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Microcirculation patterns in indocyanine green angiography and the results of plaque therapy in choroidal melanoma

Wpływ brachyterapii na zachowanie się wzorów mikrokrążenia czerniaka naczyniówki w obrazie angiografii indocyjaninowej

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Summary:

Purpose: To determine the effect of radioactive plaque therapy on blood vessel behaviour in choroidal melanomas using indocyanine green (ICG) angiography.

Material and methods: Fifty-five patients with choroidal melanoma were studied. Ruthenium-106 plaques were used in 30 eyes, in 11 the "sandwich method" (Ruthenium-106 plaque with transpupillary thermotherapy), was applied and 14 tumours were treated with Iodine-125. In all cases ICG angiography was performed prior to treatment and 12 months after, and at different time afterwards. Baseline tumour microcirculation patterns (MCPs) were studied prior to treatment and post-treatment blood vessels changes were evaluated. Total follow-up period ranged from 14-22 months (mean: 16 months).

Results: Pre-treatment ICG angiography revealed complex MCPs, combining parallel with cross-linking, arcs with branching, loops and networks patterns in 23 (41.8%) and non-complex MCPs, including straight, parallel without cross-linking and arcs without branching patterns in 32 (58.2%) melanomas. Twelve months after treatment, 38 tumours (69.1%) showed a significant changes in their MCPs. The mean ultrasonographic regression rate in tumours with complex MCPs was 57.4% as opposed to 36.2% in the group with non-complex MCPs ($p = 0.01$). No statistically significant correlation in the height regression rate was found among the various methods of therapy, however a significant difference between the type of therapy and MCPs changes was observed ($p<0.001$). Melanomas treated with Ruthenium-106 and TTT demonstrated slight or no MCPs changes, while tumours treated with Ruthenium-106 and Iodine-125 plaques alone showed a significant MCPs changes ($p<0.001$). The statistical analysis showed the correlation between the type of baseline MCPs and the degree of their changes after treatment ($p<0.001$). Tumours with networks, loops, arcs with branching and parallel with crossing showed an increased regression as compared to other MCPs. Twelve patients whose tumours contained complex MCPs developed metastatic disease.

Conclusions: This study suggests that the response of choroidal melanoma to irradiation is related to MCPs as identified by ICG angiography; the presence of complex MCPs is associated with a high regression rate after plaque therapy and a high risk of development of systemic metastatic disease.

Key words: Choroidal melanoma, radiation plaque therapy, indocyanine green angiography, microcirculation patterns.

Streszczenie:

Cel: ocena wpływu brachyterapii na zachowanie się naczyń krwionośnych czerniaka naczyniówki w obrazie angiografii indocyjaninowej.

Materiał i metody: badaniami objęto 55 chorych z czerniakiem naczyniówki. W 30 oczach przeprowadzono brachyterapię z zastosowaniem aplikatora 106Ru, w tym w 11 przypadkach łącząc ją z przezźreniczną termoterapią („metoda kanapki"), 14 guzów leczono aplikatorami z ziarnami 125I. We wszystkich przypadkach przed leczeniem oraz 12 miesięcy i następnie w różnych przedziałach czasu po przeprowadzonym leczeniu wykonano badanie angiografii indocyjaninowej, w którym oceniano wzory mikrokrążenia (microcirculation patterns – MCPs) czerniaków naczyniówki. Okres obserwacji wahał się od 14 do 22 miesięcy (średnio 16 miesięcy).

Wyniki: w 23 czerniakach (41,8%) wyjściowe badanie angiograficzne wykazało obecność złożonych wzorów mikrokrążenia (complex MCPs), wśród których występowały: naczynia równoległe z poprzecznymi połączeniami, łuki z rozgałęzieniami, pętle oraz sieci naczyniowe. Niezłożone wzory mikrokrążenia (non-complex MCPs), obejmujące proste naczynia, równoległe bez poprzecznych połączeń, łuki bez rozgałęzień, zaobserwowano w 32 guzach (58,2%). Dwanaście miesięcy po zastosowanym leczeniu 38 czerniaków (69,1%) wykazało istotne zmiany w morfologii MCPs. W badaniu ultrasonograficznym średnia regresja grubości guzów ze złożoną postacią mikrokrążenia (complex MCPs) wyniosła 57,4%, natomiast w przypadku czerniaków z niezłożonym wzorem mikrokrążenia (non-complex MCPs) odsetek ten wynosił średnio 36,2 ($p = 0,01$). Nie znaleziono istotnej statystycznie zależności, jaka zachodzi między stopniem redukcji grubości guzów a zastosowaną metodą leczenia, która jednak miała istotny wpływ na zachowanie się MCPs ($p<0,001$). W czerniakach leczonych „metodą kanapki" stwierdzono nieznaczne zmiany w MCPs lub ich brak, podczas gdy guzy leczone 106Ru i 125I wykazały istotne zmiany w MCPs ($p<0,001$). Analiza statystyczna wykazała istnienie zależności, jaka zachodzi między rodzajem wyjściowych wzorów mikrokrążenia a stopniem ich

