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Primary Mucinous Adenocarcinoma of the Appendix: A Rare Entity in the Differential Diagnosis of Ovarian Cancer

J. Sehouli,[1] O. J. Kopetsch,[1] J. Ricke,[3] E. Buchmann,[1] D. Stengel,[1] H. Riess,[4] H. Weidemann,[2] F. Schäper,[5] W. Freiesleben,[5] and W. Lichtenegger[1]

1) *Department of Gynecology, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Berlin, Germany*
2) *Department of Surgery, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Berlin, Germany*
3) *Department of Radiology, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Berlin, Germany*
4) *Department of Oncology and Hematology, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Berlin, Germany*
5) *Institute of Pathology, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Berlin, Germany*

Abstract

We report a 58-year-old female patient with the suspected diagnosis of ovarian cancer. Upon surgical exploration, examination of the appendix revealed the histological diagnosis of primary mucinous adenocarcinoma. This is an unusual consideration in the differential diagnosis of the ovarian cancer. We discuss the diagnosis, classification and treatment of the cancer of the appendix in relation to ovarian cancer.

Key words: primary adenocarcinoma of the appendix, ovarian carcinoma, differential diagnosis

Case Report

A 58-year-old woman suffered mild abdominal pain in the right lower for approximately 2 days. The physical examinations performed by gynecologist, internist and surgeon showed no abnormality.

After a 3 months symptom-free interval she presented for reevaluation. The abdominal examination revealed a palpable, $3 \times 4 \times 4$ cm tumor in the right lower quadrant. On pelvic examination there was a solid, tender and fixed pelvic mass extending the right pelvic wall. Transvaginal sonography suggested a 3.5×4 cm large tumor of the right ovary, no significant abnormality of the left ovary, and small amount of ascitic fluid. Uterine myomatosus was also diagnosed. The MRI scan disclosed a pelvic cystic tumor with a swollen wall and tumor manifestations on the liver surface and in the omentum (Figs. 1a, b and 2a, b). CA-125 concentration was 121 U/m*l* (normal range: < 35 U/m*l*), the C-reactive protein showed a level of 1.5 mg/d*l* (normal range: < 0.6 mg/d*l*). The patient was admitted

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Reprint request to: Dr. J. Sehouli, Department of Gynecology, Charité/Campus Virchow-Klinikum, Medical Faculty of Humboldt-University Berlin, Augustenburger Platz 1, 13553 Berlin, Germany

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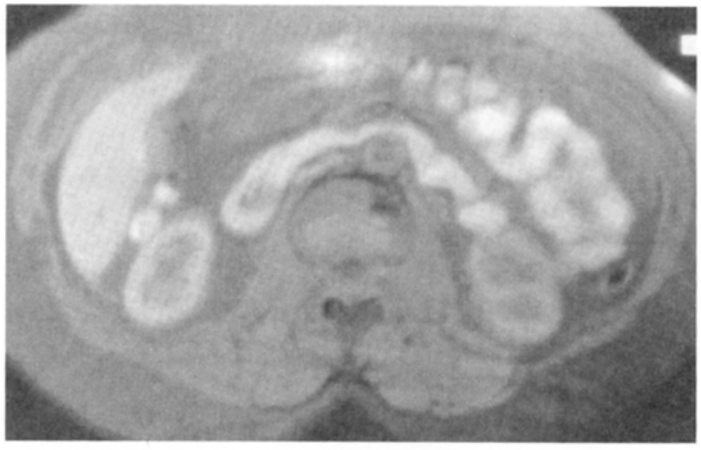

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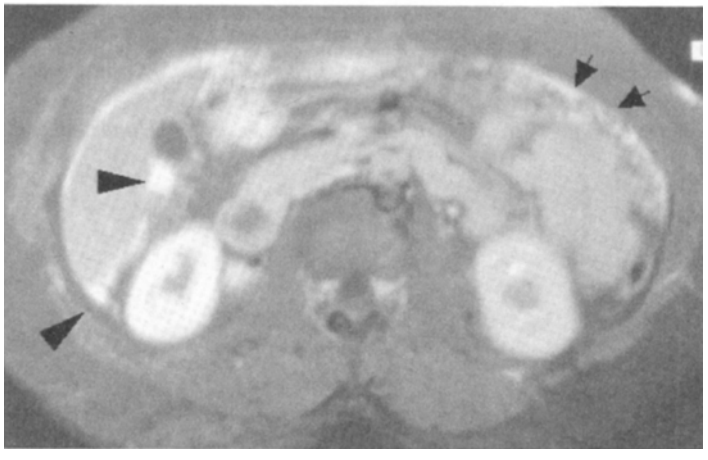

