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Case Report

Concurrent Infections in an Obese Adolescent Girl with Chronic Immune Thrombocytopenia

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ABSTRACT

Introduction

Childhood immune thrombocytopenia (ITP) affects 5 in 100,000 children per year. It is an autoimmune disease associated with impaired platelet production as well as immune-mediated platelet destruction, resulting in low platelet counts. Approximately 20% pursue a chronic course, which is defined as a platelet count that has been < 10 $\times 10^9$/L for longer than 12 months, with some cases requiring long-term immunosuppressive therapy, resulting in a greater risk of infectious complications.

Case Presentation

A 14-year-old, obese adolescent girl with chronic immune thrombocytopenic purpura, treated with a combination of dexamethasone, vincristine, and elthrombopag, presented with a 7-day history of acute fever and left hip pain, which was caused by infections from three different pathogens: (1) left hip with septic arthritis caused by Citrobacter freundii, (2) urinary tract infection caused by Escherichia coli and (3) typhoid fever caused by Salmonella typhi. The left purulent hip was operatively drained along with broad-spectrum intravenous antibiotic treatment for 3 weeks, after which the patient's condition significantly improved.

Conclusion

Children with chronic ITP who undergo long-term immunosuppressive therapy are prone to the risk of serious concurrent infections by different pathogens, as shown in our case in an obese pediatric patient in which obesity is known to be related to osteoarthritis in weight-bearing joints, but the actual risk is not well studied and needs further observational evidence.

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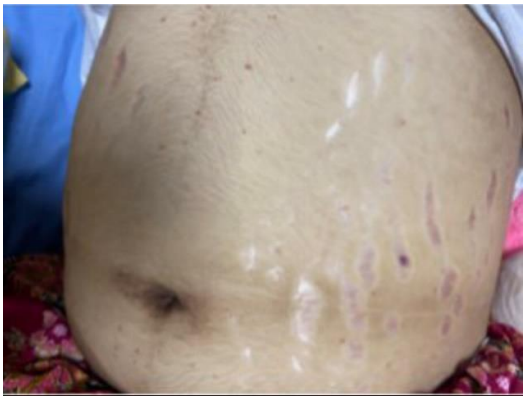
Introduction

Childhood immune thrombocytopenic purpura (ITP) is an isolated thrombocytopenia that is secondary to increased destruction of platelets by macrophages in the reticuloendothelial system (RES), particularly the spleen, resulting in the formation of antibodies against platelets in response to a viral illness [1]. Approximately 20% pursue a chronic course, which is defined as a platelet count that has been < 10 $\times 10^9$/L for longer than 12 months, with some patients requiring long-term immunosuppressive therapy, which can be prone to bacterial infection complications. In addition, obesity can have a marked effect on hip arthritis and osteoarthritis [2]. Here, we report the case of an obese adolescent girl who consequently developed severe concurrent infections caused by several different pathogens following long-term treatment with combined immunosuppressive drugs for chronic immune thrombocytopenia. The objective of this presentation is to share the risk factors for this case and the success of a quick diagnosis and accurate management.

Case presentation

A 14-year-old girl presented with a 7-day history of intermittent fever and vomiting several times accompanied by progressive left hip pain associated with restricted movement. Therefore, the patient was admitted to our Department of Pediatric Hematology, Immunology and Transfusion Medicine, National Pediatric Hospital (NPH).

Physical examination revealed that the patient was febrile (38.4°C), tachycardic (120 bpm), and experienced painful flexion and extension of the left hip. There was no evidence of organomegaly, distal neurovascular deficit, rashes, or skin lesions except for stretch marks on the abdomen **(Figure 1)** and acanthosis nigricans **(Figure 2)**. The eye examination was unremarkable. Her medical history was otherwise notable for obesity, with a weight of 90 kg and a BMI of 34.3 kg. Her past medical history revealed a diagnosis of chronic immune thrombocytopenic purpura. She is currently being treated with a combination of dexamethasone, vincristine, and elthrombopag. There was no history of trauma.



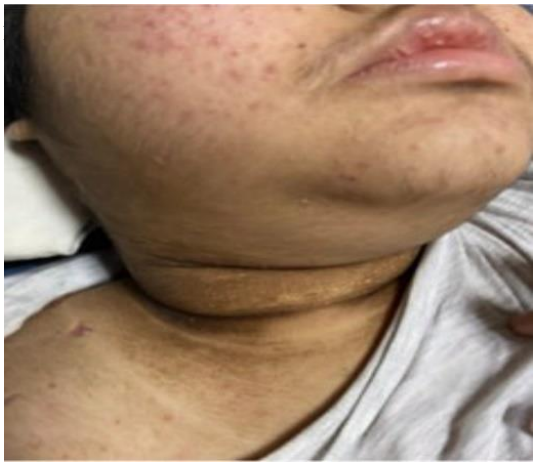
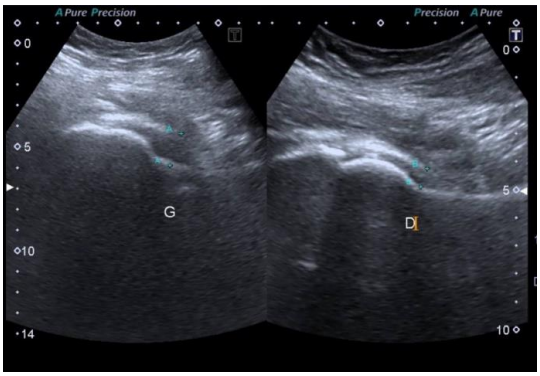


