Invasive lobular carcinoma of the breast: cytometric and immunohistochemical characteristics of 96 cases

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The aim of the study was to present microscopic, cytometric and immunohistochemical characteristics of a group of 96 invasive lobular carcinomas (ILC) of the breast. Ninety six patients treated surgically at the Department of Surgical Oncology, Centre of Oncology – Maria Skłodowska-Curie Memorial Institute, Cracow Branch, between 1983 and 1996, were included into the study. In 56 (58.3%) cases, a classical pattern of ILC was diagnosed, whereas atypical variants (solid, pleomorphic, pleomorphic with signet ring cells, signet ring cell, and tubulolobular) were recognized in 40 (41.7%) cases. ILC was characterized by lack of E-cadherin expression, high rate of steroid receptor expression, low rate of P53 and c-erb-B2 expressing tumours, low MIB-1 labelling index, and low S phase fraction, as well as high rate of diploid lesions.

Key words: invasive lobular carcinoma, flow cytometry, immunohistochemistry.

Introduction

Invasive lobular carcinoma (ILC) is the second most common histological subtype of breast cancer. The majority of authors report that ILC comprises 5-10% of all malignant neoplasms of the mammary gland. However, literature data suggest that its prevalence ranges from 1% to 20% [1-6]. This substantial difference results from a variety of studied cohorts and, particularly, from broad diagnostic criteria of ILC used by the researchers [7-10]. After the description of the classical pattern of ILC by Foote and Stewart, many authors have identified numerous, sometimes questionable, variants of this neoplasm, causing an increase in the percentage of breast cancers classified as lobular carcinoma [8, 11-14]. At the end of the 20th century the incidence of ILC has been reported to be increasing, probably due to the more common use of combined estrogen-gestagen hormone replacement therapy [15-18].

The aim of the study was to determine histological, cytometric, and immunohistochemical characteristics of ILC.

Material and methods

The analyzed group consisted of 96 patients subjected to surgical treatment at the Department of Surgical Oncology, Centre of Oncology – Maria Skłodowska-Curie Memorial Institute, Cracow Branch, from 1983 to 1996. The youngest patient was 37 years old, while the oldest – 83 years old; the mean patient age was 59 years.

Stage I tumours, according to the American Joint Committee on Cancer criteria of 2002 [19], were found

