Open Access Library Journal
2022, Volume 9, e9233
ISSN Online: 2333-9721
ISSN Print: 2333-9705

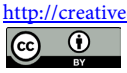
An Unusual Case of Ovarian Dysgerminoma Associated with Secondary Hemophagocytic Lymphohistiocytosis (HLH)

Nursofiah Hassan Ali[1], Anuradha P. Radhakrishnan[2], Mohd Isnisyam Saaya[3]

[1]Department of Internal Medicine, Selayang General Hospital, Batu Caves, Malaysia
[2]Department of Infectious Disease, Selayang General Hospital, Batu Caves, Malaysia
[3]Department of Pathology, Selayang General Hospital, Batu Caves, Malaysia
Email: sofiahasan86@gmail.com

How to cite this paper: Ali, N.H., Radhakrishnan, A.P. and Saaya, M.I. (2022) An Unusual Case of Ovarian Dysgerminoma Associated with Secondary Hemophagocytic Lymphohistiocytosis (HLH). *Open Access Library Journal*, **9**: e9233.
https://doi.org/10.4236/oalib.1109233

Received: August 18, 2022
Accepted: September 27, 2022
Published: September 30, 2022



Abstract

Hemophagocytic Lymphohistiocytosis (HLH) is rare fulminant disease with high mortality. High clinical suspicion is required to diagnose HLH. Malignancy can cause secondary HLH. We reported a case of 45 years old lady with hypertension, presented with bilateral loin pain. On presentation to hospital, she was clinically ill, dehydrated and laboratory parameters showed severe acute kidney injury. CECT abdomen showed huge pelvic mass. Throughout ward admission, she had period of unexplained fever and pancytopenia hence diagnosis of HLH was considered. She fulfilled criteria of HLH and decision was made to remove the mass. Her blood counts recovered after ovarian tumour removed which subsequently HPE came back as ovarian dysgerminoma. However, she succumbed due to invasive fungal infection and upper gastro intestinal bleeding as a result of prolonged period of immunosuppression. HLH is uncommon and likely underdiagnosed disease. Diagnosis of HLH is often challenging as disease manifestation is non-specific, hence early recognition and intervention will improve patient outcome and survival.

Subject Areas

Gynecology & Obstetrics, Hematology

Keywords

Pelvic Mass, Unexplained Fever, Pancytopenia, Hemophagocytic Lymphohistiocytosis, Ovarian Dysgerminoma

1. Introduction

Ovarian dysgerminoma (Figure 1 and Figure 2) is the most common type of

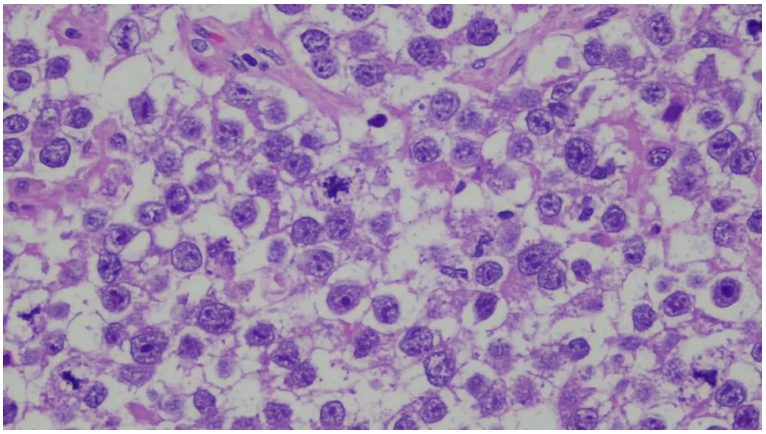


Figure 1. Slide of ovarian dysgerminoma H & E (Hematoxylin & Eosin) stain 4 ×100.

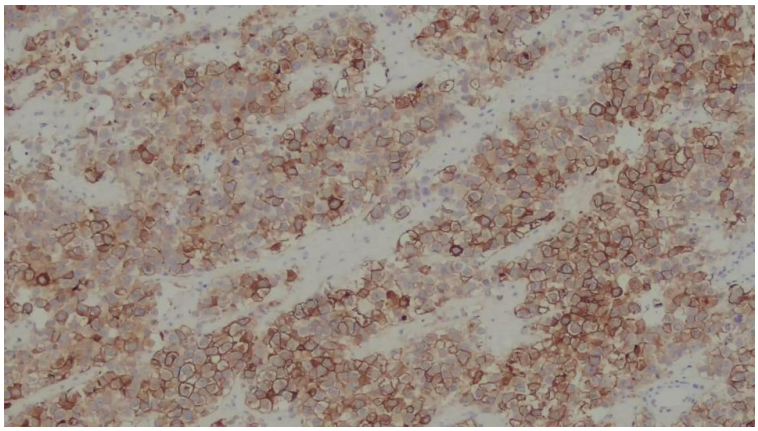


Figure 2. Slide of ovarian dysgerminoma showed PLAP (placental alkaline phosphatase) positive stain.

