CASE REPORT

PAEDIATRIC HEPATIC HAEMANGIOMA-A RARE CAUSE OF PYREXIA OF UNKNOWN ORIGIN

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Pyrexia of unknown origin (PUO) has remained a diagnostic challenge for medical professionals for decades as its aetiology remains elusive and requires extensive investigation. Hepatic Haemangioma (HH) is generally not considered a possible cause of PUO. HH is the most frequent, non-cancerous tumour in children usually presents as vague abdominal pain. We describe a case of 4-year-old female presented with the complaint of dull abdominal pain associated with low grade fever. Extensive workup was done to find out the cause. Her haemoglobin also dropped suggestive of bleeding haemangioma. She was treated with steroids (prednisolone) which significantly reduced her inflammatory markers prior to surgery. Later, hepatectomy was done after informed consent. The surgery was uneventful, and her PUO was also resolved.

Keywords: Pyrexia of unknown origin; Hepatic Haemangioma; Bleeding haemangioma

Citation: Nasir H, Bashir H, Asghar I, Tahir I, Seerat I. Paediatric hepatic haemangioma-a rare cause of pyrexia of unknown origin. J Ayub Med Coll Abbottabad 2024;36(4):824–6.

DOI: 10.55519/JAMC-04-12918

INTRODUCTION

Pyrexia of unknown origin (PUO) was first described in 1961 by Petersdorf and Beeson in adults as fever above 38 °C or 101 °F for longer than 3 weeks without an established diagnosis after a week of inpatient investigations. In children fever lasting more than 10 days without a definite cause can also be labelled as PUO.[1] Infections remain the most common cause of PUO in paediatrics age group. Other possible subcategories for causes include inflammatory disorders, malignancies and miscellaneous.[2] Hepatic Haemangioma is a very rare cause of PUO and there are very few cases that have been reported. Hepatic Haemangioma is the most common benign tumour in children often presenting as vague abdominal pain. We report here a case of preschool child presented in outpatient clinic with the complaints of dull abdominal pain and fever.

CASE

A 4-year-old developmentally normal, vaccinated girl with weight at 5th percentile and height at 10th percentile for age was admitted to Pakistan Kidney and Liver Institute and RC Lahore with complaints of gradually increasing swelling in right hypochondrium for last one month associated with dull abdominal pain, distention, occasional vomiting, persistent low-grade fever highest documented spike was of 37.8, anorexia, and weight loss. No previous medical or surgical history. Family history was unremarkable. On physical examination patient has a firm non tender single mass extending from right hypochondrium crossing midline extend up to left lumbar region 7cm below the costal margin. There was conjunctival pallor but no jaundice, ascites, or pedal oedema. No remarkable findings on CVS, CNS, and respiratory examination.

Blood tests done are as follow:

LABS	UNITS	Before Surgery	After Surgery
Total Bilirubin	mg/dl	0.24	0.18
Direct Bilirubin	mg/dl	0.14	0.09
Indirect Bilirubin	mg/dl	0.1	0.09
ALT	U/L	48	20
AST	U/L	30	25
ALP	U/L	170	150
GGT	U/L	90	80
ALBUMIN	g/dl	2.93	3.94
Haemoglobin	g/dl	9.7	10.8
WBC	10^9/L	12.9	12.5
Platelets	10^9/L	534	639
CRP	mg/dl	15.9	0.6
Procalcitonin	ng/ml	0.03	0.46

Blood tumour markers were, Serum LDH 542 IU/l (normal range 105 to 333 IU/l), Serum alpha fetoprotein 2.96 ng/ml (normal range <8.2 ng/ml), serum b-hcg less than 0.1 mIU/ml (normal range <5 mIU/ml).

As part of partial septic screening, Viral markers HbsAg, anti HCV, anti-HIV were done and came out to be non-reactive, NS 1antigen, covid 19 PCR, Quanteferon Tb were all negative and malarial parasite were not seen. All Blood, Urine and Stool cultures came out to be negative. Chest X-ray was unremarkable. All other possible causes of persistent fever were ruled out.

Ultrasound done revealed A huge heterogeneous predominantly hypoechoic mass is

noted replacing the left lobe of the liver with few internal areas of necrosis.

