

SPECTRUM OF NEOPLASTIC AND NON-NEOPLASTIC LESIONS ASSOCIATED WITH PREGNANCY- 5 YEARS EXPERIENCE IN A TERTIARY REFERRAL CENTRE

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ABSTRACT

BACKGROUND

The incidence of adnexal and non-adnexal masses in pregnancy appears to be increasing in line with the expanding use of antenatal ultrasound. Majority of such masses do not cause problems and persisting masses can lead to complications and may require emergency or elective surgical resection.

MATERIALS AND METHODS

In this study, we retrospectively analysed neoplastic and non-neoplastic lesions associated with pregnancy for a period of five years from May 2011 to May 2016 in Institute of Obstetrics and Gynaecology, Government Hospital for Women and Children, Egmore, Chennai. Our study population included all antenatal women with dysfunctional cysts, adnexal and non-adnexal masses. Most of these lesions were incidental and found during caesarean section while remaining patients underwent emergency laparotomy due to acute symptoms that endangered maternal and foetal life. We reviewed our medical records during the study period and details regarding patient age, clinical and histopathological nature of the lesions were collected.

RESULTS

There were 68,877 deliveries during the study period and 97 women were found to have these lesions, out of which 73 women had neoplastic lesions and 24 women had non-neoplastic lesions. Adnexal cysts were the most common non-neoplastic lesions associated with pregnancy. Benign lesions outnumbered the malignant counterparts. Uterine leiomyomas, benign ovarian surface epithelial tumours, sex cord stromal tumours and benign cystic teratomas were reported among benign neoplasms. Germ cell tumours were frequently encountered among malignancies, dysgerminoma being the commonest germ cell neoplasm. Two cases of bilateral Krukenberg tumour and one case of mixed germ cell tumour were recorded. We also reported a case of angiomyolipoma and well-differentiated hepatocellular carcinoma which presented as haemoperitoneum during pregnancy.

CONCLUSION

Pregnancy is associated with various neoplastic and non-neoplastic lesions and requires early diagnosis and management for better foetal and maternal outcome.

KEYWORDS

Pregnancy, Leiomyomas, Angiomyolipoma, Dysgerminoma, Mixed Germ Cell Tumour, Hepatocellular Carcinoma, Krukenberg Tumour.

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BACKGROUND

A number of neoplastic and non-neoplastic lesions are associated with pregnancy. Among non-neoplastic conditions, dysfunctional cysts are frequently encountered and most commonly identified at the time of caesarean section or puerperal sterilisation, at which time they can simply be drained or excised. Benign ovarian neoplasm and leiomyomas are also identified during pregnancy. Malignancies have an incidence of approximately 1 per 1000 pregnancies.⁽¹⁾ Genitourinary tract malignancies have higher incidence as they are diagnosed by prenatal ultrasonographic examination.

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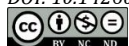
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Objective

Our purpose was to retrospectively determine the histopathological nature of various neoplastic and non-neoplastic lesions associated with pregnancy and to ascertain the frequency and distribution of these lesions.

MATERIALS AND METHODS

We reviewed cases of pregnancy complicated by haemoperitoneum, masses and dysfunctional cysts in Institute of Obstetrics and Gynaecology over a five-year period with regards to clinical and pathological aspects. Our study population included all antenatal women with dysfunctional cysts, adnexal and non-adnexal masses. Masses were removed from 58 women at the time of caesarean section, 39 women during the antepartum period and were evaluated microscopically. Patients were followed up and followup information was recorded up to the date of last contact or death.

RESULTS

A total of ninety seven cases were recorded and all these specimens were subjected for routine histopathological examination.

