Virtual Teaching Programme
Case Studies: Haemoglobinopathies Including Newborn Screening – The Challenges and Discrepancies

Session 2

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No. 824021

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Welcome & Housekeeping

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Session Etiquette

- We are unable to make recordings of these sessions public due to General Data Protection Regulations (GDPR) around the sharing of personal data.
  Remain on mute if you are not speaking.
- Use the chat box to type your questions, or use the raise hand feature if you want to ask a question.
- Nominate a member of your team to take notes during the breakout sessions.
- Contribute to the discussions.
- Return promptly from the comfort break.
- Complete the post session feedback form.
- Both sessions are CPD accredited and certificates of attendance will be awarded after the session.

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Introductions

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Session overview

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AGENDA

Introduction

Recap & Actions from previous session 20mins

University of Abuja: Case study 1
Presentation – 10mins
Group discussions – 5mins
Panel discussion – 10mins

IFAIN: Case study 2
Presentation – 10mins
Group discussions – 5mins
Panel discussion – 10mins

Break 10mins

Zankli medical centre: Case study 3
Presentation – 10mins
Group discussions – 5mins
Panel discussion – 10mins

Feedback survey

Session Summary & closing remarks (Panel)

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Presentation 1

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CASE PRESENTATION: FEMALE SCA IN HER THIRTIES PATIENT WITH IRON OVERLOAD, CARDIOVACULAR, GYNAECOLOGIC AND RENAL COMPLICATIONS.

CHALLENGES IN MANAGENENT OF CHRONIC COMPLICATIONS OF SCD IN AN ADULT PATIENT IN RESUORCE POOR SETTING.

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Female SCA patient in her 30s was referred to UATH Haematology Clinic in 04/02/2013 on account of severe anaemia (Hb – 5 gm/dL, PCV -15%).

➢ Presenting complaints:

- Weakness, easy fatigability, deepening yellowish discoloration of the eyes, LT forearm pain (pain score – 4/10) and fever x 3/7.
- No associated head ache, chest pain, GIT or GUT symptoms
- **Past medical:**
- Had two units of blood transfused 2 weeks prior to presentation
- Diagnosed with SCA at 6/12 (Hb cellulose acetate electrophoresis).
- 1st BT at toddler age (once or twice/yr, then 3x – 4x/year since 2006 (teenage years). Has had > 30 units of BT as at time of presentation.
- Steady state PCV: 18 – 20%.

➢ Assessment: Hyperhaemolysis and Fever in SCA patient? Cause.

- R/O Delay haemolytic transfusion reaction.
- R/O Malaria

- FBC: PCV-14%, MCV-76Fl, MCH-27pg, MCHC-35g/dL RBC:-SCs, Target cells, NRBCs. WBC:-15.3 x 10^9/L, N-75%, L-20%, M-3%, E-2%; PLT-347 x 10^9/L. Neutrophil toxic granulation.
- LFT – Highly elevated (total, direct & indirect) bilirubin, mildly elevated liver enzymes, normal serum proteins.
- RFT: Serum electrolytes including Ca; Urea and creatinine values were within normal reference ranges with eGFR > 90 ml/min/1.73m²
- Urinalysis: Positive for proteins, bilirubin and urobilinigen

- Viral screening for HIV, HBsAg, HCV were all negative.
- Blood film for MP showed P. falciparum trophozoites
- Alloantibody screening – DAT - negative & IAT - positive. Antibody identification not performed.
- CXR- Mild cardiomegaly, ECG- LVH, ECHO- mild dilated heart, low normal systolic function, mild tricuspid & aortic regurgitation , grade 1 diastolic dysfunction.
- Other investigations requested but were not done include: Hb Quantitation, Serum Lactate dehydrogenase, Ferritin, C-reactive protein.

➢ **Patient had Partial EBT, Antimalarial, Antibiotics and Analgesics. Post-transfusion PCV -29%.**

➢ She was regular on follow-up visits and her routine medications (Folic acid & Paludrine).

➢ FBC: PCV - 25%, Hb-8.2 g/dL, MVC- 80Fl, MCH -30 pg, MCHC-35 g/dL, few SCs, Target cells, WBC - 6.5 x 10^9/L, N-60%, L-35%, M- 3%, e -2%, Plat. – 236 x 10^9 /L

➢ Hb Quantitation: Hb A -35.9, HbA2 -3.9, Hb F – 1.2, Hb S -59.7 (performed in private laboratory – 17/04/2013):- Baseline for commencement of Hydroxyurea.

