CLINICAL, PARACLINICAL FEATURES OF PATIENTS WITH CYTOMEGALOVIRUS DISEASE AT THE NATIONAL HOSPITAL FOR TROPICAL DISEASES 2020 - 2022

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Summary

Objectives: To describe the clinical and paraclinical characteristics of patients with CMV disease at the National Hospital for Tropical Diseases.

Subjects and methods: Retrospective combined with a prospective cohort study on 58 patients diagnosed with CMV disease treated at the National Hospital of Tropical Diseases in 2 years from January 2020 to June 2022.

Results: In a total of 58 patients with CMV disease, 56.9% of patients were male and the mean age was 45.57 ± 15.7 years. HIV (55.17%), history of prolonged corticoid therapy (20.7%), diabetes (10.34%), alcoholism (3.45%), transplantation (1.72%) were major comorbidities. Common clinical symptoms were: fever (74.13%), low visual acuity (37.93%), weight loss (31.03%), productive cough (31.03%), headache (27.59%), lymphadenopathy (24.14%), dry cough (22.41%). 43.1% had monocytosis status, most patients had normal white blood cell (WBC) count, and slightly increased inflammation markers (ESR, CRP, PCT). The interquartile range of T-CD4 was48 (11.75 - 215), and 60% of patients had T-CD4 countless than 100 cells/µL. There was no difference between two groups of HIV and non-HIV patients in sex ratio. The HIV group had higher mean age than non-HIV. Low visual acuity, lymphadenopathy, and weight loss were more frequent in the HIV group, and liver damage was only seen in the non-HIV group.

Conclusion: The study showed that the clinical and paraclinical signs of CMV disease are diverse, non-specific and need to be considered for screening in patients with suspected symptoms with a history of HIV, prolonged corticoid, diabetes, alcoholism, or transplantation.

Keywords: *Cytomegalovirus, Cytomegalovirus disease, CMV.*

INTRODUCTION

Cytomegalovirus (CMV) is a common infectionthatcan be endemic worldwide, affecting 40 - 100% world's population and increasing with age1. CMV is mainly transmitted through shedding inbody secretions such as blood, saliva, urine, milk, genital secretionsand also through organ transplantation. Clinical manifestations are diverse, from no symptoms to damage to multiple organs as described in many studies around the world recently. CMV retinitis can cause visual impairment and poor visual outcome after treatment; CMV affects the whole gastrointestinal tract with non-specificsymptoms and overall mortality range from 20.4% to 39%; CMV hepatitis with acute progress and difficulty distinguishing from other viral etiologies;About 61% of patients with meningoencephalitis hadpoor prognosis after treatment[2-9].

CMV can cause multi-organ damage with non-specific symptoms, making it difficult for doctors to diagnose and treat, leading to a high mortality rate. Recently, in Vietnam this disease received much more attention in many research but mainly focused on HIV patients. To improve the quality and

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Date of receipt: *October 15, 2022*

Date of reviewed completion: *October 25, 2022*

Accepted date for publication: *December 15, 2022*

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efficiency of CMV disease diagnosis, we conducted this study: "Clinical, paraclinical features of patients with Cytomegalovirus disease at the National Hospital forTropical Diseases 2020 - 2022".

SUBJECTS AND METHODS

Research subject: 58 patients diagnosed with CMV disease treated at the National Hospital for Tropical Diseases in 2 years (01/2020 - 6/2022).

Including criteria:

- Patients 16 years old or older.

- Confirmed diagnosis of CMV disease: Clinical symptoms at least one organ and evidence of CMV infection (CMV PCR positive in blood or damaged organ'ssecretion).

- Treated with Ganciclovir.

Exclusion criteria:

- Co-infection with other pathogens in damaged organs.

- Incomplete medical records (retrospective phase) or patients were not consenting to participate in this study (prospective phase).

Research methods: Retrospective combined with a prospective cohort study on 58 patients diagnosed with CMV disease (divided into 2 groups based on HIV positive or negative) treated at the National Hospital for Tropical Diseases in 2 years from January 2020 to June 2022.

Research facilities: Quantitative CMV PCR using Real-time PCR CobasAmpli Prepperformed at Microbiology and Molecular biology Department - the National Hospital for Tropical Diseases.

Data collection and statistical analysis:

- Collect information based on research medical records.

- All statistical calculations were performed with the SPSS 25.0 software.

RESULTS

During a 2-year-study (2020-2022), a total of 58 patients with diagnosed CMV disease were included in our study. 56.9% of patients were male and the mean age was 45.57 ± 15.74 (range from 21 to 82) years, which tends to be higher in non-HIV group. The mean duration from symptoms onset to hospital admission was23.86 ± 17.06 4 - 60) days.

Table 1. Medical history characteristics

Medical History	n	%	Medical History	n	%
HIV	32	55.17	Alcoholism	02	3.45
Prolonged Corticoid*	12	20.70	Hematological disease	05	8.62
Diabetes	06	10.34	Transplantation	01	1.72

**Prolonged corticoid: Use of corticoids oral or intravenous administration, ≥ 20 mg/day of prednisolone or any equivalent for >2 weeks[5].*

Comments: There were 32/58 HIV patients, accounting for 55.17%. Other underlying conditions include: prolonged corticoid therapy (20.7%), diabetes (10.34%), hematological disease (8.62%), alcoholism (3.45%), and transplantation (1.72%).

