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Envenoming after carpet viper (*Echis ocellatus*) bite during pregnancy: timely use of effective antivenom improves maternal and foetal outcomes

A. G. Habib¹, S. B. Abubakar², I. S. Abubakar³, S. Larnyang², N. Durfa⁴, A. Nasidi⁴, P. O. Yusuf², J. Garnvwa⁵, R. D. G. Theakston⁵, L. Salako⁴, and D. A. Warrell⁶ for the EchiTab Study Group (Nigeria & UK)

¹ Department of Medicine, Bayero University Kano, Aminu Kano Teaching Hospital, Kano, Nigeria

² Kaltungo General Hospital, Kaltungo, Nigeria

³ Department of Community Medicine, Aminu Kano Teaching Hospital, Kano, Nigeria

⁴ EchiTab Study Group, Federal Ministry of Health, Abuja, Nigeria

⁵ Liverpool School of Tropical Medicine & Hygiene, Liverpool, UK

⁶ Centre for Tropical Medicine, University of Oxford, Oxford, UK

Summary

The report describes successful management of 10 women in 2nd and 3rd pregnancy trimesters with EchiTab IgG antivenom after carpet viper (*Echis ocellatus*) envenoming. All women survived but foetal loss in a victim with delayed presentation and a case of mild hypersensitivity reaction were recorded. Excellent outcomes can be achieved in rural and semi-nomadic populations without specialized care and immediate access and provision of effective antivenoms is paramount in curtailing snakebite maternal morbidity, mortality and foetal loss.

Keywords

antivenom; carpet viper; foetal loss; maternal morbidity; nomads; pregnancy

Introduction

Snakebite is a major medical problem among rural communities of the savanna region of West Africa, notably in Benin, Burkina-Faso, Cameroon, Ghana, Nigeria and Togo (Warrell & Arnett 1976). The saw-scaled or carpet viper (*Echis ocellatus*) has proved to be the most important cause of snakebite mortality and morbidity in the region. The precise incidence of snakebite is difficult to determine and is often grossly underestimated, but in parts of the Nigerian savanna its victims may occupy more than 10% of hospital beds. In the Benue valley of Nigeria, the estimated incidence is 497 per 100 000 population per year with 10–20% untreated mortality (Warrell & Arnett 1976; Pugh & Theakston 1980). The main clinical features of *E. ocellatus* envenoming are systemic haemorrhage, incoagulable blood, shock, local swelling, bleeding and occasionally necrosis (Meyer et al. 1997).

In many tropical countries men and women are equally exposed to the environmental and occupational hazards of snakebite. In a large series of hospital admissions due to snakebite reported from South Africa, pregnant women accounted for 0.4% of cases (McNally & Reitz 1987). Hospital records are misleading and the true incidence of snakebite is unknown, but it

may play a significant role in maternal morbidity, mortality and foetal loss in those societies. During a study in 2006 7 at a rural hospital in northeastern Nigeria, Kaltungo General Hospital, Gombe state, records of pregnant women who had snakebite were evaluated and are reported here.

Patients and results

In 2007, 1803 victims of snakebite with 26 deaths were seen at Kaltungo General Hospital. Snakes that bite the patients were identified when killed and brought to hospital or by incoagulable blood using the simple 20-min whole blood clotting test [WBCT20] which is diagnostic of carpet viper in this part of Nigeria (Meyer et al. 1997). More than 90% of the bites were due to *E. ocellatus*; 21 were due to *Naja* spp, four to *Bitis arietans* and the rest to *Atractaspis* spp, *Telescopus variegatus* or unidentified snakes. Eleven patients were pregnant, of whom 10 were bitten by *E. ocellatus* and one by *Naja nigricollis* (cobra). Eight of the 10 victims were nomadic or semi-nomadic Fulani maids (Table 1).

An illustrative case is that of a 17 year old Tangale Waja student who was 6 months pregnant at presentation. She was bitten on the left foot by a carpet viper 6 days prior to hospitalization while walking to the toilet. No tourniquet was applied but incisions were made at the bite site. She was treated by a traditional herbalist for 6 days and had vomited several times after ingesting concoctions. At presentation she was weak and very pale and her left leg was severely swollen to the hip joint. She had a 3-day history of gum bleeding, epistaxis and maleana; foetal heart sounds were not heard at presentation. Three millilitre of fresh whole blood placed in a clean test tube failed to clot within 20 min and she was treated with slow intravenous 20 ml of EchiTab IgG *E. ocellatus* monospecific antivenom (MicroPharm Ltd, London, UK), intravenous hydrocortisone 100 mg and normal saline alternating with 5% dextrose saline. She achieved restoration of WBCT20 1 day after admission and was transfused with a pint of fresh whole blood, after which she immediately and spontaneously delivered a stillbirth. Intravenous ampiclox and metronidazole were commenced together with oral ferrous sulphate and folic acid. Subsequently, daily WBCT20 did clot, the swelling subsided and the patient was discharged 6 days later after marked improvement with a 2-week follow up request.