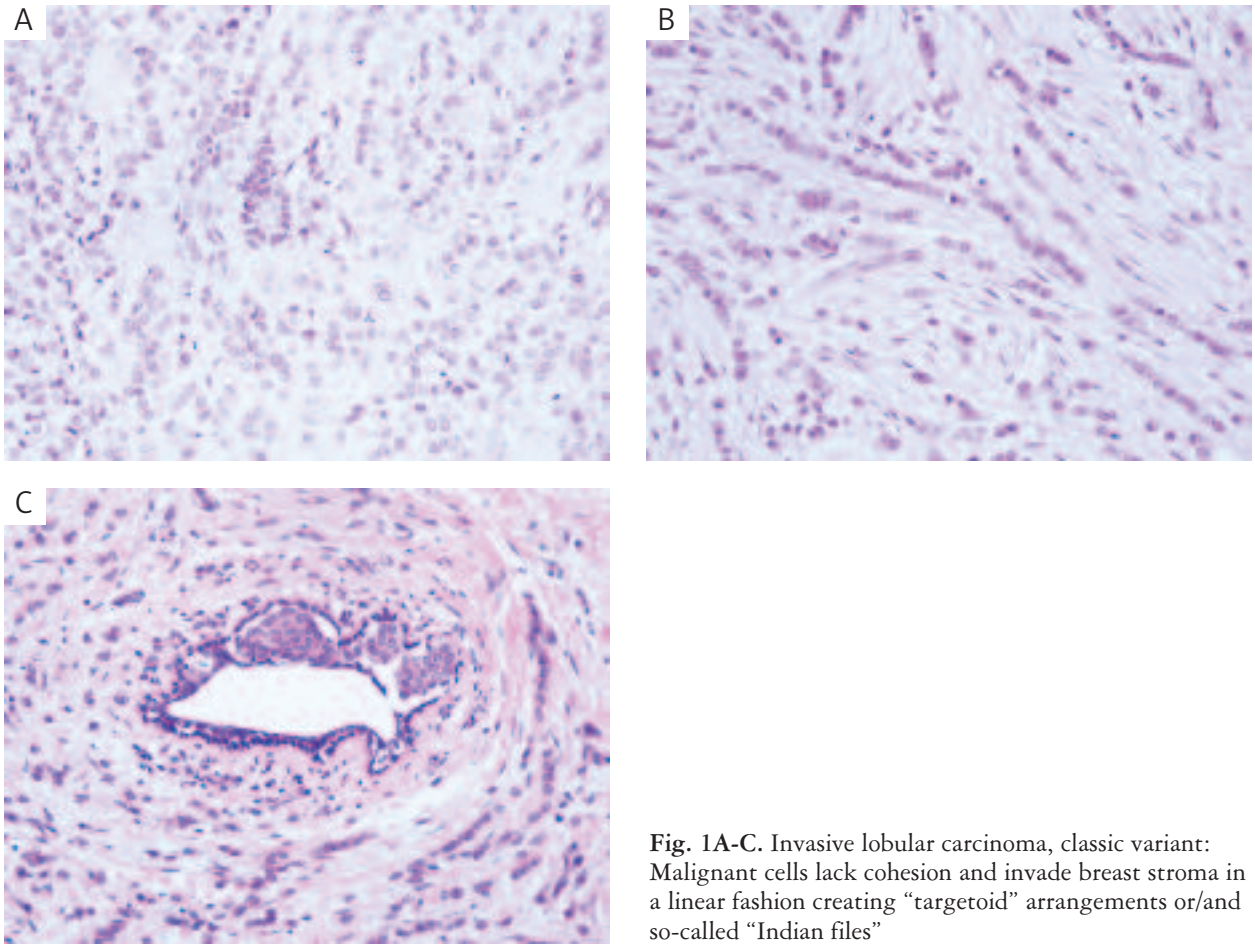

Fig. 1A-C. Invasive lobular carcinoma, classic variant: Malignant cells lack cohesion and invade breast stroma in a linear fashion creating "targetoid" arrangements or/and so-called "Indian files"

in 10 (10.4%) patients, stage IIA in 18 (18.8%) patients, stage IIB in 34 (35.4%) patients, and stage IIIA in 34 (35.4%) patients. In 30 (31.3%) patients, Halsted radical mastectomy was performed (from 1983 to 1997), in 58 (60.4%) patients – Patey modified radical mastectomy, whereas 8 (9.3%) patients underwent tumorectomy with axillary lymph node dissection followed by radiation therapy. In 56 (58.3%) cases, a classical form of ILC (Fig. 1A-C) was diagnosed, while an atypical variant – in 40 (41.7%) cases. Among 40 cases included into the atypical ILC subgroup, solid (Fig. 2), pleomorphic (Fig. 3), pleomorphic with signet ring cells (Fig. 4A-B), signet ring cell and tubulolobular (Fig. 5) variants were recognized in 8 (8.3%),

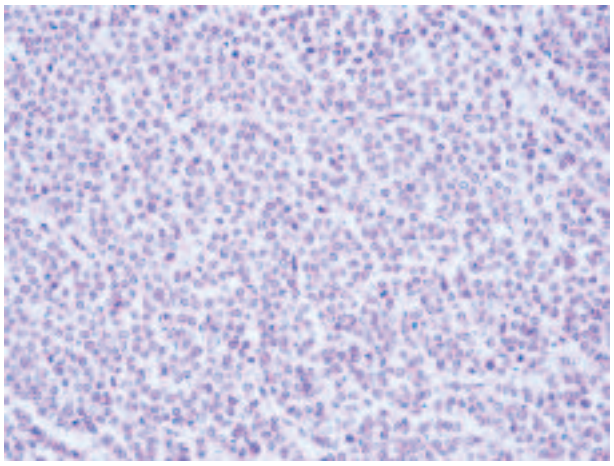

Fig. 2. Invasive atypical lobular carcinoma, solid variant. Neoplastic cells present features similar to those seen in classic variant of the tumor, but tend to form a solid mass without intervening stroma

