CARCINOMA OF THE CERVIX WITH PREGNANCY

(Report of 11 cases)

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Carcinoma of the cervix is rarely seen during pregnancy. It occurs once in about 3,000 deliveries. Corscaden gives the incidence of cancer of the cervix in pregnancy as varying from 0.005% to 0.47%. Graham *et al* from 0.005 to 0.38% listing sixteen Institutions.

Since the occurrence of carcinoma of the cervix during pregnancy is very rare, we are reporting 11 cases seen at B.Y.L. Nair Charitable Hospital (Bombay) in this article. These cases have been classified as those in the first trimesters, in the second and the third trimesters and during puerperium.

Carcinoma of the Cervix in the First Trimester of Pregnancy

Carcinoma of the cervix in the first trimester of pregnancy, particularly in the in-situ stages, is undoubtedly present much more frequently than has previously been suspected. The recent emphasis on early diagnosis of malignant disease has been more rewarding in the cases of carcinoma of the cervix than with perhaps any other malignant lesion. Primarily, this is because of the widespread publicity associated with the lesion and because of the increasing awareness of the value of the Papanicolaou smear in the diagnosis of the earliest stages of the disease.

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Received for publication on 19-4-73.

Diagnosis

Pathologists are now generally in complete accord with the fact that smears are accurate during pregnancy and that pregnancy changes in the vagina and cervical cells are easily distinguishable from those brought on by malignant change. The advantage of an accurate diagnosis of causes of bleeding during early and late pregnancy far outweighs the chance of promoting complications of pregnancy.

The majority of pregnant women are seen during the first trimester, which is the ideal time for a pattern of cancer detection to be established. Smears of the cervix should be obtained during the initial examination of each pregnant woman, whether or not she has symptoms and should be repeated six weeks' postpartum. By this method not only will many early malignancies be found during pregnancy but instructing a pregnant patient about proper follow-up care will further decrease the chance of her developing advanced lesions.

In the absence of clinical symptoms or findings initial smears of the cervix in

class I, II or II B need to be repeated only at the six weeks postpartum examination. Papanicolaou smears are 90-95% accurate. A class III report indicates a suspicion of malignancy, but local inflamation should be ruled out. Persistant class III and class IV smears must be considered indication for biopsy of the cervix. Biopsy is also essential if any suspicious local lesion of the cervix is present with or without suspicious smears.

Biopsy

Methods of biopsy during pregnancy are particularly important to establish the exact extent of all cervical lesions. Primarily, one is interested in ruling out malignancy and finding out whether it is invasive or not, and also to know its extent. The outcome of this will determine whether the pregnancy should be allowed to continue.

Local punch biopsy of the cervix should be performed if a visible or obvious area is involved. If this is positive for invasive cancer, no other diagnostic procedures are necessary. If, however, biopsy shows in-situ cancer further cold knife cone biopsy of the cervix must be done to rule out invasion elsewhere.

Treatment

With a negative cone biopsy report the patient needs no treatment. The pregnancy is allowed to continue, the smears are repeated every 3 months.

In-situ cancer diagnosed by cone biopsy also does not require further treatment, vaginal delivery should be allowed for such cases. Invasive cancer proved by biopsy, takes precedence over a pregnancy in the first trimester. There should be no attempt to conserve the pregnancy. In early stage I, radical vaginal hysterectomy is the present treatment of choice. The late stage I and early stage II lesions are treated by Wertheim's hysterectomy with lymphadenectomy. In early pregnancy even though bleeding is greater due to increased vascularity, planes of cleavage are found easily and dissection is easy. In late stage II and III radiotherapy is given. If the uterus is small and easily evacuated, by dilatation and curettage, the first course of radium should be inserted during this procedure. If it is not possible to do D & C, external radiotherapy should be given prior to the radium insertion. Radiotherapy usually results in abortion.