Table 2. Clinical features of CMV disease in HIV and non-HIV group

Medical History	Total (n = 58)		HIV (+) (n = 32)		HIV (-) (n = 26)		p
	n	%	n	%	n	%	
Fever	43	74.13	21	65.63	22	84.62	0.008
Lymph-adenopathy	14	24.14	12	37.50	02	7.69	0.004
Weight loss	18	31.03	15	46.88	03	11.54	0.001
Low visual acuity	22	37.93	18	56.25	04	15.38	0.913
Dry cough	13	22.41	07	21.88	06	23.08	0.969
Productive cough	18	31.03	10	31.25	08	30.78	0.095
Chest pain	16	27.59	06	18.75	10	39.46	0.094
Crackles	18	31.03	07	21.88	11	42.31	0.692
Respiratory failure	13	22.41	05	15.63	08	30.77	0.014
Icterus	05	8.62	00	00	05	19.23	0.681
Hepato-megaly	06	10.34	04	12.5	02	7.69	0.083
Dysphagia	10	17.24	08	25	02	7.69	0.919
Cephalalgia	16	27.59	09	28.1	07	26.92	0.1

Comments: Most of the patients (74.13%) had fever. Other clinical symptomsdepend on the organ that CMV is affected atdifferent rates. Especially, lymphadenopathy, low visual acuity, weight loss was more common in HIV groups, Icterus was only reported in non-HIV groups.

Table 3. Complete blood count characteristics

Characteristics		n	%	Mean ± SD (Min-Max)
WBC(G/L)	< 4	15	25.86	8.48 ± 6.15 1.70 - 32.7
	4 - 10	25	43.10	
	> 10	18	31.03	
Monocyte (G/L)	> 0.8	25	43.10	0.71 ± 0.5 (0.08 - 3.43)
Hb (g/L)	< 120	45	77.59	105.50 ± 19.38 63 - 144
	≥ 120	13	22.41	
PLT(G/L)	< 150	19	32.76	214.45 ± 128.34 02 - 521

Comments: Most of the patients (43.1%) have normal WBC count (The average WBC was 8.48 ± 6.15 G/L), Monocytosis status presented in 43.1% of patients on admission day.

Table 4. Inflammation markers of CMV disease

Characteristics		n	%	Characteristics		n	%
ESR1h (mm/h) (n = 41)	> 10	40	97.56	Ferritin (ng/mL) (n = 18)	> 400	18	100
	Mean ± SD (Min-Max)	75.77 ± 32.85 (4.71 - 130)			Mean ± SD (Min-Max)	4598.19 ± 11486.19 (685 - 50550)	

Characteristics		n	%	Characteristics		n	%
ESR2h (mm/h) (n = 41)	> 20	40	97.56	LDH (U/L) (n = 29)	> 460	13	44.83
	Mean ± SD (Min-Max)	93.08 ± 34.39 (12.3 - 194)			Mean ± SD (Min-Max)	435.46 ± 225.78 (146 - 902)	
CRP (mg/L) (n=58)	<10	12	20.69	PCT (ng/mL) (n = 29)	< 0.05	01	3.45
	10 -50	19	32.76		0.05 - 2	24	82.76
	> 50 - 100	13	22.41		> 2 -10	04	13.79
	> 100	14	24.14		> 10	00	00
	Mean ± SD (Min-Max)	62.56 ± 56.30 (1.5 - 206.8)			Mean ± SD (Min-Max)	0.91 ± 1.76 (0.04 - 9.32)	

Comments: Elevated ESR, CRP, LDH, PCT were presented in 97.56%, 79.31%, 44.83%, 96.55% of patients. Ferritin was higher than normal in 18 cases. The mean of CRP and PCT were 62.56 ± 56.3 mg/L and 0.91 ± 1.76 ng/mL.

