GIANT HEPATIC HEMANGIOMAS ANALYSIS OF PRESENTATION, MANAGEMENT AND OUTCOME – A SINGLE CENTER EXPERIENCE.

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirements for the Award of the degree of

M.Ch BRANCH – VI SURGICAL GASTROENTEROLOGY AND PROCTOLOGY



THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY CHENNAI

AUGUST 2014

CERTIFICATE

This is to certify that the dissertation titled "Giant Hepatic Hemangiomas – Analysis of presentation, management and outcome –A Single center experience." submitted by Dr.GNANASEKAR.M appearing for M.Ch. (Surgical Gastroenterology and Proctology) degree examination in August 2014, is a bonafide record, of work done by him under my guidance and supervision in partial fulfillment of requirement of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R. Medical University, Chennai.

Prof. D. KANNAN,M.S.,M.Ch.,FRCS., Professor, Department of Surgical Gastroenterology, Center of Excellence for Upper GI Surgery, Rajiv Gandhi Government General Hospital & Madras Medical College, Chennai-3.

Prof.S.M.CHANDRAMOHAN,

Professor and Head, Department of Surgical Gastroenterology, Center of Excellence for Upper GI Surgery, Rajiv Gandhi Government General Hospital & Madras Medical College, Chennai-3.

DEAN Madras Medical College, Chennai-3.

DECLARATION

I solemnly declare that this dissertation titled "Giant Hepatic Hemangiomas – Analysis of presentation, management and outcome –A Single center experience" was prepared by me in the DepartmentofSurgical Gastroenterology and Proctology, Center ofExcellence for Upper Gastrointestinal Surgery, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance And supervision of Prof.S.M.Chandramohan, M.Ch, FACS, Professor & Head of the Department of Surgical Gastroenterology and Proctology, Center of Excellence for Upper Gastrointestinal Surgery, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to The Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of the degree of M.Ch Surgical Gastroenterology and Proctology.

Place: Chennai Date:

Dr.GNANASEKAR.M

ACKNOWLEDGEMENT

I am extremely happy to express my gratitude towards our patients who were part of the study. I sincerely thank **The Dean**, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai for allowing me to make use of the facilities needed for my dissertation work.

It is my honor to gracefully thank my beloved chief, **Prof.S.M.Chandramohan**, Professor and Head of the Department of Surgical Gastroenterology and Proctology, Center of Excellence for upper GI surgery, for his mentorship and supervision throughout the period of this study and without whom, this project would not have seen the daylight.

I would like to thank **Prof D Kannan**, Professor, Department of Surgical Gastroenterology and Proctology, Center of Excellence for upper GI surgery, Madras Medical College, for his kind guidance during the days of preparation of this manuscript.

It is my pleasure to profoundly thank **Prof. G.Manoharan** M.Ch, Director, Institute of Surgical Gastroenterology and Proctology, Government Stanley Medical College, Chennai for his support during the project and I fondly remember the discussion in planning the management of each patient which was enlightening and thought-provoking.

It is my duty to acknowledge our Assistant Professors, **Dr.A.Amudhan, Dr.R.Prabhakaran** and **Dr.A.Benet Duraisamy** in the Department of Surgical Gastroenterology and Proctology, Center of excellence for upper GI surgery, for their continuous inspiration and support in carrying out my dissertation.

Needless to mention is the greatest support and encouragement I received from each of my fellow postgraduates, who took their time to share every piece of information regarding each of the enrolled patients and were instrumental in bringing out the thesis to its present form. I thank them with all my heart.

INDEX

Sl.No.	CONTENTS	PAGE
1.	INTRODUCTION	1
2.	AIM	3
3.	REVIEW OF LITERATURE	4
4.	MATERIALS AND METHODS	18
5.	CERTAIN INTERESTING CASES AMONGST THE ANALYSIS	23
5.	RESULTS	31
6.	DISCUSSION	33
7.	CONCLUSION	56
8.	BIBLIOGRAPHY	59
	APPENDIX	
	MASTER CHART	
	CONSENT FORMS	
	ETHICAL COMMITTEE APPROVAL	

GIANT HEPATIC HEMANGIOMAS ANALYSIS OF PRESENTATION, MANAGEMENT AND OUTCOME – A SINGLE CENTER EXPERIENCE.

Department of Surgical Gastroenterology, Center of Excellence for Upper GI Surgery, Rajiv Gandhi Government General Hospital & Madras Medical College,

(Gnanasekar.M, S.M. Chandramohan, D.Kannan, A.Amudhan, R.Prabhakaran, A.Benet Duraisamy)

Background:

Hemangiomas represents a congenital, hamartomatous proliferation (Non – neoplastic) of vascular origin, arising from mesodermal layer. Its etiology remains idiopathic, with the liver being the most common visceral organ affected. Majority of the cases are of a incidental discovery rather than a attempted search for the lesion. Therefore the natural history of the hemangioma are often asymptomatic and persists throughout the lifespan of the patient.

Only less than 10% of the lesions become symptomatic, and come for clinical attention. Within this a small percentage can meet with complications, particularly in those where the lesion is quite large, of the order of more than 10cm.

Management options are varied ranging from simple observation to interventions like resection, eunucleation, hepatic artery ligation and liver transplantation ,besides non operative procedures like angio embolisation, radiation therapy, and recently molecular target agents like Sorafenib , bevacizumab and so on .

Aim:

To study the different modes of presentation, gender predilection, symptomatology, complications, various management modalities, outcome of the varsious treatment strategies, in patients with Giant Cavernous symptomatic Hepatic Hemangioma ,who were admitted in our center, between march 2012 to 2014.

Materials and methods:

Only those cases of hemangioma liver who were persistenly symptomatic, and those presenting with complications, were included in this retrospective analysis. A total of eleven such patients were listed in this series(2012 -2014).

Asymptomatic ,incidentally diagnosed hemangioma liver were excluded from this analysis.

Variables analysed in this study:

Gender differences, Average size, Predominant symptom, Imaging modality employed, Predominant mode of intervention (resection or eunucleation anatomical or nonanatomical resection), Morphology of the tumour, Peroperative and Post operative parameters ,Duration of post operative stay and Mortality were analysed in this study.

Results:

Age incidence in this analysis ranged between 22 and 60 yrs, with a median age of 40yrs. Predominantly occurring in the female gender (90.9%), but no chronic OCP usage, or any exogenous hormonal intake were found in this study.

Majority of the lesions were in the Lt lobe(66.66%), supporting the fact that lesions in the left lobe are often symptomatic. Besides this finding, there is a linear relationship between size and symptoms in this analysis, with over 90% of the patients becoming symptomatic when the lesion is over 15 cm. And moreover pain abdomen was found to be the predominant symptom which made the patient to seek medical attention in this study.

All were diagnosed with imaging alone, with CECT being the predominant diagnostic imaging in our series .

As far as the treatment strategy is concerned ,all the patients were persistently symptomatic and therefore deserved intervention. Ten out of eleven patients(10/11 patients) underwent surgery ,either alone or with combined modality like angioembolisation ,or Sorafenib therapy, particularly for a patient who was harbouring a lesion of size (37x19x 15cm),in her right lobe.

Amongst the surgical options,Resection and not enucleation, was the surgical modality employed in this series. The reason being that we could find no well defined plane of cleavage between the liver parenchyma and the lesion in any of the patients that we operated. For those surgically high risk group, mere angio embolisation alone could be an safe alternative, which we offered as a sole management in a patient who presented with tumour rupture. Angioembolisation stopped the bleeding. Literature also reports no increase in size or any malignant transformation in the lesions that were left behind as remnants after such therapy.

Resection in this series varied between a simple stapled hepatic resection where the operative blood loss and the duration of surgery were very minimal (0.07 litre blood loss,2 hrs 15 min) to major resection utilizing thoracoabdominal access in the form of median sternotomy ,intrapericardiac IVC control ,(requiring about 14 units of blood , 4.2 litres blood loss and taking a 7 hour long surgery).

Mortality in this analysis is a patient wherein the liver is found to be fatty and after resection, bled from the remnant raw area, wherein we tried with perihepatic packing, but subsequently she succumbed to multiorgan dysfunction after second look laparotomy, even though raw area has stopped its bleeding.

Conclusion :

Hemangioma liver can sometimes be therauptically very challenging .Even though the indications for intervention are clear ,the choice of the various management options must be tailored to the patient's clinical condition and the expertise availability.

Complications that can occur in hemangioma may be life endangering too, sometimes demanding multidisciplinary approach. Offering surgery for those patients requires a great deal of knowledge and experience in liver resection and requires a well equipped center with multidisciplinary personnels for successful outcome in the management of these patients.