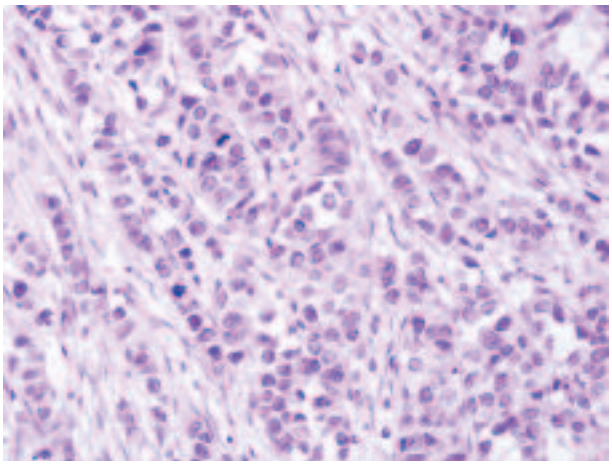

Fig. 3. Invasive atypical lobular carcinoma, pleomorphic variant. Cancer cells are characterized by lack of cohesion, however they present high nuclear polymorphism and atypia

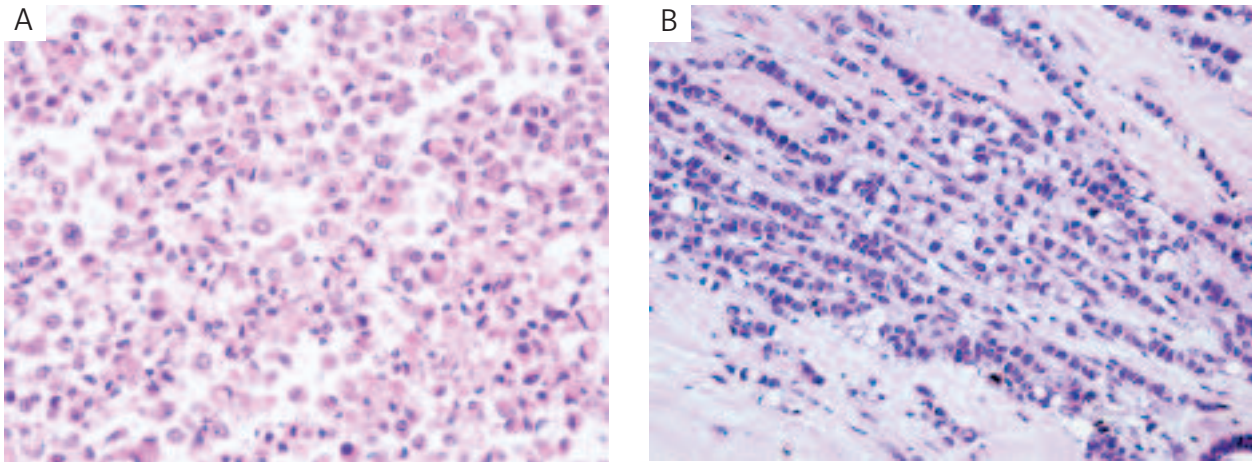

Fig. 4A-B. Invasive atypical lobular carcinoma, pleomorphic/signet ring cell variant. Numerous pleomorphic cells present cytoplasmic vacuoles filled with mucin (signet ring cells)

4 (4.2%), 18 (18.7%), 6 (6.3%), and 4 (4.2%) cases, respectively. The distribution of ILC variants in the studied cohort is presented in Table I.

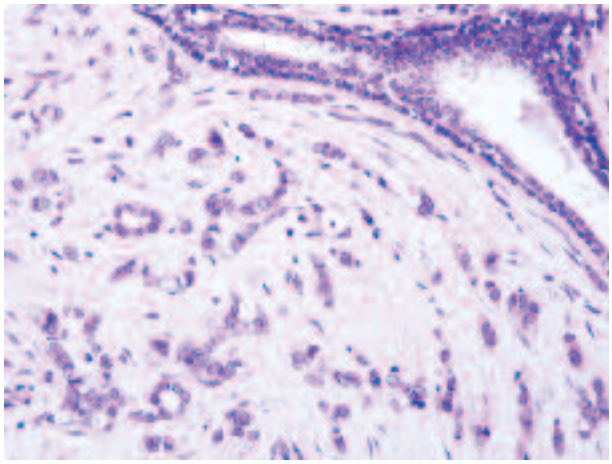

Fig. 5. Invasive atypical lobular carcinoma, tubulolobular variant. Carcinoma texture is characterized by the presence of "Indian file" arrangements, as well as microtubules built of single layer of small neoplastic cells