Fig. 1a, b. Fat saturated T1-w SE sequences before (a) and after (b) i.v. administration of 0.1 mmol GdDTPA. Note the contrast enhancement of tumor manifestations on the liver surface (arrow heads) and in the omentum (arrows). A small rim of ascites around the liver is also present.

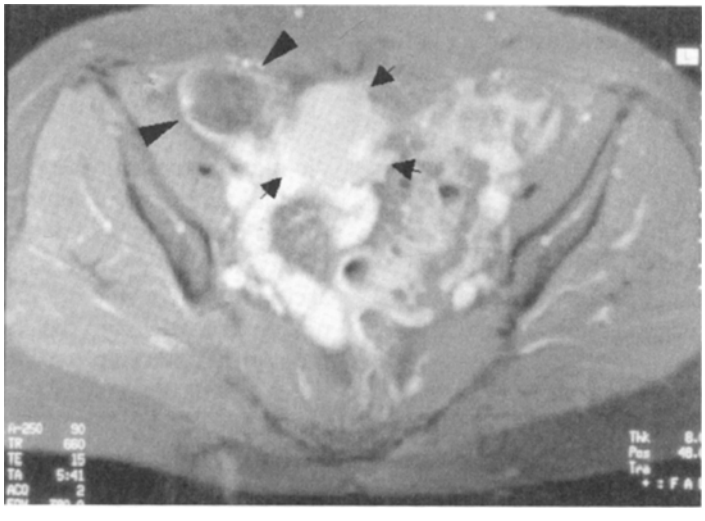

Fig. 2a. Fat saturated T1-w SE sequences postcontrast showing a cystic tumor (arrow heads) neighboring the right adnexe and the uterus (arrows).

with suspected ovarian cancer with metastasis in peritoneum and omentum majus. A median laparotomy was carried out: the omentum showed total cancerous transformation. Intraoperative ascites was found. The appendix was swollen and enlarged (Fig. 3). Both ovaries were covered with numerous small nodules. The peritoneal carcinomatosis was extensive (diaphragm, liver, bursa omentalis, abdominal wall, bladder and intestine). Following the dissection of the uterus and ovary, the appendix was removed by using a GiA-dissector.

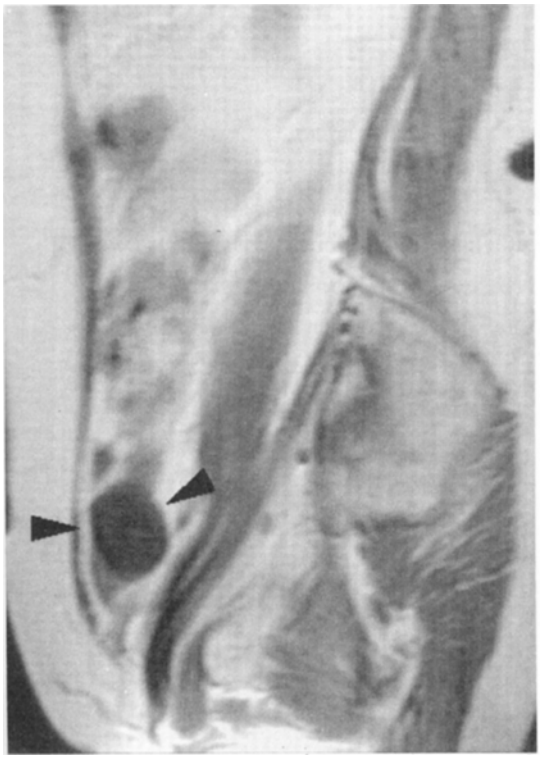

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Fig. 2b. T1 weighted postcontrast in sagital sequence showing a cystic tumor (arrow head) neighboring the caecum.

