

INDIVIDUAL STUDY

The presence of caeruloplasmin in cancer of the breast and female genital organs

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THE problem of early diagnosis of malignancy is one of the main preoccupations of the medical practitioner. The awareness of this problem stimulates his sense of observation with a view to detecting any factor which may help.

On 13 October, 1969 I was called to see a woman with shingles. On examination it was found that the herpes zoster was localised at the site of the breast amputated for carcinoma. A sample of blood was taken for virological examination. One hour later it was noticed that the blood sample had changed to a green colour. A further sample taken the following day from the same patient showed the same change.

An x-ray of the chest taken a few days later revealed disseminated metastases in both lungs.

Historical background

Caeruloplasmin, the blue copper-containing protein or serum was first isolated in 1948 by Holmberg and Laurel. They characterized this protein as an alpha 2 globulin with a copper content with approximately 0.32 per cent; a molecular weight of about 151,000 and eight atoms of copper molecule. Thompson and Watson (1949) demonstrated the increase of caeruloplasmin in the last trimester of pregnancy. Von Studnitz and Berezin in 1958 suggested that this elevation of caeruloplasmin is due to the action of endogenous oestrogen.

In 1956, Ella M. Russ and Julie Raymond showed that the administration of oestrogen, as ethinyloestradiol in doses from 0.25 mg to 1 mg caused the increase of caeruloplasmin. In 1963 Swinburne *et al.* observed the presence of caeruloplasmin in rheumatoid arthritis. H. Probst *et al.* (1969) reported the presence of haptoglobin in carcinoma of the gastro-intestinal tract. They estimated the contents of haptoglobin and iron and copper in the serum, suggesting that this evaluation could be used in the diagnosis of malignancy.

Method

Owing to the difficulty in separating the caeruloplasmin which needed special equipment and the help of expert biologists, it was decided initially to demonstrate the presence of the green plasma in blood samples by observations and by taking colour photographs of the samples every five minutes during the first two hours from (09.00–11.00 hours) and then at half-hourly intervals during the day up to 18.00 hours. This was repeated the following day at half-hourly intervals.

Different groups of patients were organised for comparison as follows: six patients with normal pregnancies, six patients taking an oral contraceptive, six patients who had stopped taking an oral contraceptive, six 'control' patients of unmarried nulliparas, one pre-menopausal patient, one post-menopausal patient, six patients with carcinoma of breast, six patients with carcinoma of the cervix, three patients with carcinoma of the vulva and ten patients with other varieties of carcinoma.

Blood samples were collected in 10 ml. non-citrated plastic tubes and disposable

syringes were used. All patients in each group were asked to attend the photographic studio at the same time to avoid delay between collection of blood and photographing.

Results

All ages given in the following tables are those at the time of the blood tests between October 1969 and June 1970.

TABLE I
PATIENTS WITH NORMAL PREGNANCIES

<i>Patient number</i>	<i>Age</i>	<i>Duration of pregnancy</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	24	8 months	Yes	intense
2	23	8 months	Yes	intense
3	25	8 months	Yes	intense
4	20	8 months	Yes	intense
5	21	4 months	No	not observed
6	26	2½ months	No	not observed

TABLE II
PATIENTS TAKING AN ORAL CONTRACEPTIVE

<i>Patient number</i>	<i>Age</i>	<i>When began pill</i>	<i>Type of pill</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	35	May 1969	'Lyndiol'	Yes	intense
2	30	April 1969	'Lyndiol'	Yes	intense
3	21	June 1969	'Lyndiol'	Yes	intense
4	26	May 1969	'Lyndiol'	Yes	intense
5	45	October 1969	'Ovulen'	Yes	intense
6	29	April 1969	'Ovulen'	Yes	intense

TABLE III
PATIENTS WHO STOPPED AN ORAL CONTRACEPTIVE

<i>Patient number</i>	<i>Age</i>	<i>When started pill</i>	<i>When stopped pill</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	47	1966	1969	No	—
2	44	1969	1969	No	—
3	26	1969	1970	No	—
4	42	1966	1969	No	—
5	26	April 1969	Sept. 1969	No	—
6**	37	1969	1969	No	—

**Patient suffered from pulmonary embolism and symptoms of intracranial pressure, therefore 'pill' stopped

TABLE IV
CONTROL GROUP OF UNMARRIED NULLIPARAS

<i>Patient Number</i>	<i>Age</i>	<i>Presence of green plasma</i>
1	19	No
2	20	No
3	17	No
4	15	No
5	17	No
6	19	No

TABLE V
PRE- AND POST-MENOPAUSAL PATIENTS

<i>Patient number</i>	<i>Age</i>		<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	46	pre-menopausal	No	—
2*	50	post-menopausal	Yes	moderate

*See text below.

TABLE VI
PATIENTS WITH CARCINOMA OF BREAST

<i>Patient number</i>	<i>Age</i>	<i>Date of operation</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	57	1969	Yes	moderate
2	48	29.7.69	Yes	moderate
3	61	29.4.68	Yes	moderate
4	59	13.4.68	Yes	moderate
5	47	23.4.68	Yes	intense
6	73	8.12.61	Yes	intense

TABLE VII
PATIENTS WITH CARCINOMA OF CERVIX

<i>Patient number</i>	<i>Age</i>	<i>Date of operation</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	44	12.12.68	Yes	intense
2	58	15.11.68	Yes	faint
3	73	Radiotherapy	Yes	intense
4	48	24.4.67	Yes	moderate
5	48	1958	Yes	faint
6	48	1969	Yes	intense

TABLE VIII
PATIENTS WITH CARCINOMA OF VULVA

<i>Patient number</i>	<i>Age</i>	<i>Date of operation</i>	<i>Presence of green plasma</i>	<i>Intensity of colour</i>
1	74	1958	Yes	moderate
2	73	March 1960	Yes	moderate
3	63	1969	Yes	intense

The green plasma was absent in the control group of unmarried nulliparas, those who stopped oral contraceptives and those in the early stages of pregnancy. The green plasma was seen in pregnant women in the third trimester, carcinoma of the breast, cervix and vulva. The post-menopausal patient (see table V) showed the presence of caeruloplasmin in June, 1970. She had a mastectomy for carcinoma of the breast on 13 September, 1971.

TABLE IX
PATIENTS WITH OTHER CARCINOMATA

Patient number	Age	Date of operation	Diagnosis	Presence of green plasma	Intensity of colour
1	64	June 1960	nephroma	Yes	faint
2	63	1970 inoperable	carcinoma of stomach	Yes	faint
3	44	April 1968	carcinoma of colon	Yes	intense
4	66		carcinoma of prostate	Yes	moderate
5	76	1969	carcinoma of larynx	No	—
6	71	1969	lymphadenoma	No	—
7	70	1969	carcinoma of antrum	No	—
8	80	1963	carcinoma of bladder	Yes	faint
9	56	March 1970	carcinoma of bronchus	Yes	moderate
10	51		meningioma	No	—

Conclusion

The detection of caeruloplasmin at various stages of carcinoma of the breast and female genital organs, before and after the operation and during the follow up period could supply valuable information and also be useful in assessing the prognosis.

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EARLY DISCHARGE FROM HOSPITAL TO HOME

(a) A relatively large proportion of patients require help with household chores, (b) and with dressing, toiletry, bathing and washing, (c) contact between hospital and community is not always satisfactory, especially when more than 50 per cent of the patients in this survey came out of hospital without the knowledge of their family doctors.

Savage, S. M. (1972). Home from Hospital, *Proceedings of the Royal Society for the Promotion of Health*, April.