Meigs syndrome, Pseudo-Meigs Syndrome, or Pseudo-pseudo Meigs Syndrome? A case report

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A case report

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ABSTRACT

Background. Meigs syndrome and its close mimics, pseudo-Meigs syndrome and pseudo-pseudo Meigs syndrome showcase a diagnostic clinical challenge faced by clinicians managing complex paediatric cases.

Case Report. We report a case of a 6-year-old girl who presented with progressive breathlessness, lethargy, and constipation for two weeks. Her twin was diagnosed with SLE a year ago and her parents are consanguineous.

Upon presentation, she had bilateral pleural effusion and gross ascites, requiring intubation and admission to the paediatric intensive care unit (PICU). Contrast enhanced computed tomography

(CECT) of the thorax, abdomen and pelvis suggested an ovarian mass with abdominal involvement. The pleural and peritoneal fluids were exudative in nature with raised tumour markers. Unfortunately, the child was not fit for mass biopsy. She slowly recovered with conservative treatment. A repeated ultrasound scan revealed normal ovarian size bilaterally with no masses. She was discharged well for a year before presenting again with constitutional symptoms. Subsequent investigations revealed diffuse large B-cell lymphoma (DLBCL). It is retrospectively apparent that this is a case of pseudo Meigs syndrome.

Conclusion. This is an unusual presentation with resolution of symptoms for a significant period. It is unclear whether repeated imaging would allow an earlier diagnosis of the lymphoma.

Keywords: Meigs Syndrome, Lymphoma, Large B-Cell, Diffuse, Intensive Care Units, Pediatric, Lupus Erythematosus, Systemic

Abbreviations:

1. Meigs syndrome (MS)
2. Pseudo-Meigs syndrome (PMS)
3. Pseudo-pseudo Meigs syndrome (PPMS)
4. Systemic lupus erythematosus (SLE)
5. Central argument (DLBCL)
6. Diffuse large B-cell lymphoma (DLBCL)
7. Paediatric intensive care unit (PICU)
8. Contrast enhanced computed tomography (CECT)
9. Alpha-fetoprotein (AFP)
10. Carcinoembryonic antigen (CEA)
11. Vascular endothelial growth factor (VEGF)
12. White cells (WBC)
13. Non-Hodgkin's lymphoma (NHL)

INTRODUCTION

Meigs syndrome and its close mimics, pseudo-Meigs syndrome and pseudo-pseudo Meigs syndrome showcase a diagnostic clinical challenge faced by clinicians managing complex paediatric cases. While all three share the clinical hallmarks of ascites and pleural effusion, their underlying aetiologies diverge significantly. This case report delves into these distinctions, exploring the unique causes of each syndrome and the difficulties navigating an acutely unwell child without a diagnosis.

Meigs syndrome manifests as ascites and pleural effusion in cases of benign ovarian tumours, with resolution of fluid collection following tumour resection [1]. Meigs syndrome (MS) is an uncommon presentation typically involving a benign ovarian tumour. It affects women over 30 and is very rare in children [1]. The prognosis is good, with no recurrence of pleural effusion and ascites after tumour removal.

Meanwhile, Pseudo-Meigs syndrome (PMS) involves ascites and pleural effusion in other pelvic tumours, [1] and pseudo-pseudo Meigs syndrome exhibits similar fluid collections due to autoimmune systemic lupus erythematosus [2,3]. Thus, although these scenarios may show similar clinical manifestations, their aetiologies are strikingly different. Yet, despite the diverse aetiologies, successful management of the underlying condition, namely by tumour resection and SLE control, results in resolution of symptoms [1-3].

CASE REPORT

We report a case of a 6-year-old girl who presented with a two-week history of progressive breathlessness, lethargy, and constipation. Notably, she had also been experiencing weight loss, loss of appetite, multiple joint pains, and intermittent vasculitic lesions for the past three years, which resolved with symptomatic treatment. She is the second child from a monochorionic, diamniotic twin pregnancy and her twin was diagnosed with systemic lupus erythematosus (SLE)

at the age of three years old. Her parents are first-degree cousins. This was her first presentation to the hospital since birth.