The appendix was 8 cm long and up to 3 cm in diameter. The apex was swollen, there were glassy mucinous masses intraluminal, intramural and serosal. Rapid section diagnosis was "infiltration of serosa and subserosa by a mucinous tumor, dignity uncertain". Pseudomyxoma peritonei due to mucinous cystadenoma or cystadenocarcinoma of the ovary or a mucinous adenocarcinoma of the appendix were considered to be the primary process. Careful examination of the paraffin-embedded tissue showed papillary hyperplasia and dysplasia of the appendix mucosa (Fig. 4), furthermore invasive tumor growth in all layers of the appendix wall, beginning in the mucosal layers with spread to subserosa and serosa. The serosa was perforated here and there, there were mucinous tumor masses on the serosa of the appendix (Fig. 5). The same thing applied for the resected parts of the omentum (Fig. 6). The ovaries showed mucinous tumor masses on the visceral peritoneum, too (Fig. 7). A genuine ovarian tumor could not be identified.

In addition to the omentectomy an infrared contact coagulation of the affected visceral and parietal peritoneum was performed. Postoperatively the patient recovered well and was discharged after 12 days. The final histological staging was pT4 Nx M1, G2. Because of the normalizing tumor markers (CA-125) and lack of symptoms the decision to closely observe the patient without treatment was made. Thereafter, every 3 to 4 weeks, monitoring of the laboratory

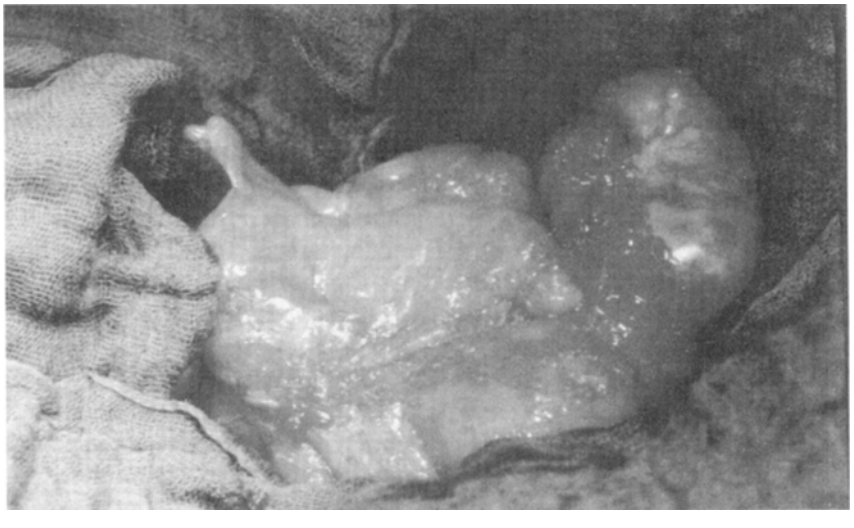

Fig. 3. Intraoperative finding of the appendix enlarged by tumor.

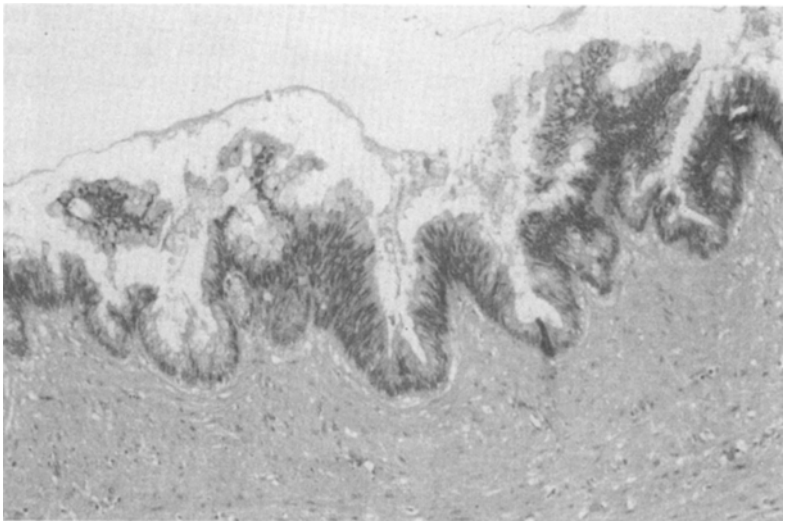

Fig. 4. The mucosa of the appendix shows papillary epithelial proliferations and dysplasia (× 65, HE).

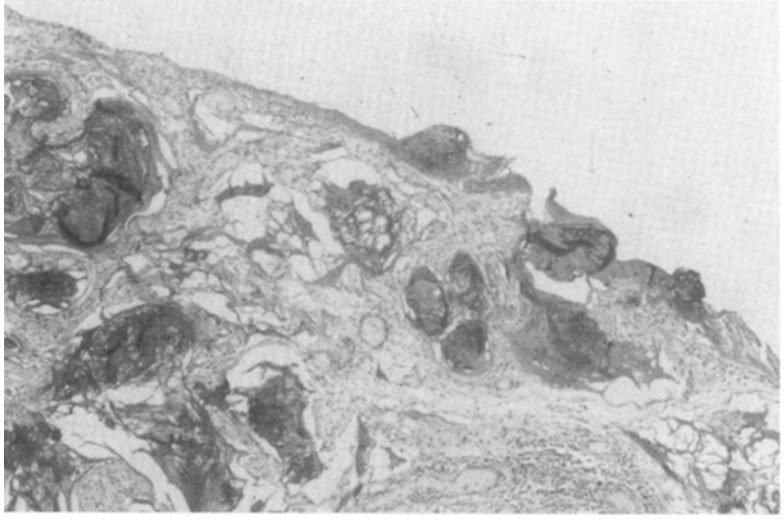

Fig. 5. Cystic and mucinous tumor with serosal perforation, appendix (× 16, PAS).

parameters were performed, as well as a sonography in the event of tumor marker concentration elevation or symptoms of recurrence. The postoperative course was uneventful. The patient is still without complaint or evidence of recurrence 10 months after surgery.

Discussion

Primary adenocarcinoma of the appendix is a rare tumor, which is usually diagnosed histopathologicaly following supposed appendicitis.[1-5] Nevertheless, in 6 to 15% of patients, a mass in the right lower quadrant or acute intestinal obstruction may be the initial clinical presentation.[6,7] The incidence is about 0.2–0.5% of all malignant G1-tumors.[7] Collins reported an incidence of 0.08% in 50,000 cases of appendectomies.[8] The coincidental presence of an ovarian cancer with primary adenocarcinoma of the appendix has been previously described.[9-11]

As the standard of classification Uihlein and McDonald[12] differentiate 3 pathological types of the primary malignoma of the appendix:

1. carcinoid types (90%, accounting for the largest group of all primary tumors of the appendix[13]
2. cystic type
3. adenocarcinomas of the colonic type.

The Duke's classification system for malignant G1-tumors is well-established as a valid prognostic factor of primary adenocarcinoma of the appendix.[2,14] Nineteen percent of patients with primary adenocarcinoma of the appendix are at

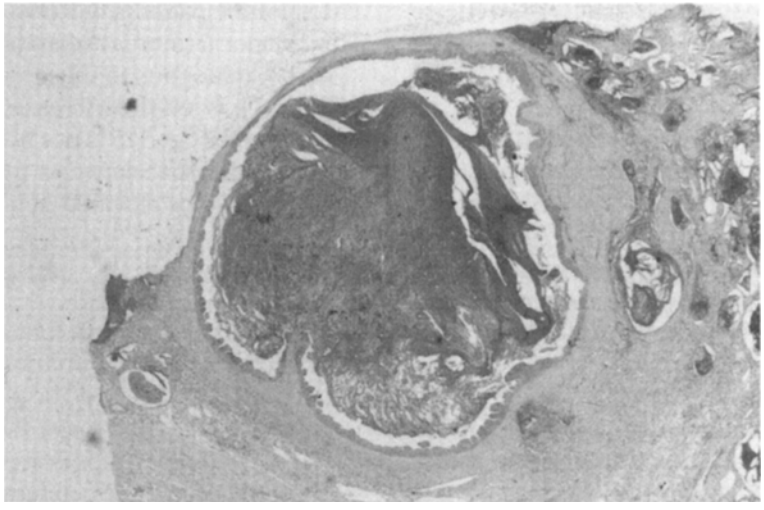

Fig. 6. Cystic and mucinous tumor in the omentum, lymphangiosis carcinomatosa (lower left corner) (× 16, PAS).

