CASE REPORT

Disseminated *Pseudomonas aeruginosa* sepsis as presenting diagnosis of X-linked agammaglobulinaemia in a previously well 16-month-old child

Naveen Kumar Bhardwaj, Daisy Khera, Neeraj Gupta, Kuldeep Singh

Department of Pediatrics,
All India Institute of Medical
Sciences Jodhpur, Jodhpur,
Rajasthan, India

Correspondence to
Dr Daisy Khera,
pushpinderdaisy@gmail.com

Accepted 18 August 2017

SUMMARY

We report a previously healthy 16-month-old child who presented to us with membranous pharyngitis and ecthyma gangrenosum. In this patient, *Pseudomonas aeruginosa* was isolated from throat swab, cerebrospinal fluid, skin swab, urine, blood and synovial fluid in a single admission. In further workup, this child was diagnosed as a case of X-linked agammaglobulinaemia. The child was treated successfully with antipseudomonal antibiotics for 6 weeks and intravenous immunoglobulin.

BACKGROUND

Pseudomonas aeruginosa is an aerobic Gram-negative bacterium causing severe infection in children with immunodeficiency. It is also responsible for serious hospital-acquired infections.¹ *Pseudomonas* can involve any organ system with various non-specific findings, but ecthyma gangrenosum is a typical skin lesion which may help in early diagnosis and deciding antibiotics for the patient with *Pseudomonas* infection.² Patients with disseminated *Pseudomonas* infections should be worked up thoroughly to rule out primary or secondary immunodeficiency.

CASE PRESENTATION

We report a 16-month-old male child who presented to us with complaint of high-grade fever, cough and history of excessive cry while swallowing food for last 4 days. There was also history of reddish-coloured skin lesions, distributed asymmetrically over limbs for 1 day. Patient was on injection amoxicillin and clavulanic acid and amikacin at the time of admission. Prior history was not significant. Perinatal history was uneventful and development of the child was normal for age. The child was second in birth order of two siblings born out of non-consanguineous parents with elder sibling a 3-year-old female, alive and healthy.

At admission the child was sick looking, febrile with temperature of 103°F, pulse of 176/min, respiratory rate 66/min with subcostal recessions. Blood pressure and peripheral perfusion were normal. He was weighing 7.8 kg (between -1 and -2 z score), pallor was present and there were 8–10 vesiculobullous skin lesions over limbs and abdomen with mild induration,

perilesional oedema and they were tender to touch (ecthyma gangrenosum) (figures 1–4). Pharynx was congested and white membrane was present over tonsils. In systemic examination, bilateral crepts were present over chest; liver was palpable 2 cm below right costal margin with span of 8 cm. In central nervous system examination, the child was irritable and terminal neck rigidity was present. After seeing typical skin lesions and clinical course of the child, we kept possibility of *Pseudomonas* sepsis and the child was started on injection piperacillin–tazobactam and gentamicin. Cerebrospinal fluid (CSF) showed pleocytosis, so antibiotics were upgraded to intravenous meropenem and gentamicin on day 1 of admission. Various body fluids' cultures isolating *Pseudomonas* were showing sensitivity to piperacillin–tazobactam, imipenem, ceftazidime and gentamicin. The child was continued on meropenem and gentamicin, and showed improvement clinically. After day 17 of admission, the child again started mounting high-grade fever with complaint of crying while changing diapers. Ultrasound hip was done and it was suggestive of effusion left hip joint which required arthrotomy and growth of *P. aeruginosa* was present in joint fluid culture. Synovial fluid was again showing same culture and sensitivity report so we completed total 6 weeks of injectable meropenem and gentamicin.

INVESTIGATIONS

Investigations of the patient are tabulated in table 1. All body fluids cultures including blood, CSF, throat swab, skin lesion swab, synovial fluid and urine revealed growth of *P. aeruginosa* sensitive to piperacillin–tazobactam, imipenem, ceftazidime and gentamicin (table 2). In view of disseminated *Pseudomonas* infection, child was worked up to rule out immunodeficiency state (table 3). Immunoglobulin levels of IgA, IgM and IgG were done and they were reduced. Flow cytometric immunophenotyping for lymphocyte subset showed that B lymphocytes are markedly decreased, consistent with the diagnosis of X-linked agammaglobulinaemia (XLA). Flow cytometric studies of father, mother and elder sibling were normal.

CrossMark

To cite: Bhardwaj NK, Khera D, Gupta N, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221006

Figure 1 Edematous and erythematous early lesions of ecthyma gangrenosum over the anterior abdominal wall.

DIFFERENTIAL DIAGNOSIS

Secondary immunodeficiency.

