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Retrospective Research exploring gestational atypical hemolytic uremic syndrome

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Abstract:

Aim

A retrospective research study revealing clinical features and prognostic parameters of 22 cases of gestational atypical hemolytic uremic syndrome.

Methodology

A retrospective research study in an analytical manner of 22 cases of gestational Atypical hemolytic uremic syndrome from the Demerdash Maternity Hospital records using diverse management protocols.

Results

12 cases underwent plasma exchange management protocol with a favourable impact regarding renal response in only 8 cases. On the contrary, 10 cases were managed with high dose plasma infusion with an excellent renal response in 7 cases by regaining renal functional capacity in managed cases.

Conclusion

The research performed by our group revealed considerable effectiveness of high dose therapy plasma infusion management of atypical HUS. Although therapeutic plasma exchange is the recommended treatment of HUS, this cumbersome procedure may not be available for all patients in an emergency. In this context, plasma infusion may represent an alternative first-line therapy.

Key words

hemolytic uremic syndrome, thrombotic microangiopathy, plasmapheresis, therapeutic plasma.

Introduction

Gestational atypical hemolytic uremic syndrome is caused by thrombotic microangiopathy due to unrestrained complement system triggering during gestation. Gestational atypical hemolytic uremic syndrome is a catastrophic clinical scienario as there is imperfect clinical knowledge and management understanding. A retrospective research approach is performed to explore and reveal in an analytical manner the clinical features and prognostic parameters of 22 patients of gestational atypical hemolytic uremic syndrome from the Demerdash Maternity Hospital records undergoing diverse management protocols. Sixteen cases clinically presented at some stage in the first gestation and nine cases demanded hemodialysis for management at the time of clinical diagnosis.13 patients had major, obstetric complications that triggered a thromboticmicroangiopathy cascade [1-5].

Postpartum stage carried the most hazardous risk for pathological development of the disease and the study category revealed a linkage and a significant correlation of cesarean delivery with gestational Atypical haemolytic uremic syndrome. 12 cases undergone plasma exchange management protocol with an encouraging impact as regards renal functional response revealed in only eight patients. Quite the opposite, 10 cases were managed by high dose plasma infusion with an outstanding renal functional response in 7 cases. Even though the group studied is somewhat small in number, however the research data obtained reveal that gestational atypical haemolytic uremic syndrome is similar to other clinical types of atypical haemolytic uremic syndrome and imply similarity of high dose plasma infusion management protocol with plasma exchange protocol. Findings obtained from this research are constructive to advance and enhance clinical prognosis in this category of case scienarios as regards gestational hemolytic uremic syndrome [6-15].

Atypical hemolytic uremic syndrome is a form of thrombotic microangiopathy linked to underlying genetic or acquired pathological basis that result from unrestrained complement system triggering, causing renal failure and other complications. Gestation associated with atypical haemolytic uremic syndrome reflects thrombotic microangiopathy occurring within the period of gestation or after delivery in the postpartum time zone, additionally it is considered a systemic morbid disease with high rate of maternal mortality. However it is a rare clinical scenario occurring 1 in every 25,000 conceptions reflecting one fifth of all cases presented with atypical heamolytic uremic syndrome in females [16-20].

HUS represents a medical emergency, the prognosis of which has been outstandingly improved by the administration of large volumes of plasma, either associated with plasmapheresis or not. The efficacy of other agents, such as steroids and antiplatelet agents, has not been validated in randomized studies and remains widely debated [11]. Indeed, their use is empirical and depends on the clinician's experience [24-28]. Large volumes of plasma are required for the management of HUS, and therapeutic plasma exchanges are usually recommended to avoid fluid overload [24, 25].