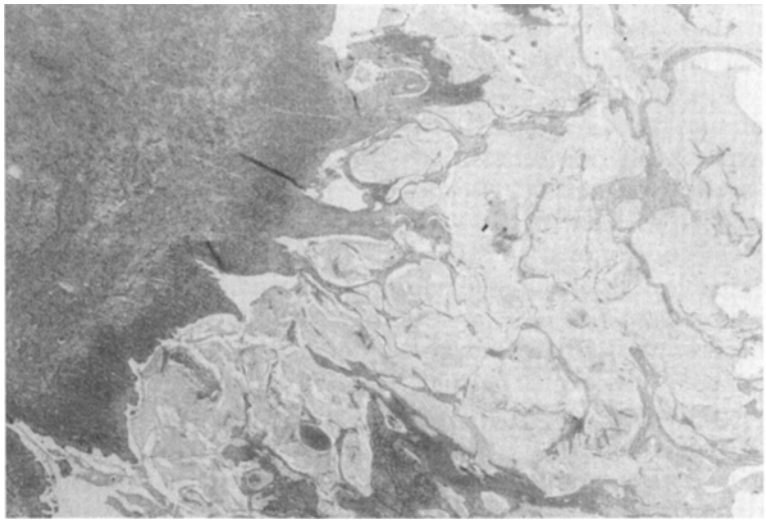

Fig. 7. Ovary (left) with regular stroma and mucinous tumor masses on the surface (× 16, HE).

stage B1 and 44% of all were at stage B2 of the Dukes' classification at the time of diagnosis.[2] The combined incidence for stages C and D is 31% in summary. It is important to consider the fact that nearly all appendical adenocarcinomas tumors were discovered at surgery for suspected appendicitis and thus that an intraoperative sampling of lymph nodes for the purpose of staging would not have been performed.

The primary therapy of adenocarcinoma of the appendix is surgical. Besides an appendectomy some authors recommend a right hemicolectomy,[1,2,14,15] normally performed a days after the appendectomy, because it is virtually impossible to diagnose an primary adenocarcinoma of the appendix pre- or intraoperatively.[1] However, other authors have found that even after right hemicolectomy, the prognosis is disappointing.[16,17] Survival is significantly correlated with the extent of tumor spread.[2] Only 11% presented in a terminal phase with wide-spread metastasis at the time of diagnosis.[1] In the current case, tumor involvement of the omentum and peritoneum was grossly evident. This extensive spread is very rare.[2]

In the described case, a hemicolectomy was not performed because of the advanced stage of the adenocarcinoma, no evidence of acute intestinal obstruction and the impaired physical condition of the patient resulting into a high postoperative risk of complications. An improvement in 5-year survival rate in patients treated by right hemi-

colectomy compared to the survival of those treated by appendectomy alone seems to be only significant in patients with low Dukes stages (B2 or C).[1,6,18]

There are only few data about appendix cancer and chemotherapy, which suggest a poor response-rate and overall survival in patients with advanced stages.[19] Sugarbaker *et al.*[20] report the most effective disease control to be feasible in patients after complete cytoreduction combined with intraperitoneal chemotherapy and no metastases.

Cancer of the ovaries carries an overall incidence of 4%,[21] although it remains one of the most common gynecological tumors.[22] In accordance to the FIGO classification[23] the staging is made surgically.[24] At time of diagnosis 75% of all patients are already in FIGO stage III or IV.[25]

Ninety percent of all malignancies of the ovary are epithelial carcinoma.[22] After surgical procedure (hysterectomy, adnectomy, appendectomy, omentectomy, pelvic and paraaortal lymphadenectomy), combination chemotherapy using paclitaxel with a platinum-based regimen is currently the standard first-line therapy for ovarian cancer and shows good results.[26,27] Diagnostic methods like ultrasonography, CT and MRI scan can be useful in the detection of ovarian cancer but they are often incapable of evaluating the full dimension of advanced disease.[27]