malignant ovarian germ cell tumour which comprises 2% - 3% of all malignant ovarian tumours [1]. It is a disease of adolescence and young female [1]. The most common symptoms are abdominal pain and abdominal swelling [2]. It has excellent prognosis [3]. Unilateral tumour, well capsulated and negative lymph node metastasis are treated by conservative surgery [3]. In advanced stage tumour radical surgery followed by chemotherapy will be the treatment of choice [3].

Hemophagocytic lymphohistiocytosis (HLH) is a rare life threatening and due to pathogenic immune dysregulation leading to prolonged fever, splenomegaly, cytopenia, hypertriglyceridemia, hypofibrinogenemia, elevated ferritin, low or absent natural killer (NK)-cell activity, or elevated soluble CD25 (interleukin [IL]-2 receptor) and hemophagocytosis in bone marrow, liver, spleen or lymph nodes [4] [5] [6]. Other supporting features include hyperbilirubinemia, hepatomegaly, transaminitis (present in the vast majority of patients with HLH), elevated lactate dehydrogenase and D-dimer levels [6] [7]. Diagnosis of HLH is tricky and mostly missed due to mixed presentation.

Early recognition of HLH is important as severe pancytopenia can lead to

morbidity and mortality as a result of delay in diagnosis due to nonspecific and varied presentation of prolonged immunosuppression [7]. The purpose of this case report is to enlighten that HLH can manifest in multiple disease background. Early disease pattern recognition can be life-saving and treatment approach can be directed early, minimize disease complication and will improve patient outcome.

2. Case Report

45 years old lady, para 8, with hypertension presented with bilateral loin pain for 2 weeks. On presentation she was clinically dehydrated with stable vital signs. Clinical examination unable to appreciate abdominal mass due to thick abdominal wall. Initial blood investigations showed normochromic normocytic anaemia with normal white cell count (WCC) and platelet, renal profile showed severe acute kidney injury and liver function test showed transaminitis with high ALP (alkaline phosphatase) and LDH (lactate dehydrogenase) (**Table 1**). US abdomen requested to rule out obstructive uropathy which revealed normal kidney size with no features of obstructive uropathy, other findings were cholecystitis and indeterminate pelvic mass. Subsequently proceeded with CECT (contrast-enhanced computed tomography of the abdomen) and pelvis which showed large heterogenous solid pelvic mass likely right ovarian mass with left ovarian cyst, calculus cholecystitis and segment II liver cyst. Throughout ward admission patient developed persistent fever and full blood count showed worsening pancytopenia with neutropenia, raised liver enzyme. Based on clinical and laboratory findings diagnosis of HLH was considered. She fulfilled HLH criteria of fever > 38˚C, cytopenia, hypertriglyceridemia, elevated liver transaminases, high ferritin level (**Table 1**) and bone marrow showed presence of hemophagocytosis (**Figure 3**) suggestive of HLH. She was admitted to critical care unit for close monitoring.

She was given subcutaneous granulocyte colony stimulating factor (GCSF) injection to increase her absolute neutrophile count (ANC) however no response after 2 weeks. She was subsequently started on iv dexamethasone tapering dose according to HLH protocol and given course of intravenous immunoglobulin (IVIG) for 4 days. Referral was made to gynaecology team to get tissue diagnosis. She underwent laparotomy right salpingo-oophorectomy and left salpingectomy for which histopathological examination (HPE) showed dysgerminoma of ovary stage 1A (**Figure 1** and **Figure 2**).

Post-surgery her counts subsequently recovered with improving pancytopenia and resolved fever. Unfortunately, patient deteriorated as complicated with invasive mold infection. She grew Fusarium solani (**Figure 4**) of her right nasal alar and extensive fungal sinusitis. Her initial treatment of invasive fungal infection was inadequate as delayed in achieving her final fungal culture result. She had prolonged period of immunosuppression as a result of delay in diagnosis of HLH and delay in surgical intervention. She succumbed to her illness due to

Table 1. Patient relevant blood investigations throughout hospital admission.