However, when compared with high-dose plasma infusion, therapeutic plasma exchange is a cumbersome [8] and invasive (23] procedure that may not be available easily, especially in emergency settings. Few studies have attempted to compare these 2 therapeutic modalities [18, 24]. The authors of a large prospective study reported therapeutic plasma exchange to be superior to plasma infusion [24]. In this study, however, the volumes of plasma administered in the plasma infusion group were low compared with those of the therapeutic plasma exchange group (15 versus 45 mL/kg per day, respectively), and therefore the clear effectiveness of high-dose plasma infusion could not be tested. In this retrospective analysis, we compared the relative efficacy of high-dose plasma infusion (25–30 mL/kg per day) and therapeutic plasma exchange to assess if high-dose plasma infusion could be used as an efficient and safe first-line therapy for TTP/HUS in emergency settings.

Methodology

Data obtained for our research is obtained from demerdash maternity hospital and hemodialysis unit hospital records and data system. Tabulated and analyzed for observation of clinical outcomes of interest.

Results

case	Dgn aHUS before	Previous pregnancies,	Age (yr)	Time of onset	Type of birth	Hb min (g/dl)	Plaq min (3 109/l)	LDH max (mg/dl	sCr max (mg/dl)	Plasma infusion	Other therapie	
1	no	no	37	11 dPP	cs	7	60	2000	HD	NO	NO	CR
2	no	no	21	5 dpp	cs	6.8	30	2620	HD	NO	FFP	CR
3	yes	no	24	7dpp	Vd	5.3	175	300	1.7	NO	NO	ESRD
4	no	no	34	6wpp	vd	6.7	70	850	HD	NO	PE,CC,CP	ESRD
5	no	no	38	5dpp	cs	7.4	23	3330	2.3	YES	PE	ESRD
6	no	1FTP, Vd	41	4wpp	cs	6	56	1900	HD	NO	PE	CR
7	no	no	21	5dpp	cs	5.8	25	4450	HD	NO	PE	CR
8	no	no	42	4dpp	cs	5.9	65	2550	HD	YES	PE	ESRD
9	no	2FTP, 2Vd	28	1dpp	Vd	6.4	55	3000	4.1	NO	heparin	ESRD
10	no	1FTP, 1Vd	37	1dpp	cs	7	56	520	5	NO	PE,FFP	CR
11	no	No	35	1dpp	cs	8	40		HD	YES	PE	CR
12	yes	1A	38	36WG	cs	6	55	850	1.9	NO	PE	CR
13	no	1FTP, 1Vd	28	36WG	Vd	6.5	50	650	4.4	YES	PE	CR
14	no	no	35	19WG	A	8.1	40	5550	1.6	NO	PE	CR
15	yes	no	32	32WG	Vd	8.4	49	7050	2.8	YES	PE	Relapse,CKD
16	no	no	33	7dpp	cs	8	66	700	HD	NO	NO	CR
17	no	no	28	1dpp	cs	6.4	55	500	4.5	YES	PE	ESRD
18	no	2A	40	36WG	cs	6.5	20	340	HD	YES	PE	CKD
19	yes	no	24	19WG	cs	7	54	800	3.4	YES	NO	Relapse,CKD
20	no	no	25	2dpp	cs	7.3	90	1400	3.9	YES	PE	CR
21	no	no	25	9dpp	cs	6	20	4000	4.1	NO	PE	Relapse,CKD
22	no	no	39	7dpp	cs	7.1	85	1600	3	YES	PE	ESRD

Table 1: demonstrates demographic data of cases studied and management modes and clinical outcomes CR :complete resolution ,CKD :Chronic Kidney Disease, PE: Plasma exchange,

Group I	Group II	P value
8/12	7/10	>0.05 (non significant)

Table 2: demonstrates non-significant differences between the two groups as regards the complete resolution rate.

Discussion

HUS is a severe life-threatening systemic disorder requiring prompt treatment. High-dose plasma therapy has improved the prognosis dramatically, permitting complete remission in 70%-80% of cases [24]. Since it allows the infusion of larger volumes of plasma, therapeutic plasma exchange has been reported to be the treatment of choice, compared with plasma infusion alone, in a comparative trial [24]. It also has been suggested that therapeutic plasma exchange may remove toxic factors from plasma and restore normal plasma viscosity [25]. However, therapeutic plasma exchange imposes a heavy demand on available resources, which may be difficult to obtain, especially in an emergency. Furthermore, the efficiency of plasma infusion alone has been largely reported, especially when large volumes of plasma are delivered [26]. Indeed, high-dose plasma infusion represents an interesting alternative therapy for HUS in emergency settings.