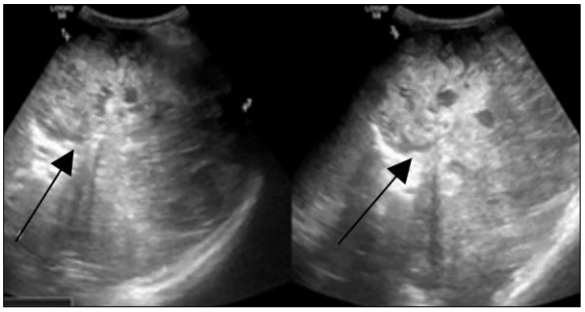

Figure-1: Ultrasound Liver (Black Arrows:Hemangioma)

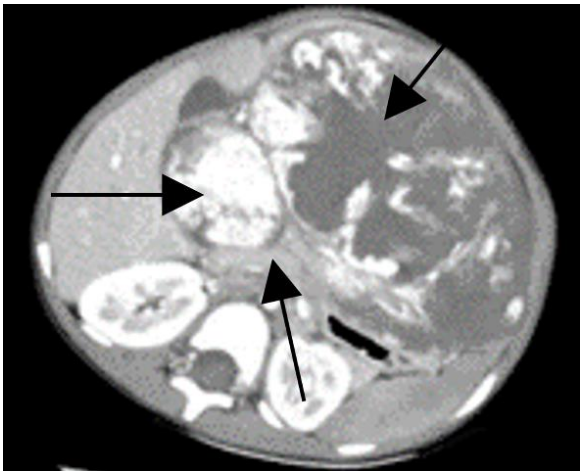

Figure-2: CT Abdomen (Black Arrows:Hemangioma)

Ct scan showed a large left hepatic lobe haemangioma measuring approximately 10×15×16 cm is re-demonstrated with peripheral contrast puddling and progressive peripheral enhancement with central area of necrosis. Left hepatic vein is severely attenuated however patent. Spleen, pancreas, gall bladder, stomach, gut loops appear unremarkable however compressed due to mass effect.

Histology was done to confirm the diagnosis. A lobulated tumour measuring 16×11×10 cm. Cut surface shows haemorrhage and some grey white areas. The tumour is 0.3 cm from the nearest parenchymal resection margin.

The sections show liver tissue involved by a vascular neoplasm composed of narrow vascular channels lined by plump endothelial cells. The cells have vesicular nuclei. Intervening spindle cell proliferation is also present. Some of the lining cells are forming papillary structures with entrapped bile ducts. There is central necrosis with some cavernous differentiation towards Centre of the lesion. There is variable nuclear atypia and mitotic figures. And CD31 was positive in tumour cells.

Patient was discharged 4 days after the surgery with no complications, without any episode of repeat fever or antibiotic requirement. Condition fairly improved. On follow up after 6 months, she was completely asymptomatic and her growth was satisfactory.

DISCUSSION

For many years, diagnosing PUO has been difficult. There have been numerous changes made to the definition, particularly in terms of the temporal criteria, which has gone from the original definition's 1 week of inpatient investigation to Durack and Street's 3 days of outpatient or inpatient investigation to Knockaert *et al*.'s most recent definition of the "pragmatic investigation period" and a structured diagnostic checklist without a time limit.[1,3,4]

After making a thorough and laborious effort to rule out the most prevalent causes of PUO, the diagnosis of exclusion for giant HH as the cause of PUO was made in our instance. The majority of benign hepatic tumours, or 70% of them, are HH.[5,6] HHs are blood-filled cavities lining the liver parenchyma that are supplied by a branch of the hepatic artery and lined with endothelial cells.5,6 0.4 to 20% of people are said to have HH.[5,6,8]

Small HH can be conservatively handled. In cases of sudden growth, unbearable pain, huge HH, or consequences including rupture, hemorrhage, or Kasabach-Merritt syndrome, surgery may be an option.[7,9] There are two peculiar characteristics of this case that demand notice; hence it is being reported. First, a low-grade fever that persisted for more than a month was the main clinical manifestation of the patient's massive haemangiomatous liver. Second, moderate dosages of prednisone had a substantial effect on the fever, and other clinical measures gradually improved as well. These improvements persisted for a long time after the use of steroids was stopped. The literature hardly ever refers to fever as a manifestation of this mass.