Table I. Microscopic patterns of ILC in a group of 96 patients

Microscopic pattern of ILC	Patients [n]	Patients [%]
classical ILC	56	58.3
atypical variants of ILC		
solid	8	8.3
pleomorphic	4	4.2
pleomorphic with signet ring cells	18	18.7
signet ring cell	6	6.3
tubulolobular	4	4.2
total	96	100.0

Histological, cytometric, and immunohistochemical studies were performed on formalin-fixed paraffin-embedded primary tumour samples. Based on slides routinely stained with haematoxylin and eosin, the histological pattern (according to the World Health Organization Classification of Tumours [16]), nuclear grade, and mitotic count per 10 high power fields (HPF) were established. In the studied cohort of 96 invasive lobular carcinomas, an E-cadherin expression, steroid receptor immunoreactive score (IRS), P53 protein expression, MIB-1 labelling index as well as external (CBE 1), and internal (CB11) HER-2/neu domains expression were studied. Immunohistochemical stainings were performed on paraffin sections up to 5 µm thick, mounted onto SuperFrost (+) slides and dried at 60°C for 24 hours, then deparaffinized in xylene (2 × 30 min), and rehydrated in absolute alcohol followed by 96% alcohol (for 5 min in both concentrations). After rinsing in distilled water, endogenous peroxidase was blocked with 3% hydrogen peroxide for 15 min. Next, the sections were immersed in sodium citrate buffer (pH 6.0), and heated 3 times in a microwave oven (540 Watt) for 7 min. In the c-erb-B2 antigen staining procedure, epitope retrieval in microwave oven was omitted, while in the Ki-67 proliferative antigen staining procedure, epitope retrieval followed additional trypsin digestion (Sigma Code-No. T7168) for 15 min at room temperature. Sections washed in TRIS were successively incubated with blocking serum, primary antibody and detection system components. The data concerning dilution and exposition time of antibodies and sera used are depicted in Table II. Finally, the slides were incubated in DAB solution (DAKO-S3000) with 3% hydrogen peroxide, counterstained in Harris haematoxylin, dehydrated and coverslipped in Canada Balsam.

Using flow cytometry, ploidy, DNA index, as well as the percentage of cells entering S phase and G2M phase were assessed in each case.

Table II. Immunohistochemical studies: antibodies and staining procedures

Antigen	Clone	Manufacturer	Dilution	Incubation Time	Detection system	Antigen retrieval technique
estrogen receptor	6F11	Novocastra	1 : 500	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min
progesterone receptor	SP2	LabVision	1 : 500	30 min room temp.	UltraVision*	citrate buffer pH = 6.0 water bath, 20 min
c-erb-B2 (external domain)	CBE1	Novocastra	1 : 80	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min
c-erb-B2 (internal domain)	CB11	Novocastra	1 : 300	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min
P53	BP53-12	Novocastra	1 : 50	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min
P53	PAb1801	Novocastra	1 : 40	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min
Ki-67	MiB1	DAKO	1 : 100	overnight, 4°C	UltraVision*	citrate buffer pH = 6.0 microwave oven, 2 × 10 min

**UltraVision Large Volume Detection System, Thermo Scientific*

During the assessment of Ki-67 antigen expression (with the use of MIB-1 antibody) all the nuclei stained were counted, irrespective of the staining intensity. In each case, 500 cells were assessed – 100 cells in 5 fields at the magnification of 400×. The score was presented as an arithmetic mean. Steroid receptor expression and P53 protein expression were assessed according to Remmele and Stegner [20] (Table III). The final IRS for estrogen and progesterone receptor expression, as well as for P53 protein expression were presented as a product of both studied parameters (range 0-12).

In the case of c-erb-B2 and E-cadherin, the presence and intensity of the membranous staining of cancer cells were assessed. The classification of the DNA ploidy histograms was based on criteria recommended by Shankey *et al.* [21]. The proliferation rate, expressed as the rate of S phase cells and proliferation index (S+G2M), was also established.