INTRODUCTION

Hemangioma is a benign tumour that affects several visceral organs. Besides the skin which remains the commonest site, the liver happens to be the commonest visceral organ affected by this vascular tumour .and conversely the most common benign lesion occuring in the liver is also this hemangioma.

Its occurrence in the liver makes it quite interesting, in that the wide spectrum with which it presents, manifests, complication it produces, and technical challenges it can pose while managing it.

Fortunately, almost 90% of the hepatic hemangiomas are asymptomatic and are incidental in its discovery, in that they are diagnosed during a routine imaging or for some other cause unrelated to it, and doesn't cause much problems throughout patient's lifespan..

But in a small proportion of patients it can produce symptoms much enough to necessitate intervention in one form or the other. Besides being symptomatic, it can occasionally present with complications, well enough to endanger the life of the affected. Since the lesion is of a vascular one, in many times the treating physician has to rely on the imaging modalities for arriving at the diagnosis of this lesion, rather than going for a tissue diagnosis. A variety of management options are available in the hands of treating physician, such as medical, surgical, radiological intervention, radiotherapy. Each one of those treatment options carries its own pros and cons, and therefore the treating person needs to have a great deal of vision into the pathological, radiological and of course in to the management perspectives of this lesion .It not only requires great deal of knowledge about the disease, but to treat such a complicated lesion in a comprehensive way, it requires a center where there are multiple specialities, with profound experience in managing liver disorders. . ours is one such center where there are multiple specialities operating with a great deal of knowledge and experience .This study analyses the various preoperative, peroperative and post operative variables that tend to occur in patients with hemangioma, particularly large, symptomatic ones, that we encountered during the study period, which could possibly influence the outcome of these patients.

AIM OF THE STUDY

To study the different modes of presentation, gender predilection, symptomatology, complications, various management modalities, , outcome of these treatment strategies, of patients with Giant Cavernous symptomatic Hepatic Hemangioma.

REVIEW OF LITERATURE

Hemangioma represents a congenital, hamartomatous proliferation (Non –neoplastic) of vascular origin, arising from mesodermal layer. Its etiology remains idiopathic. Skin remains the most common site(1), with the liver being the most common visceral organ affected. Amonst the lesions that affect the liver, Hemangiomas tops the list. Its prevalence in the general population is between 0.4% and 7.3%.(27, 28)

The incidence being increasing now, probably due to the increased no of patients undergoing . radiologic imaging of the abdomen for other reasons. More commonly diagnosed between 30 -50 years, they can present at any age.

When considering the gender predilection, it has been found to be 1.3 to 6 times higher in women than in men, (26, 27, 37) thereby, suggest that sex hormones are somehow implicated in the etio pathogenesis of hemangioma liver. Although some studies contradicted the issue of female predilection quoting that, sex hormones have not been etiologically linked to the development of hemangioma, and autopsy series have reported a nearly equal sex incidence.(29).

Macroscopically it appears as a well-circumscribed, hypervascular and compressible lesions with a clear sheath of compressed liver parenchyma between haemangiomatous tissue and normal microscopically it appears as,ectatic blood filled spaces, lined with vascular endothelium and separated by fibrous septa with a variable sclerotic components of liver. Histological variants are Fibrolamellar interface, Interdigiting pattern, Compression interface, Spongy interface.cells stains,and these lesions stain positive for elastin and trichrome, (1)

SUB TYPES

- x Typical hepatic haemangioma
- x Atypical Hepatic Haemangioma
- x Giant Hepatic Haemangioma
- x Flash Filling Hepatic Haemangioma can account for up to 16% of all hepatic haemangiomas
- x Calcified Hepatic Haemangioma
- x Hyalinized Hepatic Haemangioma

Natural history of hemangioma liver :

Majority of the cases are of a incidental discovery rather than a attempted search for the lesion. Therefore the natural history of the hemangioma are often asymptomatic and persists throughout the lifespan of the patient . this fact is being ablely supported by the fact that majority of the cases are being discovered during autopsy series (4-7% of incidental autopsy reports)

Only less than 10% of the lesions become symptomatic, and come for clinical attention .(31)**Pain ab**domen is the predominant symptom, which draws the patients to medical person .and that pain is often not so characteristic and often poorly localized . Pain in hemangioma often remains unexplained in most of the cases, though thrombosis and infarction of the lesion, hemorrhage into the lesion, or compression of adjacent tissues or organ have been implicated in the pathogenesis of the pain in hemangioma liver, (6)

Most of the studies demonstrate a well defined correlation between size of the lesion and the patient's presenting symptoms . Goodman noted that symptoms are experienced by 40% of patients when the lesion is of 4 cm, whereas with a lesion of well over 10cm, 90% of the patients, they become symptomatic.(26)

Incidence Of Complications

Even though well over 90% of the hemangioma liver patients remain asymptomatic throughout their life time, a small percentage becomes symptomatic and can meet with complications, particularly in those where the the lesion is quite big in size of the order of more than 10cm. The complications listed are

- x spontaneous rupture
- x Traumatic rupture
- x Intratumoural bleeding

And a complication that is unique to this hemangioma – **Kassabach** – **Meritt Syndrome** characterised by consumption coagulopathy and hypofibrinogenemia, in addition to thrombocytopenia.(26) The reported incidence of this complication in the literature is about 4%,but it carries about 60-75% mortality.(22) whereas the operative mortality of a ruptured hemangioma is about 36.4%(14)

Associated syndromes

The hemangioma is characteristically associated with certain syndromes .Though rare, these syndromes makes the clinical situation quite interesting.

Maffucci syndrome, : visceral hemangiomas in the syndrome of multiple enchondromas and subcutaneous hemangiomas,

Sturge-Weber syndrome (encephalotrigeminal or encephalofacial angiomatosis): Extensive capillary-venous malformation results in unilateral cerebral cortical atrophy associated with angioma on the face **Von Hippel-Lindau disease:** A combination of retinal angiomatosis and angioma that is histologically identical to hemangioblastoma, multiple hemangioblastomas, pheochromocytoma, pancreatic, renal cysts, renal tumour, hepatic lesions,

(Familial cerebro-hepato-renal cavernous angiomas): multiple cavernous hemangiomas in the liver. angiomatosis of the brain, retina and with multiple visceral tenangiectasias and cavernous lesions of the skin of the face.

Osler-Weber-Rendau syndrome Multiple dermal, mucosal, and visceral telangiectasis and arteriovenous malformations

Complications of childhood hemangioma

They are more common in older children and adolescents rather than in neonates . (20), Presenting as a solitary lesions, mostly seen in the periphery of the liver.(25)

Usually made as a palpable abdominal mass, sometimes can assume huge size sufficient to cause cardiac failure (high output cardiac failure) due to presence of A-V within the tumor (19) Other reported complications in the paediactric population are

1.Thyroid insufficiency, due to increased production of iodothyroninedeiodinase(type 3),

8

2.Hepatic failure,

3.Compartment syndrome,

4. Coagulation abnormalities,

5.Haemolysis,

6. Rupture.

Prenatal diagnosis:

A 16 weeks antenatal scans can be able to bring into light the presence of such hemangioma which appears as a mixed solid or cystic hypervascular lesions with punctate calcifications. (15). while before birth they can sometimes cause compression of IVC thereby producing Hydrops fetalis as one of the antenatal complications.

IMAGING:

Imaging plays a pivotal role in the diagnosis of the lesion .as the role of biopsy in the diagnostic workup is controversial and hazardous, it is the imaging that makes the diagnosis. The various imaging moalities in the armmentarium of the hemangioma's diagnostic workup are USG, CECT, MRI, SPECT and the newer additions such as Diffusion weighted MRI, and Contrast enhanced USG.

USG:

Well defined *hyper*echoic lesions are seen in this imaging modality however less than 10% are *hypo*echoic. Particularly when viewed in a fatty liver. Large lesions can appear heterogeneous because of complex composition. Posterior acoustic enhancement, sometimes are seen. peripheral feeding vessels on Doppler may not be seen always.The forementioned appearance is not characteristic of hemangioma alone., Adenomas, Hepatocellular carcinomas, and Metastatic disease, all can produce such lesions . However the benign nature of the hemangioma can be made out with the stable nature of the lesion upon serial imaging

CECT:

Features of typical lesions include

- x Hypoattenuating with respect to liver parenchyma in noncontrastphase
- x Characteristic nodular, peripheral enhancement in arterial phase
 (exception- small lesions may show uniform enhancement) -
- x Progressive enhancement with centripetal fill in occurring in **portal venous phase -**
- Irregular fill in, leading on to iso- or hyperattenuating with respect
 to liver parenchyma occurring in **delayed venous phase**

The sensitivity of CT in the diagnosis of hepatic hemangioma was 76.92%; specificity, 33.3%; positive prognostic value, 83.3%; and negative prognostic value, 25.0%. (5)

MRI

Typical features include

T1 - hypointense in relation to rest of the liver.