Although its exact mechanism of action is unknown, corticosteroid medication is the treatment of choice for young patients with severe cavernous haemangiomas of the skin and subcutaneous tissues.[10] Steroid therapy for hepatic haemangiomas has sometimes been documented as very useful. The quick reduction in fever together with the steady improvement in anaemia, weight, and work capacity show that the prednisone medication was effective above and beyond only serving as a generic antipyretic.

It is speculative how the fever developed and how prednisone might have had a positive effect. It is tempting to assume that damage to blood cells, particularly polymorphonuclear leukocytes, within the bounds of haemangioma results in the release of

pyrogens and, as a result, fever occurs. It is well recognized that haematomas themselves could be the source of fever, and it is undeniable that clotting frequently happens in haemangiomas, occasionally leading to calcifications in the lumens.[11,12]

Corticosteroids are long recognized to have anti-inflammatory and anti-pyretic effects. Although the exact mechanism of this fever suppression is unknown, experimental evidence supports both central effects on the hypothalamic centre that controls body temperature[13] and peripheral effects on leukocytes' production of pyrogen[14].

CONCLUSION

Patient was medically optimized with propranolol and steroid therapy successfully, prior to surgery after which her inflammatory markers, WBC count was in decreasing trend as well as the size of her haemangioma was reduced. Medical optimization with propranolol and prednisolone significantly improved her Anaemia and general wellbeing, indicating their prime significance in treatment of hepatic haemangioma. Hepatic haemangioma was the main cause of her Pyrexia of unknown origin (PUO). After surgery, her inflammatory markers were completely back to normal, no episode of fever was reported and patient's compression symptoms due to huge mass were relieved.

REFERENCES

1. Petersdorf RG, Beeson PB. Fever of unexplained origin: report on 100 cases. Medicine (Baltimore) 1961;40(1):1–30.
2. Rigante D, Esposito S. A roadmap for fever of unknown origin in children. Int J Immunopathol Pharmacol 2013;26(2):315–26.
3. Durack DT, Street AC. Fever of unknown origin-reexamined and redefined. Curr Clin Top Infect Dis 1991;11:35–51.
4. Knockaert DC, Vanderschueren S, Blockmans D. Fever of unknown origin in adults: 40 years on. J Intern Med 2003;253(3):263–75.
5. European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines on the management of benign liver tumours. J Hepatol 2016;65(2):386–98.
6. Toro A, Mahfouz AE, Ardiri A, Malaguarnera M, Malaguarnera G, Loria F, *et al*. What is changing in indications and treatment of hepatic hemangiomas. A review. Ann Hepatol 2014;13(4):327–39.
7. Montero L, Canchari PG, Peña AL, Guerra EG. Review article: A giant hepatic hemangiomas. Gastroenterol Hepatol (Bartlesville) 2017;7(5):00251.
8. Hopkins K, Bailey RJ. Hepatic hemangioma: An unusual cause of fever of unknown origin. Can J Gastroenterol Hepatol 1990;4(6):227–9.
9. Hall GW. Kasabach-Merritt syndrome: pathogenesis and management: Review. Br J Haematol 2001;112(4):851–62.
10. Zarem HA, Edgerton MT. Induced resolution of cavernous hemangiomas following prednisolone therapy. Plast Reconstr Surg 1973;51(2):207.
11. Aspray M. Calcified hemangiomas of the liver. Am J Roentgenol 1945;53:446–53.
12. Plachta A. The triad syndrome inherent to calcified cavernous hemangioma of the liver. Angiology 1965;16(10):594–9.
13. Chowers I, Conforti N, Feldman S. Local effects of cortisone in the preoptic area in temperature regulation. Am J Physiol 1968;214:538–42.
14. Dillard GM, Bodel P. Studies of steroid fever-II. Pyrogenic and antipyrogenic activities in vitro of some endogenous steroids in man. J Clin Invest 1970;49:2418–26.

Submitted: February 1, 2024	*Revised: November 21, 2024*	*Accepted: November 21, 2024*

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