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ATYPICAL RUBELLA PRESENTATION IN AN IMMUNOCOMPROMISED CHILD: A CASE REPORT AND DIAGNOSTIC CHALLENGES

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ABSTRACT

Viral exanthems in immunocompromised children can present with atypical features, complicating diagnosis and management. This case report highlights the diagnostic challenges and atypical clinical course of rubella in an immunocompromised paediatric patient with systemic lupus erythematosus (SLE) and macrophage activation syndrome (MAS). A 7-year-old girl with SLE-associated MAS presented with a 2-week history of high-grade fever and generalized maculopapular rash. Initial differentiation between rubella and measles was complicated by overlapping features. Key distinguishing findings included posterior auricular lymphadenopathy and timing of rash emergence. Notably, her immunosuppressed state due to SLE and MAS masked classic rubella symptoms, prolonging diagnostic uncertainty. Rubella infection was confirmed via serology (rubella-specific antibody). Despite severe immunosuppression, her condition stabilized with conservative care, optimised immunosuppressive therapy and nutritional support. No secondary complications were observed. This case illustrates rubella's potential for atypical and severe manifestations in immunocompromised children, particularly those with concurrent autoimmune and hyperinflammatory conditions like SLE-MAS. It underscores the need for meticulous evaluation in high-risk populations, especially those who have not been vaccinated. This report contributes to understanding viral exanthems' variable phenotypes in immunocompromised hosts, advocating for tailored diagnostic protocols in such cases.

1.0 INTRODUCTION

Rubella and measles, though clinically similar, present distinct epidemiological and diagnostic challenges with significant public health implications. Both diseases are characterised by acute febrile rash, lymphadenopathy, and systemic symptoms. Measles, caused by the *Morbillivirus* (Paramyxoviridae family), is highly contagious, spreading via respiratory droplets, and is associated with severe complications such as encephalitis and pneumonia [1-2]. In contrast, rubella caused by the single-stranded RNA *Rubivirus* (Togaviridae), typically follows a milder course in immunocompetent hosts but poses a critical threat during pregnancy due to its teratogenic potential, leading to congenital rubella syndrome (CRS) [3-4]. A key distinguishing feature lies in the progression of rash – measles rash coincides with peak fever and is often accompanied by Koplik spots, while rubella rash emerges post-fever resolution and is associated with posterior auricular lymphadenopathy [5-6]. Differentiating these diseases is crucial for both clinical management and public health response. Misdiagnosis can lead to inappropriate treatment, delayed isolation measures, and increased transmission risks. From a public health perspective, accurate identification is vital for surveillance, outbreak control, and vaccination strategies.

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In Malaysia, rubella remains a notifiable disease, with sporadic cases still reported despite elimination efforts. Global elimination efforts, including Malaysia's 2030 target, emphasize universal MMR vaccination to prevent CRS and interrupt rubella transmission [7]. However, gaps in immunization coverage, particularly in socioeconomically vulnerable populations, sustain transmission risks and hinder elimination goals [8]. According to the National Health and Morbidity Survey (NHMS) 2022, national MMR vaccine uptake stands at approximately 96% for the first dose and 94% for the second dose a modest decline from previous years [9]. Notably post-COVID-19 pandemic, there was a concerning resurgence of vaccine-preventable diseases, including a 63% increase in measles cases (from 128 to 209 cases) in 2022 underscoring the fragility of herd immunity [9]. Malaysia adheres to the WHO-recommended schedule, providing MMR at 9 and 12 months of age, with ongoing public health efforts to address vaccination gaps in underserved populations.

Juvenile systemic lupus erythematosus (SLE), a multifactorial autoimmune disorder, disrupts immune tolerance via dysregulated B- and T-cell activity, impairing pathogen defence. Concurrent macrophage activation syndrome (MAS), a hyperinflammatory complication of SLE, exacerbates immunosuppression through cytokine storms (e.g., IL-1β, IL-18) and cytolytic cell dysfunction [10]. This dual immune dysregulation heightens susceptibility to infections and obscures typical clinical signs, allowing pathogens like rubella to manifest atypically. This case report highlights the virological, clinical, and public health challenges, underscoring the need for vigilant diagnostic process and surveillance, and tailored interventions to protect high-risk populations and advance global elimination efforts.

2.0 CASE REPORT

2.1 History

A 7-year-old Malay girl with underlying SLE-MAS, presented with a two-week history of fever and generalized rash. The fever, which prolonged for 10 days, was high-grade (up to 41.9°C), intermittent, and was objectively recorded by the mother. The fever responded minimally to antipyretics. It was associated with chills and rigors. The generalised rash started two days after the resolution of fever, initially appearing as painless, non-itchy red spots over the scalp, face, and trunk before spreading caudally to the lower extremities, sparing the genital region. During illness the child experienced significant appetite loss, which led to a noticeable weight loss of 3 kilogrammes within two weeks. There was no history of conjunctivitis or other features suggestive of SLE flare. Diagnosis of SLE was made less than a year ago, which was complicated by MAS and recurrent SLE flares, with the most recent episode of flare being three weeks prior to this admission. The patient has been compliant with her SLE medication.