TREATMENT

The child received supportive care in the form intravenous fluids and free flow oxygen initially for 2–3 days along with antibiotics. Intravenous immunoglobulin was given on day 7 of admission. Intravenous therapy with two sensitive antibiotics, injection meropenem and injection gentamicin were continued for 6 weeks. Left hip joint arthrotomy was done for left hip septic arthritis on day 18 of admission.

Figure 2 Necrotic ulcer with erythematous border over the chin.

Figure 3 Large necrotic ulcer of ecthyma gangrenosum over the dorsum of hand.

OUTCOME AND FOLLOW-UP

Child was discharged successfully from hospital after 6 weeks and is under our follow-up for last 1 year, receiving regular intravenous immunoglobulin every 4 weeks and is thriving well.

DISCUSSION

XLA, first described in the year 1952 by Col Ogden Bruton, giving rise to the alternate name of Bruton agammaglobulinaemia is a humoral immunodeficiency disorder characterised by defective B-cell development with extremely reduced numbers of mature B cells causing severe hypogammaglobulinaemia.

Figure 4 Lesions of ecthyma gangrenosum with black central eschar over the leg.

Table 1 Investigations of the child

Investigations (normal range)	13 February 2016	16 February 2016	25 February 2016	31 March 2016
Hb (10.5–14 g/dL)	7.6	7.1	8.4	10
TLC (4.5–11.0 x 10 ⁹ per liter)	14	12.9	23.8	8.63
N (22%–55%)/L (15%–45%)	76/18	35/59	62/25	17/68
Platelets (150–450 x 10 ⁹ per liter)	166	320	980	620
hsCRP (<1 mg/dL)	248	249	189	5.4
Urea (5–18 mg/dL)/creatinine (0.2–0.6 mg/dL)	28/0.16	26/0.11	23/0.11	
SGPT (9–24 U/L)	47		27	
Total proteins (6–8.5 g/dL)/albumin (3.2–5 g/dL)		3.82/2.4	5.3/2.8	
Cerebrospinal fluid total/differential cell count	350 cells with 70% neutrophils			
Parainfluenza, Human metapneumovirus <i>Mycoplasma pneumoniae</i> screen	Negative			
Chest X-ray	Bronchopneumonia			
Ultrasound cranium and abdomen	Normal			
CT abdomen	Mild right pleural effusion, mild ascites, rest normal			
Ultrasound left hip	synovial effusion? septic arthritis			

Hb, haemoglobin; hsCRP, high sensitivity C reactive protein; N/L, neutrophil/lymphocyte count; SGPT, serum glutamic pyruvic transaminase; TLC, total leucocyte count.

Most common presentation of this primary immunodeficiency disorder is recurrent infections.³

In patients with XLA, recurrent sinopulmonary infections, septicaemia, pyogenic meningitis, skin infections, arthritis and gastrointestinal infections are well described in literature.^{4–6} Plebani *et al*⁴ in a large multicentric study have found that respiratory infections were most common (68%) followed by cutaneous (27%) and gastrointestinal infections (13%) in patients with XLA. Similarly Chun *et al*⁶ have described pneumonia in 68.4%, otitis media in 32% followed by arthritis and skin infection in 26.3% each in their analysis of 20 years of accumulated data on patients with XLA. In both of these studies, meningitis and urinary tract infections were the least common findings. Suri *et al*⁷ have described pneumonia and empyema to the frequency of 86% in patients with XLA. Infections among patients with XLA are mainly caused by encapsulated pyogenic organisms like *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, *Streptococcus pyogenes* and *Pseudomonas* species.⁷ Out of these *Pseudomonas* may cause severe and difficult-to-treat infections.

Respiratory tract infections are the most common infections in XLA.⁸ Likewise in our patient, the illness started with

membranous pharyngitis and involved the lower respiratory tract in due course of time. Typical skin lesions, ecthyma gangrenosum, a type of bacterial vasculitis due to necrosis of small veins representing *Pseudomonas* septicaemia were present in our patient at admission. They are described as lesions edematous at the beginning then becoming erythematous and finally evolving into haemorrhagic bullae or gangrenous ulcers with a black central eschar.¹ *P. aeruginosa* was isolated from these skin lesions in our patient.

P. aeruginosa is a classic opportunist. It rarely causes disease in people who do not have a predisposing risk factor. Compromised host defence mechanisms owing to neutropenia, mucositis,

Table 3 Immunological workup

Investigations (normal range)	18 February 2016	31 March 2016
HIV serology	Negative for HIV 1 and 2	
Immunoglobulin levels		
IgG (453–916 mg/dL)	<75	
IgA (19–146 mg/dL)	<19	
IgM (20–100 mg/dL)	<10	
Flow cytometric immunophenotyping		
CD3+ lymphocytes (T lymphocytes) percentage (53%–75%)	95.01	
CD19+ lymphocytes (B lymphocytes) percentage (14%–37%)	0.03	
CD56+ (NK cells) percentage (3%–15%)	3.10	
Flow cytometry for estimation of BTK protein expression on CD14+ monocytes	BTK expression is decreased compared with control (35.24% vs 71.49%)	

BTK protein, Bruton's tyrosine kinase protein; CD, cluster of differentiation.

