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Case Report

Pediatric Multicentric Castleman Disease Presented with Spontaneous Tumor Lysis Syndrome and Acute Kidney Injury

Alqahtani MF[1]*, Liedel JL[1], Pott T[1], Miles L[3], Douglas D[2], Nagasubramanian R[2] and Kahana MD[1]

[1]Department of Pediatric Critical Care, Nemours Children's Hospital, Orlando, FL; USA

[2]Department of Pediatric Hematology & Oncology, Nemours Children's Hospital, Orlando, FL; USA

[3]Department of Pathology, Nemours Children's Hospital, Orlando, FL; USA

***Corresponding author:** Alqahtani MF, Department of Pediatric Critical Care, Nemours Children's Hospital, 6535 Nemours Pkwy, Orlando, Florida, USA

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Abstract

Castleman disease (CD) is a rare lymphoproliferative disorder that is uncommon in the pediatric population. Tumor lysis syndrome (TLS) is a rare presentation in CD even after chemotherapy. There is only one case report for pediatric patients with CD where treatment was complicated by TLS. In this case, we report spontaneous TLS and acute kidney injury in a pediatric patient with idiopathic multicentric Castleman disease.

Here, we present the case of a 14 year old male with no significant past medical history presented with TLS and AKI (Acute kidney injury). He was found to have idiopathic multicentric CD (iMCD) based on lymph node biopsy. The child was started on Siltuximab and high systemic steroid therapy with significant improvement. A short term continuous renal replacement therapy was required for fluid overload. The patient was discharged home within a month with normal renal function on maintenance therapy.

Spontaneous TLS is a rare but significant complication that should be considered in adults and pediatric patients with MCD. Careful monitoring and immediate intervention with supportive care are essential even before the initiation of therapy.

Keywords: Idiopathic Multicentric Castleman Disease; Castleman Disease; Tumor Lysis Syndrome; Pediatric Critical Care; Continuous Renal Replacement Therapy; Siltuximab

Abbreviations

AKI: Acute Kidney Injury; CD: Castleman Disease; CT: Computerized Tomography; CRRT: Continuous Renal Replacement Therapy; HHV-8: Human Herpesvirus-8; HIV: Human Immunodeficiency Virus; iMCD: Idiopathic Multicentric Castleman Disease; IL-6: Interleukin-6; MCD: Multicentric Castleman Disease; POEMS: Plasma Cell Neoplasm Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Plasma Cell Disorder, and Skin Changes Syndrome; PICU: Pediatric Intensive Care Unit; TLS: Tumor Lysis Syndrome; UCD: Unicentric Castleman Disease.

Case Presentation

A 14 year old male was referred from an outside hospital with a chief complaint of abdominal pain and distention for two weeks. Past medical history was significant for attention deficit hyperactive disorder on Risperidone, Methylphenidate, and Guanfacine. Vital signs on admission were unremarkable; blood pressure 117/66 mmHg, temperature 37.2°C, pulse rate 76 Beats/min, and respiration rate 21 Breaths/min. His physical examination was significant for abdominal distension, mild generalized tenderness without guarding or rebound, and no appreciable hepatomegalyor splenomegaly. Two mobile, non-tender lymph nodes, one in the right deep cervical area and the other in the right axillary lymph node, both approximately one centimeter, were palpable.

Initial laboratory studies were performed at admission revealed thrombocytosis and evidence of acute kidney injury (AKI) and TLS (Table 1). The patient was admitted to the pediatric intensive care unit (PICU) for presumed tumor lysis secondary to an unknown malignancy complicated by AKI. Treatment for TLS was begun, and additional evaluation for malignancy was started. Chest X-ray revealed only a small pleural effusion. The abdominal ultrasound was significant for hepatosplenomegaly and moderate ascites (Table 2).

