatic dysfunction	Steroids	10.4	Unknown
Ercan et al.[45]	Male	16 years	2 weeks	Fever, maculopapule	Hepatic dysfunction	Methylprednisolone	4	Cured
O'Meara et al.[46]	Male	66 years	4 weeks	Fever, erythema and papules, dry cough	Hepatic dysfunction; interstitial pneumonia; renal dysfunction	Steroids and antihistamine	37.5	Remission
Webb et al.[47]	Male	73 years	23 days	Fever, maculopapule	Shock	Haemodialysis; prednisone	4	Remission
Nguyen et al.[48]	Male	62 years	32 days	Erythema, peeling and fever	Renal damage	Triamcinolone acetonide	2.83	Cured
Zafar et al.[49]	Male	30 years	4 weeks	Fever, rash	Renal dysfunction	Methylprednisolone	Acidophilic in tissue	Cured
	Female	63 years	4 weeks	Fever, maculopapule	Hepatic dysfunction	Steroids	6.8	Improved
Vauthey et al.[50]	Female	60 years	2 weeks	Fever, maculopapule	Renal failure	Methylprednisolone and antihistamine	1.25	Cured
Chamorro-Pareja et al.[51]	Male	38 years	3 weeks	Maculopapule	Hepatic dysfunction	Systemic steroids and antihistamine	6.8	Cured

(continued)

Table 3. Continued.

Author	Sex	Age	Time of onset	First symptom	Involved organs	Treatment	Eosinophil count, $\times 10^9$/l	Outcome
Güner et al.[52]	Male	73 years	27 days	Fever, maculopapule	Renal damage	Steroids	1.45	Remission
	Female	72 years	15 days	Fever, maculopapule	Hepatic dysfunction; renal damage	Prednisone and antihistamine	0.85	Cured
Littlehales et al.[53]	Male	62 years	7 weeks	Maculopapule with exfoliation and fever	Pleural infiltration; impaired cardiac function	Hydrocortisone; antihistamine	9.77	Deteriorated
Zuliani et al.[54]	Female	45 years	23 days	Fever, rash	Renal failure; hepatic dysfunction	Methylprednisolone; antihistamine; haemodialysis	1.47	Improved
Koraki et al.[55]	Female	38 years	27 days	Fever, rash	Renal failure	Methylprednisolone	2.82	Improved
Wilcox et al.[56]	Male	39 years	3 weeks	Fever, dyspnoea	Diffuse pulmonary infiltration; renal damage	Methylprednisolone	4	Remission
Vinson et al.[57]	Male	14 years	3 weeks	Low fever, headache, diarrhoea	Hepatic dysfunction; hypotension	Methylprednisolone	5	Improved
Kulkarni et al.[2]	Male	36 years	15 days	Fever, rash	Hepatic dysfunction	Prednisone	3.4	Remission
Cox et al.[3]	Female	70 years	19 days	Fever, rash	Renal function and liver enzyme derangement	Change antibiotics	11.08	Death
	Male	46 years	35 days	Rash, fever	Acute liver and kidney injury	Prednisolone	5.9	Improved
DeMaio et al.[4]	Female	50 years	4 weeks	Fever, rash	Kidney injury	Diphenhydramine, epinephrine, solumedrol	3.37	Improved
Boehmer et al.[5]	Male	41 years	5 weeks	Rash	Kidney injury	Hydroxyzine, prednisone	6.3	Improved
Hershey et al.[6]	Male	64 years	4 weeks	Rash and shortness of breath	Kidney injury, and liver enzyme derangement	Prednisone and mepolizumab	2.5	Remission
Portney et al.[7]	Female	51 years	30 days	Rash, fever	Kidney injury, liver enzyme derangement	Corticosteroids	2.02	Improved
Jackson et al.[8] Eosinophilic pneumonia	Female	58 years	4 weeks	Rash, fever	Kidney injury	Methylprednisolone	11	Remission
Isono et al.[58]	Male	65 years	3 days	Elevated eosinophil count	Lung consolidation, pleural effusion	Prednisolone	43% (alveolar lavage fluid)	Remission

(continued)

Table 3. Continued.