T2 -intensely hyperintense in relation to rest of the liver . (<u>light bulb</u> sign)

T1 C with Gadolinium : contrast retention is seen on delayed (>5 minute) contrast images..

One of the useful distinguishing features on MRI is that, whereas both hemangiomas and malignancies tend to have high signal on conventional T2 weighted images, the signal from malignancies tends to decrease as the time to echo ratio (TE) is lengthened, whereas the signal from hemangiomas tends to increase.

MRI, therefore has a reported sensitivity and specificity of greater than 90% and is the imaging modality of choice in many instances.



SPECT

⁹⁹Tc RBC labelled SPECT typically demonstrate decreased activity on initial images followed by increased activity on delayed images .SPECT significantly improves the sensitivity for hemangioma when compared over planar imaging, especially for smaller lesions less than 5.0 cm.

DIFFUSION WEIGHTED MRI

The combination of diffusion signal intensity and ADC (Approximate Diffusion Coefficient) maps and values successfully differentiates hemangiomas from other focal lesions. DWI mainly useful in distinguishing between atypical hemangiomas and other lesions e.g. metastatic tumors of liver.Malignancies have low ADC values and hypointense signal on ADC maps, whereas hemangiomas do not have low ADC values. (4)

CONTRAST ENHANCED USG

The imaging modality uses contrast agents like gas microbubbles, which is coated with surfactant (polymer like phospholipid or protein). These microbubble contrast agents are purely intravascular, safe, . These agents are not excreted by the kidneys, therefore are renal friendly in patients with renal dysfunction., which is an advantage over CT and MRI (Hyun-Jung Jang, Hojun Yu, Tae Kyoung Kim Contrast-enhanced ultrasound in the detection and characterization of liver tumors Cancer Imaging, 9 (2009), pp. 96–103). CEUS allows accurate detection of small lesions where CT and MRI fails to detect. (14)

The characteristic feature of hemangioma in CEUS is perilesional enhancement (arterial phase), perinodular enhancement (portal venous phase) and, homogeneous to liver on latel phase. The reported sensitivity, specificity, positive predictive value and negative predictive value of CEUS in hemangioma were 80%, 100%, 100% and 97.8%, respectively.

TREATMENT INDICATIONS

As already mentioned, the natural history of hemangioma is of a stable one and in many of the cases, it is often reassurance that is all necessary. Malignant transformation of the lesion has not been reported. Mere presence of the lesion in the liver is not an indication for intervention .further, in the absence of symptoms, however big the lesion, is not an indication for intervention .This so happens in a majority of the lesions.(19) An important fact in many studies regarding hemangioma liver was the absence of growth from the haemangiomas that were left in the liver remnants after resection.

However in about 10% of the patients, these lesions can assume huge proportion and can be symptomatic, and therefore deserves intervention. Besides the persistent symptoms, there are certain absolute and relative indications for interventions

Absolute indications are

- 1. spontaneous or traumatic rupture with hemoperitoneum,
- 2. intratumoral bleeding,
- 3. consumptive coagulopathy (Kasabach-Merritt syndrome).

whereas relative ones are

- 1. Persistent abdominal pain,
- 2. Obstructive jaundice,
- 3. Portal hypertension,
- Superficial location of tumors larger than five cm with a risk of trauma, Uncertain diagnosis(25)

Non indications :

1. Mere finding of the lesion in the liver

2. Patients anxiety and fear

Size of the lesion in the absence of symptoms or complications

TREATMENT MODALITIES:

Once the patient becomes the candidate for intervention, there are various options in the armamentarium of interventions. The choice of intervention often depends on patients clinical condition and location of the lesion .

The various therauptic modalities available for patients with hemangioma are : steroids, interferon alfa-2 a, embolization, radiotherapy and surgery or liver transplantation., out of which surgery remains the most consistent modality of management and was first reported by Hermann Pfannestiel. (39)

Radiation therapy, to some extent expected to produce partial reduction in size and amelioration of symptoms, but has its own inherent limitations such as radiation hepatitis, veno-occlusive disease, and hepatoma], therefore the current status of radiotherapy are only those who are unfit for or refuse surgery, so also is the hepatic artery embolization .(38)

Steroids have a role in paediactric population but their role in adults remains questionable..

Radiological Angioembolization should be considered for symp-tomatic patients in which resection is contraindication or before operation inpatients

with a ruptured haemangioma, or even in elective cases, to reduce bleeding during resection

However there are theoretical risk of ischemia of liver and possible intracavitary bleed or infection with the use of angioembolisation..T he most characteristic complication with the angioembolisation is the post-embolization syndrome in the form of pain, pyrexia, leucocytosis and nausea that lasts for a few days.

Proponents of surgical management quotes the following points against nonoperative intervention.

With non operative management

- 1. definite pre-operative diagnosis is difficult to obtain,
- 2. per-cutaneous biopsy is dangerous
- and alternative treatment options such as steroids, hepatic artery ligation and radiotherapy shows controversial results

Therefore surgery remains a promising option still today

The surgical options at hand are

- 1. Resection,
- 2. Eunucleation,
- 3. Hepatic artery ligation,
- 4. Liver transplantation.

When surgically feasible, enucleation should be the procedure of choice, even though at times, one would find it difficult to find out a plane between the lesion and the adjoining paren chyma, leading to prefer anatomical resections in most of the situations..

Liver transplantation has also shares in the surgical options available, wherein there are reports of orthotopic transplantation in in cases of diffuse hepatic hemangiomatosis and in patients with the Kassabach-Merritt syndrome,(8)

In the era of target therapy, various bio logical agents has also lended its helping hand in the management of hemangioma liver. Amonst which there are reports of resolution of the lesion with the use of Sorafenib, a multiple kinase inhibitor sed predominantly in various solid tumours . its use is based on the belief that that abnormal angiogenesis induced by i vascular endothelial growth factor (VEGF) plays an important role in the causation of hemangioma

Besides Sorafenib, agents like bevacizumab, has also been tried in the management of hemangioma liver, with promising results, thus opening up new windows in the management of this lesion. (9)

MATERIALS AND METHODS

All patients with symptomatic Giant hepatic hemangioma during the study period from March 2012 to February 2014 were included in the study. The patients' demographic data including Name, Age, Sex, place of origin and occupation were documented. An accurate history taking was done and recorded systematically.

INCLUSION CRITERIA:

Only those cases of hemangioma liver who were persistenly symptomatic and deserved intervention in one form or the other were included in this analysis.

EXCLUSION CRITERIA:

Asymptomatic ,incidentally diagnosed ,hemangioma liver were not included in this analysis.

Variables analysed in this study:

- 1. Gender predilection
- 2. Average size:
- 3. Predominant symptom necessitating intervention
- 4. compressive symptoms
- 5. Presenting with complications

- 6. Imaging modality clinching the diagnosis most
- 7. Predominant mode of intervention :conservative/Surgery/ Radiological intervention/Radiotherapy/Medical /combination of modalities.
- 8. Resection or eunucleation
- 9. Resection : Anatomical or nonanatomical
- 10. Morphology of the tumour:pedunculated/well-defined plane of cleavage/necrosis/capsular tear
- 11. Average duration of the surgery :
- 12. Average blood loss:during parenchymal transection/tumor mobilization/pedicle control
- 13. Average amt of blood transfusion/Colloids/Crystalloids.:
- 14. Inflow pedicle control :pringle/ branch artery ligation
- 15. Outflow control:intra/extra parenchymal
- Parenchymal transection: Kelly clasis / bipolar / LIGASURE / stapler
- 17. Post op ventilator support:duration
- 18. Post op inotropes :duration and dose
- 20. Liver failure: Ser. Bilirubin/INR/Encephalopathy
- 21. Duration of hospital stay
- 22. Mortality

WORKING CHART

Name Age /sex

Presenting complaints

Pressure symptoms:

Pain	
Satiety/vomiting	
breathlessness	
Pedal edema	
jaundice	

Bleeding symptoms

Anaemia	
Epistaxis	
Gingival bleeding	
Haematuria	
Recurrent abortion	

Incidental finding upon evaluation for other causes

PAST HISTORY:

OCP use	
Drug intake	
Medical illness	

PHYSICAL FINDINGS:

Anaemia

Jaundice

Abdominal mass

Ascites

INVESTIGATION

Hb	
Platelet count	
Bilirubin	

TUMOUR MARKER

CEA	
AFP	
CA19-9	

IMAGING

- x PORTAL DOPPLER(portal hypertension): yes/no
- x USG: CECT: MRI:
- x OGD(Varices): yes/no

LESION CHARACTERISTICS

- x Size of the lesion
- x Site of the lobe
- x Unifocal /Multifocal
- x Vessel infiltration /compression
- x Source of feeding vessels: single/ multiple

Management

- x Attempted angioembolisation : successful / failed
- x Alternative methods employed : medical /RFA/Radiothrapy/
- x Surgery: Emergency /elective

Resection : Anatomical/ non-Anatomical

Eunucleation

OPERATIVE DETAILS

- x Anaesthesia: GA/Regional /combined
- x Position : supine/semiprone
- x Incision: midline/Makucchi/subcostal/others

ENERGY DEVICE EMPLOYED

- x Monopolar/Bipolar/Kelly clasis/APC /Hydrodissector
- x Duration
- x Blood loss
- x Perioperative events
- x Elective ventilation/extubated

POST OPERATIVE COMPLICATIONS

- x Liver failure
- x Encephalopathy
- x Bilirubin returned to normal
- x Renal dysfunction
- x Respiratory complication
- x Discharged on
- x Mortality cause

CERTAIN INTERESTING CASES AMONST THE ANALYSIS.

CASE NO1:

(ANGIOEMBOLISATION, SORAFENIB AND FINALLY A COMBINED ABDOMINOTHOACIC APPROACH)

Here is a patient, who presented with a huge symptomatic hemangioma of size, 33x 19x 15 cm (close to largest of its kind) occupying whole Rt lobe of liver. She almost had all the possible symptoms that a hemangioma can impose on a human body such as persistent abdominal pain, breathlessness because of its pressure upon the diaphragm, besides experiencing trivial bleeding on and off too.

With a tumour of such a huge size we first decided to manage with Trans catheter embolization of the feding vessels. Though we could cannulate and embolise the feeding vessels, we could not appreciate a gross reduction in the size and symptoms of the lesion, possibly because of multiple feeding vessels.

Then with the evidence from a single case report of a successful management of a giant hemangioma with SORAFENIB, a multiple tyrosine kinase inhibitor used primarily in various solid tumours such as hepatocellular carcinoma, renal cell carcinoma, sarcoma, we tried it with her after getting consent from her and her family members. But the drug's severe side effects such as dermatologic manifestations, hypertension which is intractable to anti hypertensive drugs, prevented the drug being continued on her.

Finally after trying these modalities, we planned for surgery .Anticipating the possible technical challenges it can pose during surgery, we incorporated a multidisciplinary team comprising cardiothoracic surgeons .

Tumour was approached by a combined abdominal and thoracic access by employing median sternotomy for gaining access to intrapericardial IVC and a Makkucchi incision on the abdominal part.it toresok 7 hrs for the tumour to be resected from the liver by menas of Rt . Hepatectomy, with fourteen units of blood being transfused preoperatively.patient recuperated well .this case deserves its place for the stagewise approach and a novel surgical access which we employed in managing this lesion .



Fig: Angioembolisation



Fig: Lesion intraoperatively.



Fig: Median sternotomy.

CASE NO2 :

A DECEPTIVE ONE AT TIMES- ATYPICAL ONE .

22 yr old female in her 20th day post partum, of an uncomplicated full term normal delivery, was noticed during her routine post partum check up, by the attending medical personnel to have an intraabdominal mass, which upon cross sectional imaging showed up a picture suggesting of a Hepatocellular carcinoma.

CECT revealed a large heterogenously enhancing large necrotic lesion occupying the segment 5 and 6 of the liver with a large exophytic component. Serum AFP :1266.32 u/ ml

With the imaging and the Alpha feto protein suggesting that of Hepatocellular carcinoma, we decided to operate on her since the lesion seemed to be well resectable with the vessels well away from the lesion and with her general condition well preserved permitting us for a safe resection. A formal Rt hepatectomy was done on her, without much trouble and her post op period was also uneventful. Much to our surprise the biopsy report came as a large cavernous hemangioma.

Here in her case, the imaging and the ser. marker was found to be deceptive, in that they both led us to the diagnosis of HCC .However, retrospectively we could able explain that a raised AFP in a 20 days post partum lady is not abnormal and that the imaging belonged to an atypical hemangioma, which does notshow the characteristic enhancement pattern suggestive of hemangioma.
CASE NO3:

AT TIMES, A SIMPLE ONE TOO.

Heamangioma at times can be a simple one to both diagnose and to manage, wherein a lt lobe hemangioma of size 9x7 cm was resected with the help of vascular staplers(Stapled hepatectomy) over a period of just 20 minutes(transection part) with no per or post operative complications henceforth.this case in our series is the one with least blood loss, duration, transfusion requirements, and duration of post operative stay.



Fig: Stapled hepatectomy.

CASE NO4: RESECTION LED TO POST OP LIVER FAILURE.

60 Yr old female compounded by diabetes and hypertension as comorbid illnesses, presented with a symptomatic hemangioma of $19x \ 16 \ x \ 12$ cm occupying the left lobe of the liver, compressing the left branch of the portal vein .

The patient demanded extensive cardiac work up and optimization, so as to forfeit any cardiac catastrophe or any metabolic complication arising out of her impaired glycaemic status and compromised cardiac condition. A formal lt hepatectomy done on her, after optimization of her medical condition was an uncomplicated one, but the crux of the problem was her post operative course.

Patient went on for altered mentation in her third post operative day onwards .Being a diabetic patient we went on to have a metabolic cause for this clinical situation .But with her blood glucose and her electrolytes within the normal range, and the patient on oral alimentation from the second post operative day, and with her bilirubin and her international normalized ratio on the rise, we knew that she was on the diagnosis of post operative liver failure .

Her Ser. Ammonia level was in the higher range of the order 69 with the reported lab range (5 -30)., we started managing her with sugar free lactitol, Branched chain aminoacids, lactulose enema, correction of hypokalemia, removing all the intravenous lines that could be a source of infection which

28

could potentiate POLF.Towards the end of the first week, her mentation returned towards normalcy, and her biochemical profiles came to normal, suggesting that her liver started meeting the demands of the body's metabolic demand.

CASE NO:5

HEMANGIOMA WHEREIN WE LOST THE PATIENT

A 12x 9 cm hemangioma in the segment 6 and 7 in a 57 yr old diabetic, who weighed 84 kg with her BMI of the mildly obese, who was operated for her worsening symptoms of abdominal pain and breathlessness. Patient's cardiorespiratory, glycaemic condition, coagulation status were extensively worked up preoperatively, and optimized well before embarking on surgery.

Peroperatively after abiding to the simple rules of liver resection (adequate inflow), the resection part was not a tough one, but what made all the things worse was the texture of the remnant liver, which was fatty and was bleeding from its raw surface, refractory to all the available energy devices (monopolar, bipolar, APC), forcing us to pack it all around and then optimize the patient over a period of 48 hrs.

We reopened and unpacked and found that the bleeding has responded to the perihepatic packing, but the patient could not tolerate the insult of two laparotomies, anaesthesia, metabolic derangements, and the brunt of blood transfusions. Her renal function deteriorated, with acidosis, deranging her respiratory status and finally she succumbed to multiorgan dysfunction.

CASE NO 6:

RUPTURED AT PRESENTATION, BUT MANAGED TO SURVIVE, BY ANGIOEMBOLISATION.

An odd male in this analysis is this patient, who was referred to our tertiary care hospital from a place which is somewhere around 5 hrs from our's in a state of compensatory shock, with tachycardia, BP 100/60, and with clinical signs of pallor, with a imaging showed features of bilobar liver lesions with its characteristic enhancement pattern, and evidence of capsular breach at one point .

We could resuscitate the patient and could make him hemodynamically stable overnight, thereby he was angioembolised, the next morning .The procedure went on well with successful cannulation of the feeding vessel .Immediately his hemodynamic status responded, and he recuperated well.Though the post procedural imaging failed to show any gross reduction in the size there was not much contrast blush in the lesion with capsular breach. The Patients symptoms also subsequently subsided, but unfortunately patient was not willing for any form of treatment and therefore went on.

RESULTS

1	Sex predilection	Female(90.9%)
2	Median age of presentation	40 yrs
3	Age range	22-60yrs
4	Predominant symptom	Pain abdomen
5	OCP usage	no
6	Predominant clinical presentation	Abdominal mass
7	Predominant pressure symptoms	breathlessness
8	Anaemia	18.18%
9	Thrombocytopenia	1
10	Coagulopathy	1
11	Tumour marker(AFP)	1
12	Portal hypertension	none
13	OGD finding	Extraneous imp.
14	Imaging modality that made the diagnosis	CECT
15	Imaging modality that predicted the tumour size well	CECT
16	Lesion more than 10 cm	67%
17	Lesion more than 15 cm	33%
18	Rt lobe	33.33%
19	Lt lobe	66.66%

20	Exophytic lesion	25%
21	Atypical Hemangioma	9.09%
22	Observation	0%
23	Intervention	100%
24	Eunucleation	0%
25	Anatomical resection	80%
26	Non anatomical resection	20%
27	Angioembolisation	16.66%
28	Combination of intervention	9.09%
29	Avg duration of surgery	3 hrs.15min
30	Avg amount of blood loss	1087 ml
31	Avg. blood transfusion	3.36 units
32	Predominant method of inflow control	Pringle
33	Predominant method of transaction	Kelly clasis
34.	Raw area managed with	Suture ligation
35	Extubation or elective ventilation	81.81%
36	Duration of analgesia	4.1 days
37	Oral resumption	2.5 days.
38	Heparinisation	81.81%
39	Ambulation	4.1
40	Duration of post operative period	19.81
41	Mortality	1

DISCUSSION

Haemangioma liver, of course a rare condition, can be innocuous in most of the times, but sometimes can be troublesome and be challenging to the treating surgeon .In this analysis, only those cases that are huge and persistently symptomatic, and those with complications, who underwent intervention alone were analysed.

1. Age:

The median age of presentation in this analysis was 40 yrs, with the range being 22 to 60yrs.

2. Gender distribution

Importantly the sex predilection in this analysis is predominantly females in the proportion of 90% to 10% (M:F) However none of the female patients gave a history of OCP usage, thus raising the question of the influence of the hormonal factors in the pathogenesis of this lesion, Probably some other female factorsmight be incriminated in the etiopathogenesis of the lesion.



3. Distribution of the lesion within the liver (Rt lobe or Lt lobe):

The majority of the lesions in this analysis were found to be arising from the Lt lobe of the liver, thereby supporting the literature evidence that, Lt lobe lesions though somewhat less common in incidence when compared to Rt lobe, are often symptomatic and thereby deserves intervention, more than that occurring in the right lobe.. The incidence of Lt lobe lesions in this study is 66.66% whereas the Rt lobe lesions constitute 33.33%, thereby one again reiterating the fact that Lt lobe lesions are often symptomatic.



Fig: Distribution within the Liver.



4.Size Vs Symptoms

Also the symptoms correlated well with the tumour size in this analysis, that is only those lesions, that were more than a critical size of the order 8cm or more were associated with persistent symptoms, and came for medical intervention . Interestingly, three(3/11cases) of the patients who were harbouring lesions that were more than 15 cm, not only were symptomatic, but met with complications also.

Patient no 1:. Experienced chronic form of coagulopathy(Kassabach – Meritt Syndrome)

Patient no2:developed Post operative liver failure

Patient no 3:developed peroperative bleeding, died after we attempted with perihepatic packing.

Therefore, size of the lesion in this analysis proved to be an important factor affecting the outcome in treating these lesions.



Even though literature stresses the fact that size of the lesion is not the one which demands intervention, majority of the patients who were harbouring lesions of the order of 15 cm, invariably will be persistently symptomatic and thereby merit intervention in one form or the other.

5.Predominant symptoms:

As far as the symptoms in this analysis are concerned, the predominant symptom for which they seek the medical attention is the persistent upper abdominal pain.(91.66%). Though the pain in these patients were rarely severe and often dull achey and poorly localized, it remains the predominant mode of presentation for which they were subjected to imaging, which brings the lesion to the surgeon's notice.Besides pain, two of the patients also experienced the complications that could arise in this lesion. One patient developed a chronic form of hemolysis and persistent low platelet count (Kassabach-Meritt Syndrome), and she also developed breathlessness, due to pressure effect on the diaphragm, restricting its movement, thereby developing breathlessness, more so when she lies down., apart from suffering from bleeding complications such as repeated abortion and gingival bleeding, and another one presented with acute form of complication, tumour rupture and with hemodynamic compromise.



6.Clinical examination :

Clinically all the patients presented with palpable abdominal mass, which is non tender, confined mostly to upper abdomen, continuous with liver dullness, along with pallor which we could be able to make it out in two patients and jaundice in one patient which is of the order of 4.0 gms, and is nonobstructive in nature, we could explain it as she was also experiencing a chronic form of mild hemolysis, and also intratumoural bleeding. The blood investigation of these patients are not much informative and conclusive except for the anaemia, and low platelet count .Tumour markers in these patients were analysed in this study. we could manage to do serum AFP, CEA and CA19-9 in all these patients .None of the tumour markers were elevated except in one patient who is 1 month post partum and with elevated AFP of the order of 1266.32 units/ ml .interestingly her imaging also does not show the characteristic enhancement patten of the hemangioma, thereby we were entertaining the diagnosis of Hepatocellular carcinoma in her.per operatively the lesion was found to be hemangioma, which was very much confirmed by the biopsy from the resected specimen.

7.Imaging :

Not only the patients included in this study, but also almost 80% of the patients referred to our department, were with imaging of one type or the other related to the clinical condition. In this way the patients in this study were with either one or more of the following imaging modalities(USG, CECT, MRI). Amongst the imaging modalities cited, the CECT is the one which made the diagnosis primarily in over 90% of the cases is CECT .CT –angio was taken in one case, which could add the information about the relation of the lesion with the vessels.





Fig: CECT of hemangioma Liver (Characteristic peripheral puddling Sign).



Fig: MRI in one of our patient showing Giant hemangioma occupying the entire Rt lobe



Fig: The same patient's CT- angio (demonstrating multiple feeding vessels).

Also in this study, we could make out that, the lesion size found intraoperatively correlated well with the size made out at CECT, rather than with USG, thereby inferring about the diagnostic superiority of the CECT than with USG.We could not compare the diagnostic superiority of the MRI with CECT, because majority of the patients were analysed only with CECT, without moving on to MRI.

But the CECT failed to diagnose the atypical nature of some of these giant hemangioma, which became evident in one case of 22 yr old female and is 2 weeks post partum with raised AFP levels (1266.32), which in the absence of the characteristic contrast enhancement, was given the impression of Hepatocellular carcinoma, which when operated found to be a case of giant atypical hemangioma. The post partum state masqueraded the condition by causing pseudoelevation of AFP.

8. Tumour morphology:

As far as the tumour morphology is confirmed, three out of eleven lesions were exophytic in nature, and in none of the cases wherein we could demonstrate a interface between the lesion and the parenchyma.



This could be the main reason for which none of the patient were offered eunucleation as a surgical treatment of choice.

9. Intervention:

Amongst the intervention, all but one patient included in this study underwent surgery. The odd patient who presented with ruptured hemangioma managed to survive with angioembolisation, and further refused surgery and went on after stabilization.

Mode of intervention

Surgery alone:	81.81%
Angioembolisation alone :	9.09%
sorafenib therapy alone:	0%
Combination (Surgery+	
Angioembolisation +Sorafenib therapy):	9.09%



10. Surgical intervention :



The rest of the patients underwent surgical intervention either in the form

of anatomical or non anatomical liver resection

Anatomical liver resection :80%Non anatomical liver resection :20%



But, none of our patients were offered eunucleation as a surgical modality, because of the absence of well defined plane of cleavage between the lesion and the liver parenchyma. This is in contrast to the literature, wherein there often will be a plane of cleavage between the lesion and the liver parenchyma

11.Intraoperative parameters:

Apart from these observations, there are quite a few intraoperative parameters that became evident in this retrospective study.

12.Blood Loss and transfusion requirements:



The average amount of blood loss in the resection were 1087 ml with the maximum loss(4200ml) noted in patient with giant lesion of size 37x19x15 cm with 14 units of blood transfusion, and the least amt of 70 ml noted in laparoscopic hepatectomy, with no blood transfusion. But for that, all patients were transfused with an average amount being 3.36 units.



13. Duration of surgery:

The Average duration of surgery being 3Hrs. 15 min, with maximum time taken being 7 hrs.(who underwent median sternotomy) and the minimum being 2 hrs. 15 minutes (Stapled resection).

Stapled resection :2 hrs. 15 min

Abdomino thoracic:7 hrs.

Average :3 hrs. 15 min.



14. Technique of Hepatectomy:

The predominant mode of inflow occlusion is the pringles maneovre, and in no cases were the branch artery were ligated before proceeding on to parenchymal transection, probably the lesion overhanged the hilum in most lesions thereby leaving little room for the operating surgeon to get hold of the branch vessels over there(8/11 cases- 72.72%.) .one patient stopped short of angioembolisation and did not proceed on for surgery, and in the one who underwent stapled hepatectomy, transection was done without gaining inflow control, and the third one also underwent Lt hepatectomy (Hanging lesion from the Left lobe), without formal inflow control.

Parenchymal transection in all the cases, were done with a combination of Kelly clasis and monopolar diathermy(10/11 cases-90.09%) . harmonic was

added in three cases along with Kelly clasis and monopolar cautery (27.27%). hydrodissector (WATERJET) was employed in three cases along with the forementioned transection methods (27.27%).

