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Disseminated Intravascular Coagulation as an Adverse Event Related to Lamotrigine Use in Children

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Abstract

Disseminated Intravascular Coagulation (DIC) is a syndrome characterized by hemorrhage and microvascular thrombosis. This condition is common in critically ill patients and the most frequent causes are sepsis, trauma and malignancy. Lamotrigine is an anticonvulsant medication that has the effect of inhibiting the release of excitatory Neurotransmitters such as glutamate, by blocking sodium channels. The association between DIC and the use of lamotrigine has already been described in the literature, including pediatric patients, as a rare adverse event, which can be enhanced by the concomitant use of valproic acid, as it prolongs the half-life of lamotrigine by decreasing its hepatic clearance. The estimated incidence of lamotrigine hypersensitivity reactions ranges from 1 in every 1,000 to 10,000 exposed. The mechanism by which lamotrigine promotes this reaction in the host is not completely understood, but considering its potential for severity, it becomes a relevant topic for discussion. This study aims to describe a case of a child admitted to the Pediatric Intensive Care Unit (PICU) with DIC associated with lamotrigine.

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Case Presentation

18 months old female child, with a previous diagnosis of West Syndrome and microcephaly without a definite cause, admitted to the PICU with hemodynamic instability. Patient with a past history of difficult to control epilepsy in use of multiple anticonvulsants (valproic acid, topiramate, clobazam) besides ketogenic diet. She was hospitalized for more than 30 days due to vomiting, hydro-electrolytic disturbances and drowsiness. She was on anticonvulsant medications with lamotrigine onset 15 days before admission to the PICU, to replace topiramate. In the 24 h prior to admission, she evolved feverish peaks, respiratory distress needing supplemental oxygen therapy and hemodynamic instability been transferred to the PICU for monitorization. She required antibiotics, vasoactive drugs and orotracheal intubation to shock control. Initial tests showed severe metabolic acidosis, orotracheal, thrombocytopenia and several alterations in coagulation tests (Table 1); without active bleeding. Despite little suggestive infectious screening (including negative viral screening tests - SRV and SARS-CoV-2), she was initially treated for septic shock secondary to pneumonia. At admission, valproic acid and the ketogenic diet were also suspended. The infant evolved with a rapid improvement in hemodynamic status. The vasoactive drugs were suspended after 24 h of use, and antibiotics after 72 h. However, she persisted with changes in coagulations tests, hypofibrinogenemia and thrombocytopenia, characterizing the Disseminated Intravascular Coagulation Syndrome (DIC); maintaining without active bleeding.

As the patient did not have classic causes of DIC and did not improve after the suspension of valproic acid, a literature review was carried out and a similar case was found with the use of lamotrigine in an adolescent. Lamotrigine was suspended on the third day of admission to the PICU. Associated with this measure, to prevent escape from seizures, Phenobarbital was started and the dose of clobazam was adjusted. After lamotrigine suspension, the patient evolved with progressive improvement of laboratory changes, until the normalization of coagulation tests and platelets on the eighth day of hospitalization. She did not need platelets, plasma or cryoprecipitate transfusions. Received only red blood cell concentrate for significant anemia. During hospitalization, she also presented deep venous thrombosis in the right femoral and popliteal veins. The patient had a central venous line in this femoral vein during 11 days. Full anticoagulation started, without complications. She needed invasive mechanical ventilation with low parameters for 3 days, followed by intermittent non-invasive ventilation related to oscillations of breathing pattern associated with neurological condition and tongue fall for more 3 days. She presented with progressive neurological improvement after medication adjustment and adequate control of seizures; normalization of hydro-electrolytic

Table 1: Laboratory evolution during staying.