Discussions

This case series suggests that snakebite, in particular carpet viper bite, is a significant cause of maternal morbidity and foetal loss among underprivileged rural dwellers in the West African savanna. Foetal loss resulted from delayed presentation in a patient but there are several possible mechanisms for foetal loss after snakebite: they include the direct effects of venom on the foetus, foetal hypoxia due to maternal shock, venom-induced uterine contractions and placental bleeding due to coagulopathy. None of our patients had vaginal bleeding, although intra-uterine foetal death without bleeding [confirmed using transvaginal ultrasonography] has been reported (Nasu et al. 2004) and abruptio placentae after snakebite is a recognized cause of premature labour and foetal wastage (Zugaib et al. 1985; Adam & Gerais 2005). Snake venom is a mixture of complex biochemical compounds including potentially tocolytic substances that may induce uterine contractions but their exact role in premature labour and maternal morbidity is unknown.

In series recording bites from several types of snakes, foetal wastage rates were 28% and 43%, rising to 58% in a subgroup given antivenom, which may reflect the severity of envenoming (Dunnihoo et al. 1992; Seneviratne et al. 2002). But after bites with procoagulant/haemorrhagin-containing venoms and with evidence of systemic bleeding, foetal loss without antivenom use was (1/1) 100% after a pit viper bite (Nasu et al. 2004)

and with use of antivenom it was 0/1 (0%) after pit viper bite and 4/7 (57%) after Russell's viper bite in Sri Lanka (Seneviratne et al. 2002; Chang et al. 2005), a considerably higher rate than the 1/10 (10%) reported here with timely use of effective antivenom after carpet viper bite. Previous reports suggested that miscarriage tended to be more common during the first trimester but our cases and several others confirm that it can occur at other times during pregnancy (Dunnihoo et al. 1992; Pantanowitz & Guidozzi 1996; Seneviratne et al. 2002; Nasu et al. 2004; Chang et al. 2005; Kravitz & Gerardo 2006). However, it is possible that mechanisms of foetal loss, maternal morbidity and mortality may vary by gestational age. Indeed, in advanced pregnancy victims should not be managed supine, as supine hypotensive syndrome might exacerbate hypotensive shock from envenoming or blood loss and contribute to mortality (Sutherland et al. 1982). A maternal mortality rate of 10% has been reported but treatment with antivenoms resulted in good outcome with no death in this and other series (Dunnihoo et al. 1992; Seneviratne et al. 2002; Chang et al. 2005; Kravitz & Gerardo 2006). This was achieved mainly because effective antivenoms were used promptly (mostly within 1 or 2 days of the bite).

Hypersensitivity reactions were noted in 10%; the risk appeared lower than that observed in non-pregnant and pregnant adults (Meyer et al. 1997; Seneviratne et al. 2002) but appropriate interventions should be available when antivenoms are administered. Antivenom may be lifesaving for the mother, but management of reactions with the use of adrenaline may compromise placental circulation and should be used cautiously and only when necessary. Birth anomalies and malformations have been reported after experimentally induced envenoming in pregnant animals and/or their embryos and after bites in pregnant women (Nawar 1980; Seneviratne et al. 2002). Most (80%) of our patients were nomads, which precluded follow-up and post-delivery evaluation for defects. Biological agents such as childhood vaccines, immune globulins and some antivenoms are known to contain thimerosal [a mercury containing preservative], but prenatal exposure to it was not associated with neuropsychological deficits in children (Thompson et al. 2007). Pregnant women are excluded in clinical trials of new agents and managed with the standard of care; but if the standard of care is clearly sub-optimal, ineffective or non-existent and untreated mortality reaches 20%, then clinical and ethical decisions should be taken to treat victims with the new antivenoms after obtaining informed consent, especially when the preliminary experience is promising. Effective antivenom remains the only specific treatment for snakebite envenoming and the objective should be safeguarding maternal health while maximizing the chance of a successful pregnancy.

