Severe Vincristine-Induced Peripheral Neuropathic Weakness in Both Upper and Lower Limbs in children with acute lymphoblastic leukemia.

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INTRODUCTION

Vinca alkaloids, particularly vincristine (VCR), are cornerstone microtubule-targeting agents extensively used in polychemotherapy regimens, especially for pediatric acute lymphoblastic leukemia (ALL). Despite their efficacy, vincristine's dose-limiting neurotoxicity—commonly manifesting as peripheral neuropathy—can lead to treatment modification or discontinuation, potentially compromising therapeutic outcomes and quality of life.

We report a clinical case of vincristine-induced peripheral neuropathy (VIPN) in a child treated for T-cell ALL and to highlight associated risk factors, diagnostic challenges, and management considerations.

Case presentation

An 8-year-old chid, complaining of lateral cervical swelling, accompanied with Sleep apnea syndrome and snoring, was admitted to hematology department. The blood smear showed 93% lymphoid blasts. The bone marrow biopsy with immunophenotyping was in favor of T-ALL.

The patient received 2 cycles of COP for cytoreduction due to the significant size of the tumor mass, then followed by the FRALLE 2000 protocol .

The patient was corticosteroid-sensitive, with 3% lymphoblasts at the end of induction.

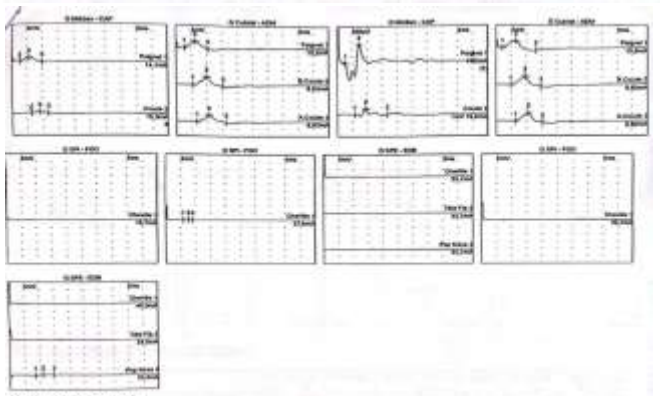
However, during consolidation, he experienced weakness in both lower limbs and walking difficulty, gradually installed within 5 days. The physical examination suggested normal muscle strength in both upper limbs, but the muscle strength in both lower limbs was graded as 2 .The electromyogram revealed an axonal motor polyneuropathy in all four limbs, more severe in the two lower limbs.

The patient received a cumulative dose of 8mg of VCR. We confirmed the diagnosis of VIPN based on his history of VCR treatment and the results of EMG.

The patient's symptoms persisted despite being treated with benfotiamine and physiotherapy.

MNC

Nerf / Sites	Muscle	Latency ms	Amplitude mV	Duration ms	Rel Amp %	Segments	Distance mm	Lat Diff ms	Velocity m/s	Vel CT m/s
D SPI - FDO										
Cheville	FDO	6,86	6,2	9,12	100	Cheville - FDO	61			
G Médian - CAP										
Poignet	APB	2,94	2,2	6,84	100	Poignet - APB	0			
Coude	APB	6,48	0,8	5,28	36,1	Coude - Poignet	180	3,54	51	50,8
D Médian - CAP										
Poignet	APB	2,77	1,3	42,52	100	Poignet - APB	0			
Coude	APB	5,94	0,8	10,71	62,8	Coude - Poignet	190	3,17	60	60,0
G Cubital - ADM										
Poignet	ADM	2,79	4,3	7,56	100	Poignet - ADM	0			
B.Coude	ADM	5,46	5,5	8,77	126	B.Coude - Poignet	200	2,67	75	75,0
A.Coude	ADM	6,57	4,2	8,52	77,5	A.Coude - B.Coude	70	1,11	59	57,9
						A.Coude - Poignet		3,88		
D Cubital - ADM										
Poignet	ADM	2,10	4,6	11,06	100	Poignet - ADM	0			
B.Coude	ADM	4,98	5,7	9,87	124	B.Coude - Poignet	190	2,88	66	66,1
A.Coude	ADM	6,35	5,7	9,00	99,3	A.Coude - B.Coude	80	1,37	58	58,3
						A.Coude - Poignet		4,25		
G SPE - EDB										
Cheville	Pédieux					Cheville - Pédieux	80			
Tête Fib	Pédieux					Tête Fib - Cheville				
Pop fossa	Pédieux	8,46	0,4	8,21		Pop fossa - Tête Fib				
						Pop fossa - Cheville				



SNC Peak Lat. Vel.