Table III. The immunoreactive score assessment criteria according to Remmele and Stegner

Staining intensity	Percentage of stained cells
0 – no staining	0 – lack of stained cells
1 – weak staining	1 – < 10% of stained cells
2 – moderate staining	2 – 10-50% of stained cells
3 – strong staining	3 – 51-80% of stained cells
	4 – > 80% of stained cells

Results

The results of all histological, immunohistochemical and cytometric analyses are depicted in Table IV.

In 26 (27.1%) studied cases, the nuclear grade was estimated as G1, in 54 (56.2%) patients as G2 and in 16 (16.7%) patients as G3. In 42 (43.8%) tumours, the mitotic count exceeded 4 mitoses per 10 HPF, whereas in 54 (56.2%) cases no more than 4 mitoses per 10 HPF were found. E-cadherin expression was observed only in one case with classical lobular histological texture. Ninety two (95.8%) tumours expressed estrogen receptor (ER). The estrogen receptor immunoreactive score, according to Remmele *et al.*, was as follows: IRS = 0 (lack of staining) in 4 (4.2%) cases, IRS = 6 in 11 (11.5%) cases, IRS = 9 in 15 (15.6%) cases and IRS = 12 in 66 (68.7%) cases from the analysed group. Progesterone receptor (PR) expression was found in 80 (83.3%) tumours. The progesterone receptor immunoreactive score, according to Remmele *et al.*, was as follows: IRS = 0 (lack of staining) in 16 (16.7%) lesions, IRS = 3 in 9 (9.4%) lesions, IRS = 6 in 25 (26.0%) lesions, IRS = 9 in (16.7%) lesions and IRS = 12 in 30 (31.2%) lesions from the studied group. Expression of P53 protein (BP53-12 epitope) was confirmed only in 16 (16.7%) tumours; in 11 of them the immunoreactive score, according to Remmele *et al.*, was 3, in 2 cases – 4 and in 3 cases – 6. Expression of P53 protein (P53-1801 epitope) was found only in 6 (6.2%) lesions; in 5 of

Table IV. The results of microscopic, immunohistochemical, and cytometric studies of a group of 96 ILC patients

Analysed parameter	Classical ILC (56 cases)		Atypical ILC (40 cases)		Total	
	[n]	[%]	[n]	[%]	[n]	[%]
nuclear grade*						
G1	25	44.6	1	2.5	26	27.1
G2	30	53.6	24	60.0	54	56.2
G3	1	1.8	15	37.5	16	16.7
mitotic count (per 10 HPF)*						
< 1	21	37.5	1	2.5	22	22.9
1–4	19	33.9	13	32.5	32	33.3
> 4	16	28.6	26	65.0	42	43.8
E-cadherin						
negative	55	98.2	40	100.0	95	99.0
positive	1	1.8	–	–	1	1.0
estrogen receptor						
positive	55	98.2	37	92.5	92	95.8
negative	1	1.8	3	7.5	4	4.2
estrogen receptor immunoreactive score according to Remmele *et al.**						
0	1	1.8	3	7.5	4	4.7
6	4	7.1	7	17.5	11	11.5
9	5	8.9	10	25.0	15	15.6
12	46	82.2	20	50.0	66	68.7
progesterone receptor						
positive	49	87.5	31	77.5	80	83.3
negative	7	12.5	9	22.5	16	16.7
progesterone receptor immunoreactive score according to Remmele *et al.*						
0	7	12.5	9	22.5	16	16.7
3	6	10.7	3	7.5	9	9.4
6	12	21.4	13	32.5	25	26.0
9	10	17.9	6	15.0	16	16.7
12	21	37.5	9	22.5	30	31.2
P53 protein expression (BP53-12 epitope)						
negative	50	89.3	30	75.0	80	83.3
positive						
according to Remmele *et al.*						
3	3	5.3	8	20.0	11	11.5
4	1	1.8	1	2.5	2	2.1
6	2	3.6	1	2.5	3	3.1
P53 protein expression (P53-1801 epitope)						
negative	53	94.6	37	92.5	90	93.8
positive						
according to Remmele *et al.*						
3	2	3.6	3	7.5	5	5.2
6	1	1.8	–	–	1	1.0
MIB-1 labelling index						
< 15	33	58.9	19	47.5	52	54.2
≥ 15	23	41.1	21	52.5	44	45.8

Table IV. cont.

