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# Intra-abdominal mass and iron deficiency anemia in a 15-year-old boy: Case report and literature review



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## ABSTRACT

Castleman's disease is rare lymphoproliferative disorder that typically presents as a mediastinal mass, although 10% of cases may be intra-abdominal. Given its rarity, diagnosis is often delayed until other pathology has been ruled out. We present the case of a 15-year-old boy with a one-year history of progressive fatigue, failure to thrive, and severe iron resistant, iron deficiency anemia. Extensive work-up revealed an intra-abdominal mass. At laparotomy, a discrete lymphoid-appearing mass was found at the base of the mesentery. Excision led to rapid and complete resolution of his symptoms, including resolution of anemia. Pathology demonstrated Castleman's disease of the hyaline vascular subtype. Increased awareness of this entity and its association with severe iron deficiency anemia through the overproduction of IL-6 may allow earlier detection and treatment.

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Castleman's disease is an uncommon lymphoproliferative disorder that may present with B-symptoms, failure to thrive, rashes, hepatosplenomegaly, and anemia. We present the case of a 15-year-old boy with Castleman's disease who presented with severe iron deficiency anemia refractory to oral iron replacement therapy. A literature review is presented reviewing the pathogenesis of Castleman's disease and its association with IL-6 and hepcidin induced iron deficiency anemia.

## 1. Case report

A 15-year-old boy was referred to the Children's Hospital at London Health Science Center (LHSC) with a history of severe iron deficiency anemia unresponsive to oral iron replacement therapy. Two months previously he had presented to his community pediatrician complaining of fatigue. He was diagnosed with iron deficiency anemia and started on oral iron replacement therapy. He subsequently presented to his local emergency department with testicular pain diagnosed as orchitis. During assessment, bloodwork revealed a hypochromic microcytic anemia with a hemoglobin of 68 g/L despite 2 months of oral iron therapy. The

patient was transferred our Children's Hospital for further inpatient work-up.

At the time of referral, the patient reported significant failure to thrive with less than 2 kg of weight gained over the past 6 years and a current weight of only 29 kg. This was accompanied by progressive fatigue, anorexia, pallor and exertional dyspnea over the past year. No other symptoms were reported including no gastrointestinal symptoms or blood loss.

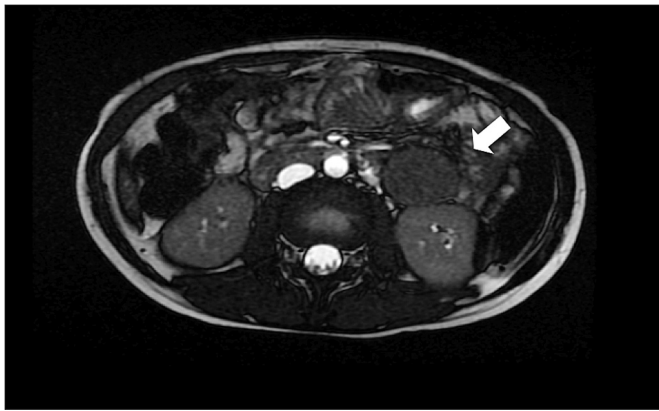
On physical exam the patient was noted to have chronic low-grade fevers. He was pale and quite thin weighing in below the 3rd percentile for age, with a BMI of 14.9 and tanner stage 2 pubertal development. No lymphadenopathy or other anomalies were noted.

Laboratory investigations revealed a hypochromic microcytic anemia with a hemoglobin of 68 g/L. White blood cell count was normal at 6.9/L with elevated platelets of 548/L. Serum iron was low at 3  $\mu\text{mol/L}$ . ESR and CRP were abnormally high at 101 mm/h and 161 mg/L respectively, while albumin was low at 28 g/L with a pre-albumin of <0.07 mg/dL. Electrolytes, renal and liver function tests were all within normal limits.

The patient was admitted to hospital for inpatient assessment by the general pediatrics team. Consultations were made to hematology, oncology, endocrinology, rheumatology, infectious disease, psychiatry, and gastroenterology. An extensive work-up followed and 2 courses of intravenous iron were administered with mild improvement in his hemoglobin to 73 g/L. Upper endoscopy and colonoscopy failed to identify any gastrointestinal blood loss or other diseases. Subsequently the patient underwent magnetic resonance enterography (MRE) and capsule endoscopy to assess for small bowel lesions. MRE revealed a homogenous ovoid mesenteric mass (Fig. 1).

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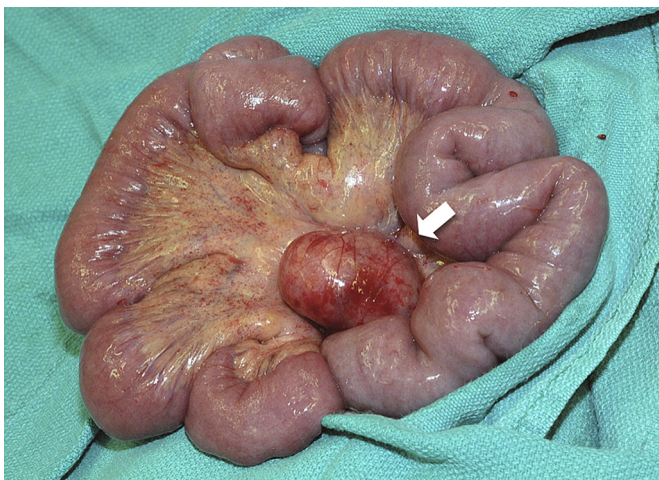
**Fig. 1.** MRE demonstrating an enlarged mesenteric lymph node [arrow] representing an intra-abdominal focus of Castleman's disease in a 15 year-old boy.