The definitive preoperative discrimination between ovarian and appendix cancer may be quite difficult[1] especially in the absence of experience with the radiologic detection of primary adenocarcinoma of the appendix. The symptoms of the appendix adenocarcinoma and those of the carcinoma of the ovaries may be indistinguishable. Most of the patients with the diagnosis of appendix adenocarcinoma are in the age group of 40–65 years,[1] analogous to those with ovarian cancer[28] (Table 1). Even the increase of the serologic tumor-marker CA-125 is not helpful in discriminating between ovarian and appendix cancer, because it may be elevated in both entities.[29]

Conclusions

1. Neither serologic tumor-markers (CA-125) nor radiological examinations (sonography, CT scan, MRI scan) are specific in the diagnosis of adenocarcinoma with regard the primary site.
2. Specific symptoms are absent in either advanced ovarian or appendecal carcinoma.
3. The distinguishing of ovarian cancer and adenocarcinoma of the appendix is unclear in most cases and will ultimately be determined operatively.
4. A certain preoperative diagnosis of the primary adenocarcinoma of the appendix is not usually possible,[1] therefore close interdisciplinary postoperative management is necessary.
5. The early radiologic diagnosis of the cancer improves the chance of effective therapy and cure. Accordingly, the early usage of sonography or MRI scans or diagnostic laparoscopy might be indicated. Although there is no mention in the medical literature of a reliable method of preoperative radiological diagnosis of primary adenocarcinoma of the appendix, the MRI scan in our case-report was capable of detecting disseminated tumor.
6. Gynecologists, as well as surgeons, radiologists and gastroenterologists should consider carcinoma of the appendix in the differential di-

Table 1. *Differences between the primary adenocarcinoma of the appendix and the ovarian cancer*

	Appendix-Ca	Ovar-Ca
Symptoms	Acute appendicitis, pain, abscess[1,3,4]	Gastrointestinal symptoms, pain, disorders in menstrual cycle[30]
Incidence	0.2–0.5% of all malignant G1-tumors[10]	4% of all cancer-diagnoses[25]
Age-group with highest incidence	40–65 years[1]	40–65 years[23]
Staging	Dukes (Surgical/Pathological)	FIGO (Surgical/Pathological)
Classification at time of diagnosis	Dukes B_1 and B_2: 62.5%[31]	FIGO III and IV: 70%[25]
Surgical therapy	Appendectomy and right-sided hemicolectomy[1,31,18]	Hysterectomy, Adnectomy, Appendectomy, Omentectomy, pelvic and paraaortal lymphadenectomy[27]
Chemotherapy	—	Paclitaxel + Platinum-based chemotherapy[32]

agnosis of a right adnexal mass in the patient without previous appendectomy.