Case Reports

Case I

Mrs. U.R.B., aged 45 years was admitted on 18-10-1970 with a history of 3 months' amenorrhoea and irregular bleeding per vaginam off and on. Her past menstrual cycles were regular. She had four full term normal deliveries.

On vaginal examination, the whole cervix was destroyed, an irregular friable growth, 2″ in diameter was felt on the cervix. The uterus was bulky about 10 weeks' size. There was no infiltration in the vagina or parametrium. Examination under anaesthesia was done to find out the exact extent of the growth, and biopsy was done. The patient had profuse bleeding following biopsy. Vaginal packing was done. Blool transfusions were given. Bipsy showed features of epidermoid carcinoma. Vaginal cytology also showed features of malignancy. Other investigations were normal.

Wertheim's hysterectomy was done with bilateral lymphadenectomy. Histopathological diagnosis was invasive epidermoid carcinoma. The patient was given postoperative deep X-Ray therapy. The patient had wound infection. Immediate follow-up showed vagina to be normal and no thickening or recurrence. One year follow-up showed an ulcer on anterior vaginal wall,

bleeding on touch. The patient is called up for further investigations—cytology and biopsy.

Case II

Mrs. B.M.A., aged 40 years was admitted on 12-5-1971 with a history of 2½ months' amenorrhoea, leucorrhoea and foul-smelling discharge. She gave a history of menorrhagia and polymenorrhoea for previous one year. She had the history of 8 full term normal deliveries. The last delivery was four years previously.

On vaginal examination, the cervix was hard, and irregular. The uterus was 12 weeks' size. The parametrium and the vagina were clear. Speculum examination revealed a big ulcer on the posterior lip of the cervix and it bled on touch. Vaginal cytology showed features of malignancy. The biopsy report was epidermoid carcinoma of the cervix. The patient had bilateral pulmonary Koch's also. Cystoscopy and intravenous pyelography were normal.

Wertheim's hysterectomy with lymphadenectomy was done on 28-5-1971. The uterus was 12 weeks' in size, blue and there was marked congestion all over, Wertheim's hysterectomy was very easy, and there was not much bleeding. The patient was given postoperative radiation. On follow-up there was no infiltration or recurrence. Patient had no symptoms. Patient developed ventral hernia.

Case III

Mrs. H.D.S., aged 45 years was admitted on 5-3-1968 with a history of irregular vaginal bleeding for six months and history of 'Contact bleeding' for six months. Her previous cycles were regular. She had four full term normal deliveries. The last delivery was four years ago.

On vaginal examination, a hard irregular mass was felt in the cervical canal, the whole cervix was balloned out. The uterus was normal in size. There was infiltration in the right parametrium, but not upto the pelvic wall. Speculum examination showed growth in the cervical canal, hard friable which bled on touch. Cervical biopsy showed features of epidermoid carcinoma. Cystoscopy and intravenous pyelography were normal.

Wertheim's hysterectomy with lymphadenectomy done on 26-3-1968. The uterus was normal in size. During lymphadenectomy of left side there was excessive bleeding, which could not be controlled by ligation or diathermy and hence tight packing was done. Later on the bleeding stopped, drainage tube was kept on left side.

On the twelveth postoperative day the patient complained of urinary leakage. Speculum examination showed urinary leakage from left side of vagina and small fistulous opening was seen. Three swab test revealed ureteric fistula on left side. Postoperative intravenous pyelography revealed that there was delay in excretion of the dye on the left side and there was lower ureteric orifice stasis. Lateral to lower end of the ureter there was a linear streak which was persistent and associated with left superolateral border of the bladder, suggestive of left uretero-vaginal fistula. Reimplantation of the left ureter in the bladder was done. Suprapubic cystostomy was done and the bladder was drained with continuous suction apparatus. The catheter was removed on the 14th day. The patient was well at the time of discharge.

The histopathology report of the specimen showed changes of pregnancy in the uterus and the section of the cervix showed features of the epidermoid carcinoma. In this case pregnancy was not suspected as the patient had irregular bleeding but no history of amenorrhoea. On vaginal examination, the uterus was normal in size. The pregnancy was missed even on the operation table since it was very early.

Case IV

Mrs. M.M.A., Muslim patient, aged 35 years was admitted with a history of 3 months' amenorrhoea and severe vaginal bleeding. Her previous cycles were regular. She had a history of three full term normal deliveries.

Vaginal examination revealed that the cervix was very hard and irregular. The internal os was open and products of conception were left. The uterus was bulky. The fornices were clear. The patient was taken up for D & C. At the time of D & C, cervical biopsy was also done. The biopsy

report was epidermoid carcinoma. The patient was advised to undergo hysterectomy operation, but refused and went against medical advice and never returned for follow-up in spite of repeated reminders.

Carcinoma of the Cervix in the Second Trimester of Pregnancy

Of the 48 cases listed from the Rosewell Park Memorial Institute, 36 were discovered postpartum, 6 occurred in the first trimester, five in the second and one in the third trimesters.

Ward in 1947 described 10 cases of cancer of the cervix with pregnancy seen at the Women's Hospital, New York, over a period of 19 years. Of these only five were seen before the 28th week of pregnancy.

Barber and Brunschwing (1963) from Memorial Hospital, New York, listed 47 cases, but discarded without further comment 15 treated less than five years previously. Of the 32 cases analysed, 5 were diagnosed at delivery, 7 from 1-4 months post-partum and 15 from 4-12 months post-partum leaving only 5 diagnosed during pregnancy and of this only 2 during the second trimester.

Liu and Meigs reviewed 473 cases of radical hysterectomy in 1955. In this series, 6 patients were pregnant at the time of surgery but of these one was so classified only because decidua and chorionic villi were found in the surgical specimen while another had carcinoma in-situ. Of the four that remained one only was in the 2nd trimester.

Treatment

Radical hysterectomy in a pregnant patient is technically feasible and not dangerous. Liu and Meigs record 5 cases without an operative death, Lash 15 and Barber and Brunsehwig 5.

Radiation therapy may be highly effective in cervical cancer even in pregnancy, is attested to by many others.

Case Reports

Case I

Mrs. L.G.K., aged 30 years was admitted on 11-2-1971 with a history of six months' amenorrhoea and bleeding per vaginam. The patient was transferred from a peripheral maternity hospital. Her previous cycles were regular. She had history of four deliveries. One was stillbirth, and 3 were full term normal deliveries.

On examination, there was marked pallor. The uterus was 28 weeks in size, presentation was vertex 1 and the head was floating. Foetal heart sounds were regular.

Vaginal examination revealed a growth on the cervix which was hard and irregular and friable. There was moderate bleeding per vaginam.

Vaginal cytology showed features of malignancy. The cervical biopsy report was squamous cell carcinoma. Other investigations were normal.

Since the patient was already 30 weeks' pregnant by the time the diagnosis was confirmed it was decided to do Caesarean Wertheim's at term. Classical caesarean section was done on 7-4-1971. Baby was female, and weighed 2.5 Kg. The bladder was adherent to the cervix and could not be pushed down on right side. It was found that the infiltration had already occurred and the cancer was inoperable. Tube ligation was done. The patient was sent to Tata Memorial Hospital for radiation. The patient took full course of radiotherapy. She was well for 2 months. Later on she developed loss of appetite, loss of weight, had bleeding per vaginam, and urinary symptoms and expired after 5 months.

Case II

Mrs. S.V.K., aged 30 years was admitted on 19-11-1972 with a history of 6 months' amenorrhoea, pain in the abdomen and bleeding per vaginam. She had four full term normal deliveries in the past. The last delivery was 2 years back.

The uterus was 26 weeks in size with

the foetus lying in breech presentation. The foetal heart sounds were normal.

On vaginal examination a hard, irregular, friable growth was felt on the anterior lip of the cervix. Speculum examination showed that the growth was mainly on the cervix, and it bled on touch. There was no infiltration of the vagina or the parametrium.

The cervical biopsy report was squamous cell carcinoma. The vaginal cytology also showed evidence of malignancy. The other investigations were normal.

Wertheim's hysterectomy with lymphadenectomy was done on 7-12-1972. The uterus was 26 weeks' size. The operation was easy and there was not much bleeding. On the 5th postoperative day patient developed distension of the abdomen and profuse purulent discharge from the abdominal incision. The incision was opened up to allow free drainage. The purulent discharge continued for 3 weeks and hence re-exploration was done on 20-12-1972. There were multiple cavities of pus in the paracolic gutter, in both iliac fossa and under the liver. The pelvic cavity was also full of pus. 500 c.c. of pus was drained. Two drainage tubes were kept, one in each iliac fossa and one under the liver. The patient's condition deteriorated in spite of treatment and she expired on 13-1-1973.

Carcinoma of the Cervix in the Third Trimester of the Pregnancy

Approximately only 1% of cases of carcinoma of the cervix occurs in pregnant women in the third trimester. Thus, no individual physician has had sufficient personal experience with the management of third trimester carcinoma of the cervix to base valid opinions regarding its proper management.

Stander and Lein have emphasized that the chief threat to the patient is not alteration of the biologic behaviour of the neoplasm by the pregnancy but the delay that may occur before the carcinoma is detected. They noted delay in diagnosis averaging 4-5 months in 62 per cent of this group. Delay in most instances was as a result of attributing symptoms to some obstetric complication.

Todd noted that the patient's chances for successful treatment diminished by about 15% for each month that treatment was delayed after the onset of vaginal bleeding.

MontGomery and Lash among others have emphasized the importance of prompt investigations of any abnormal vaginal bleeding during pregnancy. Irrespective of the duration of gestation, the cervix can safely be exposed for inspection, cytological study and biopsy. Considerable evidence exists that the prognosis is worse when the diagnosis is not made until late pregnancy.

Maino and Mussey noted that 17% with stage I carcinoma of the cervix were at or near term at the time of diagnosis, 31% with stage II, 50% with stage III and 67% with stage IV. Kottmeier supported the observation of Hunt and Mussey that the results are very poor in cases of carcinoma of the cervix involving a viable foetus. Of the 8 patients treated during the last week of pregnancy, none survived.

Kistner and Gorbach (1957) indicated that before the 34th week of pregnancy the five year survival rate did not appreciably differ from that of non-pregnant patients when compared stage for stage, whereas the apparent cure rate declined considerably after the 34th week, or during the postpartum stage. Hormonal alteration together with increased vascularity was suggested as the responsible factor.

Treatment

It is the carcinoma diagnosed between the twenty-seventh and the thirty-third week of pregnancy that places the obste-

trician in a difficult position. He must balance the added risk to the mother of delaying treatment for 4-8 weeks against the increased possibility of foetal survival. Mcduff Corney & Watterman expressed the opinion that the delay of this magnitude may spell the difference between success and failure of treatment.

Despite the observation of Strauss in 1940, that the 20% pregnancies subjected to radiation result in production of microcephalic infants, some authorities like Hayden continue to advise "containing dose of radium" and the deferment of complete therapy until the possibility of obtaining a living infant has improved. The objecetives of this therapy are to retard the carcinoma and to secure a normal infant.

Whereas there is not sufficient evidence that partial therapy will accomplish retardation of the neoplasm, there is wealth of information to demonstrate that it may produce an abnormal microcephalic infant (6-20%) and theoretically it may produce other abnormalities, present and future. The price of the above therapy seems too high. If delay for better viability is elected under certain special circumstances, delay for few weeks without radiation therapy would be advisable.

The definitive treatment would be after evacuation of the uterus to do radical hysterectomy with dissection of lymph nodes for all third trimester patients with an operable carcinoma cervix and conventional radiation therapy for inoperable lesions.