Examination upon admission showed mild dehydration with significant reduction in muscle bulk. She was hemodynamically stable but showed moderate to severe respiratory distress with diminished breath sounds bilaterally and scattered crepitations. Palpation of the abdomen revealed massive hepatomegaly, a large, painless abdominal mass in the centre with ascites. She had vasculitic lesions over bilateral soles and onycholysis over the first to fourth toenails of the right foot. There were no palpable cervical, axillary, and inguinal lymphadenopathies. Otherwise, cardiovascular and neurological examinations were normal.

Her initial blood results showed leucocytosis and thrombocytosis with total white cells of 22.4 $x10^9$/L and platelet of 662 $x10^9$/L, with normal kidney and liver function tests. Chest radiograph showed bilateral pleural effusion, while an urgent ultrasound revealed a heterogeneous pelvic mass with right mild hydronephrosis (Figure 1).

She was subsequently electively intubated and transferred to the paediatric intensive care unit (PICU). Bilateral chest drains were inserted, draining a large amount of straw-coloured fluid. The chest radiograph taken after chest drain insertion is shown in Figure 1. A day later, she developed worsening abdominal distension associated with hypotensive shock, attributed to progressive ascites. A peritoneal drain was inserted, and the peritoneal fluid was similar in colour and consistency with the pleural fluid. Peritoneal and pleural fluid suggested an exudative origin, however, immunophenotyping from these fluids were inconclusive. Cytology from both fluids showed no atypical cells. The results of these body fluids are shown in Table 1.

A contrast enhanced computed tomography (CECT) of the thorax, abdomen and pelvis was performed on day 5 of admission, which showed bilateral ovarian/adnexal solid masses with omental caking, right paracolic peritoneal thickening and abdominal and pelvic lymphadenopathy. In addition, it also exhibited gross ascites, moderate bilateral pleural effusion, and bilateral enlarged kidneys. Autoimmune screenings were negative. She had an elevated CA-125 level of 1300 U/ml, with normal levels of other tumour markers, namely alpha-fetoprotein and carcinoembryonic

antigen. Thrombophilia and tuberculosis screening yielded negative results. These results are summarised in Table 2.

The case was discussed with interdisciplinary teams, including gynaecology-oncology, paediatric haemato-oncology, and paediatric surgery. Several potential diagnoses were considered, such as Krukenberg syndrome, Burkitt's lymphoma, an ovarian tumour with Meigs' syndrome, and systemic lupus erythematosus (SLE). She was planned for an ovarian biopsy once her condition stabilised. Due to the patient's Mediterranean background and a history of consanguinity within the family, consideration was given to autoinflammatory conditions such as familial Mediterranean fever.

Treatment commenced with intravenous hydrocortisone and oral colchicine as anti-inflammatory agents. Investigations for autoinflammatory disorders were sent. Cytokine analysis revealed elevated levels of interleukin-6, fibrinogen, and d-dimer, with normal immunoglobulin levels, although these findings lacked specificity for any disorder.

Throughout her stay in PICU she was supported on mechanical ventilation with a mild to moderate settings and required up to three inotropic medications. There was significant kidney injury and electrolyte imbalances that were attributed to hypovolemia, sepsis, and tumour lysis syndrome. At this point, the clinical presentations indicated an oncological aetiology; however, definitive confirmation was challenging in the absence of histopathological evidence.

These biochemical parameters responded well to hyperhydration, allopurinol and furosemide. Subsequently, her renal function gradually showed significant improvement. Due to persistent fever and raised inflammatory markers, she received multiple courses of antibiotics. However, no positive cultures were yielded from blood, tracheal, pleural, or peritoneal fluids.

Notwithstanding these challenges, she showed clinical improvement on the anti-inflammatory medications. Drains were removed two weeks later. No subsequent reaccumulation of fluid was observed. She managed to be extubated at day 21 of admission and made a full neurological recovery thereafter. A repeat ultrasound performed after a month of admission showed mild hydronephrosis of the right kidney and both adnexal masses appear to reduce in size. Considering

the patient's clinical improvement and the observed decrease in the size of the masses, the initial biopsy plan was rescinded.

She was well for a year and was followed up under the paediatric rheumatology team during this period. She then presented again with left lumbar mass and constitutional symptoms. A renal biopsy was performed during this admission, and histopathological examination suggested diffuse large B-cell lymphoma. She underwent multiple courses of chemotherapy, but succumbed due to the aggressive nature of the disease.

DISCUSSION

This case illustrates a diagnostic challenge for the managing team. Considering the presentation, Meigs syndrome (MS) was one of the main differential diagnoses, especially given the presentation of ovarian mass, pleural effusion, and ascites. However, similar presentations can also be seen in many other metastatic malignancies.

