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# Atypical erythema Migrans with generalized maculopapular rash in a child: A case report of Lyme disease and review of the literature

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**Abstract**
Lyme disease (LD) is a multisystem zoonosis caused by *Borrelia species* and is transmitted by ticks. Erythema Migrans (EM) is the most common early manifestation and a key diagnostic sign, but atypical morphologies are frequent and may be underrecognized. Generalized rash concurrent with EM is rare in paediatric LD.

We report a 6-year-old girl presenting with acute right lower limb pain, low-grade fever, and a generalized blanchable maculopapular rash. Physical examination revealed an atypical EM lesion on the right thigh, characterized by an almost homogeneous erythematous patch with diamond-shaped borders, lacking the classic "bull's eye" configuration. Laboratory findings showed elevated inflammatory markers, normal blood count, and negative microbiological tests for alternative aetiologies. Serology was positive for *Borrelia burgdorferi* IgM and confirmed by Western blot. The patient was treated with oral doxycycline, achieving rapid symptom resolution. At 15-month follow-up, she reported occasional limb arthralgia without neurological symptoms or need for medication.

This case adds to the scarce literature describing generalized rash in association with EM in children. The coexistence of these cutaneous features may indicate early disseminated LD and warrants clinical suspicion, even in the absence of a known tick bite. Recognition of atypical EM morphologies is crucial for timely diagnosis and treatment, particularly in endemic areas. Long-term follow-up is advised due to the risk of post-treatment Lyme disease syndrome (PTLDS), which can present with persistent musculoskeletal or neurocognitive symptoms.

**Keywords:** Lyme Disease, Erythema Migrans, *Borrelia burgdorferi*, Child, Post-Treatment Lyme Disease Syndrome

## Introduction

Lyme Disease (LD) is a multisystem zoonosis caused by *Borrelia* species and transmitted to humans primarily through the bite of infected ticks. In children, LD may present in early localized, early disseminated, or late stages [1-3]. The early localized stage is most often characterized by Erythema Migrans (EM), a cutaneous lesion that develops at the site of inoculation due to local multiplication of spirochetes in the skin [4, 5]. EM occurs in approximately 77-89% of symptomatic paediatric cases [3]. It usually develop within 3 days to 3 months after a tick bite, most commonly between 3 to 30 days. The anatomical distribution of EM lesions varies with the tick bite location. In children, the head and neck are commonly involved. Typically, EM appears as a pink-to-red, oval or round macule or papule, enlarging centrifugally and sometimes developing central clearing with a darker border, exceeding 5 cm in diameter [4]. This configuration resembles a ring or ring-within-a-ring pattern, often referred to a bull's-eye lesion. Classic EM is considered pathognomonic and therefore represents a key diagnostic feature. However, EM morphology is variable. While medical literature and training often emphasize the classic bull's-eye appearance, uniform or atypical lesions are frequently underrecognized. Atypical EM may present with an irregular shape, uniform coloration, a diameter <5 cm, increased central erythema, red-violet spots, vesiculation and petechiae [2, 4, 5]. Patients may also report pruritus or pain. Other dermatologic manifestations of LD have been described.

Non-specific manifestations such as fever, fatigue, headache, myalgia and arthralgia are common in LD and may mimic viral infections, particularly in children [1]. In this age group, the disease may follow a different course, as distinguishing between stages is more challenging and the immune system is still immature. Furthermore, signs and symptoms of early disseminated LM may appear earlier, often while skin lesions are still present, whereas late-stage disease is rare [3]. Consequently, LD in the paediatric population poses unique diagnostic challenges, requiring an integrated approach that combines semiology, epidemiologic context and careful clinic observation. Without timely diagnosis and treatment, the infection may progress to long-term complications affecting the musculoskeletal, neurologic, and cardiac systems [5].

Routine serologic testing is not recommended for patients with EM due to low sensitivity in early localized LD [5]. However, it may be useful in selected cases, particularly when the presentation is atypical. Initial antibody detection is performed using highly sensitive methods such as enzyme-linked immunosorbent assays, chemiluminescent immunoassays or multiplexed microsphere-based immunoassays [7]. Positive or equivocal results require confirmation with Western blot, which offers high specificity and establishes the diagnosis. However, these methods have temporal limitations as IgM antibodies typically become detectable 3-4 weeks after infection and disappear within approximately 6 months, whereas IgG antibodies appear later - after 6-8 weeks - and may remain detectable for many years [7]. Additional diagnostic procedures, including skin biopsy, are rarely required to establish the diagnosis.

