Mediterranean Journal of Hematology and Infectious Diseases

Case report

Kikuchi-Fujimoto Disease and Hemophagocytic Lymphohistiocytosis: A Rare Combination of Two Rare Diseases

Supplementary files

Supplementary Table 1: References

1. **Komp DM et al.** Kikuchi histiocytic necrotizing lymphadenitis: association with parvovirus B19 infection. *J Pediatr Hematol Oncol.* 1997;19(2):185–188.
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4. **Rajasekaran S et al.** Kikuchi-Fujimoto disease and hemophagocytic lymphohistiocytosis. *Pediatrics.* 2000;106(3):E41.
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15. **Park JS et al.** Kikuchi-Fujimoto disease complicated by hemophagocytic lymphohistiocytosis in subcutaneous panniculitis-like T-cell lymphoma. *Korean J Hematol.* 2016;51(2):146–149.
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17. **Chou TY et al.** Kikuchi-Fujimoto disease-associated hemophagocytic lymphohistiocytosis following staphylococcal skin infection. *Clin Case Rep.* 2021;9(8):e04512.
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19. **Ko JH et al.** Central nervous system-involved hemophagocytic lymphohistiocytosis secondary to Kikuchi disease. *J Korean Med Sci.* 2020;35(13):e80.
20. **Yu HH et al.** Kikuchi-Fujimoto disease complicated by hemophagocytic lymphohistiocytosis and systemic lupus erythematosus: successful recovery with corticosteroids. *Medicine (Baltimore).* 2021;100(5):e24463.

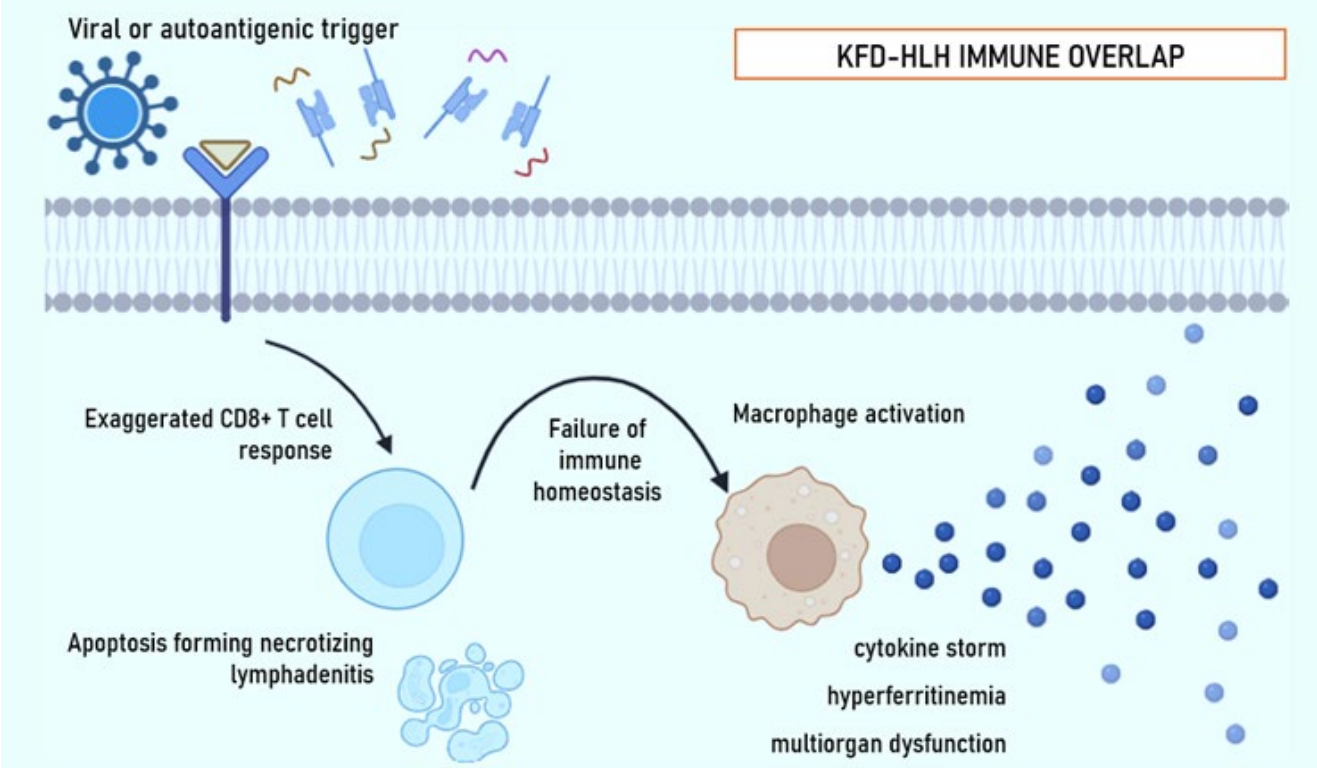
Supplementary Table 2. Literature review.