In this study, the incidence of these lesions were found to be 1.4/1000 deliveries. Of the total 97 women, 42 were primigravida, remaining were multigravida. Among 97 women, 59 were diagnosed during antenatal period and others were incidentally found at caesarean section. The average age range of the patient was 20-40 years. Mean time of diagnosis was 16-26 weeks of gestation. Mean time of surgical intervention was around 37-39 weeks. Asymptomatic women were found to have these lesions during caesarean section while remaining patients presented with abdominal pain, distension and haemoperitoneum. Histopathological diagnosis included dysfunctional cysts, uterine and cervical leiomyomas, benign ovarian surface epithelial tumours, ovarian germ cell tumours, angiomyolipoma, well-differentiated hepatocellular carcinoma and Krukenberg tumour.

In this study, non-neoplastic cysts accounted for 25% cases. Among these cysts, paratubal/paraovarian cysts were common which is followed by haemorrhagic cyst, endometriotic cyst, follicular cyst and corpus luteal cyst.^(2,3)

Most of these cystic lesions were incidental finding and cystectomy done during caesarean section. Lesions more than 5 cm presented with acute abdominal pain and showed features of torsion.

Neoplastic lesions constituted about 75% cases and include both benign and malignant tumours. 67% were benign and remaining 8% were malignant.

Leiomyoma complicating pregnancy was more frequently encountered compared to other benign and malignant conditions. 19 cases of uterine leiomyomas and 2 cases of cervical leiomyoma were reported. Pregnancy induced changes like red degeneration, hyaline degeneration and cystic degeneration were noted.⁽⁴⁾

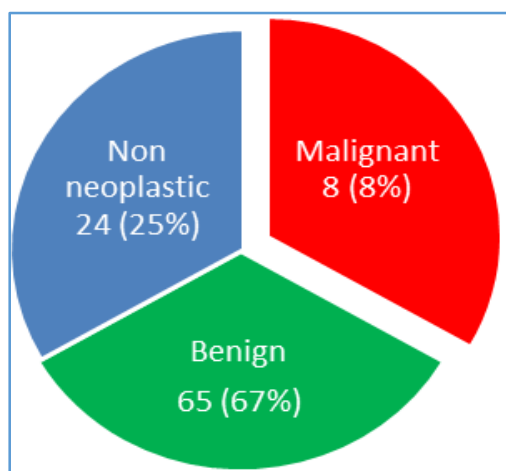
Among benign surface epithelial ovarian neoplasm, serous cystadenoma predominated in comparison to mucinous cystadenomas.^(5,6) 17 cases of benign cystic teratomas were recorded, of which one showed monodermal specialisation – Struma ovarii.⁽⁷⁾

Dysgerminomas were the common malignant germ cell neoplasms.^(8,9) One case of mixed germ cell tumour (yolk sac tumour & immature teratoma) and two cases of Krukenberg tumour were reported.⁽¹⁰⁾

A case of angiomyolipoma and hepatocellular carcinoma were recorded.^(11,12)

Clinical Data	Number of Women	Percentage of Women
Time at Diagnosis:		
I trimester	12	12
II trimester	47	49
Caesarean section	38	39
Presenting Symptoms:		
Symptomatic	39	40
Asymptomatic	58	60
Time at Surgical Intervention:		
I trimester	8	8
II trimester	31	32
Caesarean section	58	60

Table 1. Time at Diagnosis, time at Surgical Intervention and Presenting Symptoms



Proportion of Non-neoplastic and Neoplastic Lesions Complicating Pregnancy

Histological Diagnosis	Number of Women	Age in Years	Size of Cyst in cm
Paratubal/Paraovarian cyst	10	20-30	2-12
Haemorrhagic cyst	5	20-30	8-15
Endometriotic cyst	4	20-30	3-13
Follicular cyst	2	20-35	1.5 & 8
Corpus luteal cyst	3	20-30	2-3