There are limited reported cases of MS in children in literature [4,5], with the youngest reported patient being 9 years old. Pathophysiology of MS is not well established. The initial theory proposed by Meigs suggests that the tumour presses upon abdominal lymphatics causing exudative ascites, and the ascitic fluid transudates into the pleural space [6]. Other theories mention the possibility of fluids entering the peritoneum through the ovarian tumour capsule and seeping through the pleural cavity via diaphragmatic defects or lymphatic channels [6]. More recent studies suggest protein-induced vascular permeability, such as VEGF (vascular endothelial growth factor) [7].

Although serum CA-125 is typically elevated in MS, it is also raised in many other malignancies involving female reproductive system (ovarian cancer in particular) and mesothelial cells (i.e., pleura, pericardium, and peritoneum), as well as many benign conditions such as during

endometriosis, peritonitis, cirrhosis [8]. Surgery is both therapeutic and diagnostic, with histopathology results confirming the diagnosis.

SLE or pseudo-pseudo Meigs (PPMS) was suspected as the other twin has established SLE, with vasculitis rashes, musculoskeletal and systemic manifestations. The genetic contribution to SLE development is considerably high, [9] estimated at a 25% concordance rate in monozygotic twins [10] and up to 66% heritability in twin studies [11]. Abdominal masses in SLE are usually due to other malignancies, such as gastric cancer in the older population [12]. However, there is a documented case report of lupus mesenteric vasculitis (LMV) presenting with painless abdominal pain [13].

Pseudo-Meigs syndrome (PMS), on the other hand, is usually caused by other abdominal malignancies, namely ovarian malignancies, and germ cell tumours [14,15]. To our knowledge, there is no reported case of paediatric lymphoma with PMS in the literature. Although pleural effusion is a common complication of lymphoma due to pleural involvement, this is not the case in our patient considering the pleural fluid cytology result. The probable pathogenesis is related to the thoracic duct obstruction and impaired lymphatic drainage in Hodgkin lymphoma, while direct pleural infiltration is the predominant cause in non-Hodgkin's lymphoma (NHL) [16]. As for ascites, it is typically seen in many peritoneal lymphomas [17,18]. Both effusions are associated with a poor outcome in lymphoma [16].

Retrospectively, considering the abdominal masses, constitutional symptoms, pleural effusions, and ascites, along with occurrence of tumour lysis syndrome and leucocytosis, her presentation aligns with PMS. Her other symptoms are also seen in neoplasm aetiology. Vasculitic rashes and arthralgias are not exclusively seen in infections and autoimmune and may appear as a paraneoplastic symptom [19, 20]. However, the inconclusive results from the pleural and peritoneal fluid cytology and immunophenotyping presented a challenge in reaching an earlier diagnosis.

Paediatric diffuse large B cell lymphoma (DLBCL) is a rare but aggressive form of lymphoma, constituting about 10-20% of paediatric NHL [21]. Paediatric DLBCL has a higher incidence of c-myc translocation [22], extra nodal disease, and is more likely to demonstrate centroblastic or

immunoblastic morphologies [23], hence the more aggressive disease progression as seen in this case. Involvement of the ovary in DLBCL is rare and it is usually a manifestation of disseminated lymphoma [24].

There are several learning points from this case. First, histopathological results are crucial for early diagnosis, especially considering the inconclusive immunophenotyping and atypical clinical manifestations. Close follow up on her general condition and surveillance imaging is important to catch recurrence of ovarian mass. The other twin and other family members will also benefit from abdominal imaging surveillance. There is a 23-fold higher risk of NHL in monozygotic twins of patients with NHL [25]. First-degree relatives of NHL patients also have approximately 1.7-fold risk of developing NHL [25].

CONCLUSION

This is an unusual presentation of NHL with complete resolution of symptoms for a significant period. It is unclear whether repeated imaging after discharge would allow an earlier diagnosis and prompt treatment of the lymphoma. DLBCL is a rare and aggressive form of NHL, in which outcomes are generally poor.

PATIENT CONSENT

Informed consent was received from the patient and her parents.

CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

AUTHOR'S CONTRIBUTIONS

Conceptualization, AMK, AJAN.; writing—original draft preparation, AJAN, LCY, AWAR, AMK writing—review and editing, AJAN, AMK, supervision, AMK. All authors have read and agreed to the published version of the manuscript.