References

1. Hesketh KT. The managment of the primary adenocarcinoma of the vermiform appendix. *GUT* 1963; 4: 158–168
2. Lenriot J, Huguier M. Adenocarcinoma of the appendix. *Am J Surg* 1988; 155: 470–475
3. Lesnick G, Miller D. Adenocarcinoma of the appendix. *Cancer* 1949; 2: 18
4. Niceberg DM, Feldman S, Mandelberg A. Adenocarcinoma of the vermiform appendix: A case presentation and review of literature. *Surgery* 1956; 40: 560
5. Yamada T, Murao Y, Nakamura T, Tabuse H, Miyamoto S, Imai S, Nakano H. Primary adenocarcinoma of appendix, colonic type associated with perforating peritonitis in an elderly patient. *J Gastroenterol* 1997; 32: 658–662
6. Hopkins GB, Tullis RH, Kristensen KAB. Primary adenocarcinoma of the vermiform appendix: Report of seven cases and review of the literature. *Dis Colon Rectum* 1973; 16: 140–144
7. Steinberg M, Cohn I. Primary adenocarcinoma of the appendix. *Surgery* 1967; 61: 644–660
8. Collins DC. A study of 50,000 specimens of the human vermiform appendix. *Surg Gynec Obstet* 1955; 101: 437–445
9. Campbell JS, Lou P, Ferguson JP, Krongold I, Kemeny T, Mitton DM, Allan N. Pseudomyxoma peritonei et ovarii with occult neoplasms of the appendix. *Obstet Gynecol* 1973; 42: 897–902
10. McKenna H, Ritchie G, Monks P. Pseudomyxoma peritonei et ovarii with an occult neoplasm of appendix: Case report. *Pathology* 1978; 10: 157–160
11. Shanks HGI. Pseudomyxoma peritonei. *J Obstet Gynaecol Br Commonw* 1961; 68: 212–224
12. Uihlein A, McDonald JR. Primary carcinoma of the appendix resembling carcinoma of the colon. *Surg Gynec Obstet* 1943; 76: 711–714
13. Sieracki JC, Tesluk H. Primary adenocarcinoma of the vermiform appendix. *Cancer* 1956; 9: 997
14. Thaler W, Riedler L, Bacher G, Barbareschi G. Zum Appendixcarcinom. *Aktuel Chir* 1986; 21: 246–248
15. Proulx GM, Willett CG, Daley W, Shellito PC. Appendiceal carcinoma: Patterns of failure following surgery and implications for adjuvant therapy. *J Surg Oncol* 1997; 66: 51–53
16. Gamble RA. Adenocarcinoma of the appendix: An unusual case and review. *Dis Colon Rectum* 1976; 19: 621–625
17. Gilhorne RW, Johnston DH, Clark J, Kyle J. Primary adenocarcinoma of the vermiform appendix: A report of a series of ten cases and review of the literature. *Br J Surg* 1984; 71: 553–555
18. Andersson A, Bergdahl L, Boquist L. Primary carcinoma of the appendix. *Ann Surg* 1976; 24: 176–180
19. Goldthorn JF, Powars D, Hays DM. Adenocarcinoma of the colon and rectum in the adolescent. *Surgery* 1983; 93: 409–414
20. Sugarbaker PH. Intraperitoneal chemotherapy and cytoreductive surgery for the prevention and treatment of peritoneal carcinomatosis and sarcomatosis. *Semin Surg Oncol* 1998; 14: 254–261
21. Yanick R. Ovarian cancer: Age contrasts in incidence, histology, disease stage at diagnosis, and mortality. *Cancer* 1993; 71: 517
22. Parker SL, Tong T, Bolden S, Wingo PA. Cancer statistics. *Cancer* 1996; 46: 5
23. Schwartz PE. Surgical management of ovarian cancer. *Arch Surg* 1981; 116: 99
24. Ozols RF, Schwartz PE, Eifel PJ. Ovarian cancer, Fallopian tube carcinoma, and peritoneal carcinoma. In: DeVita VT, Hellman S Rosenberg SA, eds. Cancer: Principles and Practice of Oncology. Philadelphia: 1997 5(5), 1506
25. Annual report on the results of treatment in gynecological cancer. Pettersson, F. International Federation of Gynecology and Obstetrics. Stockholm: Panorama Press, 1991 AB. 21
26. Judson PL, Watson JM, Gehrig PA, Fowler WC Jr, Haskill JS. Cisplatin inhibits paclitaxel-induced apoptosis in cisplatin-resistant ovarian cancer cell lines: Possible explanation for failure of combination therapy. *Cancer Res* 1999; 59: 2425–2432
27. Lichtenegger W, Sehouli J Buchmann E, Karajanev C, Weidemann H. Operative results after primary and secondary debulking-operations in advanced ovarian cancer (AOC). *J Obstet Gynaecol Res* 1998; 24: 447–451
28. Yanick R, Ries LG, Yates JW. Ovarian cancer in the elderly: An analysis of surveillance, epidemiology and end results program data. *Am J Obstet Gynecol* 1986; 154: 639
29. Shimizu T, Shimizu M, Kawaguchi K, Yomura W, Ihara Y, Matsumoto T. Mucinous cystadenoma of the appendix with raised serum carcinoembryonic antigen concentration: Clinical and pathological features. *J Clin Pathol* 1997; 50: 613–614
30. Igoe BA. Symptoms attributed to ovarian cancer by women with the disease. *Nurse Pract* 1997; 22: 127–128
31. Jamieson JK, Dobson JF. The lymphatic system of the caecum and appendix. *Lancert* 1907; 1: 1137
32. Travis LB, Holowaty EJ, Bergfeldt K, *et al.* Risk of leukemia after platinum-based chemotherapy for ovarian cancer. *N Engl J Med* 1999; 340: 351–357