Figure 2: Acanthosis nigricans.

Laboratory and imaging findings

The initial laboratory findings were as follows: white blood cells (WBCs) 13.6×10^9/L (neutrophils: 11.83×10^9/L, lymphocyte count of 1.22×10^9/L), hemoglobin of 9 g/dl, normal glycated hemoglobin (HbA1c) of 5.4%, platelet count of 81×10^9/L, erythrocyte sedimentation rate (ESR): 80 mm/hour and C-reactive protein (CRP): 12 mg/dL. Serum urea and creatinine were increased to 62 mg/dL and 1.8 mg/dL, respectively. The thyroid stimulating hormone (TSH) level was increased to 6.6 µIU/mL (range: 0.35-5.1), the normal free T4 level was 1.19 ng/dL (range: 0.5-1.4), and the normal free T3 level was 3.42 pg/ml (range: 1.8-4.2). The electrolyte levels and liver function test results were within normal ranges. The urinalysis revealed bacteria 1+, red blood cells (RBC) > 100/HPF, and WBC 38/HPF. In addition, X-ray of the left hip revealed no bone/joint abnormalities, whereas ultrasound revealed an intra-articular collection of approximately 16 mm (**Figure 3**).

The clinical assessment of functional left hip limitations, pain, fever, elevated ESR, CRP and increased leucocyte count suggested a diagnosis of septic arthritis. Initially, she was referred to the surgery department for surgical intervention after urine and blood were collected for microbiological culture.



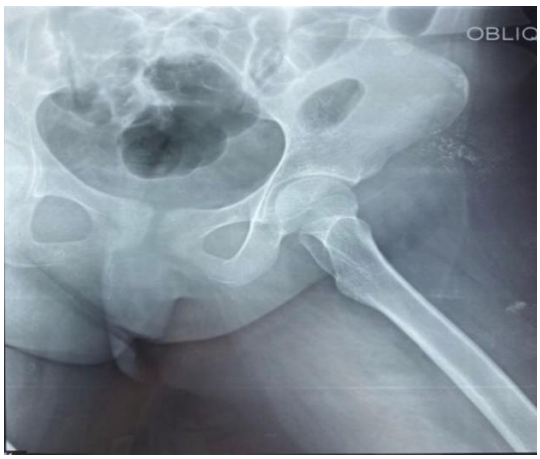


Figure 3: Intra-articular collection of images of the left hip joint (by ultrasound and X-ray)

Treatment

An urgent decision was made for surgical arthrotomy and debridement by a team of pediatric surgeons on 03 February 2024. The aspirational intra-articulation of the hip joint was performed and confirmed with bloody-purulent fluid, which was also sent for microbiological culture (Figure 4). An incision was carefully made through the articular capsule, which was then cleaned with normal saline mixed with diluted betadine and subjected to skin traction to prevent flexion and internal rotation. Antibiotic tri-therapy, namely, ceftriaxone, gentamycin and ciprofloxacin, was intravenously indicated.

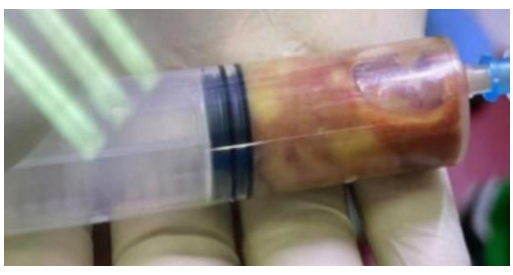


Figure 4: Blood-purulent fluid from the left hip joint

The results of the culture of the purulent fluid showed a facultative anaerobic gram-negative bacillus (Citrobacter freundii) was susceptible to the current treatment. The patient's clinical condition remained stable after surgery, but the fever continued. The blood culture showed Salmonella typhi, and the urine culture revealed Escherichia coli **(Table 1)**.

Left purulent drainage of the hip joint was continued along with broad-spectrum intravenous antibiotic therapy. Three weeks later, the patient's condition significantly improved, and traction was removed. The patient was discharged and instructed to continue oral ciprofloxacin and cloxacillin for 3 more weeks. The subclinical hypothyroid was initially treated with levothyroxine.