	Admission Day	Day 1	Day 2	Day 4	Day 5	Day 8	Day 10
Hb (g/dL) | Htc (%)	9.2 | 29	7.7|25.1	7.2|22.8	7.0|22.5	7.1|22,8	5.1|16.2	11.5 | 35.1
Global Leucocyte (/mm³)	17960	7530	5290	6770	8300	23330	
B/S/L/M (%)	4 |43|51|1	11|57|25|6		0|50|40|9	7|52|32|8	0|34|48|16	
Platelets (/mm³)	37000	18000	16000	87000	137000	429000	
CRP (mg/L)	21,2	27,5	31				
Fibrinogen (mg/dL)	30		<35	<35	39	61	
Protrombin Activity (%) INR |	<10%|>10	<10%|>10	<10%|>10	<10%|>10	51%|1.64	79%|1.18	
aTTP (Seconds)	> 120	>120	> 120	35,1	29,4	20,9	
AST (U/L) | ALT (U/L)		46|32	48|32		196|83		
BUN (mg/dL) | Creatinine (mg/dL)	44|0.32	44|0.36	49|0.5	40|0.15	38|0.35	33|<0.15	
Sodium (mmol/L)	157	154	153	153	151	128	136
Potassium (mmol/L)	3.5	3.1	2.7	3.8	4.0	4.0	4.6
Chloride (mmol/L)	144	132	131	121	121	94	96
Calcium (mg/dL)	5.6	5.52	5.37	4.92	5.23	3.94	4.44
Phosphorus (mg/dL)	3.7	3.1	2.7	2.7	1.9	4.3	4.6
Magnesium (mg/dL)	1.7	1.7	1.6	2.0	2.0	1.6	2.1
Lactate (mmol/dL)	3.5	3.5	2.4	1.8	5.4	5.1	
pH/pCO2/pO2 /BIC/BE/ SatO2	7.02/42/36 /10/-18.5/ 59	7.21/31/17 9/13/-14.5 /99	7.30/26/16 7/14/- 13/98	7.28/50.4/ 57.3/21.7/ -2.7/84.4	7.22/57.3/29.5/20.8/-3.2/47%	7.48/31.7/ 163/25.1/0.8/99.2	

disorders being discharge to PICU after 12 days of staying.

Discussion

DIC is a syndrome characterized by hemorrhage and microvascular thrombosis. The diagnosis is confirmed by changes in coagulation tests as platelet count, Prothrombin Time (PT), INR, Activated Partial Thromboplastin Time (aPTT) and fibrinogen. It is a common diagnosis in the PICU and its main cause is sepsis. Usually, the resolution of this condition is associated with the treatment of the underlying cause. However, some patients may not respond to these measures and may need clotting factors, which is reserved for those with major bleeding. Anticoagulation with heparin is also a possibility, with few studies and evidence in pediatric population. Seems that it can be beneficial to patients with predominantly thrombotic, symptomatic or life-threatening manifestation and it's contraindicated in the presence of traumatic brain injury or liver failure. The cases previously reported in the literature about the association between DIC and lamotrigine describe an initial condition of flu-like syndrome, with subsequent evolution to DIC and multiple organ dysfunctions, similar to that observed in our case report. In addition, the onset begins about 1 to 12 weeks after the onset of lamotrigine, which is also compatible with the patient's condition. It is also important to remember that the changes cannot be attributed to a state of epileptic illness, since the patient had good crisis control during hospitalization, as was observed in other case reports [1-6].

Conclusion

The association between DIC and lamotrigine is rare, and was described for the first time in 1992, being the first report in pediatric patients published in 1997. Despite a mechanism not yet well established, previous studies have identified immune serological changes associated with this condition, corroborating the hypothesis that a DIC may result from a hypersensitivity reaction to lamotrigine, even considering that studies of the drug's efficacy and safety do not show such an adverse reaction. In addition, it is already known that DIC could be triggered due to hypersensitivity to various drugs. So far, the identification of the detailed condition is essentially done through the association of clinical and laboratory data and it is important as a differential diagnosis, since it is a serious condition, in which the suspension of medication can reverse the DIC.

References

1. Chang Rsk, Cole AJ. Lamotrigine-induced lupus-like syndrome: A case report and literature review. Am J Ther. 2014;21(3):e85-7.
2. Chattergoon DS, McGuigan MA, Koren G, Hwang P, Ito S. Multiorgan dysfunction and disseminated intravascular coagulation in children receiving lamotrigine and valproic acid. Neurology. 1997;49(5):1442-4.
3. Mackay FJ, Wilton LV, Pearce GL, Freemantle SN, Mann RD. Safety of long-term lamotrigine in epilepsy. Epilepsiy. 1997;38(8):881-6.
4. Jem S, Williamsom PJ, Barnes EW, Trewby PN. Multisystem adverse reaction to lamotrigine. Lancet. 1994;344(8920):481.
5. Taillia H, Alla P, Fournier B, Bounolleau P, Ouologem M, Ricard D, et al. [Anticonvulsant hypersensitivity syndrome and lamotrigine associated anticonvulsant hypersensitivity syndrome]. Revue Neurologique. 2009;165(10):821-7.
6. Takeshima M, Ishikawa H, Shimizu T, Toyoshima A, Manabe M. Lamotrigine-induced disseminated intravascular coagulation with hypersensivity syndrome: A case report. Psychossomatic. 2016;57(5):540-2.