15. Transection methods

Kelly classis alone	0%
Kelly classis+Diathermy	63.63%
Kelly +diather+harmonic	27.27%
Kelly +Diatherm+waterjet	27.27%
Vascular stapler	9.09%



16.Management of Raw area:

Hemostasis in the raw area managed with suturing with 000 silk in 10out of 11 operated cases(90.9%).Besides suture ligation the raw area in the remnant liver is managed with Argon Plasma Coagulator(1/11 case-9.09%), surgiseal(2/11 cases-18.18%), and tissue seal(FIBRIN)-1/11(9.09%) case .the parenchyma is transected with the combination of Kelly clasis and diathermy.

Suture alone	63.63%
Suture +APC	9.09%
Suture +Surgiseal	18.18%
Suture+Fibrin	9.09%



The odd patient in this analysis whom we lost after perihepatic packing was the one I whom the bleeding from the raw area failed to respond to these agents, thereby we attempted to optimize the situation by perihepatic packing and then the patient underwent relaparotomy after 48hrs. Even though the bleeding from the raw area responded to the perihepatic packing, patient subsequently developed sepsis, and multiorgan dysfunction leading to death, the only reported mortality in this analysis.



Fig:Raw area managed with sutures .



Fig: With Argon Beam Coagulation.



Fig: with Surgiseal.



Fig: With Tissue sealant (FIBRIN GLUE)

19.Immediate post operative course:

All the operated patients except two (2/11 cases), were extubated, immediate post operatively and were managed in the ICU for an average of one day and were shifted to post operative ward.

Post operative course:

All the operated patients received anticoagulation (heparin) in the post operative period (81.81%), except two patients wherein because of their bleeding we did not attempted heparinisation in them .the two patients were the one whom we angioembolised, and the other one whom underwent perihepatic packing.the average duration duration of days of hepaininsation was found to be 2.4 days.



The one (perihepatic packing)for an average period of 2.4 days, till they are ambulant.

oral resumption was on an average of 2.5 days .The earliest one to resume oral alimentation was the one who underwent stapled resection. Analgesics are mostly continued for an average period of of 4.1 days, mostly with epidural Analgesia (lignocaine, Tramadolol) to start with and to taper with oral tramadolol. Again the patient who underwent median sternotomy required a maximum duration of analgesics, whereas the one who underwent stapled resection required the least duration in this analysis.

Almost all the patients were discharged after suture removal, that is on the 9 -11 POD, with an Avg of 19.81 days, as the two patients, one who underwent abdominothoracic approach and the one who had post operative liver failure had a prolonged post operative stay.



Mortality in this analysis was one patient who bled from the raw area of the remnant liver due the fatty nature of the liver and was initially managed with anged with perihepatic packing and then underwent relaparotomy and then developed multiorgan dysfunction and death.

CONCLUSION

Hemangioma liver, though highly prevalent amongst the population and often diagnosed as a a incidental finding during imaging, the symptoms and the complications arising out of the lesion are quite rare.when symptomatic, the lesions are always quite large, much bigger than what the literature quotes as a giant hemangioma (>4cm).Distinctively, the lesions associated with complications are much larger than the lesionswhich are persistently symptomatic. Even though literature quotes that the size of the lesion is not the criteria for undertaking intervention, larger hemangiomas are invariably associated with persistent symptoms and of course with complications. This is evident in this analysis, in which there is linear relationship of size with symptoms.

Undoubtedly, hemangiomas are common in female gender, however the reason for this female predilectionstill remains unravelled. The role of chronic OCP usage in the etiopathogenesis of the hepatic hemangioma is not well established as that of the case of Hepatic adenoma, but still there are reports of hemangioma liver increasing in size upon the effect of progesterone during pregnancy.. In this analysis we too have encountered a case of hepatic hemangioma in a twenty days old post partum .probably the lesion would have increased in size throughout the pregnancy upon the influence of progesterone.

This female predilection and the influence of the female hormones needs further appraisal in this regard.

The absolute and the relative indications of intervention for giant hemangioma are well established. And the role of conservative approach for incidentally diagnosed lesion is also well established. Though the role of CECT and MRI in the diagnosis of classical hemangioma is undoubtedly evident, with atypical hemangioma, wherein the classical enhancement pattern of the hemangioma will not be present, the role of Contrast enhanced USG, and the Diffusion weighted MRI has to be established. With these imaging modality able to pick up both typical and atypical variants of the hemangioma, the role of preoperative biopsy is not only needed, but also catastrophic and is ruled out nowadays.

Amongst the interventions, Surgery clearly has got an edge over others in patients for whom the risk of surgery is low. But even in such patients, where the lesion is too large much similar to what we encountered in this analysis, one could adopt a rather stepwise approach like an initial angioembolisation followed by surgical intervention seems to be an attractive option.

For patients whom the surgical risk is too high, therauptic angioembolisation alone could be an safest approach, since malignant transformation in hemangioma liver is unknown and unheard of, and therefore the lesion can be best left as such.

57

And there are reports of target agents in the therapy of hemangioma liver too, such as Sorafenib and Bevacizumab based on the fact that the growth of the lesions were influenced by VEGF.

Eventhough the literature advocates eunucleation as a preferential surgical modality than resection, because it allows for a greater preservation of liver parenchyma, leaving behind minimal morbidity, no patient were offered eunucleation in this series, as there was no well defined plane of cleavage between the lesion and the parenchyma.

The principles of resection in hemangioma liver is the same as in standard hepatic resection, that is adequate inflow and outflow control

But the surgical resection demands a high degree of surgical expertise and a great deal of knowledge in hepatic resections, and invariably requires well equipped center and a multidisciplinary personnels for successful outcome of the procedure.

Studies were able to establish the fact that the left over lesions after resection remains as such and does not grow subsequently, reveals that no long term follow up is needed for these patients who were offered treatment in form or the other for these giant symptomatic hemangioma.

BIBLIOGRAPHY

- Liver and intrahepatic bile ducts TumorBenign tumors Hemangioma, Reviewers: Deepali Jain, M.D. Revised: 9 January 2013, last major update February 2012Adx
- Liver hemangioma: the need for a well-defined differential diagnosis and the therapeutical timing dilemma]. <u>Russo A</u>. 9 January 2013, last major update February 2012 Jan-Feb;25(1-2):47
- Fetal and neonatal liver tumours. *Early Human Development* 2010;86(10):637-642,5. Makin E, Davenport M
- Diffusion-weighted MR Imaging of the Liver. Radiology 2010;254:47–66. Bachir Taouli and Dow-Mu Koh.
- 2010;46(5):329-35.Comparative diagnostic value of contrastenhanced ultrasonography, computed tomography, and magnetic resonance imaging in diagnosis of hepatic hemangiomas.Zviniene K1, Zaboriene I, Basevicius A, Jurkiene N, Barauskas G,.
- Contrast-enhanced ultrasound in the detection and characterization of liver tumors Hyun-Jung Jang, Hojun Yu, Tae Kyoung Kim Cancer Imaging, 9 (2009), pp. 96–103.
- Hemangioma, Hepatic: emedecine < Gastroenterology < Liver, Dec
 22, 2008) David C Wolf, MD, FACP, FACG, AGAF Unnithan V

Raghuraman, MD, FCRP, FACG, FACP

- Living donor liver transplantation in a patient with giant hepatic hemangioma complicated by Kasabach-Merritt syndrome: Report of a case <u>Makoto Meguro</u>, <u>Yuji Soejima</u>, <u>Akinobu Taketomi</u>, <u>Toru Ikegami</u>, May 2008, Volume 38, <u>Issue 5</u>, pp 463-468
- Incidental reduction in the size of liver hemangioma following use of VEGF inhibitor bevacizumab.<u>Mahajan D¹</u>, <u>Miller C</u>, <u>Hirose</u> <u>K</u>, <u>McCullough A</u>, <u>Yerian L</u>
- Wen- Yao- Yin et al.: Early treatment for symptomatic giant hepatic hemangioma report of three cases and literature review. Medwell surgery journal 2(4):45-49,2007.
- Margot Brannigan, Peter N. Burns, Stephanie R. Wilson, Blood flow patterns in focal liver lesions at microbubble-enhanced US Radiographics, 24 (2004), pp. 921–935
- Q. L. Zeng, Y. H. Li, Y. Chen, Y. Ouyang, X. He and H.Zhang, "Gigantic Cavernous Haemangioma of the Liver Treated by Intra-Arterial Embolization with Pingyang- mycin-Lipiodol Emulsion: A Multicentric Study," *Car- diovascular and Interventional Radiology*, Vol. 27, No. 5, 2004, pp. 481-485.
- Margot Brannigan, Peter N. Burns, Stephanie R. Wilson, Blood flow patterns in focal liver lesions at microbubble-enhanced US Radiographics, 24 (2004), pp. 921–935

