

Letter to the Editor

Hormone Receptors in Gastric Cancer

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RECENTLY, papers reporting the presence of hormone receptors for estrogen, progesterone and androgen in some tumors which have been thought to be non-target organs have been published by McClendon *et al.* [1], Ranelletti *et al.* [2] and Greenway *et al.* [3]. Thus there is a possibility that the hormone receptors may be detected more widely than was previously thought in tumors derived from the non-endocrine system and these tumors may also be hormone-dependent, as in breast cancer.

In this study the presence of receptors for estrogen and progesterone in gastric cancer is reported and the possibility of hormone dependency in gastric cancer is briefly discussed.

Resected stomach from 10 patients with primary gastric cancer was used for this study. Specimens of gastric cancer were obtained immediately after gastrectomy, were washed by cold saline to remove blood, and stored at -70°C until the time of assay. Frozen tissues were homogenized in 5 mM of phosphate buffer (pH 7.5) containing 0.5 mM of dithiothreitol and 10% glycerol with Spex homogenizer (Spex Ind., CA, U.S.A.) in liquid nitrogen and then centrifuged at 105,000 g for 90 min. The supernatant fraction was used for the assay. Receptor assay for estrogen and progesterone was performed by the methods of McGuire *et al.* [4, 5] with [³H]estradiol and [³H]-R5020 using dextran-coated charcoal. The data were analyzed by a

Scatchard plot and the receptor contents were expressed as fmol of estradiol and R5020 bound per mg cytosol protein.

Scatchard analysis of receptors for estradiol and R5020 in cytosol of gastric cancer are shown in Fig. 1(a, b). The distribution of receptors for estradiol and R5020 in gastric cancer is shown in Table 1. Two cases of gastric cancer had positive levels of binding activity. The highest level of binding activity for estradiol was 200 fmol/mg protein, this level corresponding to the value found in breast cancer [4, 5]. In the two positive

Table 1. Receptor contents for estradiol and R5020 in gastric cancers

Case No.	Age	Sex	Receptors		Histological findings
			Estradiol (fmol/mg protein)*	R 5020 (fmol/mg protein)**	
1	69	M	negative	negative	Moderately Differentiated
2	60	M	negative	negative	Moderately Differentiated
3	52	F	40	6	Undifferentiated
4	60	M	negative	negative	Well Differentiated
5	50	F	200	22	Undifferentiated
6	66	F	negative	negative	Mucinous
7	65	M	negative	negative	Moderately Differentiated
8	74	F	negative	border line (5)	Poorly Differentiated
9	53	M	negative	negative	Moderately Differentiated
10	48	M	negative	negative	Moderately Differentiated

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*Positive level of binding activity is over 3 fmol/mg protein.

**Positive level of binding activity is over 5 fmol/mg protein.

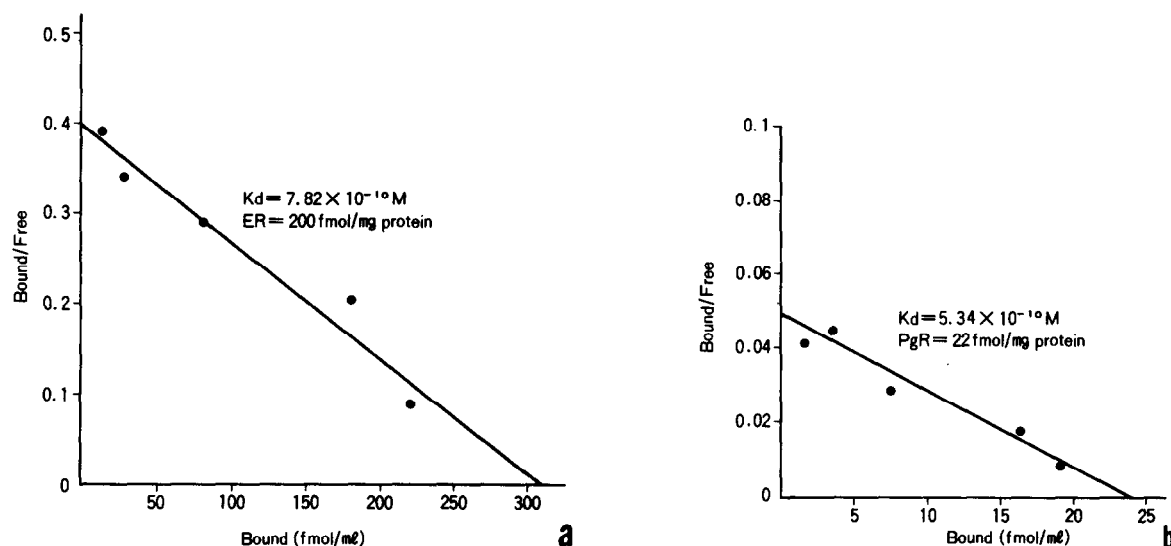


Fig. 1. (a) Scatchard plot of receptor for $[^3\text{H}]$ -estradiol in gastric cancer (case 5). Aliquots of cytosol (1.56 mg protein/ml) were incubated with $0.05\text{--}2.8 \times 10^{-9} \text{ M}$ of $[^3\text{H}]$ -estradiol alone or in the presence of a 200-fold excess of non-radioactive estradiol. Specific binding was assayed by dextran-coated charcoal. Non-specific binding has been subtracted. ER: contents of estrogen receptor; (b) Scatchard plot of receptor for $[^3\text{H}]$ -R5020 in gastric cancer (case 5). Aliquots of cytosol (1.09 mg protein/ml) were incubated with $0.04\text{--}2.2 \times 10^{-9} \text{ M}$ of $[^3\text{H}]$ -R5020 alone or in the presence of a 200-fold excess of non-radioactive R5020. Non-specific binding has been subtracted. PgR: contents of progesterone receptor.