	Normal Values	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 44
WCC (109/L)	4 - 10	7.17	7.96	0.99	0.6	0.46	0.32	5.87	7.78
ANC (109/L)	2 - 7	5.7	6.6	0.1	0	0.02	0.03	5.2	7.3
Haemoglobin (g/dL)	12.5 - 16	10.2	9.9	9.6	7	6.4	7.5	7.4	6.3
Platelet (109/L)	150 - 410	247	256	183	76	51	38	166	219
Urea (mmol/L)	1.7 - 8.3	31	20.6	13.6	7.7	9.3	10	11.2	17
Creatinine (umol/L)	80 - 115	1012	462	173	181	54	38	42	49
Sodium (mmol/L)	133 - 145	132	129	122	145	144	135	133	136
Potassium (mmol/L)	3.3 - 5.1	3.1	5	2.6	3	3.4	3.5	3.3	4.4
Albumin (g/L)	38 - 51	29	30	23	15.3	27.4	27	23.5	23
Ast (u/L)	5 - 41	289	186	990	97.9	29	35	39	32
Alt (u/L)	5 - 37	364	156	577	106	20	109	87	75
Ferritin (ng/mL)	10 - 120	1971							
Triglyceride (mmol/L)	≤2.4	5.3							
Fibrinogen (mg/L)	200 - 400	165							
C-RP (mg/dL)	≤0.8		8.58	8.08	11	13			2
CEA (ng/mL)	≤5	7.2							
AFP (ng/mL)	≤9	42.9							
Ca 19-9 (u/mL)	≤35	<0.8							
Ca 125 (u/mL)	≤35	61.6							
Beta-HCG (IU/L)	(0 - 3.1)	1.5							
Hepatitis B	Nonreactive								
Hepatitis C	Nonreactive								
HIV	Nonreactive								
Syphilis	Nonreactive								

Abbreviations: WCC, white cell count; ANC, absolute neutrophile count; Ast, aspartate aminotransferase; Alt, alanine aminotransferase; CRP, C-reactive protein; CEA, carcinoembryonic antigen; AFP, alpha fetoprotein; CA19-9, cancer antigen 19-9; CA-125; cancer antigen 125; Beta-HCG, beta human chorionic gonadotropin; HIV; human immunodeficiency virus.

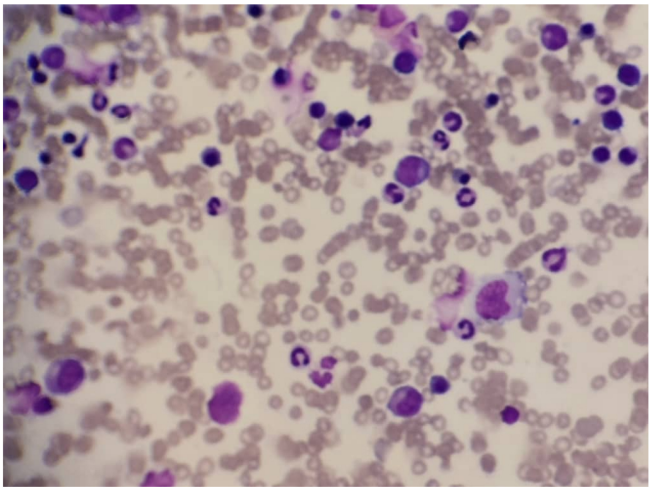


Figure 3. HLH seen in patient's bone marrow smear.

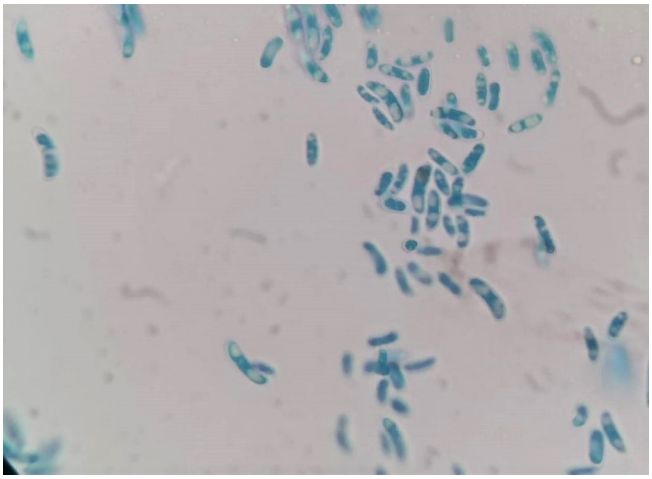


Figure 4. Picture of Fusarium solani.

severe septicaemia and hypovolemic shock as a result of gastrointestinal bleeding.

3. Discussion

This is a rare case reported for secondary HLH associated with malignant ovarian germ cell tumour. Secondary HLH can be due to many causes mainly triggered by infections followed by malignancies, autoimmune diseases, metabolic diseases and acquired immune deficiencies [7].