Table 2 Cultures from various body fluids

Investigations	13 February 2016	25 February 2016	31 March 2016
Blood culture and sensitivity	Growth of <i>Pseudomonas aeruginosa</i> sensitive to piperacillin–tazobactam, imipenem, ceftazidime and gentamicin	No growth	No growth
Throat swab, cerebrospinal fluid, urine culture	Growth of <i>P. aeruginosa</i> sensitive to piperacillin–tazobactam, imipenem and ceftazidime		
Synovial fluid and wound swab culture and sensitivity			

immunosuppression and impaired mucociliary transport explain the predominant role of this organism in producing opportunistic infections.⁹ We isolated *Pseudomonas* from throat swab, CSF, skin swab, urine, synovial fluid and blood in a single patient which is quite a rare finding. Urine culture in our patient was positive for *Pseudomonas* and its isolation rate in such patients is relatively low.¹⁰ We investigated this child for immunodeficiency in view of such disseminated *Pseudomonas* infection.

In a recent study from India by Suri *et al*⁷ mean age of onset of symptoms in XLA cohort was 1.6 years with a mean delay of 4.2 years in diagnosis. The child, we are reporting, was totally asymptomatic till the age of 16 months and was diagnosed in first admission due to disseminated infection by *Pseudomonas* and high index of clinical suspicion of immunodeficiency. There are articles in literature describing *Pseudomonas* infection in healthy children,^{1,2} but patients with such serious *Pseudomonas* infections should be thoroughly evaluated to rule out immunodeficiency.

Learning points

- ▶ Knowledge of typical skin lesions of ecthyma gangrenosum seen in *Pseudomonas* infection may help in early diagnosis.
- ▶ Patients with disseminated *Pseudomonas* infections should be thoroughly evaluated for primary or secondary immune deficiency.
- ▶ Early recognition and prompt treatment with antipseudomonal antibiotics is vital to reduce morbidity and potential mortality.

Contributors NKB and DK were involved in the conception and design of the manuscript, drafting the article and revising it critically for important intellectual content and final approval of the version published and agreed to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of

the article are investigated and resolved. NG and KS were involved in the conception and design of the manuscript and revising it critically for important intellectual content and final approval of the version published and agreed to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved.

Competing interests None declared.

Patient consent Obtained from guardian.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Viola L, Langer A, Pulitano S, *et al*. Serious *Pseudomonas aeruginosa* infection in healthy children: case report and review of the literature. *Pediatr Int* 2006;48:330–3.
- 2 Fang LC, Peng CC, Chi H, *et al*. *Pseudomonas aeruginosa* sepsis with ecthyma gangrenosum and pseudomembranous pharyngolaryngitis in a 5-month-old boy. *J Microbiol Immunol Infect* 2014;47:158–61.
- 3 Preece K, Lear G. X-linked Agammaglobulinemia with Normal Immunoglobulin and Near-Normal Vaccine Seroconversion. *Pediatrics* 2015;136:e1621–4.
- 4 Plebani A, Soresina A, Rondelli R, *et al*. Clinical, immunological, and molecular analysis in a large cohort of patients with X-linked agammaglobulinemia: an Italian multicenter study. *Clin Immunol* 2002;104:221–30.
- 5 Conley ME, Rohrer J, Minegishi Y. X-linked agammaglobulinemia. *Clin Rev Allergy Immunol* 2000;19:183–204.
- 6 Chun JK, Lee TJ, Song JW, *et al*. Analysis of clinical presentations of Bruton disease: a review of 20 years of accumulated data from pediatric patients at Severance Hospital. *Yonsei Med J* 2008;49:28–36.
- 7 Suri D, Rawat A, Singh S. X-linked Agammaglobulinemia. *Indian J Pediatr* 2016;83:331–7.
- 8 Aadam Z, Kechout N, Barakat A, *et al*. X-Linked Agammaglobulinemia in a Large Series of North African Patients: Frequency, Clinical Features and Novel BTK Mutations. *J Clin Immunol* 2016;36:187–94.
- 9 Thomas SM, Pseudomonas RSB, In Kliegman RM, *et al*. Burkholderia and Streptotrophomonas. *Nelson textbook of Pediatrics*. 20th edn. Philadelphia: Elsevier, 2016.
- 10 Conley ME, Howard V. Clinical findings leading to the diagnosis of X-linked agammaglobulinemia. *J Pediatr* 2002;141:566–71.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow