BRENNER TUMOUR OF OVARY

(Report of two cases with review of literature)

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The position of Brenner tumour in the classification of ovarian tumours has changed. Previously it was classified as one of the tumours arising from congenital rests (Hertig and Gore 1961) whereas in the W.H.O. Classification of ovarian tumours (Serov *et al* 1973) it has been included under the larger group of epithelial tumours of ovary.

The tumour was first described by Fritz Brenner in 1907 under the name of Oophoroma folliculare thinking it to arise from the follicle. The true nature and origin of the tumour, however, remain obscure though many views about its genesis have been expressed since then (Meyer 1932; Jondahl *et al* 1950; Greene 1952; Fox *et al* 1972).

The tumour is not frequently seen; the incidence is 1.7% of all the ovarian tumours (Hertig and Gore 1961). The tumour may be associated with other ovarian tumours (Ehrlich and Roth 1971; Silverberg 1971; Balasa *et al* 1977). Brenner tumour is usually benign in nature, however, some of the cases with malignant Brenner tumour have been reported (Mackinlay 1956; Abell 1957; Woodruff and Acosta 1962 and Idelson 1963).

A brief report of 2 cases of Brenner tumour is presented herewith one of which was a proliferating tumour or potentially malignant.

While studying the histopathological pattern of 130 ovarian tumours in the Department of Pathology, J.N. Medical College, A.M.U., Aligarh 2 cases were diagnosed as Brenner tumour of ovary—thus giving the incidence as 1.54% of all the ovarian tumours.

Both the tumours occurred in the fifth decade of life—average age being 45.5 years.

Case 1

A., Hindu female aged 50 years, P_3 + O, was admitted with the complaints of a lump and pain in abdomen for 1 year and postmenopausal bleeding for last 6 months. She was of thin built and pale. No edema or lymphadenopathy was noticed.

Menstrual History: Menopause 6 years back; before that cycle was regular.

Vaginal Examination: Uterus retroverted; mass was felt through the right fornix.

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Abdominal Examination: A solid, freely mobile palpable mass occupying the lower abdomen midway between xiphisternum and umbilicus was felt.. No free fluid in the abdomen was noticed. Skiagram of chest did not reveal any abnormality.

Clinically the tumour appeared malignant as it was firm to solid in consistency, hence bilateral salpingo-ophorectomy and hysterectomy was done. No adhesions were found. Lymphnodes were not palpable. No free fluid in the abdomen was noticed.

Gross Pathology

There was a right sided ovarian tumour measuring 19 x 10 x 9 cm. in size. Its weight was 850 gms. Surface was irregular, nodular and grayish-white in colour. Nodules were ranging from 1 to 6 cm in diameter. Consistency was firm to solid.. Cut surface presented a multilocular picture, the loculi being filled with solid fibrous tissue having fasiculated appearance. Small areas of haemorrhage and cysts were seen filled with mucinous material.

Uterus appeared to be normal.

Microscopic Pathology

Multiple blocks were prepared. Section revealed focal collection of rather broad, spindle-shaped cells separated by thin fibrous septa (Fig. 1). In some areas cystic spaces were seen filled with mucinous material. The nuclei were elongated, vasicular and at times hyperchromatic showing division figures (Fig. 2).

At places these cells resembled fibroblasts and formed interlacing fasiculi. In some nuclei grooved structures like 'coffee bean' was seen. The stroma was cellular and at places continuous with the cellular mass. The overall picture was that of a proliferating Brenner tumour.

Section from the uterus showed endometrial hyperplasia.

Case 2

In this case the tumour was a small whitish nodule of 1 cm. diameter in the left ovary. It was an incidental finding in a case aged 41 years, P_3 + O, witd right ovarian tumour showing the morphological picture of papillary serous cystadenocarcinoma. All the complaints and clinical findings were due to other tumour. Histologically, the tumour of the left ovary presented the classical picture of benign cortical Brenner tumour where solid groups of epithelial cells were separated by cellular stroma. In some of the epithelial strands the central area was cystic and contained pink round protoplasmic mass. The cells contained grooved 'coffee-bean nuclei'.