In the tropics, poisonous snakebite is a problem of vulnerable hard-to-reach societies such as pastoral or rural communities. To optimize resources, health facilities should be designated and stocked year-round with the relevant antivenoms to care for victims in high risk areas like the Benue and Niger valleys and the West African savanna. As at Kaltungo General Hospital, care-givers should be trained and public awareness increased through media coverage and sensitization so that victims know where to access care without delay, avoiding useless, time wasting and potentially harmful traditional remedies. Of our patients with favourable outcomes eight were treated within 1 day of the bite and one within 2 days. The delay between bite and antivenom administration may have important consequences for managing pregnant patients.

We found that excellent outcomes can be achieved even in rural hospitals without specialized care and that immediate access and provision of effective antivenoms is paramount in curtailing snakebite maternal morbidity and the double tragedy of maternal and foetal loss, especially as dangerously inappropriate foreign products are commonly being marketed by unscrupulous manufacturers in rural Africa (Warrell 2008).

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Table 1
 Characteristics, presentation and management of 10 pregnant women bitten by carpet viper

SN	Initials age tribe DOA	Gestational age in weeks	Circumstance of snakebite	Presentation	WBCT20 at admission	Antivenom at KGGH [Bite to antivenom time (h/day)]	Management	LOS	Outcome
1	M. B. 35 year Tangale- Waja 11/2/07	28	Bitten by CV on foot 16 h; snake killed	Severe right foot swelling	Non-clotting	SAIMR 10 ml [16 h]	Tetanus toxoid Paracetamol vitamin C	12 day	Restored clotting and cured; viable pregnancy
2	A. A. 20 year Fulani 11/7/07	Pregnant; 20	Bitten but snake not seen or killed	Severe right leg swelling up to knee joint	Non-clotting	EchiTab 10 ml [16 h]	Tetanus toxoid Paracetamol vitamin C	6 day	Restored clotting and full recovery; intact pregnancy
3	A. R. 30 year Fulani 13/5/07	32	Bitten by CV on right hand; snake killed	Moderate swelling up to the wrist	Non-clotting	EchiTab 10 ml [18 h]	Tetanus toxoid Paracetamol vitamin C	4 day	Restored clotting; had bloody bullae; recovered
4	S. A. 23 year Fulani 31/8/07	28	Bitten by CV on right foot; snake not killed	Severe swelling of right foot	Non-clotting	EchiTab 20 ml and 10 ml repeated [7 h]	Tetanus toxoid Paracetamol	4 day	Restored clotting; improved; intact pregnancy
5	L. A. 25 year Fulani 26/3/07	20	Bitten by CV on left foot	Severe swelling up to mid thigh	Non-clotting	EchiTab 20 ml [9h]	Tetanus toxoid Paracetamol	5 day	Restored clotting; improved; discharged
6	M. M. 15 year Fulani 19/4/07	36	Bitten by CV on left foot; snake killed	Severe swelling up to the knee joint	Non-clotting	EchiTab 20 ml [5h]	Tetanus toxoid Paracetamol Adrenaline Hydrocortisone Chlorpheniramine	5 day	Restored clotting; severely reacted to ASV
7*	J. M. 17 year Tangale-waja 14/4/07	24	Bitten by CV on left foot; 6 day before presentation	Severe swelling; anaemia epistaxis gum bleeding maleana	Non-clotting	EchiTab 20 ml [6 day]	Blood transfusion Ampiclox Flagyl	6 day	Stillbirth; restored clotting and improved
8	M. B. .25 year Fulani 2/4/07	36	Bitten by CV on left foot	Severe swelling up to knee joint; bleeding at bite site	Non-clotting	EchiTab 20 ml [? 2 day]	Hydrocortisone Paracetamol	5 day	Restored clotting; intact pregnancy
9	M.H. 26 year Fulani 4/10/07	28	Bitten by CV on left foot	Gross swelling up to mid thigh	Non-clotting	EchiTab 20 ml [6h]	Tetanus toxoid Paracetamol	4 day	Restored clotting; improved with intact pregnancy

Initials	age	tribe	Gestational age in weeks	Circumstance of snakebite	Presentation	WBCT20 at admission	Antivenom at KGH [Bite to antivenom time (h/day)]	Management	LOS	Outcome
SN	DOA									
10	U. H.	14 years Fulani	28	Bitten by CV on left foot	Gross swelling; haematuria; foetal heart sounds – present	Clotting [had received SAIMR 10 ml × 3]	Nil at KGH [1 day; received antivenom in another town]	Tetanus toxoid Paracetamol Wound debridement	6 day	Restored clotting; improved; intact pregnancy

CV, carpet viper; DOA, date of admission; KGH, Kaltungo General Hospital; LOS, length of stay in days; SAIMR, South African Institute for Medical Research; WBCT20, 20 min whole blood clotting test.

* Illustrative case described under patients and results..