Prompt initiation of antibiotic therapy generally leads to full resolution of LD. Nonetheless, a subset of patients, including children, may develop Post-Treatment Lyme Disease Syndrome (PTLDS), a condition characterized by persistent fatigue, arthralgia, and neurocognitive symptoms [1]. PTLDS is thought to result from post-inflammatory processes and permanent tissue damage rather than active infection [8]. In such cases, management should focus on symptomatic treatment, as repeated antibiotic courses have not been shown to improve quality of life and carry significant risks of adverse effects [9].

This report describes a paediatric case of early localized LD presenting with an atypical EM lesion and generalized rash, highlighting the importance of clinical recognition, awareness of morphological variability, and the need for follow-up to monitor for PTLDS. Further efforts are required to address knowledge gaps among healthcare providers and improve recognition of atypical EM to support accurate and timely clinical decision-making.

## Case Report

A previously healthy 6-year-old girl presented to the emergency department with acute right lower limb pain, night awakenings, and refusal to bear weight. She had fever and a generalized maculopapular rash. She resided in a rural area with frequent exposure to farm animals.

Physical examination revealed a solitary target-like lesion with central clearing on the right thigh, measuring approximately 4 centimetres, consistent with atypical EM (Figure 1A). A mild, generalized, blanchable macular rash was also noted, without petechiae or purpura (Figure 1B). No swelling or erythema of the affected limb was observed. There was no clinical evidence of a distinct tick bite or an attached tick. Neurological examination findings were unremarkable

Laboratory studies showed elevated C-reactive protein and erythrocyte sedimentation rate, with normal complete blood count (Table 1). Radiographic and ultrasonographic evaluation of the right lower limb were unremarkable. Further diagnostic investigation revealed that renal function and hepatic function were within normal limits, with no evidence of hepatocellular injury. Additionally, electrocardiogram and cardiac enzymes were also normal. *Streptococcus pyogenes* was not detected on throat swab, and nasal swab was negative for respiratory viruses. Blood culture was also negative. Serologic tests ruled out acute infections due to *Toxoplasma gondii*, *Epstein-Barr* virus and parvovirus B19. There was evidence of previous contact with cytomegalovirus, but no active infection. Test for human immunodeficiency virus and were negative. However, serologic testing was positive for *Borrelia burgdorferi* IgM and was confirmed by Western blot, showing reactivity to Outer Surface Protein C (OspC) band, according to the manufacturer's interpretation criteria (Table 1).

The patient was started on oral doxycycline and showed progressive symptom improvement. She remained afebrile after 48 hours, with resolution of the exanthem within 10 days, followed by palmar and plantar desquamation. She has been under follow-up for the past 15 months, reporting occasional lower limb arthralgia, without neurological complaints or need for medication.

## Discussion

This case illustrates early localized LD in a child with atypical EM and a generalized rash – a rare combination in paediatrics patients [4]. In most series, generalized rash concurrent with EM suggests early disseminated disease due to hematogenous spread [3]. The timely recognition of the lesion was crucial for diagnosis and initiation of the treatment.

EM is the hallmark of early LD and can appear within days to weeks after tick exposure. However, its morphology is highly variable. In a recent prospective study, only 6% of EM lesions presented with the classic ring-within-a-ring configuration [10]. Most were oval, pink, homogenous plaques, frequently mistaken for cellulitis, insect bites, or contact dermatitis. In our patient, EM had an almost homogeneous colour and diamond-shaped borders, consistent with atypical EM morphology, which occurs in the majority of paediatric cases [2, 4]. Moreover, the present case adds to the limited literature describing the coexistence of EM and generalized maculopapular rash in children. Similar to a previous case reported, our patient developed a widespread exanthem in addition to a localized EM lesion. In both instances, systemic symptoms were present, and the diagnosis was confirmed by serology. However, in our case, the temporal overlap between the generalized rash and EM was more synchronous, whereas in the Banadyha case the exanthem preceded EM by several days [4]. Generalized maculopapular rash may represent a cutaneous hypersensitivity phenomenon or systemic immune response to *Borrelia* dissemination [3].

The pain and antalgic gait seen in this case, despite unremarkable imaging, are consistent with early LD-related musculoskeletal manifestations [3, 5]. Arthralgia and

migratory limb pain are common in the early stage and may precede arthritis. Different *Borrelia* species exhibit organotropism: *B. burgdorferi* is linked to arthritis and neurological symptoms, *B. garinii* to neurologic involvement, and *B. afzelii* to late cutaneous disease [3].