Analysed parameter	Classical ILC (56 cases)		Atypical ILC (40 cases)		Total	
	[n]	[%]	[n]	[%]	[n]	[%]
CBE 1 (external domain of HER-2/neu)						
negative	56	100.0	40	100.0	96	100.0
positive	–	–	–	–	–	–
CB11 (internal domain of HER 2/neu)						
negative	56	100.0	38	95.0	94	97.9
positive	–	–	2	5.0	2	2.1
ploidy*						
diploid tumours	42	75.0	22	55.0	64	66.7
aneuploid tumours	14	25.0	18	45.0	32	33.3
ploidy index (PDI)						
1	42	75.0	22	55.0	64	66.7
1.1-1.9	10	17.9	16	40.0	26	27.1
≥ 2.0	4	7.1	2	5.0	6	6.2
S phase cells (PS)						
< 10.0	33	58.9	17	42.5	50	52.1
10-20.0	15	26.8	16	40.0	31	32.3
> 20.0	8	14.3	7	17.5	15	15.6
G2 phase cells (PG2M)						
< 4.0	24	42.8	20	50.0	44	45.8
4.1-8.0	15	26.8	14	35.0	29	30.2
> 8.0	17	30.4	6	15.0	23	24.0
proliferation index (SG2M)						
< 10.0	21	37.5	13	32.5	34	35.4
10.0-20.0	19	33.9	14	35.0	33	34.4
> 20.0	16	28.6	13	32.5	29	30.2
total	56	100.0	40	100.0	96	100.0

**statistically significant, log rank test, $p < 0.05$*

them the immunoreactive score, according to Remmele *et al.*, was 3 and in 1 lesion – 6. In 52 (54.2%) tumours MIB-1 labelling index was lower than 15, whereas in 44 (45.8%) patients its value equalled or exceeded 15. None of the studied tumours expressed CBE1 (external domain of HER-2 neu) and only in 2 (2.1%) atypical ILCs, the presence of CB11 (internal domain of HER-2neu) was observed. Sixty four (66.7%) tumours were diploid (D1 = 1.0) and 32 (33.3%) – aneuploid (hyperdiploid, D1 > 1.0). Among 32 aneuploid lesions, DNA index ranged from 1.1 to 1.9 in 26 cases and in 6 cases it exceeded 1.9. In 50 (52.1%) lesions from the studied group, the rate of S phase cells was lower than 10.0, in 31 (32.3%) lesions it ranged from 10.0 to 20.0, and in 15 (15.6%) lesions it exceeded 20.0. In 44 (45.8%) tumours the rate of G2 phase cells (PG2M) was lower than 4.0, in 29 (30.2%) tumours it ranged from 4.1 to 8.0, and in 23 (24.0%) tumours it exceeded 8.0. In 34 (35.4%) tumours, the proliferation index (SG2M) was lower than 10.0, in 33 (34.4%) tumours it ranged from 10.0 to 20.0, and in 29 (30.2%) tumours it exceeded 20.0.

Detailed analysis of data presented in Table III revealed that the group of atypical ILC, in comparison with the classical pattern of ILC, is characterised by:

- lower rate of tumours expressing both ER and PR (92.5% vs. 98.2% and 77.5% vs. 87.5%, respectively),
- lower rate of tumours with a high (9-12) PR immunoreactive score (37.5% vs. 55.5%),
- higher rate of P53 protein expressing tumours (BP53-12 epitope) (25.0% vs. 10.7%),
- higher rate of tumours with MIB-1 labelling index ≥ 15 (52.5% vs. 41.1%),
- higher rate of tumours with S phase cells index > 10.0 (57.5% vs. 41.1%),
- higher rate of tumours with proliferation index > 10 (67.5% vs. 62.5%).

However, the above-mentioned differences were not statistically significant (log rank test, $p > 0.05$).

Statistically significant differences between the classical and atypical type of ILC were confirmed with regard to the nuclear grade, mitotic count, intensity of ER staining, and ploidy of tumour cells. In 55 (98.2%) classical ILCs, the nuclear grade was low or moderate (G1, G2), whereas in the group of atypical ILCs, a low or moderate nuclear grade was observed only in 25 (62.5%) cases (log rank test, $p < 0.01$). In 26 (65%) atypical ILCs, the mitotic count exceeded 4 mitoses per 10 HPF, while in the group of classical ILC such high value of mitotic count was found only in 16 (28.6%) cases (log rank test, $p < 0.001$).