This approach was influenced at least in part by the fact that in previous studies [19,24]. Clinical and standard biologic parameters on admission were reported to have a poor prognostic value, particularly in terms of response to treatment. Despite the retrospective nature of our study and the fact that therapeutic decisions were not randomized, neurologic involvement was represented equally in both groups, including the more severe variants, and laboratory values on admission were comparable in the 2 groups. Importantly, patients with HUS associated with bone marrow or hematopoietic stem cell transplantation, metastatic cancer, or CDC stage C HIV disease were excluded because the disease course was determined by the primary underlying disease, regardless of initial treatment.

In both groups, patients received large volumes of plasma daily, with similar treatment duration. We found that complete remission and mortality rates in the HD-PI group were comparable to those of the TPE group.

However, the parenteral administration of large doses of protein (protein content of infused plasma is at least 5 g/dL, with 60% albumin) [27] is believed to enhance the glomerular epithelial cell absorption of albumin [28]. Studies on experimental rat models of overload proteinuria induced by infusion of bovine serum albumin have shown that increased transcapillary movement of proteins causes degenerative changes of glomerular epithelial cells. These lesions are characterized by swelling, vacuolization, increased reabsorption droplets, and detachment of glomerular epithelium from the underlying glomerular basement membrane, which lead to large pore defects. In these studies, however, changes were completely reversible [29]. In our patients, the possibility that preexisting glomerular lesions related to HUS may have facilitated an alteration in glomerular membrane pore structure cannot be ruled out.

In both groups, steroids were administered inconsistently compared with others [30], largely because in both groups of our study, infectious diseases hampered the use of steroids in many patients (8 patients in the HD-PI group and 6 in the TPE group).

Particularly, Rock et al [31] conducted a prospective and randomized study that compared therapeutic plasma exchange (45–60 mL/kg daily) with plasma infusion (15 mL/kg per day). The outcomes in the 2 groups were compared 9 days and again 6 months after entry into the trial. At both 9 days and 6 months, response rates were significantly higher in the TPE group than in the plasma infusion group (TPE group: 24/51 and 40/51, respectively; plasma infusion group: 13/51 and 25/51, respectively). However, one may hypothesize that higher volumes of plasma in the plasma infusion group may have improved the response rate in this group.

In a retrospective study, Novitzky et al [32] compared 10 patients treated with plasma infusion (25.9 mL/kg per day) as first-line therapy with 9 others treated with therapeutic plasma exchange. They found that with plasma infusion, 6 patients responded while 4 others did not and died. Three of these patients were switched to therapeutic plasma exchange with no efficacy.

As in other studies [33-35], no prognostic factors could be defined on admission, which emphasizes that specific therapies based on initial clinical and standard biologic parameters remain challenging in HUS.

Conclusion

Our results suggest that high-dose plasma infusion (25–30 mL/kg per day) is an efficient treatment of TTP/HUS in an emergency, especially when therapeutic plasma exchange is not available, since neither complete remission and mortality rates, nor median duration of clinical and biologic abnormalities are worsened. Moreover, high-dose plasma infusion may reduce the duration of central catheter use, which may prevent complications such as thrombosis or infections. However, high-dose plasma infusion may be rapidly hampered by fluid overload, and may thus require a switch to therapeutic plasma exchange until complete remission. Other side effects such as transient proteinuria may also be observed in prolonged high-dose plasma infusion treatment. Therefore, the occurrence of proteinuria or the exacerbation of preexisting proteinuria during high-dose plasma infusion treatment may not systematically indicate a renal manifestation of HUS, and should not warrant a renal biopsy.

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