Table 1. Pathogens and susceptibility

Specimens	**Pus culture**	**Urine culture**	**Blood culture**
Pathogens	***Citrobacter freundii***	***Escherichia coli***	***Salmonella typhi***
Susceptibility			
Ceftriaxone	S	S	S
Gentamicin	S	S	–
Ciprofloxacin	S	S	S
Ceftazidime	S	S	–
Trimethoprim/Sulfamethoxazole	S	S	S
Amoxicillin/Clavulanic Acid	S	–	–

Progression of follow-up

The patient was regularly followed up for both clinical and hematological progression. The immunosuppressive drugs were discontinued during antibiotic treatment, and thereafter, the platelet counts progressively and spontaneously increased during infection from 81×10^9/L to 861×10^9/L and then declined to 250×10^9/L after a 4-month period following the infection (**Table 2)**. To date, the patient has recovered well and is in excellent condition.

Table 2. Variation of platelet counts and HbA1C prior to surgical intervention and thereafter

Date	**Platelet count** $\times10^9$/L	**HbA1c (%)**
31/01/2024	171	-
02/02/2024	105	-
03/02/2024	**81 – Surgical intervention**	
09/02/2024	592	-
14/02/2024	**861**	5.40
22/02/2024	713	-
03/03/2024	766	-
10/05/2024	564	-
17/06/2024	**250**	3.21

Discussion

Septic arthritis in the pediatric hip joint is relatively rare, with an incidence of 1–10 in 100,000 individuals and is considered an orthopedic emergency. It has 3 sources: hematogenic spread, direct inoculation and spread from adjacent tissue [3]. This condition can lead to permanent damage to the joint if it is not treated promptly and effectively. Early diagnosis and treatment are crucial for avoiding long-term complications. The case reported two interesting aspects of this uncommon condition.

First, septic arthritis is often secondary to the hematogenic spread of bacteria from other locations, but in our case, there was no apparent primary source. The pathogen isolated from the aspirated pus of the affected hip was different from that isolated from the blood and urine cultures.

Second, septic arthritis is more prevalent among individuals with a weakened immune system, joint problems, or certain medical conditions [4]. Additionally, weight load due to obesity is another risk that places an excess load on the hip joints and leads to hip osteoarthritis [5].

Corticosteroids are known as the main immunosuppressants associated with severe infections in patients with ITP who are exposed to long-term treatment [6]. Our patient was an obese child with chronic ITP who was under long-term use of immunosuppressive therapy, such as dexamethasone and vincristine, which seem to be risk factors for serious concurrent infections caused by three different pathogens.

To date, the recommended treatment for septic arthritis, including antibiotics and surgical debridement of the inflammatory tissue, is to administer culture-specific intravenous antibiotics for seven days and then switch to oral antibiotics for two to three weeks [7]. To treat typhoid fever due to Salmonella typhi and urinary tract infection due to Escherichia coli, the choice of antibiotics is generally based on susceptibility. In our case, those 3 pathogens were susceptible to similar antibiotics.

Being overweight is known to be an independent risk predictor for type 2 diabetes mellitus [8]. In addition to weight load, the presence of acanthosis nigricans potentially caused by insulin resistance is a warning signal to indicate potential prediabetic states that increase the likelihood of developing type 2 diabetes mellitus. However, these two indications in our obese patient were not consistent with her normal levels of HbA1c during the two successive follow-ups over the past 1.5 years.

The latest report by Aggarwal et al. demonstrated that thyroid dysfunction was present in approximately 25.7% of children aged more than 12 years with ITP (25.7%). Among these patients, 16.4% (21/128) presented with hypothyroidism, 7.0% (9/128), and subclinical hypothyroidism [9] since we detected increased TSH with normal free T4. The role of glucocorticoids, estrogens and systemic illness (acute/chronic) can probably alter the levels of thyroid hormones, including T4 and TSH [9].

The unexpected thrombocytosis, which declined to normal levels after antibiotic therapy, was probably due to an infection event. It may also have been a response to the combined course of high-dose dexamethasone and vincristine.

Conclusion

Long-term treatment with combined immunosuppressive drugs for chronic ITP in obese patients is prone to serious concurrent infections, such as typhoid fever, urinary tract infection, and septic arthritis of the hip joint. Being vigilant with patients showing these risk factors can lead to a correct diagnosis and timely management. The key success of treatment for our patient is the collaboration between orthopedic surgeons and hematologists.

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Author Contributions

The manuscript was written by Try Lytheang and Long Laiya, and revised by Lam Pechkethia, Robyn Devenish and Chean Sophâl. All the authors have read and approved the final manuscript.

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Declaration: Informed consent was provided to a child's parents as they agreed to the case publication.

Competing interest: The authors declare that they have no competing interests.

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