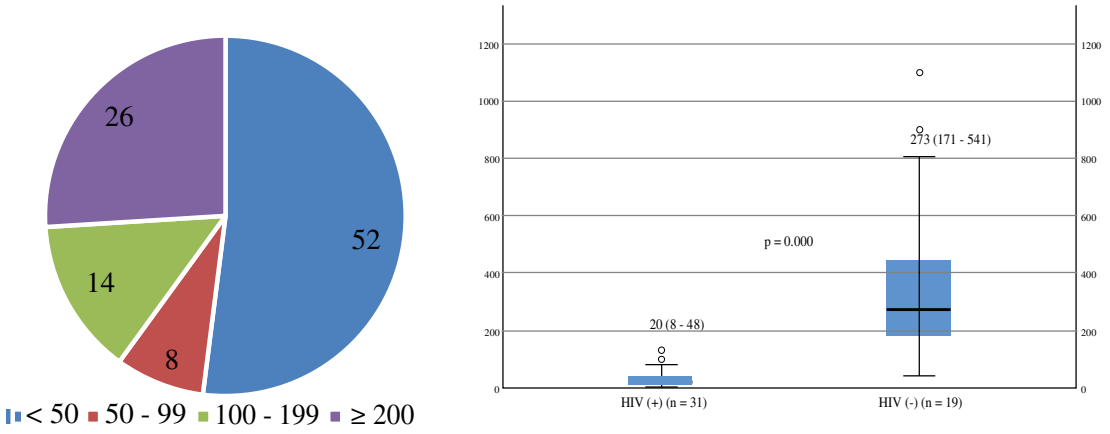

Figure 1. Characteristic of T-CD4 number

Comments: The number of T-CD4 below 100 cells/µL accounted for 60%, T-CD4 less than 50 cells/µL accounted for 52%. The interquartile range was 48 (11.75 - 215), the HIV group was 20 (8 - 48), which is significantly lower than the non-HIV group with an interquartile range was 273 (171 - 541) cells/µL.

DISCUSSION

The male and female ratio in our study was about 1.32/1. The average age was 45.57 ± 15.74, ranging from 21 to 82 years. Common medical histories included: HIV (55.17%), prolonged corticoid use (20.7%), diabetes (10.34%), hematological disease (8.62) alcoholism (3.45%), transplantations (1.72%). A study of Pai-Jui Yehin 54 patients diagnosed with CMV gastritis also showed some major comorbidities included: a history of immunosuppressive therapy (57.4%), diabetes (25.9%), transplantations (9.3%), HIV (7.4%) and alcoholism (7.4%). Besides, hypertension and malignancies were presented with high rates (38.9% and 37.0%)[5].

Our research showed that CMV disease had chronic progress, the mean duration from the onset of the first symptoms to the day of hospital admission was 23.86 ± 17.06 days, ranging from 4 to 60 days. Systemic symptoms were common in CMV disease. Most of the patients (74.13%) had fever and this rate did not significantly differ between two groups, higher than a study of Pai - Jui Yeh (31.5%), Panu Wetwittayakhlang (25.8%), Guy-Handley(42%)[5,7,9].

There were 24.14% of cases had lymphadenopathy, weight loss happened in 31.03% of cases, these symptoms were more common in HIV patients.

Clinical symptoms were diverse and depend on the damaged organ. Low visual acuity was reported in 22 patients (37.93%), more common in HIV group, ratio between HIV and non-HIV was 18/04, higher than in the study of Mary Ho (06/21) and Doong Joon Kim (21/57)[2,10]. The number of HIV patients varies across countries leading to this difference. Cough was most common among respiratory symptoms (productive cough - 31.03%, dry cough - 22.41%), other symptoms such as chest pain (27.59%), and crackles (31.03%). Moreover, there were 22.41% of patients with respiratory failure that need respiratory support (non-invasive and invasive ventilation). CMV infects the whole alimentary tract, can cause several symptoms including: Icterus (8.62%), hepatomegaly (10.34% - which was only seen in non-HIV group), dysphagia (17.24%). There was 27.59% of patients that had cephalalgia rate similar between two groups of patients. Our study had a similar symptoms rate to a study of Do Minh Hoang such as: low visual acuity (55.6%), cough (37.8%), chest pain (11.1%), dyspnea (4,4%) and study in the same region[3,5,9,11].

Most of the patients had normal WBC counts in complete blood count at the first admission, 43.1% of patients had monocytosis status. Inflammatory markers such asESR, CRP, and PCT, elevated in 97.56%, 79.31%, and 96.55% of cases, almost slightly elevated. Research by Yu - Xue, Đo Minh Hoang, and Pai - JuiYeh showed similar results, which are suitable forthe body's immune response to virus infection in genera[l5,11,12]. LDH was increased in 44.8% of patients, this is an enzyme that represents the body's tissues, and elevated levels of this enzyme reflect the extent of tissue damage. Ferritin was increased in 18 cases, it was released from macrophage cells or during red blood cell phagocytosis, however, it was not specific for CMV disease.

In our study, 60% of patients had T-CD4 below 100 cells/µL and 52% of patients had T-CD4 count less than 50 cells/µL, the interquartile range of T-CD4 count was 48 (11.75 - 215) cells/µL and lower in HIV group. This result was similar to the study of Yu-Xue and Đo Minh Hoang[11,12].

CONCLUSION

From our research results on 58 CMV patients treated at the National Hospital for Tropical Diseases from 2020 to 2022, we drew some conclusions:

* *Epidemiological features:* CMV disease is common in patients with risk factors such as HIV, history of immunosuppressive drugs, and hematology diseases. It is necessary to screen for CMV disease especially in this group of patients when clinical symptoms are suspected and other etiologies have been excluded.

* *Clinical and paraclinical characteristics:* Chronic disease with multi-organ damage, different clinical symptoms between two groups of patients. Leukocytosis was rare but monocytosis status and slightly increase inflammation markers were common. LDH and Ferritin can be elevated. T-CD4 is usually under 100 cells/µL.

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