Her vaccination history revealed incomplete immunization, with no documented MMR (Measles-Mumps-Rubella) vaccine. The missed immunization was primarily due to competing family healthcare priorities as her brother was undergoing intensive treatment for acute lymphoblastic leukaemia, requiring multiple hospital admissions for chemotherapy.

2.2 Physical Examinations

At presentation the girl was febrile (40.2°C) but alert. A maculopapular erythematous rash was present on her face, trunk, and limbs, with some lesions showing vasculitis features and post-inflammatory hyperpigmentation (Figure 1(a), Figure 1(b) and Figure 1(c)). Oral ulcers were noted on the buccal mucosa. Systemic examination revealed hepatomegaly of 3 centimetres below her right costal margin. Traube's space was dull on percussion. Multiple posterior auricular and right jugular cervical lymph nodes were palpable. Cardiovascular, respiratory and neurological examinations were unremarkable.

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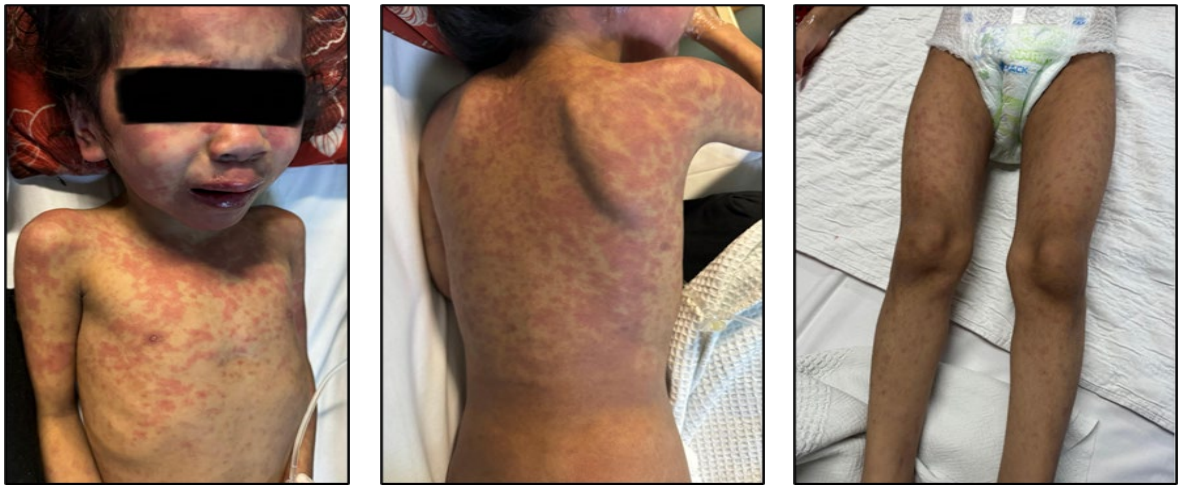

(a) (b) (c)

Figure 1. (a) maculopapular rashes with distribution over the face spreading to the anterior chest; (b) similar rash over the back; (c) discrete maculopapular rash on bilateral lower limbs

2.3 Investigation

Laboratory findings upon admission revealed mild anaemia with neutropenia and a normal platelet count. Ferritin level was significantly elevated, indicative of MAS. Liver enzymes showed mild elevation, while lactate dehydrogenase (LDH) was significantly raised. Renal and coagulation profiles were normal. Abdominal ultrasound indicated hepatomegaly, with no additional abnormalities reported. Detailed results are summarised in Table 1.

Table 1. Summary of investigations

Tests	Results	Normal range
Haemoglobin (Hb)	10.4 g/dL	11 – 16 g/dL
Total white cell	4.38 $x10^9$/L	4.5 – 13.5 $x10^9$/L
Neutrophil counts	1.03 $x10^9$/L	2 – 7.5 $x10^9$/L
Platelet	155 $x10^9$/L	150 – 400 $x10^9$/L
Serum ferritin	4037.2 µg/L	7 – 140 µg/L
Alanine transaminase (ALT)	26.9 U/L	< 40 U/L
Aspartate transaminase (AST)	101 U/L	< 40 U/L
Serum albumin	38.6 g/L	35 – 58 g/L
Lactate dehydrogenase (LDH)	1106 U/L	150 – 300 U/L
C-reactive protein (CRP)	7.14 mg/L	< 5mg/L

The initial blood culture identified *Kocuria marina*, with sensitivity to oxacillin. However, this result was deemed a contaminant considering the nature of her clinical presentation. Rubella-specific IgG was positive (obtained two weeks after onset of fever), while measles serology and Epstein-Barr virus (EBV) PCR were negative.