Discussion

Though the tumour is designated as Brenner tumour but actually the first person who clearly described this tumour as a separate entity in 1898 was Macnaughton-Jones. Later on Orthmann (1899) reported six unusual cases of ovarian tumour, the last one resembling Brenner tumour and this he labelled as 'Fibroma papillare superficiale carcinomatosum'.

The incidence of Brenner tumour in the present study was 1.54% of all the ovarian tumours—a finding similar to that of Hertig and Gore (1961), though other Indian workers (Tyagi *et al* 1967; Ramachandaran *et al* 1972 and Talib *et al* 1974) have reported a low incidence of 0.83%, 1.2% and 0.63% respectively. The rarity of the tumour could also be judged by the fact that Meyer (1932) could collect only 4 cases in the large amount of material of his laboratory during 20 years.

Bilateral Brenner tumours are extremely rare, the incidence being 5 to 7% (Jondahl *et al* 1950; Farrar *et al* 1960; Kendall and Bowers 1960 and Jorgensen *et al* 1970). So far 25 such cases are on record (Novak and Woodruff 1974).

Brenner tumour is generally seen in the postmenopausal age group, average age being 58.5 years (Berge and Borglin 1967) and 53.4 years (Jorgensen *et al* 1970) or 45 to 50 years (Silverberg 1971; Erhlich and Roth 1971; Fox *et al* 1972). In the present series both the cases were in the 5th decade. Novak and Jones (1939) on the other hand have observed only 3 cases out of 14 above the age

group of 50 years, majority of cases being of 3rd and 4th decades of life. No genuine Brenner tumour has been seen in a child (Novak and Woodruff 1974).

The size of the tumour is extremely variable—from merely a microscopic size to a huge one weighing 19 pounds as reported by Averbach *et al* (1957). In one case the tumour was an incidental finding —a small nodule in the cortical area associated with serous cystadenocarcinoma in the other ovary. Other workers (Jondahl *et al* 1950; Ehrlich and Roth 1971; Silverberg 1971) have also reported Brenner tumour diagnosed incidentally with mucinous or serous cystomas or benign cystic teratomas. Balasa *et al* (1977) have narrated that 90 to 95% tumours are discovered incidentally at surgery.

The second tumour presented the morphological picture of a rather highly cellular maligant tumour. Langley (1975), however, reviewed the slides and was of the opinion that the tumour should be designated as proliferating Brenner tumour. Roth and Sternberg (1971) and Miles and Norris (1972) have emphasized that the malignant Brenner tumour should be diagnosed only when carcinomatous changes result into transitional or squamous cell carcinoma. A predominently mucinous carcinoma in which Brenner epithelial cell nests are seen should be labelled as mucinous cystadenocarcinoma or mixed epithelial tumours (Serov *et al* 1973).

In proliferating Brenner tumour there is unusual degree of epithelial proliferational and biological resemblance to low grade carcinoma (Transitional cell type) as seen in urinary bladder (Roth and Sternberg 1971). Mitoses are seen as had been observed in the case under review. Chang *et al* (1977) added their own case to the list of 17 cases of proliferating Brenner tumour reported so far. The present case is probably the first to be reported in the Indian literature. These tumours are generally large, of variable consistency and present with postmenopausal bleeding (Chang *et al* 1977). All the above qualities were noticed in the present case. Proliferating Brenner tumour is generally considered benign with better prognosis as local recurrences and distant metastases have not yet been documented (Balasa *et al* 1977). In the present case the patient could be followed only upto 3 years without any metastases.

Histogenesis of Brenner Tumour

Many views have been expressed about the histogenesis of Brenner tumour that the tmour develops from:

(a) Follicular granulosa cells—originally thought by Brenner and later on supported by Teoh (1953) and Jones (1959).

(b) Ovarian mesenchyme as a transition between the epithelial and stromal elements can occasionally be seen (Reagan 1950; Greene 1952; Woodruff and Acosta 1962).