zmiany po przeprowadzonym leczeniu ($p<0,001$). Guzy z sieciami naczyniowymi, pętlami, łukami z rozgałęzieniami oraz równoległymi naczyniami z poprzecznymi połączeniami wykazały większą regresję niż guzy z innymi MCPs. U dwunastu chorych, u których czerniaki naczyniówki charakteryzowały się złożoną postacią MCPs, pojawiły się odległe przerzuty.

Wnioski: wyniki naszych obserwacji sugerują, że odpowiedź czerniaka naczyniówki na leczenie metodą brachyterapii jest uwarunkowana rodzajem mikrokrążenia guza, które można zobrazować w badaniu angiografii indocyjaninowej. Obecność złożonego typu mikrokrążenia jest związana z wysokim wskaźnikiem regresji guzów oraz wysokim ryzykiem wystąpienia odległych przerzutów.

Słowa kluczowe: czerniak naczyniówki, brachyterapia, angiografia indocyjaninowa, wzory mikrokrążenia.

Introduction

Indocyanine green (ICG) angiography allows more accurate visualization of the choroidal vasculature compared with fluorescein angiography (FA). While it is an essential method of diagnosis and evaluation of treatment in some ocular diseases, there are only some reports demonstrating the value of ICG angiography in the diagnosis and differentiation of intraocular tumours, including choroidal melanomas (1-5). Until now the evaluation of choroidal melanoma is based on clinical visualization and ultrasound measurement of the tumour (6-8).

Malignant tumour growth, metastasis and mortality rate are facilitated by various factors, including the architecture of the intrinsic microvasculature (9,10). Histological analysis of primary uveal melanomas has led to the identification of nine different patterns of extracellular matrix formation, which are also known as "Folberg patterns" (11). It has been suggested that these patterns contain or represent blood-conducting channels and they can be detected by angiography, indicating that these channels and normal blood vessels are interconnected (12). Certain patterns such as arcs, loops and networks have been related to tumour progression and bad prognosis (9,10).

This prospective study was performed to determine the value of ICG angiography in the evaluation of efficacy of radioactive plaque therapy in choroidal melanomas. The purpose of this study was also to evaluate the usefulness of ICG angiography results in taking the decision about additional treatment in tumours with unchanged microcirculation patterns (MCPs) after primary therapy. Analysis was based on changes in the MCPs in comparison with changes in tumour thickness as measured by ultrasonography.

Material and methods

The study included fifty-five patients with choroidal melanoma, treated conservatively with plaque therapy. There were 28 males and 27 females, with an age range of 24-79 (mean 56) years. Patients were enrolled prospectively according to the following criteria: a clinically diagnosed choroidal melanoma, not previously treated, a tumour location posterior to the equator and clear optical media which allow optimal visualization and interpretation of ICG angiography. Exclusion criteria were: a contraindication to ICG angiography, heavy tumour pigmentation, extensive exudative retinal detachment, peripheral location of the tumour and lack of transparency of optical media. Baseline ocular examination included: best-corrected visual acuity (BCVA), intraocular pressure, slit-lamp examination, fundoscopy, ultrasonography and ICG angiography. In all cases fundus photography was performed. The diagnosis of choroidal melanoma was based on ophthalmoscopic examination and A and B mode ultrasonography. Ultrasonographic tumours characteristics were recorded for each patient: tumour thickness ranged from 3.2 to 8.7 mm (mean thickness: 5.8 mm) and basal diameter ranged from 3.4 to 15.2 mm (mean diameter: 10.2 mm). Orange pigment was observed in 35 eyes, limited exudative retinal detachment was present in 11 eyes. All tumours demonstrated a medium degree of pigmentation.

A Ruthenium-106 plaque was used in 41 eyes (tumour thickness: 3.2 – 6.4 mm), in 30 cases with additional transpupillary thermotherapy ("sandwich method"). In 14 cases (tumour thickness: 7.0 – 8.7 mm) Iodine-125 plaques were used.

Ruthenium-106 plaques delivered a dose of 90-100 Gy to the tumour apex and 240-580 Gy to the tumour base, Iodine-125 plaques delivered 100 -110 Gy to the tumour apex and 320 -410 Gy to the tumour base.

