Ovarian reported to arise from the epithelium of

Ovarian Cancer Of all gynecologic malignancies, ovarian cancer continues to have the highest mortality and is the most difficult to diagnose. In the United States female population, ovarian cancer ranks fifth in absolute mortality among cancer related deaths (13, 000/yr). In most reported cases, ovarian cancer, when first diagnosed is in stages III or IV in about 60 to 70% of patients which further complicates treatment of the disease (Barber, 3). Early detection in ovarian cancer is hampered by the lack of appropriate tumor markers and clinically, most patients fail to develop significant symptoms until they reach advanced stage disease. The characteristics of ovarian cancer have been studied in primary tumors and in established ovarian tumor cell lines which provide a reproducible source of tumor material. Among the major clinical problems of ovarian cancer, malignant progression, rapid emergence of drug resistance, and associated cross-resistance remain unresolved. Ovarian cancer has a high frequency of metastasis yet generally remains localized within the peritoneal cavity. Tumor development has been associated with aberrant, dysfunctional expression and/or mutation of various genes.

This can include oncogene overexpression, amplification or mutation, aberrant tumor suppressor expression or mutation. Also, subversion of host antitumor immune responses may play a role in the pathogenesis of cancer (Sharp, 77). Ovarian clear cell adenocarcinoma was first described by Peham in 1899 as “ hypernephroma of the ovary” because of its resemblance to renal cell carcinoma. By 1939, Schiller noted a histologic similarity to mesonephric tubules and classified these tumors as “ mesonephromas.” In 1944, Saphir and Lackner described two cases of “ hypernephroid carcinoma

of the ovary” and proposed “ clear cell” adenocarcinoma as an alternative term. Clear cell tumors of the ovary are now generally considered to be of mullerian and in the genital tract of mullerian origin. A number of examples of clear cell adenocarcinoma have been reported to arise from the epithelium of an endometriotic cyst (Yoonessi, 289).

Occasionally, a renal cell carcinoma metastasizes to the ovary and may be confused with a primary clear cell adenocarcinoma. Ovarian clear cell adenocarcinoma (OCCA) has been recognized as a distinct histologic entity in the World Health Organization (WHO) classification of ovarian tumors since 1973 and is the most lethal ovarian neoplasm with an overall five year survival of only 34% (Kennedy, 342). Clear cell adenocarcinoma, like most ovarian cancers, originates from the ovarian epithelium which is a single layer of cells found on the surface of the ovary.

Patients with ovarian clear cell adenocarcinoma are typically above the age of 30 with a median of 54 which is similar to that of ovarian epithelial cancer in general. OCCA represents approximately 6% of ovarian cancers and bilateral ovarian involvement occurs in less that 50% of patients even in advanced cases. The association of OCCA and endometriosis is well documented (De La Cuesta, 243). This was confirmed by Kennedy et al who encountered histologic or intraoperative evidence of endometriosis in 45% of their study patients. Transformation from endometriosis to clear cell adenocarcinoma has been previously demonstrated in sporadic cases but was not observed by Kennedy et al. Hypercalcemia occurs in a significant percentage of patients with OCCA. Patients with advanced disease are more typically affected than patients with nonmetastatic disease.

Patients with OCCA are also more likely to have Stage I disease than are patients with ovarian epithelial cancer in general (Kennedy, 348). Histologic grade has been useful as an initial prognostic determinant in some studies of epithelial cancers of the ovary. The grading of ovarian clear cell adenocarcinoma has been problematic and is complicated by the multiplicity of histologic patterns found in the same tumor. Similar problems have been found in attempted grading of clear cell adenocarcinoma of the endometrium (Disaia, 176). Despite these problems, tumor grading has been attempted but has failed to demonstrate prognostic significance. However, collected data suggest that low mitotic activity and a predominance of clear cells may be favorable histologic features (Piver, 136). Risk factors for OCCA and ovarian cancer in general are much less clear than for other genital tumors with general agreement on two risk factors: nulliparity and family history. There is a higher frequency of carcinoma in unmarried women and in married women with low parity.

Gonadal dysgenesis in