

A Malignant Itch

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We report an unusual presentation of a previously healthy three-year-old Chinese girl with a four-week history of apparently unexplained generalized intense itch. She had no past history of atopy or xerosis. Despite the severe itch, she had only minimal scratch marks on her right gluteal region but no flexural involvement. The girl was treated as having scabies and eczema and with oral antihistamines by various dermatologists without much improvement. She subsequently presented to a regional hospital with right hip pain and fever. Radiological and histopathological investigations confirmed that she had a peripheral T-cell lymphoma. The itch pattern prior to and following chemotherapy, as documented by the DigiTrac wrist-held movement monitor, showed a dramatic reduction of her nocturnal itch. The pattern was also very different from that of atopic dermatitis in that the scratching was of much higher intensity but lower frequency. Intractable pruritus associated with a peripheral T-cell lymphoma has not been previously reported in the pediatric literature. This report serves to alert clinicians of the gold paradigm that in a patient with an unexplained generalized itch, lymphoma and other malignancies must be considered.

Key words: itch ■ lymphoma ■ malignancy

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INTRODUCTION

It is a well-known paradigm that malignancies, among other differential diagnoses, must be considered in any patients with a generalized itch of recent onset.¹ This consideration is especially important if the patient does not have an apparent rash to account for the symptom. We report a previously healthy young girl with a recent-onset, apparently unexplained, generalized intense itch who was subsequently diagnosed as having a peripheral T-cell lymphoma. To our knowledge, intractable pruritus associated with a peripheral T-cell lymphoma has not been reported in children.

CASE REPORT

A previously healthy three-year-old Chinese girl presented with a four-week history of generalized intense itch without a rash. She had no past history of atopy or dryness of the skin. There was no history of night sweats. She was treated as having scabies by one dermatologist and atopic dermatitis by another who gave her various antihistamines such as chlorpheniramine and cetirizine. There was not much improvement. She developed an antalgic gait and was taken to see a bone setter. She subsequently presented with right hip pain (for 10 days) and fever (for three days) to a regional hospital.

Radiologic study at the regional hospital revealed multiple osteolytic lesions with fracture in the right femoral neck. She was initially treated as osteomyelitis with intravenous penicillin and cloxacillin. Bone marrow biopsy revealed the presence of abnormal lymphoid infiltration with medium-to-large lymphoid cells showing irregular nuclei, stippled chromatin and small nucleoli. The atypical lymphoid cells (CD3, CD8 positive and CD4 negative) were positive for LCA, CD5, MT1 (CD43), Fli-1; and negative for TdT, CD34, CD15, CD20, CD79a, CD30, ALK-1, CD56, CD57 and TIA. The histopathologic findings confirmed that she had a peripheral T-cell lymphoma. She was then referred to the pediatric oncology unit of a teaching hospital for further management.

Upon examination at the teaching hospital, the patient was febrile (38.2°C) but hemodynamically stable. Her weight was 14 kg (50th percentile) and height 95.3 cm (50th percentile). Despite the intense itch, as evident by onycholysis involving half of her left index finger (Figure 1), there were only a few scratch marks over the ears and buttocks, and there was no flexural involvement. There was a 3x2-cm soft-tissue swelling over the right temporal region, a subconjunctival hemorrhage in the right eye, and a few shotty lymph nodes in the cervical and inguinal areas. Liver edge was 1 cm below the right costal margin, and the spleen was not palpable. She refused to bear weight on the right leg. There was no swelling or tenderness in the right hip, but the range of movement was generally decreased at the right hip. Her hemoglobin level was 10.6 g/dL, white cell count $4.3 \times 10^9/L$ with a normal differential, and

platelet count $393 \times 10^9/L$. The peripheral blood smear did not reveal any blast cells. Her renal and liver functions were normal. Her C-reactive protein (5.5 mg/l), serum urate (0.23 mmol/l) and serum alkaline phosphatase (80 IU/l) were normal, but ESR (40 mm/hr), serum phosphate (1.46 mmol/l) and serum lactate dehydrogenase (3,040 U/l) were elevated. Computerized tomography (CT) and triphasic skeletal scintigraphy revealed a large nonhomogeneous anterior mediastinal mass (4.5x5.5 cm) and multiple lytic lesions involving the right skull base, left mandible, right femoral head, right fourth rib and left sacrum. CTs of the abdomen and pelvis were normal.