- N. Coriglian, P. Mercantini, P. M. Amodio, G. Balducci, S. Caterino, G. Ramacciato, *et al.*, "Hemoperitoneum from a Spontaneous Rupture of a Giant Heamangioma of Liver: Report of a Case," *Surgery Today*, Vol. 33, No. 6,
- Makin E, Davenport M. Fetal and neonatal liver tumours. *Early Human Development* 2010;86(10):637-642,5. Roos JE, Pfiffner R, Stallmacj T *et al.* Infantile hemangioendothelioma. *Radiographics* 2003;23:1649-55
- S. Warmann, H. Bertram, R. Kardorff, M. Sasse, F. G.Hausdor and J. Fuchs, "Interventional Treatment of In- fantile Hepatic Haemangioendothelioma," *Journal of Pe-diatric Surgery*, Vol. 38, No. 8, 2003, pp. 1177-1181.
- Stallmacj T *et al*. Infantile hemangioendothelioma. *Radiographics* 2003;23:1649
- 2002 Oct;89(10):1240-4.Size of lesion is not a criterion for resection during management of giant liver haemangioma. <u>Terkivatan T¹, Vrijland WW</u>, <u>Den Hoed PT</u>, <u>De Man RA</u>, <u>Hussain</u> <u>SM</u>, <u>Tilanus HW</u>,.
- 19. Prokurat A, Kluge P, Chrupek M, Kosciesza A, Rajszys P. Hemangioma of the liver in children: proliferating vascular tumor or congenital vascular malformation? Med Pediatr Oncol 2002; 39:524-529.

- 20. Siegel M. Pediatric liver imaging. Semin Liver Dis 2001; 21:251-269.
- 21. Roos JE, Pfiffner R, Huang SA, Tu HM, Harney JW *et al.* Severe hypothyroidism caused by type 3 iodothyroninedeiodinase in infantile hemangiomas. *NEngl J Med* 2000;343(3):185-189
- Cappellani, A. Zanghi, M. Divita, G. Zanghi, G.Tomarchio and G.Petrill, "Spontaneous Rupture of a Gi- ant Haemangioma of the Liver," *Annali Italiani Di Chi-rurgia*, Vol. 71, No. 3, 2000, pp. 379-383.
- 23. J, Most D, Bresnick S, et al. Proliferative hemangiomas: analysis of cytokine gene expression and angiogenesis. Plast Reconstr Surg. 1999;103:1–9. doi: 10.1097/00006534-199901000-00001.
- Pietrabissa, P. Giulianotti, A. Campatelli, G. Di Can- dio, F. Farina,
 S. Signori, *et al.*, "Management and Fol- low-Up of 78 Giant Haemangiomas of the Liver," *British Journal of Surgery*, Vol. 83, No. 7, 1996, pp. 915-918.
- Powers C, Ros P, Stoupis C, Johnson W, Segel K. Primary liver neoplasms: MR imaging with pathologic correlation. RadioGraphics 1994; 14:459-482.
- 26. O. Nishida, N. Satoh, A. S. Alam and J. Chino, "The Effect of Hepatic Artery Ligation for Irresectable Cav- ernous Haemangioma of the Liver," *The American Sur- geon*, Vol. 54, No. 8, 1988, pp.
483-486

- 27. Goodman Z. Benign tumors of the liver. In: Okuda K, Ishak K G. Neoplasms of the liver. Tokyo: Springer-Verlag; 1987:105-125.
- Dennis th M. Fatal pulmonary embolism due to thrombo- sis of a hepatic cavernous hemangioma. Med Law1980;20:287–8.
- 29. Ishak KG, Robin L. Benign tumors of the liver. Med ClinNorth Am 1975;59:995–1013.
- 30. Ochsner JL, Halpert B. Cavernous hemangioma of the liver.Surgery 1958;43:577–582.
- 31. Henson SW, Gray HK, Dockerty MB. Benign tumors of the liver. II. Hemangiomas. Surg Gynecol Obstet1956;103:327–31.),female predilection still remains in all the major studies on the hemangioma liver.
- 32. Official Journal of the American Society of Abdominal Surgeons, Inc.Giant Cavernous Hemangioma of the Liver: A Case Report and Review of Literature, Dr. Ali Bendjaballah, Dr. M. Taieb.
- 33. Comparative diagnostic value of contrast-enhanced ultrasonography, computed tomography, and magnetic resonance imaging in diagnosis of hepatic hemangiomas.<u>Zviniene</u> <u>K¹, Zaboriene I, Basevicius A, Jurkiene N, Barauskas G</u>,.
- 34. Role of contrast enhanced ultrasound in characterization of focal liver lesions <u>Shruti Thakur Anupam Jhobta¹</u>, <u>D.S. Dhiman²</u>, <u>R.G.</u>

Sood³,

- 35. E. Moreno, M. R. Del Pozo, M. C. Vicente and J. A.Abellan, "Indications for Surgery in the Treatment ofHepatic Haemangioma," *Hepatogastroenterology*, Vol. 43,
- O. Nishida, N. Satoh, A. S. Alam and J. Chino, "The Effect of Hepatic Artery Ligation for Irresectable Cav- ernous Haemangioma of the Liver," *The American Sur- geon*, Vol. 54, No. 8, 1988, pp. 483-486.
- S. I. Schwatz and W. C. Husser, "Cavernous Haeman- gioma of the Liver; A Single Institution Report of 16 Re- sections," Annals of Surgery, Vol. 205, 1987, pp. 456-465. <u>doi:10.1097/00000658-</u> <u>198705000-00003</u>
- Shumacker HB. Hemangioma of the liver. Discussion of symptomatology and report of a patient treated by operation. Surgery 1942;11:209–22.

MASTER CHART

Name	Age.	Sex	Presenting symptoms		compressiv	e symptoms	bleeding d	iatheses		OCP intake	comorbid illnesses
				satiety	jaundice	dyspnoea	gingival ble	eeding	abortion		
Zareena	34	f	pain-abdomen	no	no	yes	yes		yes	no	no
jebamalai	60	f	pain-abdomen	no	no	no	no		no	no	Diabetic/HT
vinodhini	22	f	pain-abdomen	no	no	no	no		no	no	Postpartum
kandasamy	40	m	shock	no	no	no	no		no	no	no
laxmi	35	f	pain-abdomen	no	no	no	no		no	no	no
kalaivani	53	f	pain-abdomen	no	no	no	no		no	no	Diabetes
kasiammal	42	f	pain-abdomen	yes	no	no	no		no	no	no
mariammal	38	f	pain-abdomen	no	no	no	no		no	no	HBSAg
mohana	43	f	pain-abdomen	no	no	no	no		no	no	no
Dhanalaxmi	39	f	pain-abdomen	no	no	no	no		no	no	no
Murugayee	54	f	pain abdomen	no	no	no	no		no	no	diabetic

Name	Pallor	Jaundice	Dyspnoea	Easy bruisability	Abdominal mass	Ascites	Meleana	Hb	Bilirubin	PT/INR	AFP	Platelet count
Zareena	yes	yes	yes	no	yes	minimal	no	6.8	3.2	14.4/1.02	0.5	0.68
jebamalai	yes	no	yes	no	yes	no	no	10.6	3.2	17.4/1.29	no	2.21
vinodhini	no	no	no	no	yes	no	no	9.5	1	13.6/1.02	1266.32	6.42
kandasamy	yes	yes	yes	no	yes	yes	no	5.9	4.2	12.8/1.01	no	1.78
laxmi	no	no	no	no	yes	no	no	9.4	0.9	12.7/.94	1.42	1.47
kalaivani	no	no	no	no	yes	no	no	8.2	0.6	13.1/.98	2.04	1.64
kasiammal	no	no	no	no	yes	no	no	12.8	0.6	12.7/0.9	2.1	1.68
mariammal	no	no	no	no	yes	no	no	9	0.7	12.7/0.9	1.2	1.42
mohana	no	no	no	no	yes	no	no	10.2	0.8	13.2/.9	1.59	2.58
Dhanalaxmi	no	no	no	no	yes	no	no	9.5	1	13.9/1.00	0.74	1.31
Murugayee	no	no	no	no	yes	no	no	10.2	1.1	12.8/1.00	1.1	1.55