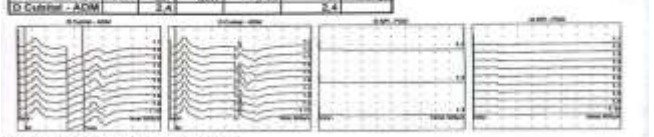
Nerf / Sites	Rec. Site	Peak Lat ms	Amp.2-3 µV	Segments	Distance mm	Vel. Pk m/s	TC Vel Pk m/s
G Médian - Orthodromic (Dig III, Mid paume)							
Dig III	Poignet	2,15	60,4	Dig III - Poignet	82	42,9	42,9
D Médian - Orthodromic, (Dig III, Mid paume)							
Dig III	Poignet	1,75	30,1	Dig III - Poignet	70	40,0	40,0
G Cubital - Orthodromic, (Dig V, Mid paume)							
Dig V	Poignet	1,75	32,1	Dig V - Poignet	70	40,0	40,0
D Cubital - Orthodromic, (Dig V, Mid paume)							
Dig V	Poignet	1,83	29,0	Dig V - Poignet	70	38,2	38,2

SNC

Nerf / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	Amp.2-3 µV	Segments	Distance mm	Velocity m/s	Vel CT m/s
D Sural - Cheville (Mollet)								
Mollet	Cheville	1,52	2,15	20,3	Mollet - Cheville	90	58	58,3
G Sural - Cheville (Mollet)								
Mollet	Cheville	1,83	2,46	19,5	Mollet - Cheville	110	60	60,0

F Wave

Nerf	F Lat ms	M Lat ms	F-M Lat ms	Min F Lat ms	Min M Lat ms	Min F-M ms
D Cubital - ADM	33,0	3,7	29,3	24,8	2,7	22,1
D Cubital - ADM		2,4			2,4	



MUP (Amplitude trigger and Delay)

Muscle		Dur. ms	Ampl. µV	Phases	Turns	Area µVms	SizeIdx	SpikeDur ms	Rate Hz	Rise µs
D Abducteur du pouce	Moyenne TDUT	35,0	1549	3	3	28441	17,5	8,9	50	7045
	Std YOUT	0,0	0,00	0	0	0	0	0	0	0
	Moyenne XIMPL P	35,0	1549	3	3	28441	17,5	8,9	50	7045
	n	35,0	1549	3	3	28441	17,5	8,9	50	7045

Electroneuromyography (ENMG) of all four limbs demonstrates findings consistent with a motor axonal polyneuropathy involving both upper and lower limbs, with more severe impairment observed in the lower limbs.

DISCUSSION

Vincristine is a key drug used in the treatment of ALL, but its most significant side effect is neurotoxicity. Several factors contribute to the development of vincristine-induced peripheral neuropathy (VIPN).

VIPN is a dose-limiting side effect, with the dose of administration being one of the main contributing factors. When the cumulative dose of VCR exceeds 2–6 mg/m2, approximately 35–45% of patients are at risk for developing VIPN.
Another contributing factor is the frequency of VCR administration. Studies have found that when VCR is administered at shorter intervals, the incidence of VIPN also increases. Additionally, the method of administration plays a role in the risk of developing VIPN. The standard route of administration for VCR is bolus push injection, while continuous infusion seems to increase systemic exposure.
Certain genetic variations can also affect the metabolism and clearance of VCR, influencing the risk of VIPN.

Currently, there is no standardized approach for preventing or treating VIPN. It is recommended to avoid prolonged or repetitive use of VCR. If VIPN develops, the VCR dose should be reduced or discontinued based on the patient's condition. Pyridoxine can be used in the treatment of VIPN. Additionally to pyridoxine, pyridostigmine and Glutamate.

CONCLUSION

In conclusion, we presented a case of VIPN in a child presenting with severe bilateral lower-limb weakness. We also reviewed the risk factors and treatment strategies for VIPN. Further studies are needed to develop a comprehensive risk assessment system to better understand the safe and individualized use of VCR in patients.

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