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FIGURES, TABLES AND SCHEMES

FIGURES

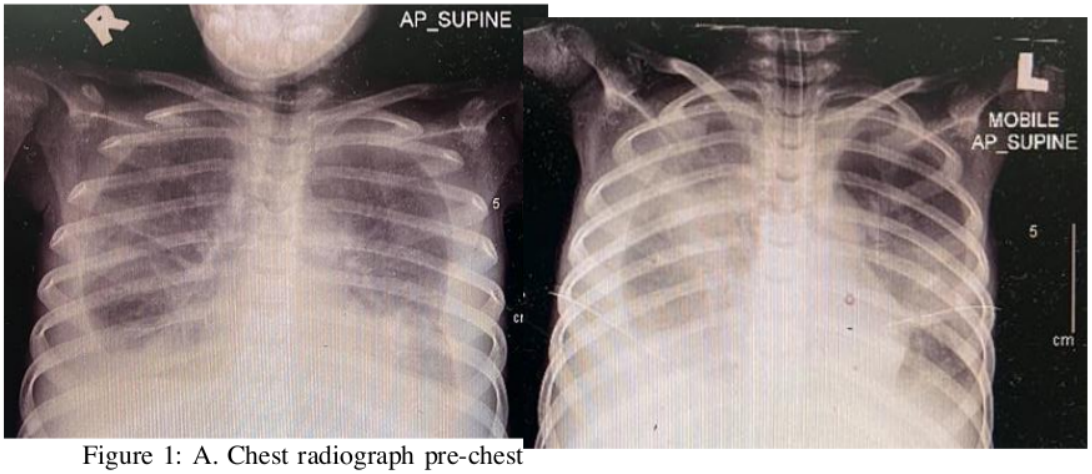

Figure 1: A. Chest radiograph pre-chest tube insertion (left) B. Chest radiograph post-chest tube insertion (right).

TABLES

Table 1: Results of pleural and peritoneal fluid.

Parameter	**Pleural fluid**	**Peritoneal fluid**	**Remarks**
pH Total protein (g/L) LDH (U/L)	7.8 40.84 3861	NA	Serum: Protein 70.13 LDH 2663
Gram stain Appearance WBC (x 10^6/L) RBC (x 10^6/L) Mononuclear cell (x 10^6/L) Polymorphonuclear (x 10^6/L) Total Count WBC (x 10^6/L) Culture & Sensitivity	Nil Cloudy 6965 12000 6037 928 7800 No growth	Nil Slightly cloudy 2419 5000 2264 155 2444 No growth	
AFB Mycobacterium C&S	Negative No growth	Negative No growth	

Cytology	No atypical cells	No atypical cells	
Immunophenotyping	Inconclusive results.	Blood tap sample. 7% cluster of small sized B cells lacking surface light chains.	

AFB: Acid fast bacilli, C&S: culture and sensitivity, LDH: Lactate dehydrogenase, RBC: red blood cell, WBC: white blood cell.

Table 2: Investigation results

Investigations	Results	Reference Range	Interpretation
Complement C3	1.34 g/L	0.82 – 1.85 g/L	Normal
Complement C4	0.24 g/L	0.15 – 0.53 g/L	Normal
ANA screening and immunofluorescence	Negative		
Anti-mycoplasma antibody	Negative		
Coombs test	Negative		
Antiphospholipid antibody panel	Negative		
Extractable nuclear antigen (ENA)	Negative		
Rheumatoid factor	Negative		
Immunoglobulin level			
Immunoglobulin G	3.87 g/L	0.52 – 16.31	Low
Immunoglobulin A	2.86 g/L	0.21 -2.82	Elevated
Immunoglobulin M	0.99g/L	0.47- 2.4	Normal
Alpha feto-protein	2.457 ng/mL	0 – 8.1	Normal
Beta human chorionic gonadotropin	< 2 mIU/mL	0 - 6	Normal
Cancer antigen (CA) 125	1 300 U/mL	0 - 35	Elevated
Carcinoembryonic antigen (CEA)	<0.5 ng/mL	0 – 5.1	Normal
Parathyroid hormone	3.04 pmol/L	1.58 – 6.03	Normal
25-hydroxyvitamin D	17.63 ng/mL	20-40	Low

Procalcitonin	17.05 ng/mL	0.03 – 0.1	Elevated