Author	Sex	Age	Time of onset	First symptom	Involved organs	Treatment	Eosinophil count, $\times 10^9$/l	Outcome
Eosinophilic meningitis								
Kazi et al.[59]	Male	32 years	14 days	Fever, vomiting, headache	Eosinophilic meningitis	Only drug withdrawal	84%	Improved
Eosinophilic peritonitis								
Deweese et al.[60]	Female	37 years	12 days	Hypotension	The proportion of eosinophils in peritoneal fluid increased (69%)	Not described	Not described	Improved
Rosner et al.[61]	Female	61 years	7 days	Asymptomatic	The proportion of eosinophils in peritoneal fluid increased (39%)	Drug withdrawal	Not described	Remission
Interstitial nephritis								
Wai et al.[62]	Male	64 years	42 days	Fever, maculopapule	Interstitial nephritis; renal failure	Haemodialysis	2.76	Improved
Interstitial lung and interstitial nephritis								
Kwon et al.[63]	Male	50 years	18 days	Maculopapule, fever	Interstitial pneumonia; interstitial nephritis	Drug withdrawal; methylprednisolone	1.6	Improved
Stevens–Johnson Syndrome								
Alexander et al.[64]	Male	36 years	17 days	Fever, maculopapule	Hepatic dysfunction	Methylprednisolone	2.38	Cured
No symptoms								
Lintel et al.[65]	Female	46 years	33 days	Eosinophilia	Leukopenia, thrombocytopenia	Change antibiotics	0.94	Cured
This current case	Female	2 months	4 days	Eosinophilia	None	Untreated	8.14	Cured

ALT, alanine aminotransferase.

Table 4. Analysis of eosinophilia induced by vancomycin use as reported in 44 cases in the published literature.[2–8,35–65]

Characteristic	Number of cases/ total number	Proportion, %
Sex, female	17/44	38.6%
Median age, years	46.8	
Age range, years	2 months–79 years	
First symptom		
Fever	32/44	72.7%
Skin rash	36/44	81.8%
Respiratory symptoms	3/44	6.8%
Digestive symptoms	3/44	6.8%
Blood dyscrasia	2/44	4.5%
Hepatic dysfunction	2/44	4.5%
Hypotension	1/44	2.3%
No symptom	2/44	4.5%
Involved organs		
Liver function involvement	21/44	47.7%
Kidney involvement	23/44	52.3%
Lung involvement	6/44	13.6%
Eosinophilic peritonitis	2/44	4.5%
Neurological system involvement	1/44	2.3%
Haematological system	1/44	2.3%
Cardiac insufficiency	1/44	2.3%
Hypotension, shock	2/44	4.5%
None	1/44	2.3%
Mean eosinophil count, $\times 10^9$/l	5.22	
Eosinophilic count range, $\times 10^9$/l	0.85–37.5	
Mean duration of medication before symptoms, days	23.5	
Days of medication before symptoms, range	3–49	
Treatment		
Steroids	38/44	86.4%
Haemodialysis	3/44	6.8%
Untreated, only drug withdrawal and/or antihistamine	4/44	9.1%
Outcome		
Remission	41/44	93.2%
Deterioration/death	3/43	6.8%

gone into remission. This proportion was higher than previously reported.[66] The three patients that experienced deterioration or death were over 60 years old.

The pathogenesis of eosinophilia induced by vancomycin remains unclear, but it is speculated to be related to increased inflammatory cytokines, especially interleukin-5, which reach a peak a few days before the peak of eosinophilia.[67] It is thought that inflammatory cytokines might be involved in organ damage and the subsequent induction of eosinophilia.[67] This current case report described the induction of eosinophilia by oral vancomycin in a 2-month-old infant without it causing organ damage. The lack of organ damage in the current case might be related to the infant's immune system not being fully developed so it did not initiate a strong response.

With the wide application of vancomycin in the clinic, understanding its association with adverse reactions can help avoid organ damage in a timely manner.

It should be noted that repeated use of metronidazole did not cause eosinophil elevation in the current case, so it was inferred that eosinophil elevation in this infant was related to the newly added oral vancomycin treatment. However, there was no evidence to prove that the eosinophilia observed in this current patient was caused by the combined action of oral vancomycin and metronidazole, although this remains a small possibility.

In conclusion, a case of eosinophilia induced by oral vancomycin in an infant was reported for the first time in this current case report. A summary and analysis of the previously reported adverse reactions caused by oral vancomycin and eosinophilia caused by vancomycin confirm the need for physicians to pay close attention to vancomycin-related adverse reactions, to monitor the required concentration and to measure eosinophil counts in patients with rash-related adverse reactions.

Author contributions

Study concepts: Yali Wu, Fang Wang; literature research: Yali Wu, Shan Guo, Fang Wang; clinical information collection: Yali Wu, Fang Wang; data analysis/interpretation: Yali Wu, Shan Guo; manuscript preparation: Fang Wang, Wei Yin; manuscript final version approval: Fang Wang.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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