Table 2. Incidence of Non-neoplastic Lesions

Histological Diagnosis	Number of Women	Age in Years	Tumour Size in cm
Surface Epithelial Tumours: Serous cystadenomas	14	20-30	1.5-20
Papillary serous cystadenofibroma	3	20-30	3-15
Benign mucinous cystadenoma	7	20-35	3.5-25
Sex Cord Stromal tumours: Ovarian fibroma	2	20-30	12 & 15
Germ Cell Tumours: Benign cystic teratoma	16	20-35	6-12
Monodermal/specialised teratoma, struma ovarii	1	27	11
Dysgerminoma	4	20-30	16-22
Mixed germ cell tumour	1	23	25
Leiomyomas	21	20-40	3-15
Miscellaneous Bilateral Krukenberg	2	30-35	10 & 15
Angiomyolipoma	1	33	15
Hepatocellular CA	1	32	2.5

Table 3. Incidence of Neoplastic Lesions

Outcome

Histological Diagnosis	Maternal Outcome			Foetal Outcome	
	Alive	Expired	Lost to Followup	Alive	Expired
Dysfunctional cyst	24	-	-	24	-
Benign neoplasms	65	-	-	65	-
Malignancy	5	1	2	6	2

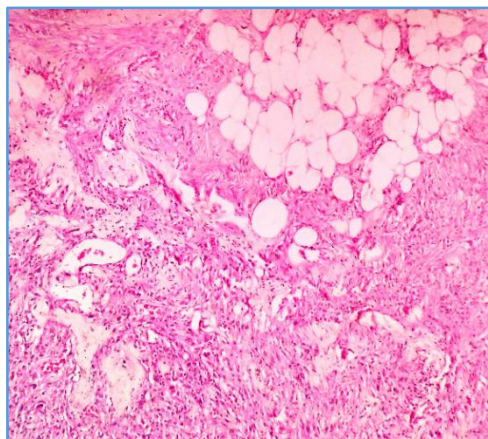


Figure 1. Angiomyolipoma: Composed of Variable Amounts of Adipose Tissue, Smooth Muscle and Blood Vessels. 400X H&E

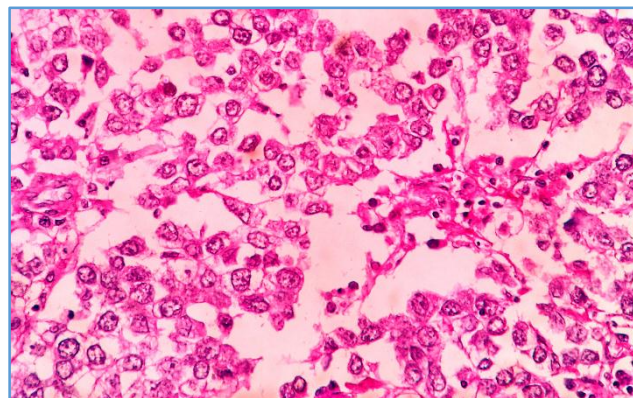


Figure 3. Dysgerminoma - Round to Polygonal Cells with Vesicular Nuclei & Prominent Nucleoli. Stroma shows Numerous Lymphocytes. 400 X H&E

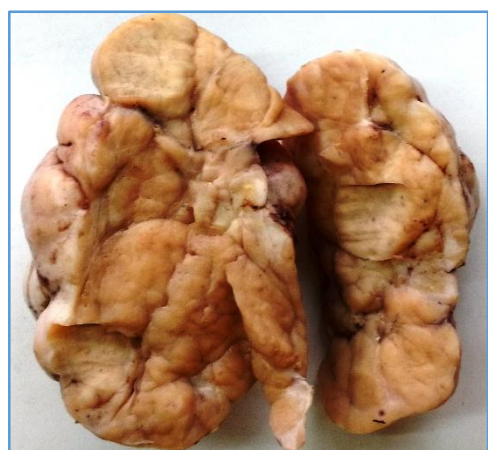


Figure 2. Dysgerminoma - Grossly Tumour is Solid, Fleshy and Lobulated



Figure 4. Hepatocellular Carcinoma - Tumour showing Rupture Site and Macerated Foetus that was Expelled Spontaneously