Case	Age / Sex	Affected LNs	Ferritin (ng/mL)	LDH (U/L)	Associated Disorders / Triggers	Treatment	Outcome	Reference
1	15 / F	C	2,500	1,941	Parvovirus B19 infection	Oral prednisolone 60 mg/day	Recovery	1
2	37 / F	C, A	6,330	4,228	SLE	IV methylprednisolone 1 g × 3 days	Recovery	2
3	14 / M	C	128	1,238	None	Prednisolone + IVIG	Recovery	3
4	10 / F	C	1,083	852	None	Prednisolone + IVIG	Recovery	3
5	6 / M	A	35,500	8,340	RSV + streptococcal infection + sickle cell trait	Prednisolone, dexamethasone, etoposide, cyclosporine	Recovery	4
6	17 / F	C	>1,000	1,573	—	IVIG	Recovery	5

7	13 / F	C	14,955.2	NA	None	IVIG + methylprednisolone + etoposide + dexamethasone taper	Recovery	6
8	1 / F	G	41,500	1,317	sJIA	Cyclosporine + low-dose steroids	Recovery	7
9	26 / F	C	7,000	2,200	EBV + SLE	Corticosteroids	Recovery	8
10	1.7 / M	NA	500	NA	JMML	Prednisolone 2 mg/kg	Initial improvement, later death (JMML)	8
11	40 / M	C	NA	NA	None	Naproxen 500 mg BID	Recovery	5
12	13 / M	A, I	94	417	Atopic dermatitis, asthma	Prednisolone 1.5 mg/kg × taper over 4 wks	Recurrences	9
13	12 / M	C	1,003	1,105	None	Prednisolone	Initial improvement, recurrence in 2 years	9
14	14 / M	G	2,541	682	EBV infection	IVIG + dexamethasone + etoposide + acyclovir	Initial improvement, recurrence after 7 years	9
15	5 / F	G	3,371	1,540	None	Prednisolone + dexamethasone + etoposide	Death	9
16	14 / F	C	472	627	None	IVIG + dexamethasone + etoposide + cyclosporine	Recovery	9
17	8 / M	G	1,168	1,308	EBV infection	Prednisolone	Recovery	9
18	50 / M	G	NA	3,056	SLE	IV methylprednisolone pulses	Death	10
19	16 / M	C, A	892.9	NA	EBV infection	Supportive care	Recovery	11
20	0.75 / M	G	3,090	1,615	CMV infection	Supportive care	Recovery	12
21	41 / M	G	5,100	NA	HHV-6 + cutaneous lupus	Oral corticosteroids	Recovery	13
22	21 / M	C	Normal	436	Sweet's syndrome	Prednisolone 30 mg/day (taper)	Recovery	13
23	16 / F	A	777	2,150	Dengue fever	Empiric antimicrobials	Recovery	14
24	21 / M	G	6,691	752	SPTL	Prednisolone + pralatrexate + bexarotene	Recovery	15
25	30 / M	G	1,730	1,111	None	Prednisolone 1 mg/kg (taper 3 weeks)	Recovery	14
26	35 / F	C	4,567	NA	Pregnancy	IV methylprednisolone + dexamethasone + etoposide	Death	16
27	54 / F	G	41,147	2,420	None	None	Recovery	16
28	36 / F	G	40,000	3,056	EBV + Parvovirus B19	Dexamethasone	Initial improvement, relapse (coronavirus)	14
29	16 / F	C, A, I	9,329	1,682	None	Methylprednisolone + prednisone + cyclosporine	PRES complication, eventual recovery	15
30	17 / M	C	4,027.4	608	SLE	Methylprednisolone × 3 days + prednisolone 60 mg	Recovery	20
31	18 / M	C, I	1,410.4	NA	None	Methylprednisolone 48 mg + IVIG 2 g/kg + hydroxychloroquine + intrathecal dexamethasone	Recovery	19
32	4 / M	C	1,500	1,361	None	IVIG 2 g/kg + methylprednisolone + dexamethasone + cyclosporine + etoposide + plasma exchange + hemodiafiltration	Recovery	19
33	49 / F	C, A	Elevated	NA	Staphylococcal skin infection	IV methylprednisolone pulses	Recovery	17
34	19 / M	C, MD	19,640.61	NA	Recurrent KFD	IV dexamethasone 10 mg/m² (taper 8 weeks)	Recovery	18

35	26 / M	C	16,500	23,499	SLE	Oral prednisolone 0.5-1 mg/kg (taper) + hydroxychloroquine 6.5 mg/kg	Recovery	20

Abbreviations: A, Axillary; C, Cervical; CMV, Cytomegalovirus; d, day; F, Female; EBV, Epstein-Barr virus; G, Generalized; HHV-6, Human Herpes virus – 6; HLH, Hemophagocytic lymphohistiocytosis; I, Inguinal; IVIG, intravenous immunoglobulin; JMML, Juvenile myelomonocytic leukemia; KFD, Kikuchi-Fujimoto disease; LDH, Lactate dehydrogenase; LNs, Lymph nodes; M, Male; MD, Mediastinal; NA, Not available; PRES, Posterior reversible encephalopathy syndrome; RSV, Respiratory syncytial virus; sJIA, systemic Juvenile Idiopathic Arthritis; SLE, Systemic lupus erythematosus; SPTL, Subcutaneous Panniculitis-like T-cell lymphoma; Y, Years.



Supplementary Figure. The pathophysiological link between KFD and HLH involves hyperactivation of $CD8^+$ T cells and histiocytes, suggesting a shared immune dysregulation. In KFD, an aberrant or exaggerated $CD8^+$ T-cell response—often in reaction to a viral or autoantigenic trigger—leads to apoptosis and formation of necrotizing lymphadenitis, when this process becomes systemic-