➢ **In June 2013, she presented to the clinic with complaints of Heavy menstrual flow associated with lower abd. Pain, dysuria & fever x 2/7. She was referred for Gynae consultation. Diagnosed as Menorrhagia with UTI ? Cause**

- **FBC: PCV – 17%, MCV – 80 Fl, MCH – 30 pg, MCHC 35g/dL, few SCs, Target cell, no NRBCs. WBC: 9.5 x 10^9/L, N-78%, L-20%, E-2%. Platelet: 234 x 10^9/L**
- **Transvaginal USS** – Uterine myoma (4.1cm x 3.8cm)
- Urine m/c/s – Klebsiella pneumoniae sensitive to Ofloxacin & Ciprofloxacin.

- Was co-managed appropriately with the Gynae team (partial EBT, Antibiotics, HU, Mefenamic acid).

➢ **Serum Ferritin: 3481 ng/ml (10 150ng/ml) performed at a private laboratory 04/04/2014. Baseline at which Deferasirox was commenced. Serum Ferritin: ?? 1104 ng/ml (12/06/14)**

➢ **By 2015 she had developed Hypertension (BP – 150/90 mmHg); RFTs: serial elevation of serum urea & creatinine, and diminishing estimated GFRs with worsening anaemia, PCV – 13%, no SCs, no NRBCs; she three episodes of seizures; . She was reviewed by Cardiology, Neurology, Nephrology & Gynae teams.**

- **CT Scan / MRI: Not performed.**
- **Abdominopelvic USS: Grade 1 bilateral renal parenchymal disease.**

- **She is currently being co-managed with these teams on partial EBT/simple BT, EPO, Antihypertensive drugs; Norethisterone (Primolut N) & Mefenamic acid menstrual cycles.**

➢ **2015 – 2016/2017, she was not regular on follow-up visits, discontinued HU. Had multiple BT.**

- **Hb Quantitation: Hb A – 76.6%, Hb A2-3.6%, Hb F 1.8 Hb S -18% (05/09/2019).**
- **?? >2000ng/ml (10 -150ng/ml - 22/11/2019); 6442 ng/ml (10 - 150ng/ml - 23/01/2020)**

➢ **Challenges in Management of Chronic Complications of SCD in Adult Patients.**

- Lack of essential ancillary investigation tools such as Reagent RBCs, ELISA,HPLC, IEF, TCD, MRI, for accurate diagnosis & effective monitoring of treatment of chronic complications of SCD.
- Availability of safe and quality blood components.

➢ **I thank and commend Daimler & Benz Foundation (ARISE) for their support in human capacity development & other various ways to ameliorate some of these challenges.**

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Group Discussion 1

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In your group discussion: Consider

- Are there any good practice points from the case presentation?
- What would our laboratory / clinical service have done differently?
- What are the main learning points from the case?
- 1-2 examples of what we might change e.g. laboratory / clinical processes and pathways

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Panel Discussion 1

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Challenges faced in current diagnostic methodologies, clinical outcomes and potential interventions

Grace Olanipekun *(MPH,BMLS)*

International Foundation Against Infectious Diseases in Nigeria (IFAIN)

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Case Study

- A baby with no previous history of anaemia presents to the clinic with the following symptoms:
  - Short duration of illness
  - Irritability
  - Fever
  - Pallor
  - Shallow breathing
  - Yellowness of the whites of the eyes

- Previous laboratory test for Hb genotype = AS
- Method used for the previous test- Not known

What was done to resolve the discrepancies?

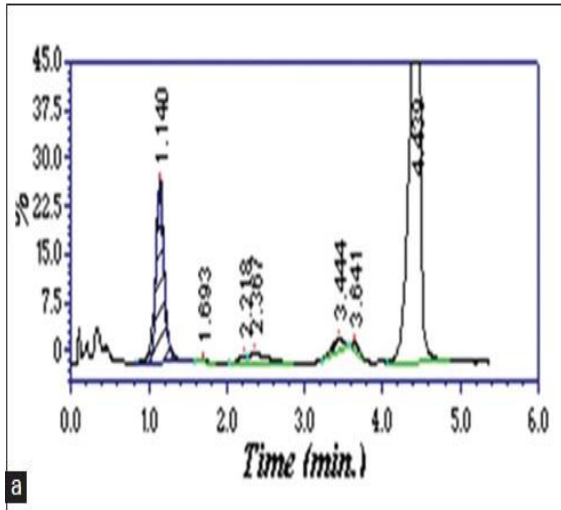
- Repeat test was done for baby using alkaline electrophoresis at Zankli medical centre.
- Test of baby previously reported as AS was identified as SS.

- Parental investigation(done in the past) :
  - Baby's Mother was said to have an AA genotype by verbal information
  - Baby's father as said to have an AS Genotype, also by verbal information.