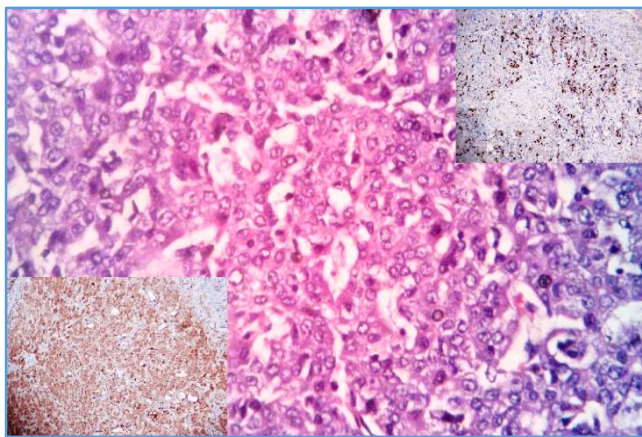


Figure 5. Hepatocellular Carcinoma - Tumour Cells showing Atypia and Few Mitotic Figures seen. 400X H&E. Upper Inset: Ki 67 Index showing more than 30% Positivity in Tumour Cells. Lower Inset: Alpha Fetoprotein Positive in Tumour Cells

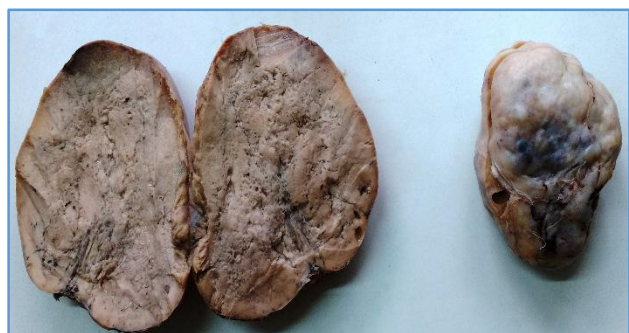


Figure 6. Krukenberg Tumour - Grossly Bilateral Solid Ovarian Mass

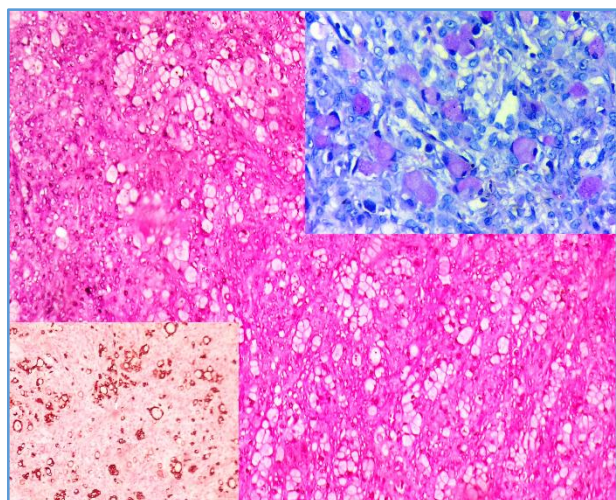


Figure 7. Krukenberg Tumour - Signet-ring of Cells which are PAS Positive & CK 20 Positive

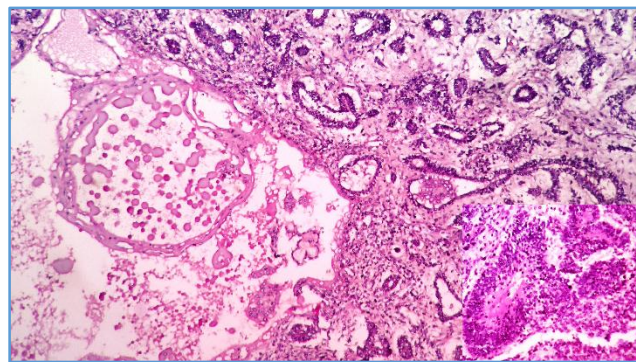


Figure 8. Mixed Germ Cell Tumour - Yolk Sac Elements with Hyaline Globules are seen. Lower Inset showing Immature Neuroepithelium