On hospital day 1, the patient underwent paracentesis, which resulted in 1500mL of serous straw-colored fluid with no evidence of malignancy by cytologic examination. Bone marrow biopsyruled out a myelodysplastic process, including leukemia. On hospital day 2, computerized tomography (CT) of the chest, abdomen, and pelvis showed diffuse lymphadenopathy involving the supraclavicular, axillary, mediastinal, peritoneal, retroperitoneal, and bilateral inguinal regions. Additionally, it showed worsening bilateral pleural effusions, massive abdominal ascites, diffuse body wall edema, and mild hepatosplenomegaly (Figure 2). No focal mass was identified on CT. Noninvasive positive pressure ventilation and peritoneal drain were required due to worsening ascites and pulmonary edema. On hospital day 3, the patient underwent axillary lymph node biopsy. The lymph node contained uniform follicleswevenly dispersed in the cortex and medulla. Many atrophic geminal centers were penetrated by a blood vessel. There was no evidence of significant plasma cell infiltration. The final diagnosis of Castleman disease (CD), hyaline-

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Table 1: Complete blood count during admission and serology.

White blood cellK/UL	Hemoglobin g/dL	Platelet Count	Serology	Hospital Day
11	12	776		1
12	10	428	HHV8 and HIV negative	8*
9	10	443		12**
26	9.5	303		29 ***

*start of IL6 and methylprednisolone
**start of CRRT
***discharge date

Table 2: Chemistry profiles during admission.

Potassium	Phosphorous	Uric acid	Urea	Creatinine	Ionized Calcium	Albumin	Hospital Day
7.3	7.5	15.4	59	2.5	1	2.3	1
4	5.5	2.4	37	1.2	0.93	3.5	8*
3	5.7	4.6	75	1.4	1.05	3	12**
4.3	4.9	5.3	25	0.4	1.2		29***

*start of IL6 and methylprednisolone
**start of CRRT
***discharge date

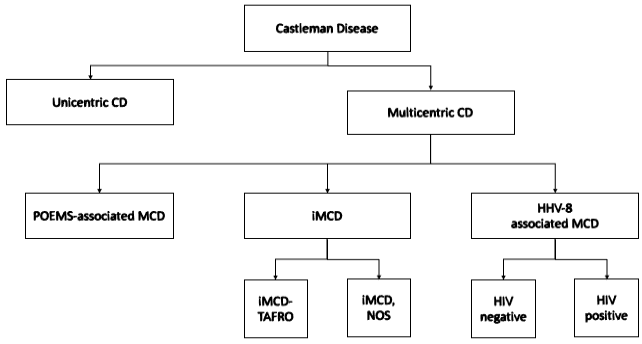

Figure 1: Classification of Castleman Disease.
Monoclonal plasma cell disorder, Skin changes (POEMS) syndrome, Idiopathic MCD (iMCD), iMCD–not otherwise specified (iMCD-NOS). iMCD–Thrombocytopenia, Ascites, Reticulin Fibrosis, Renal dysfunction, Organomegaly (iMCD-TAFRO).

vascular type was made (Figure 3). At this point, more labs were performed to classify CD and to help with the selection of targeted therapy, mainly interleukin-6 (IL-6) and HHV-8.

On hospital day 8, the HHV-8 result was negative, and IL-6 was elevated at 8.1pg/mL, therefore the patient was classified as severe idiopathic multicentric CD (iMCD). Treatment was started based on the international, evidence-based consensus treatment guidelines [1], which recommends Siltuximab, an IL-6 monoclonal antibody, 11mg/kg weekly dosing and high dose methylprednisolone 500 mg for 7 days. On day 12, a dialysis catheter was placed, and the patient was started on continuous renal replacement therapy (CRRT) due to worsening renal function and fluid overload refractory to maximum diuretic therapy. Siltuximab was continued weekly, and methylprednisolone was weaned. CRRT was stopped on hospital day 16 (8 days after initiation of immunotherapy) as renal function improved. Three weeks following the initiation of therapy, his lab results were normal, and ascites was improved, allowing for removal of the dialysis catheter and peritoneal drain. On day 25of admission, he was transferred to the hematology/oncology service for continued

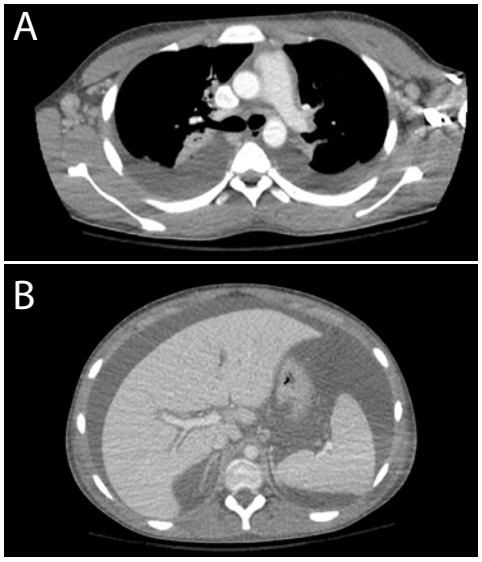

Figure 2: CT scan images for the chest shows bilateral axillary lymph nodes (A). CT abdomen with hepatosplenomegaly and ascites (B).