Lucci, Barber and Brunschwig advocated for all trimesters of pregnancy the use of Betatron supervoltage external radiation with a minimum of 4000r given to the total pelvis for I and II and 6000 for stage III and IV. Radium is used to complete therapy. Pregnancy is ignored during the I and the II trimesters and high classical caesarean section is performed in the third trimester, to be followed as soon as possible by the supervoltage radiation. Advantages of surgery are:

1. Radical surgery provides a soft pliable and functional vagina in contrast to the fibrotic fixed and contracted vagina, encountered after radiation.
2. With hysterectomy significant infection of the post caesarean uterus can be avoided.
3. Surgery affords the opportunity to delineate the extent of the disease which is clinically difficult to determine during pregnancy.

Case I

Mrs. S.R.B., aged 35 years was admitted on 29-9-1970 with a history of seven months' amenorrhoea and blood stained discharge. The patient had 4 full term normal deliveries and one twin delivery.

On examination there was marked pallor. The uterus was 28 weeks, presentation was vertex, the head was floating and foetal heart sounds were regular.

Vaginal examination revealed an irregular growth on both the lips of the cervix. It was friable and bled on touch. Biopsy was taken from the grwth and the report was poorly differentiated squamous cell carcinoma of the cervix. Colposcopy and vaginal cytology also showed features of malignancy. The patient was discharged against medical advice on 28-11-1970. She never came for antenatal check up. She was readmitted on 1-1-1971 with labour pains. Classical caesarean section was done on the same day. During the operation the cancer was found to be advanced, and inoperable. The patient was referred to Tata Memorial Hospital for radiation. She did not return for follow up.

Case II

Mrs. B.M.P. was admitted on 4-11-1948 with seven months' amenorrhoea, and foul

smelling discharge per vaginam for four months. The patient also gave history of bleeding per vaginam in the first trimester. The uterus was 30 weeks, vertex, floating and foetal heart sounds were good. Vaginal examination revealed a growth arising from the posterior lip of the cervix, filling the vagina, but did not involve the vagina or the parametrium. The biopsy report was squamous cell carcinoma of the cervix. Caesarean section plus Wertheim's was done at term. The entire specimen was sent for histopathological section. It confirmed the diagnosis of carcinoma of the cervix. The patient expired after few months.

Case III

Mrs. S.L.V., aged 26 years was admitted on 20-7-1971 with a history of 9 months' amenorrhoea and bleeding per vaginam. She had 3 full term normal deliveries. The last delivery was 7 years previously. The uterus was 36 weeks size, vertex presentation, the head was floating, the fetal heart sounds were regular.

Vaginal examination showed a hard irregular and cauliflower like growth on the posterior lip of the cervix and it bled on touch. There was no infiltration of the vagina but the parametrium on the right side was infiltrated upto the pelvic wall. The patient went into labour on 21-7-1971. A classical caesarean section was done with tube ligation. The baby was male and weighed 1.9 kg. On palpation the left parametrium was free but on the right the growth was infiltrating the parametrium upto the pelvic wall. It was a case of inoperable cancer. The patient was sent to Tata Memorial Hospital for radiation. The patient could not be called for follow up, since she was a road side patient.

Carcinoma Of The Cervix In The Puperperium

Although carcinoma of the cervix diagnosed within 6 months following delivery or abortion is rare except for carcinoma of the breast, it is most common malignant neoplasm in this period of life.

The prognosis is poor, irrespective of the particular type of treatment employed. It is remarkable that once the immediate postpartum period is passed the cure rate returns to a normal level.

Pathology

This histological appearance of carcinoma of the cervix during puerperium is different from that in the non-pregnant state. This is due to marked inflammation of the stroma demarcating the tumour and due to derangement of the architectural and cellular norms in the cervical glands with hyperplastic proliferation, decidual formation and enlarged vessels. Gluksmann reports that anaplastic, mixed carcinoma occur more frequently in association with pregnancy and that they have much worse prognosis when occurring in such conjunction. He reports a cure rate of only 5% in mixed adeno-epidermoid tumours.