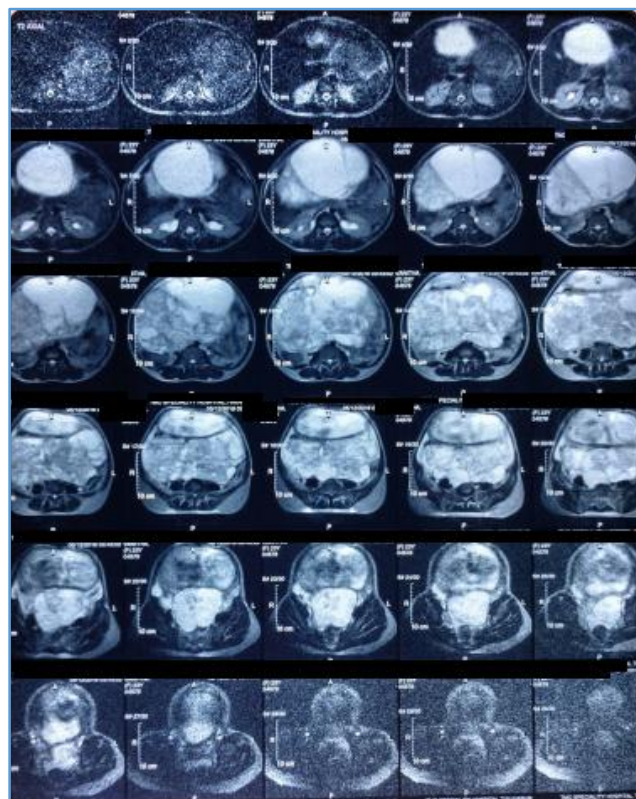


Figure 9. Mixed Germ Cell Tumour - MRI showing Solid and Cystic Right Ovarian Mass

Maternal Outcome

All women who underwent operative intervention for dysfunctional cysts and benign neoplasms were followed up and their post-operative period were uneventful. A case of hepatocellular carcinoma was treated with radiofrequency ablation and lost to followup after a period of two years. All four cases of dysgerminoma were in Stage I and three cases were in regular followup and one case lost to followup after a period of two years. One case of Krukenberg tumour with primary gastric carcinoma expired within three months of diagnosis. Another Krukenberg tumour which was found per operatively was evaluated for primaries and found to have growth in distal gastric region and referred at request to higher cancer institute for further management. A case of mixed germ cell tumour was followed up with tumour markers and patient was referred at request to higher cancer institute for further management.

Foetal Outcome

The neonatal outcome in pregnancies complicated by dysfunctional cysts and benign neoplasms were good where as those complicated by malignant tumours had dismal prognosis. Pregnancies complicated by dysgerminoma and Krukenberg tumour had favourable foetal outcome. Mixed germ cell tumour patient delivered a female child weighing 800 g and succumbed to respiratory distress. Due to circulatory insufficiency, patient with hepatocellular carcinoma had spontaneous expulsion of foetus.

DISCUSSION

The overall incidence of ovarian masses in pregnancy was 2.4-5.7%.⁽¹³⁾ Of these masses, approximately 5% were malignant. Most patients with ovarian masses have no specific symptoms. This asymptomatic character of these lesions makes early diagnosis difficult. Currently, an ultrasound is routinely used early in pregnancy, and this has led to an early diagnosis and management of asymptomatic ovarian tumours.^(2,14)

The management of these masses during pregnancy can be challenging for the clinician. The spectre of a possible malignancy can sway the decision for intervention versus expectant management. The aetiologies of ovarian masses were reflective of the patient's age; and therefore, benign entities such as dysfunctional ovarian cysts, benign cystic teratomas, and serous cystadenomas predominate. In the unusual cases when malignancy is present, they are typically germ cell and borderline ovarian tumours, and are commonly low stage and low grade.⁽¹⁵⁾ Tumour markers are used primarily to monitor disease status after treatment rather than establishing diagnosis as a result of lack of specificity. Several studies have reported that the histologic types of ovarian masses during pregnancy were similar to those for non-pregnant women in the corresponding reproductive age group.⁽¹⁰⁾

Expectant management is recommended for most pregnant patients with asymptomatic, non-suspicious masses. Surgical intervention during pregnancy is indicated for large and/or symptomatic tumours and those that appear highly suspicious for malignancy on imaging. Conservative management is appropriate for benign masses and borderline ovarian tumours. Rarely, chemotherapy has been used during pregnancy when the risk of maternal mortality outweighs the foetal consequences.