The patient was treated with chemotherapy as per the protocol for acute lymphoblastic leukemia ALL IC-BFM 2002 High Risk Group. The itch pattern prior to and on day 6 following chemotherapy, as documented by the DigiTrac wrist-held movement monitor (IM Systems, Baltimore, MD),² showed a dramatic reduction of her nocturnal itch (Figures 2 and 3). Five weeks following chemotherapy, her bone marrow was clear of lymphomatous infiltration.

DISCUSSION

Systemic disease may be associated with generalized pruritus. In the adult population, the prevalence of the association ranges from 10–50%.^{1,3} In the pediatric age group, the prevalence of the association is not known but presumably a lot less common.¹ Systemic diseases associated with pruritus include iron deficiency anemia; hyper-

thyroidism; hypothyroidism; diabetes mellitus; hepatobiliary diseases; chronic renal failure; drugs (e.g., erythromycin estolate, phenothiazide, morphine, isoniazid); polycythemia rubra vera; leukemia; lymphoma; internal malignancy; and psychogenic causes (e.g., stress, anxiety disorder, psychosis).^{1,4} Delays in diagnosing a malignancy such as lymphoma may result in widespread dissemination and irreversibly loss of time for treatment.⁵

The DigiTrac monitor is a wrist-worn device for recording the frequency and amplitude of limb movements. In our pilot testing on 17 patients with atopic dermatitis, the DigiTrac provided essential data on a wide spectrum of frequencies of wrist movements and quantity of movements in term of acceleration or g values.⁶ We previously documented that wrist activities between 0–3 Hz for the first three hours of sleep are a

Figure 1. Onycholysis involving half of the left index finger nail



Figure 2. Average acceleration (g/min) activities at (A) baseline, (B) on day 6 following chemotherapy, and (C) a normal subject as reference. The vertical axis indicates the total amount of wrist activities as a g value, and the horizontal axis indicates the time and date when the movements occur.

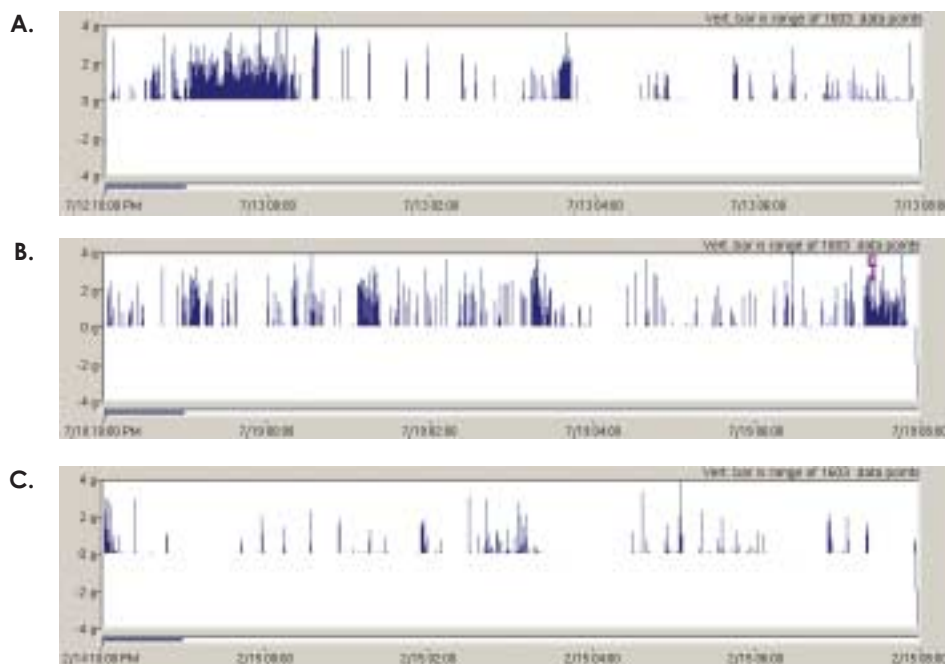
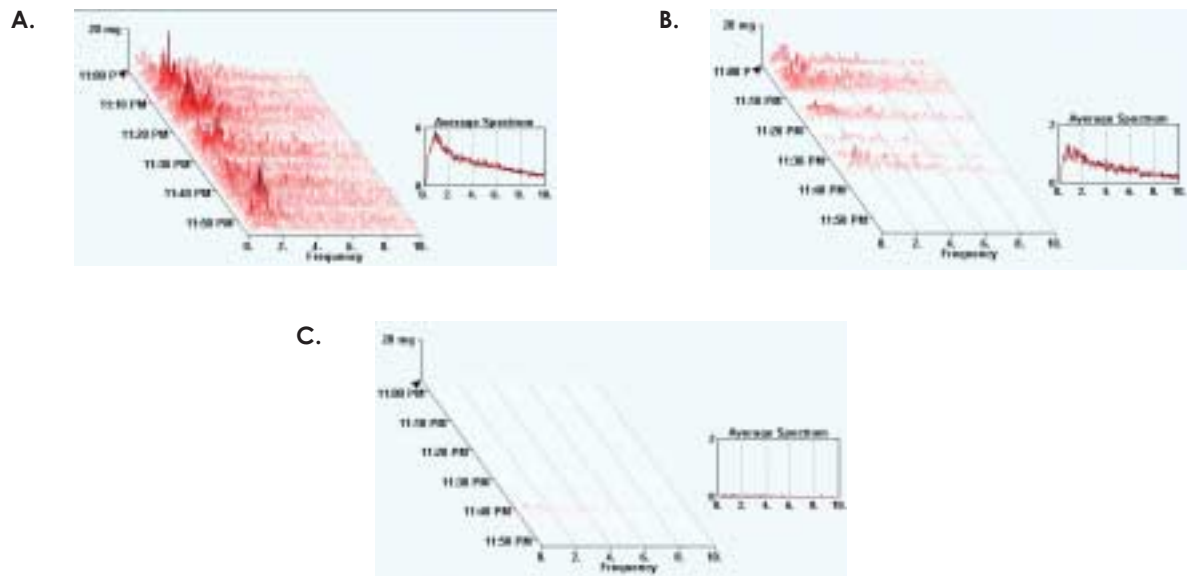