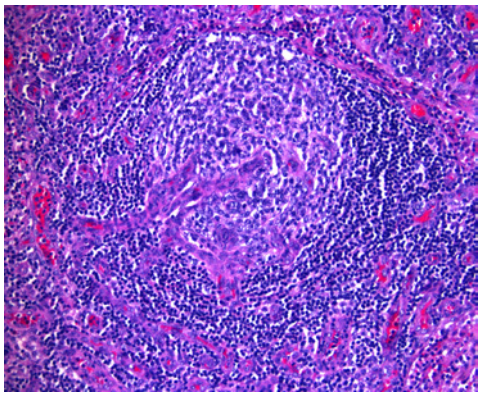

Figure 3: Cross section for axillary lymph node.
Section from the axillar lymph node revealed a radially penetrating blood vessel in an atrophic geminal center.

management. On hospital day 29, the patient was discharged home. He had received four doses of Siltuximab and one week of high dose methylprednisolone. The patient has remained in remission with maintenance therapy of Siltuximmabevery three weeks and daily prednisone.

Discussion and Conclusion

Castleman disease is a rare lymphoproliferative disorder that is uncommon in the pediatric population [2]. CD was initially described by Dr. Castelman in the 1950s. Most recently, it was subdivided into different categories based on centricity and HHV8 infection [3]. CD exists along a clinical spectrum with 4 distinct presentations (Figure 1) [3,4]. Each category of CD has different etiology, presentation, treatment, and outcome. The most common type of CD seen in pediatric patients is Unicentric CD (UCD) [5]. It involves a single enlarged lymph node or multiple lymph nodes in the same region. Multicentric CD involves lymph nodes in different regions. There are 3 types of Multicentric CD (MCD): associated with

human herpesvirus-8 (HHV-8), idiopathic, and POEMS (plasma cell neoplasm polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes syndrome) [3]. Most pediatric patients with MCD are HHV negative [5], since HHV8-MCD is most associated with immunocompromised conditions, especially human immunodeficiency virus (HIV).

Treatment options are specific depending on the type of CD. For patients with UCD, treatment options include surgical resection, steroids, and radiotherapy. Whereas for MCD, tocilizumab, rituximab, anakinra, steroids, chemotherapy, and splenectomy are indicated. Tumor lysis syndrome (TLS) is most commonly associated with hematological malignancy after chemotherapy. Rarely, it occurs spontaneously after CD treatment. Reports of TLS in CD patients post chemotherapy are rare in the literature [6-8].

After a thorough review of the literature, we could identify only four case reports of tumor lysis syndrome with Castleman disease [6-8]. Only one of these occurred in a child. There are two adult cases with spontaneous TLS with MCD, one in an HIV seropositive patient and another in an HIV-negative patient [7,8]. In the pediatric report, the child developed TLS after starting a high-dose parenteral steroid for MCD [9]. In contrast, our patient initially presented with spontaneous TLS, which was the catalyst for the development of AKI and fluid overload state. This was prior to a diagnosis or any therapy. This case illustrates the successful treatment of iMCD with an accelerated Siltuximab protocol and high dose methylprednisolone [1]. Initially, electrolytes derangement from TLS were treated, and ascitic fluid was removed until a definitive diagnosis emerged. AKI and fluid overload required CRRT for a short period of time, ultimately allowing kidney function to return to normal.

This case represents a rare pediatric disease with a similarly rare complication. The initial presentation with spontaneous tumor lysis syndrome is unique. Close laboratory monitoring for TLS is warranted as soon as the diagnosis is made, even before therapy is initiated to prevent renal failure and fatal arrhythmia. Early initiation of supportive therapy can clearly result in a favorable outcome.

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