The most common pregnancy associated adnexal masses were functional cysts like the corpus luteal cyst and theca lutein cysts. Most of these cysts will resolve after the first 14-16 weeks of gestation but some, like the theca lutein cysts, can persist until after delivery.⁽¹⁶⁾ Masses that persist after 16 weeks of gestation were considered as non-functional. Most frequent complication was torsion and found to be associated with lesions greater than 5 cm in diameter.⁽¹⁶⁾

The majority of ovarian tumours associated with pregnancy were diagnosed at an early stage, when disease was still confined to the ovary.⁽¹⁰⁾ Germ cell tumours and epithelial tumours of low malignant potential were much more prevalent than other types of malignancies in pregnancy.⁽¹⁷⁾ Among epithelial tumours, serous cystadenomas were common followed by mucinous cystadenomas.⁽¹⁸⁾ These epithelial tumours were of low malignant potential. Benign cystic teratoma was the most common benign germ cell tumour associated with pregnancy. Dysgerminoma was the

most common malignant germ cell tumour followed by mixed germ cell tumours.⁽¹⁹⁾

Leiomyomas were the common uterine tumours associated with pregnancy and their incidence during pregnancy was approximately 2%.⁽¹⁾ Leiomyomas vary in location and may develop as submucosal, subserosal, or intramural growths. Less frequently, these develop in cervix or broad ligament. In this series, two cases of cervical fibroid were reported and these were excised or else this would have caused cervical dystocia. Pregnancy induced changes like red degeneration, hyaline degeneration and cystic degeneration were noted.⁽⁴⁾

Common causes of spontaneous haemoperitoneum in pregnancy were ectopic pregnancy, ruptured ovarian cyst, endometriosis and uterine rupture. In this series, we reported two uncommon cases of spontaneous non-traumatic haemoperitoneum-angiomyolipoma and well-differentiated hepatocellular carcinoma. Hepatocellular carcinoma is very rare during pregnancy and has a worse prognosis in pregnant women compared to those who are not pregnant. Hepatocellular carcinoma is aggressive during pregnancy and has a poor prognosis with an overall one-year survival of 23%,⁽²⁰⁾ which could be explained by two main aetiologies: oestrogen elevation which accelerates the evolution of hepatocellular carcinoma and immune suppression during pregnancy.⁽²¹⁾ It is associated with foetal loss in 42% of cases.⁽²²⁾

In this series, we reported a case of well-differentiated hepatocellular carcinoma in which patient presented with haemoperitoneum at 20 weeks of gestation and a macerated foetus was expelled. Even though common cause of haemoperitoneum in pregnancy was ruptured ectopic, the possibility of bleeding intra-abdominal tumours should always be considered as a differential diagnosis in such clinical settings.

We reported two cases of Krukenberg tumour and these tumour accounts for 1-2% of all ovarian tumours. These tumours during pregnancy were even rarer, as the incidence of gastric cancer in women of reproductive age group was only 0.4%-0.5%.⁽²³⁾

CONCLUSION

Pregnancy can be complicated by dysfunctional cysts and malignancies. Management of these conditions poses unique problems related to foetal outcome. Thus, a careful clinical examination helps in early diagnosis and treatment of such conditions. Even though common cause of haemoperitoneum in pregnancy is ruptured ectopic, the possibility of bleeding intra-abdominal tumours should always be considered as a differential diagnosis in such clinical settings.

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