The diagnosis was supported by positive *B. burgdorferi* IgM and confirmatory Western blot. While serologic testing is standard, it is limited in early disease due to delayed seroconversion. Therefore, EM should be considered sufficient for clinical diagnosis and initiation of empirical therapy, especially in endemic areas. Treatment with doxycycline, though traditionally avoided in children under 8 years, is now considered safe for short courses in paediatric LD. Studies have shown no significant risk of dental discoloration or enamel defects when used appropriately [5].

While the patient improved with antibiotics, clinicians should be aware of the potential for PTLDS. Though less frequently reported in children than adults, persistent symptoms such as fatigue, myalgia, and neurocognitive disturbances have been documented. A recent paediatric study found that up to 22% of children reported lingering symptoms 6 months post-treatment, including concentration difficulties and musculoskeletal pain [6, 10]. The pathogenesis of PTLDS remains debated. Hypotheses include immune dysregulation, neuroinflammation, and antigen persistence. Notably, *Borrelia* peptidoglycan has been detected in synovial fluid of patients with Lyme arthritis months after bacterial eradication, suggesting persistent antigenic stimulation [8]. In conclusion, this case reinforces the diagnostic value of EM, including its non-classical morphologies. Clinicians should maintain high suspicion for LD in children with unexplained musculoskeletal symptoms and skin lesions, particularly in endemic regions. Prompt treatment can prevent progression, but continued surveillance is warranted due to the potential for PTLDS. Given these findings, children treated for LD who present with persistent musculoskeletal symptoms should be carefully monitored over time in a paediatric consultation. Management should focus on symptom control and functional recovery, with referral to paediatric rheumatology or infectious disease specialists when appropriate.

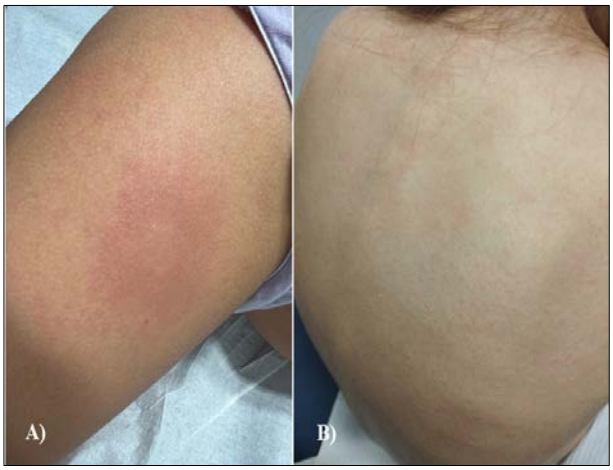


**Fig 1:** A) Atypical erythema migrans lesion on the lateral aspect of the right thigh, presenting as an almost homogeneous erythematous patch with diamond-shaped borders, lacking the classic ring-within-a-ring pattern. The lesion measured approximately 4 centimeters in diameter and was non-tender, without scaling or induration. B) generalized blanchable maculopapular rash involving the back, with no associated petechiae or purpura

**Table 1:** List of complementary diagnostic tests

| Test | Result | Reference Range |
|---|---|---|
| **Complete Blood Count** | | |
| Hemoglobin | 11.7 | 11.5 – 13.5 g/dl |
| Hematocrit | 34.3 | 34 – 40% |
| Leukocytes | 10700 | 5000 – 14500 /ul |
| Neutrophils | 8200 | 1500 – 8000 /ul |
| Lymphocytes | 1200 | 1500 – 7000 /ul |
| Platelets | 230000 | > 150000 /ul |
| Erythrocyte sedimentation rate | 62 | 1 – 20 mm/h |
| **Blood Chemistry** | | |
| Glucose | 105 | 74 – 106 mg/dl |
| Urea | 21 | 19 – 49 mg/dl |
| Creatinine | 0.4 | 0.24 – 0.41 mg/dl |
| Sodium | 135 | 135 – 145 mmol/l |
| Potassium | 3.7 | 3.5 – 5.1 mmol/l |
| Chloride | 106 | 98 – 107 mmol/l |
| Aspartate aminotransferase | 20 | < 50 U/l |
| Alanine transaminase | 19 | 7 – 40 U/l |
| Total Creatine Kinase | 68 | 34-145 U/l |
| Creatine Kinase - MB | < 0.18 | < 5 ng/ml |
| Troponin I | < 0.002 | < 0.045 ng/ml |
| Myoglobin | 14 | < 110 ng/ml |
| C-Reactive Protein | 22.80 | < 5 mg/l |
| Procalcitonin | 0.17 | < 0.05 ng/ml |
| Coagulation profile | | |
| International Normalized Ratio | 1.15 | 0.8 – 1.2 |
| Prothrombin Time | 13.6 | 8 – 14 seconds |
| Activated Partial Thromboplastin Time | 43.2 | 25 – 37 seconds |
| Microbiology | | |
| Hemoculture | Negative | - |
| Serologies | | |