The patient was consented for excisional biopsy of this lesion. At laparotomy a discrete 4 cm lymphoid-appearing mass was found at the base of the mesentery (Fig. 2). The mass was removed without complication and no other abnormalities were found. Pathology revealed Castleman's disease of the hyaline vascular subtype. His post-operative course was unremarkable. Ten weeks following surgery, his appetite had normalized and he had gained 7 kg with a 54 g/L increase in his hemoglobin to 127 g/L.

## 2. Discussion

Castleman's disease, first described by Dr. Benjamin Castleman in 1954, represents a rare lymphoproliferative disorder with a diverse clinical spectrum [1,2]. Mediastinal involvement is the most common disease site but any lymph node basin may be involved. 10% of cases are intra-abdominal [1,3].

Two clinical presentations predominate: unicentric and multicentric. Unicentric disease comprises two-thirds of cases, with the remainder being multicentric. Unicentric disease is usually of the hyaline vascular subtype and often remains asymptomatic until detected incidentally during the work-up of other medical conditions. In contrast, multicentric disease is usually plasmacytic or mixed cellularity variant and typically presents with a wide range of non-specific symptoms including B-symptoms (fever, night sweats, weight loss), fatigue, anorexia, rashes, anemia, thrombocytopenia, and



**Fig. 2.** Operative photo of an enlarged, 4 cm, mesenteric lymph node [arrow] in a 15 year-old boy. Pathology revealed hyaline vascular Castleman's disease.

hepatosplenomegaly [1,4]. Studies have shown that symptoms correlate with the histological variant: patients with plasmacytic or mixed cellularity disease tend to become symptomatic while systemic symptoms in patients with hyaline vascular disease are rare [1–5]. Interestingly, our patient had unicentric hyaline vascular disease yet presented with an array of systemic symptoms including failure to thrive and iron deficiency anemia unresponsive to iron therapy.

Interleukin 6 (IL-6) is a pro-inflammatory cytokine implicated in the pathogenesis of Castleman's disease. Studies show over-expression of IL-6 in the hyperplastic lymph nodes affected by Castleman's disease [1,5]. Furthermore, animal models demonstrating over-expression of IL-6 reproduce the phenotype of Castleman's disease, while blockage of IL-6 leads to symptom resolution [2]. IL-6 over-expression is thought to mediate the iron deficiency anemia seen in Castleman's disease through regulation of hepcidin [4].

Hepcidin is a regulator of iron homeostasis. It mediates iron metabolism through the inhibition of intestinal absorption of iron and blocking iron release from macrophages and hepatocytes [4]. Hepatic production of hepcidin is stimulated by IL-6. Over-expression of IL-6 by hyperplastic lymph nodes in Castleman's disease creates a chronic inflammatory state and drives the over-expression of hepcidin, which in turn inhibits intestinal absorption of iron, resulting in an iron deficiency anemia refractory to oral iron replacement therapy [1,4,5].

Our patient underwent inpatient assessment with multiple consultations and investigations prior to an MRE that finally demonstrated the enlarged, mesenteric lymph node that ultimately led to his diagnosis of Castleman's disease. The primary care team was puzzled by the degree of anemia and its refractory nature. Increased awareness of the association between B-symptoms, failure to thrive and refractory iron deficiency anemia may have pointed toward Castleman's disease earlier in the course of investigation and limited the morbidity associated with prolonged hospitalization and an extensive diagnostic work-up.

Unicentric disease carries an excellent prognosis with complete resolution of symptoms in over 90% of cases following treatment [2]. Surgical excision is the treatment of choice for unicentric disease, however location may prevent excision. Radiation therapy is considered second line. There is no standard treatment of multicentric disease. Options include steroids, thalidomide, cyclophosphamide, vinblastine, rituximab, radiation, or bone marrow transplantation [1,3]. Surgical debulking has been used in the past. Debulking provides a degree of symptom control but is not curative and has been largely replaced by medical management [1]. Tocilizumab, an anti-IL-6 receptor antibody, has shown promising results in the treatment of Castleman's disease [2–5]. Studies have shown that Tocilizumab decreases IL-6 binding leading to symptom resolution in both adult and pediatric populations [5,6]. Specifically Tocilizumab is thought to decrease hepcidin levels through the IL-6 pathway and thus be effective against the associated iron deficiency anemia [4].

## 3. Conclusion

Castleman's disease is a rare lymphoproliferative disorder that can cause a variety of insidious and progressive symptoms. Awareness of this disease entity can lead to earlier diagnosis and treatment limiting associated morbidity.

## Conflict of interest statement

Authors have no conflicts of interest to disclose.

## Consent

Written informed consent has been obtained from the patient for publication of this case report and accompanying images. A copy

of the written consent is available for review by the Editor-in-Chief of this journal on request.

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