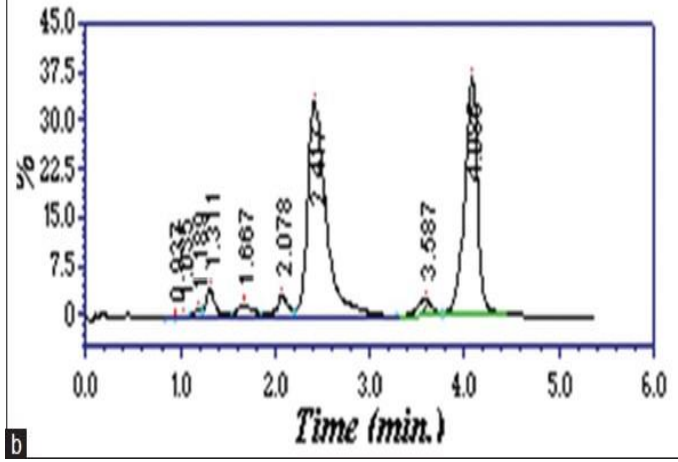
- We re-tested baby's sample using HPLC by IFAIN, also identified as SS
- Mother's sample was also tested, identified as AS.

Snapshot of typical HPLC results

HPLC results



Peak Name	RT	Area	Area %	Concentration
F	1.140	461713		21.2*
P3	1.693	2010	0.1	
Unknown	2.218	17666	0.8	
Ao	2.367	58628	2.6	
A2	3.444	45615		1.8
Unknown	3.641	17595	0.8	
S-window	4.439	1645248	73.2	



Peak Name	RT	Area	Area %	Concentration
Unknown	0.937	1054	0.0	
F	1.035	6571		0.3*
Unknown	1.189	18941	0.9	
P2	1.311	76646	3.6	
P3	1.667	55600	2.6	
Unknown	2.078	71297	3.3	
Ao	2.417	1060978	49.7	
A2	3.587	55306		2.4
D-window	4.085	788042	36.9	

Hb SS

Advice between diagnosis and treatment plan

- Accurate diagnosis was key to inform appropriate treatment plan. Focus was to:
  - Manage the pain
  - Treat possible infection
  - Prevent any further complications
  - Prevent end organ damage

Social consequences of delay in accurate and timely diagnosis

- For the patient:
  - An earlier (at birth), accurate diagnosis and with appropriate follow-up could have resulted in avoidance of clinical complications (sickle cell crisis).
- For the Father:
  - On confirmation of baby's result, the father walked out on the mother in anger probably due to shock.
  - there may have been some concerns of deceit
- For the Mother:
  - She experienced avoidable trauma and heartbreak

Take home lessons for medical team

- Appropriate age sensitive methods for screening should be used.
- Alkaline electrophoresis for neonates may not give accurate results.
- Misdiagnosis may sometimes need to be ruled out where laboratory results are not consistent with the clinical presentation. Repeat test using a different method.
- If the baby had been screened at birth, further investigations and appropriate follow-up would have been initiated earlier:
  - This could have prevented the significant costs (medical and social) to the family, as was observed in this case.

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In your group discussion: Consider

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Presentation 3

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Case Report

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- Baby D. I. M,1year 10months,Male.
- He was born in a private hospital at term via Elective C/section for foetal macrosomia
- BW-4.45kg.
- Blood Group-0 negative.
- Genotype-Not done at birth
- Child had mild neonatal jaundice at birth
- fully immunised for age

- Presented to our centre at 8 months of age with cough, fever and diff in breathing.
- Had severe anaemia with a PCV of 15%
- Diagnosis of sickle cell anaemia was made – HPLC
- He has had about 5 crises since diagnosis and has had 2 blood transfusions
- Last admission was 11/10/2020

- Steady state PCV – 21%
- Clinic visits were set for monthly, however have been irregular……comes only when unwell
- He is currently on Tabs Folic Acid,Paludrine and hydroxyurea…..recommenced on these after admission because mother had stopped medication.

Current parameters

- Reticulocytes 7.4%
- PCV-21%
- WBC 21 X 10^9/L
- Neut-31%
- Lymp-60%
- Mono-6%
- Eos-3%

- Sodium 134mmol/l
- Potassium-3.9mmol/l
- Sodium Bicarb-18mmol/l
- Urea-8mg/dl
- Creatinine-0.2mg/dl

- Liver Function Test:
- AST-46u/L.
- Alt-32u/l.
- Alk-277u/l.
- Total Bilirubin:1.6mg/dl
- Conj Bilirubin:0.8mg/dl

DISCUSSION

- DIAGNOSIS AT BIRTH – ideal situation
  feasibility
- PROBLEMS – follow up, medication
- Laboratory support – diagnosis

  follow up

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Please Complete the Session Feedback Survey

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Session Summary & Close

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