

COMBINED TRANSCATHETER ARTERIAL EMBOLIZATION AND REGIONAL CHEMOTHERAPY FOR LOCALLY ADVANCED CARCINOMA OF THE BREAST

A preliminary investigation

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Abstract

Seventeen patients with carcinoma of the breast received a combination of transcatheter arterial embolization and regional chemotherapy before surgery. A gelatin powder mixed with an anticancer agent and blood clotting factors (own technique) was selectively injected into the internal mammary artery, the lateral thoracic artery, and the thoracodorsal artery. Marked regression of both primary tumor and metastatic regional lymph nodes was observed. The potential of this method as presurgical treatment is discussed.

Locally advanced carcinoma of the breast has been shown to be poorly managed by surgery alone and to have a very high incidence of loco-regional recurrence. For this reason, different types of additional or alternative therapy have been used for this group (4).

While transcatheter arterial embolization has been used widely for various purposes during the past few years, we have applied this technique for locally advanced breast malignancy, with a new embolic material, as a presurgical treatment. The method is described in this report and also the early observations in a pilot series of patients.

Material and Methods

From October 1981 through July 1983, 17 patients were treated (Table).

A catheter was introduced through the femoral

artery or the axillary artery. A modified cerebral catheter (H 1 H, 6.5 F Cook) and a femoral internal mammary catheter (7 F Cordis) were introduced through the femoral artery, and a home-made J-shaped catheter through the axillary artery, respectively. The embolic material consisted of a new absorbable gelatin powder mixed with an anticancer agent (mitomycin-C or adriamycin) and blood clotting factors (factor XIII and thrombin). In the first two patients, this embolic material was used without an anticancer agent. The embolic material was dissolved in a solution of calcium chloride and a contrast medium (76% Urografin).

Following subclavian arteriography, selective catheterization into the internal mammary artery, the lateral thoracic artery and the thoracodorsal artery was performed. The embolic material was infused into each vessel under fluoroscopic control. The infusion was given slowly and gently in order to prevent backflow of the embolus. Surgery was performed 7 to 24 days (average 14 days) after embolization. All patients received adjuvant chemotherapy and hormonal therapy after surgery.

Results

The early observations are shown in the Table. Selective catheterization was successfully performed into the internal mammary artery, the lateral

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Table

Seventeen patients with locally advanced mammary carcinoma treated with intraarterial infusion and embolization

Case No.	Age (years)	Tumor size (cm)	Stage*	Embolized artery			Anticancer agent	Regression rate (per cent)	Histologic effect**		Complication	Recur-rence
				I.M.	L.T.	T.D.			Pri-mary	Lymph node		
1	54	6.4×5.5	III B		+	+	—	23	II B	II B	—	+
2	45	5.7×5.4	III B	+		+	—	87	II B	II A	L.P.	+
3	43	3.8×3.6	II	+			MMC 3 mg	43	II B	II A	S.D.	—
4	59	5.1×4.6	III A			+	ADM 10 mg	23	II B	—	L.P.	—
5	41	6.5×5.5	III B		+		MMC 4 mg	50	II A	II A	—	—
6	59	5.4×4.5	III A			+	MMC 4 mg	40	III	II B	—	—
7	59	3.8×3.2	II			+	ADM 20 mg	10	II B	I	—	—
8	50	5.0×3.5	III A	+		+	ADM 60 mg	100	III	—	S.D.	—
9	41	5.2×5.0	III A	+	+	+	ADM 180 mg	92	III	—	L.P. H.L. S.D.	—
10	32	14×13	III B	+	+	+	ADM 100 mg	48	III	IV A	H.L.	+
11	39	5.3×4.8	III A	+	+	+	ADM 100 mg	100	II A	II A	H.L.	—
12	64	3.4×2.6	III B	+		+	ADM 100 mg	100	II B	I	H.L.S.D.	—
13	43	4.5×4.0	III B			+	ADM 20 mg	10	II A	II B	—	—
14	50	5.5×4.5	III B			+	ADM 25 mg	27	II B	II B	—	—
15	43	5.7×5.0	III B	+	+	+	ADM 50 mg	56	II A	I	—	—
16	66	8.0×6.0	III B		+	+	ADM 100 mg	40	IV A	—	S.D.	—
17	45	6.0×5.6	III B	+	+	+	ADM 100 mg	100	II A	I	H.L. S.D.	—

* According to the criteria of UICC. ** According to the criteria of SHIMOSATO et coll. (8).

I.M.: Internal mammary artery. L.T.: Lateral thoracic artery. T.D.: Thoracodorsal artery. L.P.: Local pain. S.D.: Skin disorder. H.L.: Hair loss. ADM: Adriamycin. MMC: Mitomycin C.

thoracic artery, and the thoracodorsal artery in 9, 8 and 15 patients, respectively. In 5 patients all three vessels were catheterized. In all patients macroscopic regression of the primary tumors was observed. The size of the tumor was expressed as the maximum diameter × the corresponding perpendicular diameter. The regression rate was 10 per cent to 100 per cent (average 55.8%).

The histologic changes were evaluated according to criteria described by SHIMOSATO et coll. (8):

Grade I. Characteristic changes in tumor cells but tumor structures not destroyed (no defect in tumor nests resulting from lysis of individual tumor cells).

Grade II. In addition to characteristic cellular changes, tumor structures have been destroyed as a result of disappearance of tumor cells. Some viable cells still remain. a) Destruction of tumor structures of mild degree (viable tumor cells frequently observed). b) Destruction of tumor structures of severe degree (viable tumor cells few in number).

Grade III. Markedly altered, presumably non-viable tumor cells present singly or in small clusters and viable cells hardly seen.

Grade IV. No tumor cells remain in any sections (local cure). a) Extensive areas of coagulation ne-

crosis present. b) Granulation tissue with or without small foci of necrosis including keratotic debris remains. c) Only a cicatrix observed.

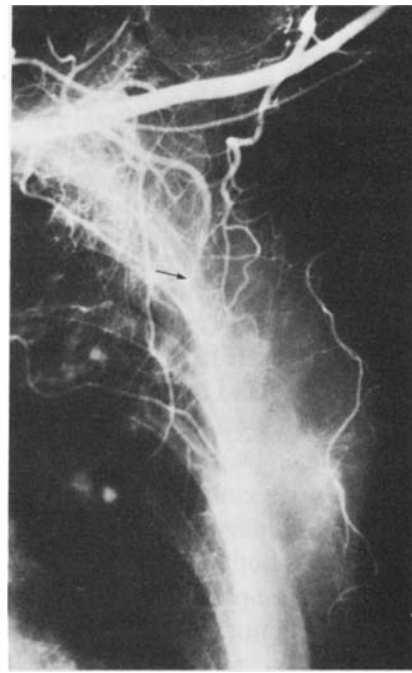
The primary tumors showed marked necrosis in all cases (grade II a, 5 patients; grade II b, 7 patients; grade III, 4 patients, grade IV a, 1 patient). Also metastatic regional lymph nodes showed necrotic changes (grade I, 4 patients; grade II a, 4 patients; grade II b, 4 patients; grade IV a, 1 patient). No lymph node metastases were observed in 4 patients.

The side effects were skin disorder such as redness or erosion (6 patients), local pain (3 patients), and hair loss (5 patients). Although necrotic changes in the chest wall, probably due to over-dosage of the anticancer agent, were observed in one patient (case 9), no complication interfering with surgery was observed. All patients underwent surgery successfully (radical mastectomy in 11 patients, extended radical mastectomy in 6 patients).

During a follow-up time of 2 to 23 months, pulmonary metastases were found in two patients (cases 2 and 10) and ipsilateral supraclavicular lymph node metastases in one patient (case 1). All patients were alive at the time of writing.



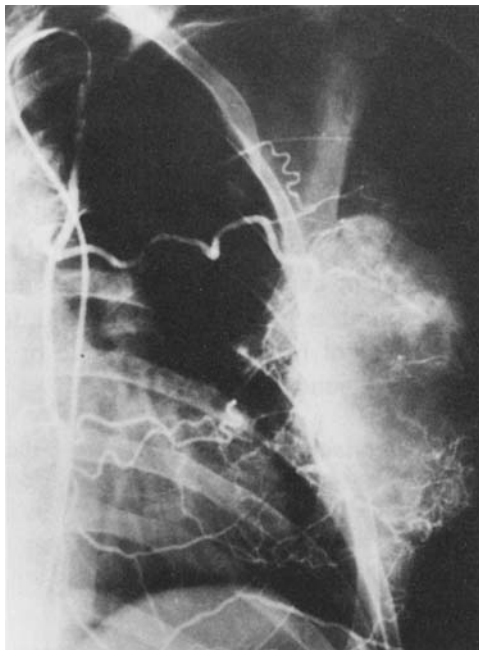
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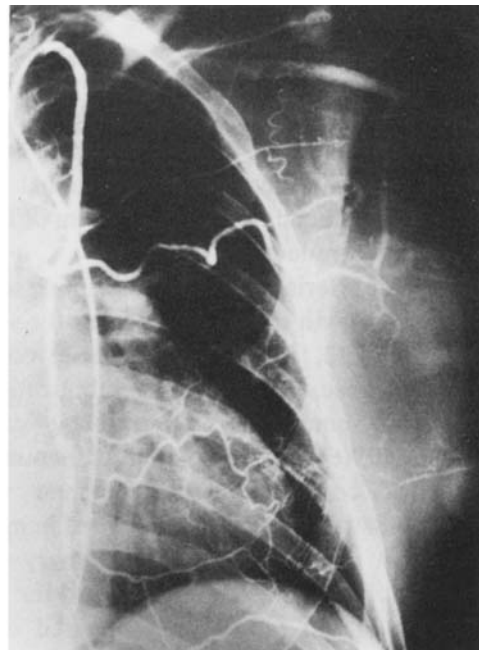
b

Fig. 1. Case 6. Selective thoracodorsal arteriography. a) Accumulation of contrast medium in axillary lymph node metastases

(→). b) Thoracodorsal artery obliterated (→) and no accumulation of contrast medium after transcatheter arterial embolization.



a



b

Fig. 2. Case 10. Selective internal mammary arteriography. a) Marked accumulation of contrast medium in the primary tumor.

b) No contrast accumulation in the tumor after transcatheter arterial embolization.

Case reports

Case 6. A 59-year-old female with a 5.4 cm×4.5 cm breast malignancy in the outer half of the left breast (T3N1BM0). Left thoracodorsal arteriography showed accumulation of contrast medium in

metastatic axillary lymph nodes (Fig. 1 a). The embolus-forming material with 4 mg mitomycin-C was injected into the thoracodorsal artery (Fig. 1 b). The two other vessels could not be catheterized selectively. Extended radical mastectomy was per-

formed after 7 days of transcatheter arterial embolization. The regression of the primary tumor was 40 per cent. Histologically, the primary tumor showed grade III and the metastatic regional lymph nodes grade II b, respectively. No complications occurred.

Case 10. A 32-year-old female noticed a rapidly growing tumor in the left breast during lactation. When admitted to this hospital, the tumor measured 14 cm×13 cm (T4BN2M0). Subclavian arteriography revealed accumulation of contrast medium in a large tumor, and tumor vessels in the left breast (Fig. 2 a). The embolus was injected into all three vessels with a total dose of 100 mg of adriamycin. An extended radical mastectomy was performed after 22 days of transcatheter arterial embolization (Fig. 2 b). The regression of the primary tumor was about 50 per cent. Histologically, both the primary tumor and the metastatic regional lymph nodes showed remarkable necrosis (primary tumor, grade III; metastatic regional lymph nodes, grade IV a). Hair loss was noted, but no other complications. Pulmonary metastases were found 6 months after the transcatheter treatment.

Discussion

Locally advanced carcinoma of the breast shows a high incidence of local recurrence after surgery. Various types of additional treatment, such as radiation therapy, chemotherapy, and hormonal therapy, have therefore been used with the aim of reducing the local recurrence rate (4).

Transcatheter arterial embolization aiming to control the tumor growth has been reported for several organs (1, 2, 7, 13, 14). HARRINGTON et coll. (3) reported that transcatheter arterial embolization offered hemostatic control in recurrent breast cancer. MCLEAN et coll. (6) reported on percutaneous alcohol injection for control of internal mammary artery bleeding, and SMITH et coll. (9) described hemostatic control of a ruptured internal mammary artery secondary to blunt chest trauma. As far as is known, however, no report has appeared on the application of this technique for administering an anticancer agent to a breast malignancy before surgery.

As regards the catheterization, a transaxillary approach was employed in the early patients. However, with this approach, complete catheterization of all three vessels was sometimes unsuccessful. In the later patients, a transfemoral approach with a modified cerebral catheter for the lateral thoracic artery

and the thoracodorsal artery, and a femoral internal mammary catheter for the internal mammary artery was employed. These catheters made selective catheterization easy.

Intra-arterial infusion of anticancer agents may be an effective measure for locally advanced breast carcinoma. However, it causes several complications such as myeloproliferative suppression, digestive tract disturbances, or hair loss, due to high concentration of the infused anticancer agent in the systemic circulation (5, 12). The new embolic material has the property of releasing an anticancer agent slowly into the systemic circulation (11), and our method while allowing high doses of the anticancer agent to reach the tumor site, produces no such systemic disturbances except hair loss.

Moreover, the new embolic material remains thrombotic for a longer period than previously used materials (10), simultaneously cutting off the arterial blood supply to the tumor and, due to the small particle size of the embolic material, allowing the anticancer agent to be distributed diffusely within the chest wall. The method seems to be effective not only in primary tumors but also in metastatic regional lymph nodes.

The described method may have a good potential as preoperative treatment in locally advanced breast carcinoma. The possible value of the method for increasing recurrence-free survival or survival must, however, be carefully evaluated by controlled clinical trials, including long-term observation, before a definite statement can be made. Another possible use of the method, not tried at this hospital, may be palliative treatment in locally inoperable or recurrent breast malignancy.

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