cases the dissociation constant (K_d) was $1.5 \times 10^{-10} \text{ M}$ and $7.8 \times 10^{-10} \text{ M}$ for estradiol and $0.41 \times 10^{-10} \text{ M}$ and $5.34 \times 10^{-10} \text{ M}$ for R5020 respectively. The K_d s for estradiol in the two positive cases showed a high affinity with those found in breast cancer. Histological findings of two cases showed undifferentiated carcinoma of the stomach [Fig. 2(a, b)]. Physical and laboratory examinations revealed no other cancer, including the endocrine system-derived tumors in the two positive cases. All of the stomach cancers employed in this study were primary and not metastatic cases.

In this study the presence of receptors for estrogen and progesterone in some gastric cancers

was confirmed. It is noteworthy that the two positive cases were undifferentiated carcinoma, which is not a common type of gastric cancer like differentiated adenocarcinoma. Results suggested that some gastric cancers may have been influenced by hormonal factors, although it is still open to question whether these tumors are hormone-dependent. No reports about hormonal treatment for gastric cancer are available, and for future gastric cancer treatments it would be expected to employ chemo-endocrine therapy using an anti-estrogen in addition to conventional therapy.

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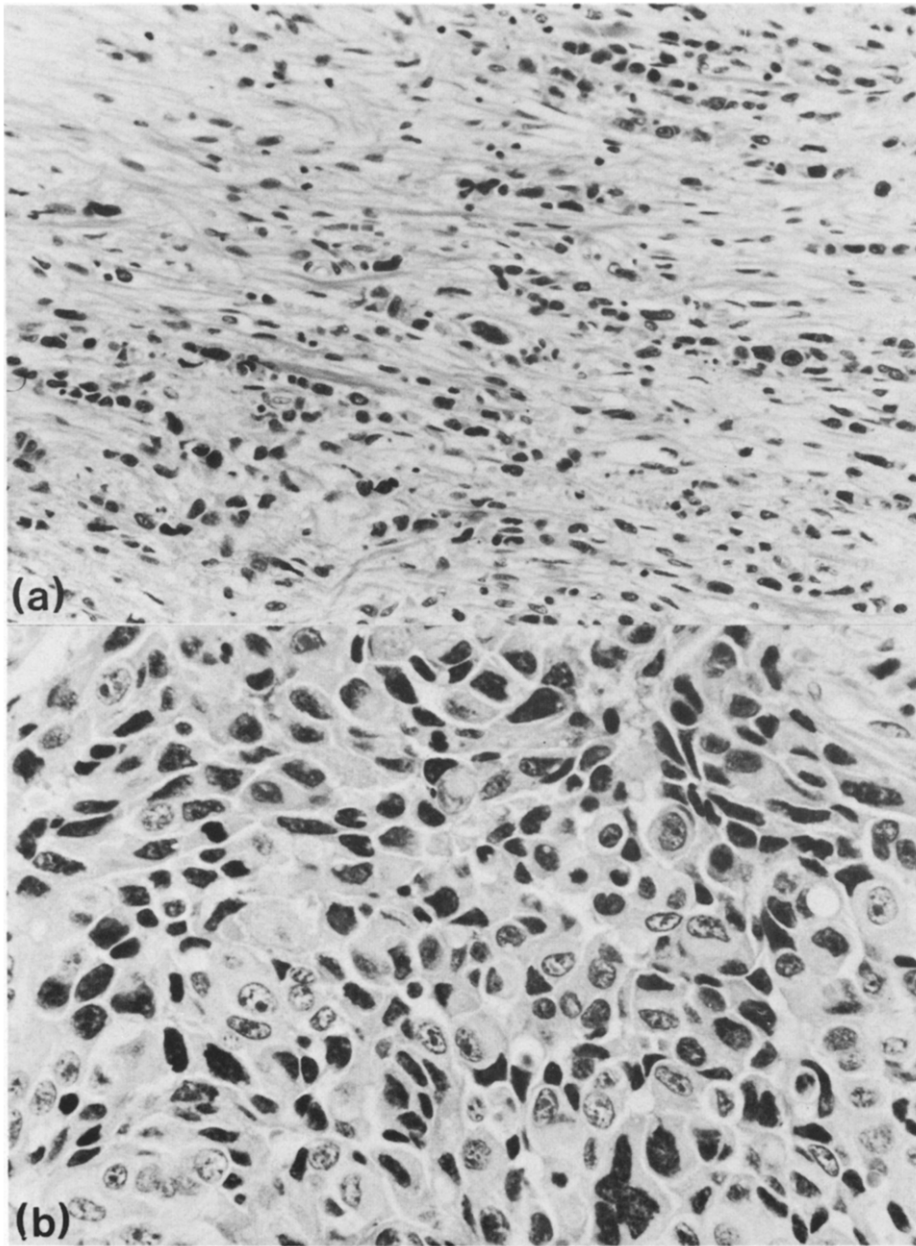


Fig. 2. (a) Histological findings of undifferentiated carcinoma of the stomach (case 5), with tumor cells infiltrating the muscularis propria ($\times 100$); (b) metastatic lymph node of the undifferentiated carcinoma shown in (a) ($\times 200$).