(c) Teratomatous origin as the tumour was frequently associated with benign cystic teratomas (Jondahl *et al* 1950) or with struma ovarii (Klein *et al* 1968).

(d) Rete ovarii—a view expressed by Schiller (1934) and supported by Greene (1952) and Stoher (1956).

(e) Walthard rest—due to morphological resemblance between Walthard rests and epithelial cell nests of Brenner (Meyer 1932; Fox 1942).

(f) Ovarian surface epithelium (mesothelium)—the tumour is generally associated with mucinous or serous cysto-

mas (Arey 1961; Ehrlich and Roth 1971; Silverberg 1971; Fox *et al* 1972).

(g) Uroepithelial metaplasia (Sternberg 1963; Battifora *et al* 1964; Langley *et al* 1972; Cummins *et al* 1973).

Last view is now commonly accepted as there is a marked ultrastructural resemblance between uroepithelial cells and those found in the epithelial islands of Brenner tumour. The mucous secreting cells in the Brenner tumour do not resemble those of either endocervical or enteric epithelium and appear to be uroepithelial cells that have adopted a secretory function (Langley *et al* 1972; Cummins *et al* 1973). The cortical Brenner tumours are derived from the surface epithelium of the ovary by uroepithelial metaplasia.

Associated Lesions with Brenner Tumour

Mucinous cystomas have commonly been reported to be associated with Brenner tumour (Mackinlay 1958; Freda and Montimurro 1959; Ramachandaran *et al* 1972; Talib *et al* 1974). Woodruff and Acosta (1961) have observed coexistence of Brenner tumour in the same ovary with mucinous cystomas in 3 cases; serous cystomas in 2 cases and endometriosis in one in the same ovary and the coma in 2 cases and fibroma in one in the opposite ovary. Klein *et al* (1968) have reported a case where Brenner tumour was associated with struma ovarii. Balasa *et al* (1977) on reviewing seven big series of Brenner tumour have reported that out of 302 Brenner tumours there were 101 (33%) other concurrent histologic types of ovarian neoplasms (62 cystomas, 17 teratomas, 13 carcinomas and 9 fibromas thecoma). In the present series in one case there was a serous cystadenocarcinoma of ovary and the Brenner tumour was an incidental finding in the contralateral ovary.

Endocrine Effect

Brenner tumour is generally regarded as an inert tumour, having no hormonal influence, however, there are case reports where this tumour is associated with oestrogenic effect as evident by associated hyperplasia or even adenocarcinoma of endometrium Te linde 1930; Schiffman 1932; Biggart and Macafee 1955; Eton and Parker 1958; Shay and Janovaski 1963). Farrar *et al* (1960) reviewed the world literature and narrated that out of 402 cases an oestrogenic effect was seen in 7.5% cases.

In one of case under review the patient had postmenopausal bleeding for the last six months but it is very difficult to relate this bleeding with the tumour as such bleeding can occur even in the absence of any tumour. Woodruff and Acosta (1961) have reported that 40% of their cases (Out of 90) had postmenopausal bleeding.

Ullery *et al* (1963) on the other hand have reported a Brenner tumour associated with a testosterone synthesis. Hameed (1972) has documented the occurance of Leydig cell hyperplasia in a Brenner tumour.

Extraovarian Brenner Tumour

This is extremely rare. So far two cases have been reported in females, one in the broad ligament (Robinson 1950) and the other in the uterus (Arhelger and Bocian 1976). Three paratesticular lesions have been observed in man (Vechinski *et al* 1965; Ross 1968; Goldman 1970).

Summary

Two cases of Brenner tumour of the ovary are presented, giving the incidence as 1.54% (2/130 tumours). One of the case was a proliferating type associated with post menopausal bleeding.

The other was a small cortical Brenner tumour diagnosed incidentally on surgery done for papillary cystadenocarcinoma of the contralateral ovary. The salient features of the cases have been discussed in the light of brief review of literature.

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See Figs. on Art Paper IV