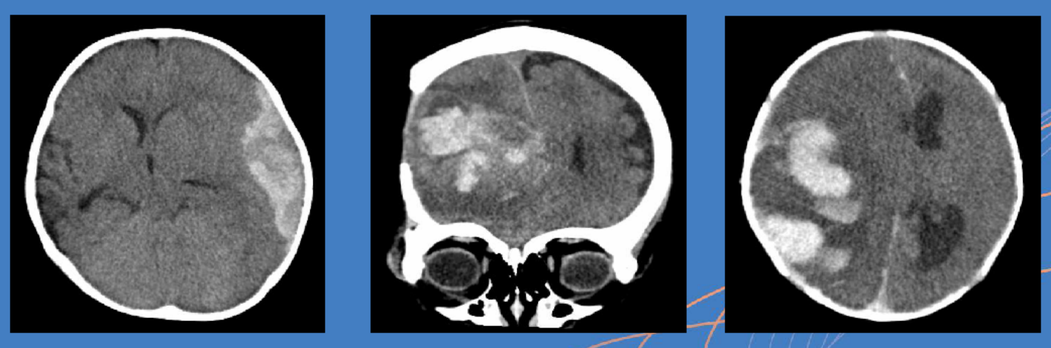

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Diagnostic and Management Delays in Children with Haemophilia Presenting with Intracranial Haemorrhage

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INTRODUCTION

Intracranial haemorrhage (ICH) can be the presenting bleed in children with haemophilia and causes significant morbidity and mortality. Successful management of ICH in these children hinges on early diagnosis and appropriate treatment with clotting factor replacement therapy and / or neurosurgical intervention. We aimed to look at factors influencing the diagnosis and management of children with haemophilia presenting with ICH at our institution over a 12-year period from 2002 to 2013.

RESULTS

There were 5 patients who presented with ICH at diagnosis, who made up 16% of 32 new cases of haemophilia diagnosed over the same period. The median age at presentation was 119 days. The most frequent presenting symptoms were fever (80%), tense fontanelle (80%), seizures (60%) and vomiting (60%). There was no preceding history of trauma in any patient. All cases were diagnosed via neuroimaging within 24 hours of admission.

Table 1 shows the clinical details of these patients at diagnosis:

Patient	Age (Days)	Symptom (Duration in days)	Site of Bleed
1	108	Fever (3), Vomiting (3), Tense fontanelle (1)	Right parietotemporal ICH
2	119	Fever (3), Vomiting (1), Focal seizure (1)	Left frontal intraparenchymal, subdural and subarachnoid haemorrhage
3	152	Irritability (2), Lethargy (1), Tense fontanelle (1)	Right frontotemporal ICH
4	122	Fever (4), Seizures (1), Tense fontanelle (1)	Right subdural and subarachnoid haemorrhage in right cerebral hemisphere
5	16	Fever (3), Poor feeding (3), Lethargy (1), Tense fontanelle (1)	Right frontotemporoparietal ICH

Although the APTT was raised in all 5 cases, clotting factor assays were not sent prior to infusion of FFP infusion in 40% of cases. The time taken from acknowledgment of a prolonged APTT to haematologist referral ranged from 0 to 3 days. The median time interval between diagnosis of an ICH to appropriate clotting factor replacement therapy was 17 hours (range 1 to 84 hours). Factors associated with a faster time to diagnosis and appropriate clotting factor concentrate therapy included initial admission to the Intensive Care Unit and early referral to a haematologist. 80% of patients survived, with neurodevelopmental delays noted in 50%.

Table 2 shows the management details of the 5 patients:

Patient	Known Family History	Admitting Unit	Clotting Assays Sent Before Blood Product Infusion	APTT	Coagulation Factors	Diagnosis	Management Details
1	No	General Ward	No	89.4s (19/12/04 1026h)	Factor VIII 6% (22/12/04 1220h) – sent after FFP transfusion	Severe Haemophilia A	Referred haematologist on 22/12/04 – 3 days after APTT result FFP infusion from 19/12/04 to 22/12/04 Factor VIII concentrate from 22/12/04 2240h – 84h after APTT result Total 10 doses, 4700 units (~670 units/kg)
2	Yes	General Ward	No	152.9s (09/08/09 1609)	Factor IX 3% (11/08/09 1233h) – sent after FFP transfusion	Severe Haemophilia B	Referred haematologist on 11/08/09 – 2 days after APTT result FFP infusion from 09/08/09 to 10/08/09 Factor IX concentrate from 11/08/09 2030h – 52h after APTT result Total 7 doses, 3500 units (~450 units/kg)
3	No	Intensive Care Unit	Yes	81.5s (05/03/11 1901h)	Initial sample sent for coagulation factors on 05/03/11 clotted Repeat Factor VIII <1% (05/04/11)	Severe Haemophilia A	Referred haematologist on 05/03/11 – day of APTT result FFP infusion from 05/03/11 to 06/03/11 Factor VIII concentrate from 06/03/11 1209h – 17h after APTT result Total 14 doses, 6350 units (~790 units/kg)
4	No	Intensive Care Unit	Yes	149s (30/01/12 0250h)	Factor IX <1% (30/01/12 0454h)	Severe Haemophilia B	Referred haematologist on 30/01/12 – day of APTT result FFP and cryoprecipitate infusion on 30/01/12 Factor IX concentrate from 30/01/12 1700h – 14h after APTT result Total 25 doses, 13000 units (~1625 units/kg)
5	Yes	Intensive Care Unit	Yes	139.5s (05/07/13 0220h)	Factor IX < 1% (05/07/13 0405h)	Severe Haemophilia B	Referred haematologist on 05/07/13 – day of APTT result Factor IX concentrate from 05/07/13 0226h – immediately on receipt of APTT result Total 13 doses, 6500 units (~1750 units/kg)

CONCLUSION

Haemophilia as an underlying cause of ICH is still under-recognised even in a tertiary paediatric institution, and associated with diagnostic and management delays, especially in children without a prior family history of a bleeding disorder. Even a positive family history of haemophilia in one of the children presenting with ICH (Case #2) did not prompt early, appropriate investigations to exclude a bleeding disorder. More efforts were made in our institution to raise awareness of congenital bleeding disorders as a possible cause of spontaneous ICH amongst general paediatricians. As a result, the time to diagnostic investigations, haematologist referral and appropriate treatment has improved over recent years.