HLH associated with malignancy is a huge challenge to clinicians due to nonspecific and overlaps symptoms leading to misdiagnosis and mortality [8].

Solid tumour with HLH incidence reported about 3% in overall adult HLH patient [8] [9]. HLH is severe hyperinflammatory syndrome which in this case malignant cells initiate immune response producing dysfunctional cytotoxic CD8+ T lymphocytes and natural killer NK cell unable to initiate adequate response against target cells [8] [9]. This results to uncontrolled proliferation of cytotoxic T cells, large production of interferon gamma (INF-γ) and proliferation of macrophages that invade other organs, such as liver, spleen and lymph nodes, and produce further cytokine storm [8] [9]. The proliferating macrophage will engulf red cells, white cells, platelets and are called hemophagocytes [8] [9].

Treatment of malignancy associated HLH aims to control the overactive immune system and treat underlying malignancy [6] [9]. Treatment decision are usually made base on clinical experience, expert opinion and clinical cases as lack of clinical trials [7].

In this case, patient requires early surgical intervention as HLH was diagnosed later after her presentation and surgical intervention was delayed. She had prolonged period of neutropenia hence she was given immunosuppressed treatment for long duration leading to risk of invasive fungal infection. Invasive fungal infection can be detrimental if not diagnosed and treated early [10].

4. Conclusion

In summary, we report the rare case of secondary HLH associated with ovarian dysgerminoma. Incidence of malignancy associated HLH especially non-hematolymphoid malignancy is very low given the nature of the disease with varieties and nonspecific presentation [8]. It is life threatening condition that carries high disease burden with great mortality [4]. With increase understanding, high clinical suspicion and recognition of disease pattern, more HLH related disease can be diagnosed early to improve patient outcome. Multidisciplinary approach and collaboration are required to improve overall survival of patient with malignancy associated HLH [4].

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Kilic, C., Cakir, C., Yuksel, D., Kilic, F., Kayikcioglu, F., Koc, S., *et al.* (2021) Ovarian Dysgerminoma: A Tertiary Center Experience. *Journal of Adolescent and Young Adult Oncology*, **10**, 303-308. https://doi.org/10.1089/jayao.2020.0087

[2] Sailer, S. (1940) Ovarian Dysgerminoma. *The American Journal of Cancer*, **38**, 473-482. https://doi.org/10.1158/ajc.1940.473

[3] Arndt, T., Taube, E.T., Deubzer, H.E., Rothe, K., *et al.* (2022) Management of Malignant Dysgerminoma of the Ovary. *European Journal of Gynaecological Oncology*, **43**, 353-362. https://doi.org/10.31083/j.ejgo4302041

[4] George, M.R. (2014) Hemophagocytic Lymphohistiocytosis: Review of Etiologies and Management. *Journal of Blood Medicine*, **5**, 69-86. https://doi.org/10.2147/JBM.S46255

[5] Filipovich, A.H. (2009) Hemophagocytic Lymphohistiocytosis (HLH) and Related Disorders. *Hematology*, *ASH Education Program*, **1**, 127-131. https://doi.org/10.1182/asheducation-2009.1.127

[6] Farkas, J. (2016) PulmCrit-Sepsis 4.0: Understanding Sepsis-HLH Overlap Syndrome. https://emcrit.org/pulmcrit/sepsis-hlh-overlap-syndrome-shlhos/

[7] La Rosee, P., Horne, A.C., Hines, M., von Bahr Greenwood, T., Machowicz, R., Berliner, N., *et al.* (2019) Recommendations for the Management of Hemophagocytic Lymphohistiocytosis in Adults. *Blood*, **133**, 2465-2477. https://doi.org/10.1182/blood.2018894618

[8] Wang, H.L., Xiong, L.X., Tang, W.P., Zhou, Y. and Li, F. (2017) A Systematic Review of Malignancy-Associated Hemophagocytic Lymphohistiocytosis That Needs More Attentions. *Oncotarget*, **8**, 59977-59985. https://doi.org/10.18632/oncotarget.19230

[9] Nosratian-Baskovic, M., Tan, B., Folkins, A., Chisholm, K.M. and Dorigo, O. (2016) Hemophagocytic Lymphohistiocytosis as a Paraneoplastic Syndrome Associated with Ovarian Dysgerminoma. *Gynecology Oncology Report*, 38-41. https://doi.org/10.1016/j.gore.2016.05.013

[10] von Lilienfeld-Toal, M., Wagener, J., Einsele, H., Cornely, O.A. and Kurzai, O. (2019) Invasive Fungal Infection. *Deutsches Ärzteblatt International*, **116**, 271-278. https://doi.org/10.3238/arztebl.2019.0271