Figure 3. Frequency spectrum in the early hours of sleep at (A) baseline, (B) on day 6 following chemotherapy, and (C) a normal subject as reference. In the three-dimensional diagrams, the vertical axis represents the wrist activities as a g value, the horizontal axis indicates the frequency in Hz that the dominant hand scratches, and the remaining axis indicates the time when the movements occur. Note that most activities occur at 0–1 Hz.



good indicator of severity of atopic dermatitis, nocturnal itch and sleep disturbance in children.² We found that wrist activities in this patient, defined as average acceleration in the early hours of sleep, were especially intense in the first few hours of sleep at baseline (Figure 2). The intensity of these movements is even higher than that in patients with severe atopic dermatitis, with an average value of 223.63 ± 97.57 g/min (mean \pm standard error) for the first three hours vs. 84.47 ± 8.53 g/min for the group of 24 subjects with atopic dermatitis (unpublished data). The intensity decreased to 69.17 ± 9.93 g/min on day 6 following the initiation of chemotherapy. The frequency pattern also showed a dramatic improvement after chemotherapy. Most wrist activities are slow movements at 0–1 Hz. This is in striking contrast to the scratching activities at 0–3 Hz in subjects with atopic dermatitis. Interestingly, the itch was relieved by chemotherapy treatment for the underlying lymphoma but not by multiple antihistamines, implying that mechanisms other than histamine may be involved in the pathophysiology. Centrally acting mediators such as opiate-like endorphins and serotonins may have a role to play in the pathogenesis of generalized pruritus.¹

Peripheral T-cell lymphomas are a heterogeneous group of malignancies that result from clonal proliferation of postthymic T-cells.^{7,8} Peripheral T-cell lymphomas are very rare and are more common in Asians than Caucasians.^{7,8} The malignancies typically affect adult males, and children are very rarely affected.^{7,8} Affected adult patients may present with pruritus.⁷ The present report

demonstrates that peripheral T-cell lymphomas may present with pruritus in the pediatric age group.

Although atopic dermatitis is the most common cause of pruritus in children,⁹ this report serves to alert clinicians of the importance of considering the various differential diagnoses in the evaluation of a child with an unexplained generalized itch. This case also illustrates that DigiTrac may be clinically useful in confirming the diagnosis of significant itch as well as monitoring its intensity and frequency before and following treatments.

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