In 46 (82.2%) cases of classical ILC, the ER immunoreactive score was 12, according to Remmele *et al.*, whereas in the group of atypical ILC such intense ER expression was observed only in 20 (50.0%) cases (log rank test, $p < 0.01$).

Aneuploidy was found in 18 (45.0%) atypical ILCs and in 14 (25.0%) classical ILCs (log rank test, $p < 0.05$).

Discussion

An analysis of a group of 96 ILC patients treated surgically at the Department of Surgical Oncology, Centre of Oncology – Maria Skłodowska-Curie Memorial Institute, Cracow Branch, from 1983 to 1996, was performed. The studied group was selected from 2347 breast carcinoma patients based on the reassessment of the archival histological tumour samples. The selected ILCs comprised 4.1% of breast carcinoma cases managed at the Institute in the referred period, which is consistent with ILC prevalence according to literature data (i.e. 1-20%) [1, 2, 4, 5, 13, 16].

Classical ILC was observed in 58.3% of cases, whereas atypical ILC – 41.7% of cases of the analysed cohort. In the atypical ILC subgroup, 5 variant patterns have been recognized: solid, pleomorphic, pleomorphic with signet ring cells, signet ring cell, and tubulolobular. In the available literature, numerous additional variants of ILC have been described, including alveolar, trabecular, histiocytoid, pleomorphic with apocrine or histiocytoid differentiation, and others [3, 8, 11-14, 16, 22-32]. If the lesion is composed of more than one ILC variant, and none of them constitutes more than 80-85% of the microscopic texture, the tumour is referred to as mixed ILC [8, 16]. The prevalence of particular ILC forms varies in published literature, due to patients selection criteria and different interpretation of microscopic appearance of ILC by the authors [8, 16, 24]. Dixon *et al.* reported 30% of classical ILC cases, 22% – solid, 19% – alveolar and 29% – mixed ILC variants [33]. In the study by Ellis *et al.* the classical pattern constituted 40% of cases, solid – 10%, alveolar – 4%, tubulolobular – 6%, and mixed – 40% [34]. In a group of 230 ILC patients, DiCostanzo *et al.* from the Memorial Sloan-Kettering Cancer Center recognized the classical variant in 176 (77%) cases, solid in 10 (4%) cases, alveolar in 14 (6%) cases and mixed in 30 (13%) cases [8]. Distinct distribution of ILC forms was presented by du Toit *et al.*; in their material mixed ILC constituted 45.6% of cases, classical ILC – 30.4%, tubulolobular – 13.5%, solid – 6.4%, and alveolar – 4.1% [25]. Finally, Mise *et al.* documented 33 (66%) cases of classical ILC and 17 (34%) cases of atypical patterns, in a group of 50 patients [35].

The studied subgroups of classical and atypical variants of ILC differed significantly with regard to the following parameters: nuclear grade, mitotic count, intensity of ER expression as well as ploidy of tumour cells. An atypical ILC subgroup was characterized by a higher grade (G3: 16.7% vs. 1.8%), higher mitotic count (>4 mitoses per 10 HPF: 65% vs. 28.6%), lower ER immunoreactive score (12 according to Remmele and Stegner: 50% vs. 82.2%), and higher rate of aneuploid lesions (45% vs. 25.0%) as compared with classical ILC.

Immunohistochemical and cytometric analyses performed on the studied material revealed that both the high rate of ER expressing lesions (95.8%) and high ER immunoreactive score according to Remmele and Stegner (12 in > 66% of cases), as well as a high rate of PR expression (83.3%) and a relatively high PR immunoreactive score according to Remmele and Stegner (6-12 in almost 75% of cases) are characteristic of ILC.