| | | |
|---|---|---|
| Anti-Human Immunodeficiency virus I/II | Negative (0.072 index) | Negative: ≤ 1 index |
| | | Positive: ≥ 1 index |
| Treponemal test – *Treponema pallidum* | Negative (0.14 index) | Negative: ≤ 1 index |
| | | Positive: ≥ 1 index |
| IgG *Borrelia burgdorferi* | Negative (<5.0) | Negative: < 9.0 EU/ml |
| | | Equivocal: 9.0-11.0 EU/ml |
| | | Positive: > 11.0 EU/ml |
| IgM *Borrelia burgdorferi* | Positive (40.58) | Negative: < 9.0 EU/ml |
| | | Equivocal: 9.0-11.0 EU/ml |
| | | Positive: > 11.0 EU/ml |
| IgG *Borrelia burgdorferi Western blot* | Negative (0 index) | Positive: each band (OspC/p23, p39, p41) positive if index ≥ 6 |
| IgM *Borrelia burgdorferi Western blot* | Positive (OspC – 8 index) | |
| IgG *Toxoplasma gondii* | Negative (< 0.5) | Negative: < 6.4 UI/ml |
| | | Equivocal: 6.4-9.9 UI/ml |
| | | Positive: > 10 UI/ml |
| IgM *Toxoplasma gondii* | Negative (0.4 index) | Negative: < 0.90 |
| | | Equivocal: 0.90-0.99 |
| | | Positive: > 1 |
| IgG Cytomegalovirus (CMV) | Positive (25.82 index) | Negative: < 0.9 |
| | | Equivocal: 0.9-1.1 |
| | | Positive: > 1.1 |
| IgM CMV | Negative (0.52 index) | Negative: < 0.9 |
| | | Equivocal: 0.9-1.1 |
| | | Positive: > 1.1 |
| IgG Epstein-Barr virus (EBV) Early Antigen | Negative (<< 5.00) | Negative: < 5 U/ml |
| | | Equivocal: 5–10 U/ml |
| | | Positive: > 10 U/ml |
| IgG EBV Viral Capside Antigen | Negative (<< 10.00) | Negative: < 20 U/ml |
| | | Equivocal: 20–40 U/ml |
| | | Positive: > 40 U/ml |
| IgM EBV Viral Capside Antigen | Negative (<< 10.00) | Negative: < 20 U/ml |
| | | Equivocal: 20–40 U/ml |
| | | Positive: > 40 U/ml |
| IgG EBV Nuclear Antigen | Negative (<< 3.00) | Negative: < 5 U/ml |
| | | Equivocal: 5–20 U/ml |
| | | Positive: > 20 U/ml |
| IgG parvovirus B19 | Negative (<< 0.10) | Negative: < 2.00 UI/ml |
| | | Doubtful: 2.00 – 2.49 UI/ml |
| | | Positive: > 2.49 UI/ml |
| IgM parvovirus B19 | Negative (<< 0.10 index) | Negative: < 0.9 |
| | | Doubtful: 1 - 1.1 |
| | | Positive: > 1.1 |
| Antigen-based nasal swab | | |
| Syncytial respiratory virus | Negative | - |
| Influenza A | Negative | - |
| Influenza B | Negative | - |
| Parainfluenza 1 | Negative | - |
| Parainfluenza 2 | Negative | - |
| Parainfluenza 3 | Negative | - |
| Adenovirus | Negative | - |
| Metapneumovirus | Negative | - |
| SARS-CoV-2 | Negative | - |
| Coronavirus OC43 | Negative | - |
| Antigen-based throat swab | | |
| *Streptococcus pyogenes* | Negative | - |

## Conclusion

Early identification of LD in children hinges on recognizing EM, including its atypical forms. In endemic areas, clinicians should maintain a high index of suspicion for LD in paediatric patients with unexplained musculoskeletal complaints and skin lesions, even when typical features are absent. In this case, prompt clinical diagnosis and treatment led to rapid resolution and prevented disease progression. Given the potential for persistent symptoms such as arthralgia, long-term follow-up remains essential.

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