Diagnosis

Whenever prolonged bleeding or discharge occurs it is essential to perform a thorough pelvic examination and to institute the necessary diagnostic procedures to rule out the presence of malignant growth. Cytology, colposcopy and biopsy must be done in suspected cases.

Treatment

Radiotherapy or radical hysterectomy is the treatment of choice in invasive carcinoma.

Case Report

Case I

Mrs. J.M.S., muslim patient, aged 30 years was referred on 1-2-1972 for irregular, profuse bleeding and white discharge following normal delivery. The patient had six full term normal deliveries. The last delivery was 3½ months back.

On vaginal examination, the cervix was found to be irregular, there was a growth

on the posterior lip of the cervix, which was friable very vascular and bled on touch. The uterus was normal in size. The parametrium and the vagina were not infiltrated. Colposcopic findings suggested that there was marked inflammation, and the growth was benign, no malignant changes were detected. Vaginal cytology showed atypical cells with changes strongly suggestive of malignancy. Cervical biopsy report showed muco-epideroid carcinoma of the cervix. Cytoscopy and intravenous pyelography was normal. On 17-2-1972 Wertheim's hysterectomy was done. There was infiltration in the parametrium on both the sides but not upto the pelvic wall. Bilateral lymphadenectomy was also done.

Postoperatively the patient had continuous fever. Urine culture and routine examination showed plenty of pus cells, R.B.Cs, epithelial cells and E-Coli were grown which were resistant to all the antibiotics except Reverin and Ampicillin. The patient was treated with Reverin and was discharged against medical advice on 15-3-1972. On 4-4-1972 the patient was re-admitted for severe anaemia and urinary infection. The patient continued to have fever at home. Haemoglobin levels were falling constantly in spite of blood transfusions and other antianaemic treatment. Urine examination showed presence of albumin, plenty of pus cells, R.B.C. and casts. Intravenous pyelography showed non-functioning kidney on the right side. Post-micturating cystogram was suggestive of urinary tract infection. Blood urea nitrogen levels were 31 mg.%. The patient continued to have high fever in spite of intravenous Reverin and Gentamycin Sulphate. She went into uraemia and expired on 5-4-1972.

Case II

Mrs. S.M.F., aged 35 years was admitted at B. Y. L. Nair Charitable Hospital on 11-3-1969 for nine months' amenorrhoea and cord prolapse. An emergency caesarean section was done. Baby was male and weighed 2.8 Kg. The patient was discharged on the 10th day. The patient was called for postnatal check up after one month. At this time the patient complained of leucorrhoea. On speculum and vaginal examinations a growth was found on the posterior lip of the cervix which was friable and bled on touch. The uterus was normal in size and the fornices were clear. Cervical biopsy report showed squamous cells carcinoma—poor to moderate differentiation. The patient was advised admission but refused because there was no one to look after her child. She was admitted after one month. All the other investigations were normal. Wertheim's hysterectomy and bilateral lymphadenectomy was done. The patient was given postoperative radiation also.

The patient could not be called up for follow-up since she was a road side patient and proper address was not available.

Summary

In this article we have reported 11 cases of carcinoma of the cervix, 10 cases seen from 9.3.1968 to 19.11.72 and one case was seen in the year 1948. There were four cases in the first trimester, only two in the second trimester, three in the third trimester, and two cases were seen in the puerperium. The cases are discussed in detail and the available world literature has been reviewed. There were four deaths out of 11 cases. Five patients were well on follow-up examination, and 2 could not be contacted because the proper address was not available.

Acknowledgement

We are grateful to Dr. E. J. Sequeira, Head of the Gyn. and Obst. Department for his valuable guidance and the Dean, Dr. M. S. Kekre for allowing us to publish the hospital data.

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