2.4 Management

The patient was treated conservatively with antipyretics, intravenous hydration, and the continuance of her immunosuppressive therapy. Initial administration of intravenous methylprednisolone was replaced by oral prednisolone. Ceftriaxone was initially prescribed for suspected bacterial superinfection but was later de-escalated upon negative growth on repeat culture. Nutritional support was optimised during the admission, with attention to the dental care for oral ulcers. Public health authorities were informed regarding the diagnosis, and the need to address her incomplete immunization. At the time of discharge after 12 days of admission, the child showed notable improvement. Her fever subsided, rashes diminished albeit with residual hyperpigmented patches and her appetite normalised. Follow-up appointments were arranged to evaluate disease activity, assess vaccination status, and re-examine her growth parameters. Referral to medical social worker was made to address the family's socioeconomic barriers to healthcare access.

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3.0 DISCUSSION

This case highlights the atypical and severe presentation of rubella in a child with SLE and MAS, underscoring the profound impact of immune dysregulation on viral infections. The clinical overlap with measles both presenting with fever, maculopapular rash, and lymphadenopathy posed diagnostic challenges. However, key differentiating features, such as posterior auricular lymphadenopathy and rash onset post-fever resolution, supported rubella diagnosis, later confirmed by rubella-specific antibody [2]. To our knowledge, this is the first documented case in literature describing confirmed rubella in a child with SLE and MAS. Similar cases remain rare, though a few reports have noted atypical rubella or measles-like illnesses in immunocompromised hosts, often complicated by diagnostic delays and increased morbidity [10-11].

The interplay between SLE-MAS and rubella infection exacerbated disease severity. SLE impairs both innate and adaptive immunity, while MAS induces a hyperinflammatory state characterized by a cytokine storm and cytolytic cell dysfunction [12]. In this patient, rubella virus triggered excessive T-cell and macrophage activation, further suppressing immune function and prolonging viremia. The resultant cytokine storm caused widespread inflammation, manifesting as hepatosplenomegaly and elevated ferritin levels [12]. This case illustrates how pre-existing immune dysregulation can transform a typically benign infection into a life-threatening condition, highlighting the importance of early recognition and tailored management in such complex scenarios. This case also underscores the vital role of herd immunity. Immunocompromised individuals, such as children with SLE, rely heavily on community-wide immunisation to prevent exposure to vaccine-preventable diseases. When vaccination coverage falls below threshold levels, these vulnerable individuals face heightened risks, even when medically ineligible for vaccination themselves [12]. Vaccination plays a critical role in mitigating rubella severity too, particularly in high-risk populations. Although global rubella elimination efforts aim for 2030, incomplete immunization in vulnerable groups, such as children with chronic immunosuppression, remains a concern [9]. Unvaccinated immunocompromised individuals face elevated risks of prolonged viremia, severe complications, and atypical presentations, as seen in this case.

Socioeconomic barriers significantly contributed to this patient's susceptibility. Financial constraints and competing healthcare priorities, including her brother's leukaemia treatment, led to missed MMR vaccinations, leaving her unprotected against rubella. Addressing these social barriers through targeted interventions, such as mobile vaccination clinics and financial support, is critical to closing immunization gaps and supporting Malaysia's rubella elimination goals [7, 13]. This case contributes to scientific understanding by demonstrating the severe consequences of rubella in immunocompromised children and the diagnostic complexities in differentiating it from measles. It also underscores the need for integrated healthcare approaches that address both clinical and socioeconomic factors to improve outcomes in high-risk populations.

4.0 CONCLUSIONS

This case report underscores the complexities of diagnosing and managing rubella infection in an immunocompromised child, specifically SLE-MAS. Unlike its typically mild and self-limiting course in healthy individuals, rubella manifested severely in this patient, featuring prolonged fever, hepatosplenomegaly, and multi-organ involvement. The clinical resemblance to measles also posed diagnostic challenges. Diagnosis was later confirmed by laboratory testing. The patient's underlying SLE-MAS exacerbated the infection, as immune dysregulation and hyperinflammation from a cytokine storm impaired viral clearance and amplified tissue damage. Socioeconomic factors, including financial strain and competing healthcare needs, led to missed vaccinations, leaving her vulnerable to this preventable disease. This case highlights the critical need for heightened vigilance in immunocompromised hosts, robust vaccination strategies to protect high-risk populations, and integrated healthcare approaches that address both medical and socioeconomic barriers.

5.0 KEY LEARNING POINTS

Rubella can present atypically in immunocompromised paediatric patients, mimicking measles or other viral exanthems. Next, immunosuppressive state of host may obscure classic clinical signs and prolong diagnostic timelines. On top of that, missed or delayed vaccinations, often due to social or family-related

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barriers, can lead to preventable infections. Finally, herd immunity is essential to protect vulnerable individuals who are ineligible for certain vaccinations.

6.0 CONFLICT OF INTEREST

The authors declare no conflicts of interest. Informed consent for publication was obtained from the child's parents, including for clinical information and images presented in this report.

7.0 AUTHORS' CONTRIBUTION

Crissny, C. N. T. T., (Methodology; Validation; Formal analysis; Investigation; Writing -original draft)
Khaiyin, L., (Formal analysis; Investigation)

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