Table V. Steroid receptor expression in invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC) patients

AUTHOR, YEAR [REFERENCE NO.]	ILC		IDC	
	ER+ [%]	PR+ [%]	ER+ [%]	PR+ [%]
Silverstein *et al.* 1994 [38]	67	67	55	55
Yeatman *et al.* 1995 [39]	88	68	72	66.8
Cocquyt *et al.* 2003 [40]	79	42	44	25
Molland *et al.* 2004 [41]	92	82	75	75
Mathieu *et al.* 2004 [37]	91	71	68	61
Cristofanilli *et al.* 2005 [42]	90	90	62	62
Tubiana-Hulin *et al.* 2006 [17]	65.5	65.5	38.8	38.8

In available literature, there prevails an opinion that hormonal receptor expression is more frequent in ILC than in invasive ductal carcinoma (IDC) [1, 3, 5, 9, 10, 16, 17, 24, 36-42], what is depicted in Table V.

According to published data, 66-95% of lobular carcinomas presented a positive ER status [5, 16, 17, 39, 41-43], and 25-90% were characterized by a positive PR status [5, 16, 17, 39, 41]. In the studies by Sastre-Garau *et al.* and du Toit *et al.*, ER expression was found more frequently in ILC as compared with IDC, while PR expression was equally frequent [5, 44]. The World Health Organization Classification of Tumours emphasizes the difference in hormonal receptor expression between particular ILC variants, e.g. nearly 100% of alveolar ILCs have a positive ER status, whereas only 10% of pleomorphic ILCs have such status [16].

Ninety five (99%) studied tumours lacked E-cadherin expression. In the literature, a complete loss of E-cadherin expression is documented in 80-100% of ILCs, while a reduced E-cadherin expression is observed in 30-60% of IDCs [16].

The analysed cohort was also characterized by a low rate of P53 expressing lesions and lack of c-erb-B2 expression. P53 expression was found only in 6.2% (P53-1801 epitope) and 16.7% (BP 53-12 epitope) of tumours. No CBE-1 expression was observed in any of the studied cases, and only in 2 (2.1%) cases, CB11 was expressed.

Many authors accentuate that c-erb-B2 (HER2/neu) as well as P53 expression is less frequent in ILC than in IDC [1, 5, 10, 16, 36, 37, 40, 42]. Cocquyt *et al.* found c-erb-B2 in 4% of ILC cases and in 18% of IDC cases, whereas P53 – in 17% and 19% of cases, respectively [40]. Mathieu *et al.* observed c-erb-B2 expression in 1 of 19 (5%) ILCs and in 37 of 110 (34%) IDCs; P53 was expressed in 1 (5%) and in 52 (47%) cases, respectively. The differences have reached statistical significance [37]. Pleomorphic ILC is an exception among ILC variants, which frequently overexpresses HER2/neu and accumulates P53 protein [16, 45, 46].

Studied tumours were characterized by a relatively low MIB-1 labelling index that in 54.2% cases did not exceed 15 (mean: 14). Many authors emphasize that the MIB-1 labelling index is generally low in ILCs [5, 16, 36, 37]. In the study by Mathieu *et al.*, a mean MIB-1 labelling index was 14% in the ILC group, and 27% in the IDC group [37].

In the analysed group, diploid tumours constituted ~66% of cases, which is consistent with literature data that demonstrate a higher rate of diploid ILCs than IDCs [1, 40]. According to the WHO Classification of Tumours, diploid lesions account for ~50% of ILC cases [16].

A relatively low S phase cell index was also observed. It did not exceed 10 in > 50% of cases of the analysed group; in 85.4% of cases, the S phase cells index did not exceed 20. In many studies a lower S phase cells index was found in ILC as compared with IDC [1, 38, 40].

Several other studies reported features of ILC, which were not subject of the present study, are worth noticing. Invasive lobular carcinoma rarely expresses an epidermal growth factor receptor [1, 40] and in this type of breast carcinoma immunohistochemical reaction to vimentin is also usually negative [47]. Expression of bcl-2 was demonstrated in 89% of ILC cases and in 67% of IDC cases [37]. Gross cystic disease fluid protein 15 expression was identified in ~33% of ILCs and in almost 100% of cases of a signet ring carcinoma variant [16].

To conclude, cytometric and immunohistochemical analyses reveal that ILC differs significantly from IDC; in ILC hormonal receptors are expressed more frequently, P53 and c-erb-B2 expression is rare, E-cadherin is expressed sporadically, MIB-1 labelling index as well as S phase cells index are low, and diploid lesions constitute a high proportion of cases.

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