Name	OGD	first imaging done	USG size	CECT impression	MRI impression	CT Angio	Rt.lobe	Lt lobe	exophytic	At Surgery
Zareena	Extraneous imp. DI	CECT	22.8x14.6x26.7 cm	33x19x15 cm	24X14X20 cm	29x16x14	yes	no	yes	35x20x15 cm
jebamalai	Extraneous imp. DI	CECT	16x12cm	19x16x 12.6cm	not done	not done	no	yes	yes	20x25cm
vinodhini	Extraneous imp. in DI	USG	9x6 cm	9x7x6 cm	not done	not done	yes	no	no	11x10cm
kandasamy	not done	CECT	14x12 cm	15x15 cm	not done	not done	yes	no	no	not operated
laxmi	Extraneous imp. DI	CECT	9.8x7.1 cm	9.7x9.8x10cm	not done	not done	no	yes	no	10x10 cm
kalaivani	Normal	CECT	8x8 cm	9x 7.8 cm	not done	not done	yes	no	no	15x12 cm
kasiammal	LaxLES	USG	10x12 cm	13.5 x 9 cm	not done	not done	no	yes	yes	13x 13 cm
mariammal	Distal Esophagitis	USG	9x8 cm	11x 12 cm	not done	not done	no	yes	no	11x11 cm
mohana	normal study	CECT	10x 8.8 cm	7x6.5x6	not done	not done	no	yes	no	9x7 cm
Dhanalaxmi	normal study	CECT	9.8 X 8 cm	8x6 cm	not done	not done	no	yes	no	7x6cm
Murugayee	normal study	USG	11.8x7.5	9x7x6 cm	not done	notdone	no	yes	no	10x8cm

Name	Observation	Intervention			
		surgery	Angioembolisation	Sorafenib	Others
Zareena	no	yes	yes	yes	no
jebamalai	no	yes	no	no	no
vinodhini	no	yes	no	no	no
kandasamy	no	no	yes	no	no
laxmi	no	yes	no	no	no
kalaivani	no	yes	no	no	no
kasiammal	no	yes	no	no	no
mariammal	no	yes	no	no	no
mohana	no	yes	no	no	no
Dhanalaxmi	no	yes	no	no	no
Murugayee	no	yes	no	no	no

Name	Inflow occlusion]	parenchtma	I transection	1			Raw Are	a treated v	vith		packing	Duration of Surgery	Blood loss	TRANSF	USION	
	Pringle	Branch ligation	kelly clasis	Diathermy	Harmonic	Stapler	waterjet	Suture	Surgiseal	APC	tissue seal	no			Blood	Colloids	FFP
Zareena	yes	no	yes	yes	no	no	no	yes	no	yes	no	no	7 hrs	4200ml	14	2	: 11
jebamalai	yes	no	yes	yes	yes	no	no	yes	yes	no	yes	no	4 hrs. 20 min	1000 ml	4	1	4
vinodhini	yes	no	yes	yes	yes	no	no	yes	no	no	no	no	3 hrs.	1000ml	2	2	3
kandasamy	not operated	not operated	not	not	not	no	not	not	not	not	not	no	not operated	not	3	no	4
laxmi	no	no	yes	yes	no	yes	no	yes	yes	no	no	no	2 hrs. 15 min	70 ml	0	0	0
kalaivani	yes	no	yes	yes	yes	no	no	yes	no	no	no	yes	3hrs	900ml	2	0	2
kasiammal	no	no	yes	yes	no	no	yes	yes	no	no	no	no	2 hrs 40min	1200ml	3	1	4
mariammal	yes	no	yes	yes	no	no	yes	yes	no	no	no	no	3 hrs 50 min	750 ml	3	1	4
mohana	yes	no	yes	yes	no	no	no	yes	no	no	no	no		550	2	1	4
Dhanalaxmi	yes	no	yes	yes	no	no	no	yes	no	no	no	no		600	2	1	4
murugayee	yes	no	yes	yes	no	no	yes	yes	no	no	no	no	3 hrs	600ml	2	1	3

name	VENTILATION	inotropes	heparin upto	oral resmptio	pain killers	Encephalopa	Bile leak	post op stay
Zareena	yes	yes	4 days	Day6	7 days	no	no	18 da ys
jebamalai	extubated	no	4days	day4	5days	yes	no	16 days
vinodhini	extubated	no	4days	day2	3 days	no	no	7 days
kandasamy	no	yes	no	no	2 days	no	no	12 days
laxmi	extubated	no	2 days	day2	2 days	no	no	6 days
kalaivani	extubated	yes	no	no	3 days	no	no	expired
kasiammal	extubated	no	2 days	day2	5 days	no	no	10 days
mariammal	extubated	no	2 days	day2	5 days	no	no	10 days
mohana	extubated	no	2 days	day3	5days	no	no	7 days
Dhanalaxmi	extubated	no	2 days	day2	5 days	no	no	7 days
murugayee	extubated.	no	2 days	day2	5 days	no	no	10days

CONSENT FORM

Information to Participants

Title: -

"Giant Hepatic Hemangiomas – Analysis of presentation, ,management and outcome – our experience

Principal Investigator: DR. M. GNANASEKAR Co-Investigator(if any):

Name of Participant:

Site :

You are invited to take part in this research/ study/procedures/tests. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of research?

To study the sex predilection ,presenting symptoms ,predominant management options ,complications ,outcome of these management options of the patients with giant symptomatic hemangioma liver

We have obtained permission from the Institutional Ethics Committee.

The study design

Retrospective study

Study Procedures

The study involves evaluation of giant ,symptomatic hemangioma for which we will need tumor markers, USG,UGIscopy , CECT Abdomen & Pelvis. The planned scheduled involve visits at

and _____(days/ weeks) after your initial visit. You will be required to visit the hospital _____ number of times during the study.

At each visit, the study physician will examine you. Some [blood / urine /imaging/clinical examination other] tests will be carried out at each visit. [... ... ml of blood will be collected at each visit. Blood collection involves prick with a needle and syringe.] These tests are essential to monitor your condition, and to assess the safety and efficacy of the treatment given to you.

In addition, if you notice any physical or mental change(s), you must contact the persons listed at the

end of the document.

You may have to come to the hospital (study site) for examination and investigations apart from your scheduled visits, if required.

Possible risks to you - If any, Briefly mention

Possible benefits to you - If any, Briefly mention

Possible benefits to other people

The results of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, Institutional Ethics Committee and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not loose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment/discontinuing of procedures etc.

Signature of Investigator

Signature of Participant

Date

Date

INSTITUTIONAL ETHICS COMMITTEE MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013 Telephone No : 044 25305301 Fax : 044 25363970

CERTIFICATE OF APPROVAL

To

Dr. M. Gnanasekar, PG in Surgical Gastroenterology, Department of Surgical Gastroenterology, Madras Medical College, Chennai-3.

Dear Dr. M. Gnanasekar,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Giant Hepatic Hemangioma – Analysis of Presentation, Management and Outcome – A Single Center Experience" No.44032014

The following members of Ethics Committee were present in the meeting held on 11.03.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	Chairperson
2.	Prof. Kalaiselvi, MD	Member Secretary
	Vice-Principal, MMC, Ch-3	
3.	Prof. Nandhini, M.D.	Member
	Inst. of Pharmacology, MMC, Ch-3.	
4.	Prof. Bhavani Shankar, M.S.	Member
	Prof & HOD of General Surgery, MMC, Ch-3.	
5.	Prof. V. Padmavathi, M.D.	Member
	I/c Directory of Pathology, MMC, Ch-3.	
6.	Thiru. S. Govindasamy, BABL	Lawyer

7. Tmt. Arnold Saulina, MA MSW

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

-- Social Scientist

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

1111

Member Secretary, Ethics Committee

turnitin

Digital Receipt

This receipt acknowledges that Turniin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is cisplayed below.

Submission author:	Gnanasekar murugaiyan
Assignment Millar	Medical
Submission	Giant Hepatic Hemangiomas – Analysis of presentation, management and outcome –A Single center experience".
Filename	INTRODUCTION.docx
2012/02/19/203	289.03K
Fage count	55
Wordcount	6,826
Charactér count	39,446
Submission cate	31-Mar-2014 12:45PM
Submission 199	411455683

Giant Hepatic Hemangiomas – Analysis of presentation, management and outcome –A Single center experience".

ORIGIN	ALITY REPORT						
6 SIMILA	% RITY INDEX	5 %	2% PUBLICATIONS	1 % STUDENT PAPERS			
PRIMAR	YSOURCES						
1	radiopaeo	dia.org		1%			
2	moon.ou	nsc.edu		1%			
3	brighamrad.harvarc.edu						
4	WWW.MeC	licine.cu.e(u.eg		1%			
5	"Studies f Departme data on n August 30 Publication	rom Kaunas Un ent of Radiology nagnet", Health o 2010 Issue	iversity of Med have provided & Medicine We	icine, < 1 % new eek,			
6	theaccent	s.org		< 1 %			
7	emedicine Internet Source	e.medscape.cc n	ו	<1%			