Transpupillary thermotherapy (TTT) was performed using an infrared diode laser at 810 nm through a slit-lamp adaptor (Iris Medical Instruments, Mountain View, California, USA). Treatment was initiated by using a 60-second exposure and a low energy level at 300 mW with a 2.0 or 3.0 mm beam width. The energy was gradually increased by 50 – 100 mW till the surface of the tumour showed a light greyish discoloration. Spots were overlapping, including a border of 0.5 mm of normal tissue around the tumour margins.

For follow-up, a complete ophthalmological examination with A and B scan ultrasonography and ICG angiography were performed. Total follow-up period ranged from 14 – 22 months (mean: 16 months).

Indocyanine green (ICG) angiography using a Heidelberg retina angiograph (Heidelberg Engineering, Heidelberg, Germany) was performed in all patients before treatment and 12 months after therapy. Then in 52 patients ICG angiography was performed at 18 months and in three – at 20-22 months of follow-up (these three patients missed their visit at 18 months of follow-up). A bolus of 25mg of ICG (ICG-Pulsion; Pulsion Medical Systems, Munich, Germany) dissolved in 5 ml of aqueous solvent was injected into the antecubital vein followed by a 5 ml aqueous solvent flush. ICG study was analysed according to the standard protocol used for intraocular tumours (4). The visibility of microcirculation patterns as well as their post-treatment changes were evaluated. Special care was taken to achieve visualization of deep microcirculation within the tumour by obtaining comparable confocal serial optical sections of the melanoma. Signs of MCPs within the tumour mass in the ICG angiography were compared to the angiograms obtained previously. At baseline examination, the tumour microcirculation was analysed and classified according to the criteria as published by Folberg et al. and Mueller et al. (10,13,14). The tumours were

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divided into two groups depending on the type of "Folberg patterns", known also as microcirculation patterns (MCPs): noncomplex MCPs, which included normal, silent (avascular), straight, parallel without cross-linking and arcs without branching patterns, and complex MCPs: parallel with cross-linking, arcs with branching, loops and networks.

The criteria of the evaluation of treatment efficacy included the decrease in thickness as measured by ultrasound of at least 30% and angiographic changes of MCPs which was categorized as thickening, thinning, obliteration and distortion of previously imaged vessels within the tumour borders as described by Schaller et al. (15). The persistence of unchanged MCPs after primary therapy was an indication to perform additional treatments.

The difference between the baseline types of MCPs and tumour ultrasonographic thickness and the values of follow-up were statistically analyzed using the Mann-Whitney test. Correlations between the type of performed treatment and the changes in MCPs were analyzed using the Fisher exact test. The Fisher exact test was also used to relate the type of baseline melanomas MCPs with the degree of their changes after plaque therapy.

A probability value of less than 0.05 was considered to be statistically significant for all statistical analysis.

Results

At the baseline examination, early frames of ICG angiography revealed various MCPs in all 55 tumours. Complex MCPs were seen in 23 (41.8%) melanomas and included: parallel with cross-linking in 18 (32.7%), arcs with branching in 20 (36.4%), loops in 18 (32.7%), and networks in 30 (54.5%). Noncomplex MCPs were present in 32 cases (58.2%) with the straight pattern in 22 (40%), parallel without cross-linking in 25 (45.5%), and arcs without branching in all of these 32 (58.2%) tumours. In five tumours with noncomplex MCPs large calibre vessels were observed.

Twelve months after treatment in 38 (69.1%) melanomas a variety of changes in the MCPs were observed. In 20 (36.4%) of them the total obliteration of MCPs was seen on ICG angiography (Fig. 1a, 1b). All of these melanomas had demonstrated complex MCPs at the baseline examination and their thickness ranged from 4.8-8.7 mm (mean: 6.8 mm). The treatment used in this group of tumours included: Ruthenium-106 in 2 cases, Ruthenium-106 with TTT in 12 cases and Iodine-125 in 6 patients. In this group of tumours the regression rate on ultrasonography ranged from 36.2-100% (mean: 59.5%).

In 18 cases (32.7%), thinning and/or distortion of the previously imaged MCPs was observed. This group contained 3 tumours with complex MCPs and 15 with non-complex MCPs. At the pre-treatment examination tumour thickness ranged from 4.2-8.0 mm (mean: 5.95 mm). The treatment methods used in this group of melanomas included: Ruthenium-106 in 6, Ruthenium-106 with TTT in 9, and Iodine-125 in 3 cases. The regression rate on ultrasonography ranged from 34.8-82.5% (mean: 52.7%).

In the remaining 17 cases (30.9 %) 12 months after therapy no changes in tumour MCPs were observed. All of these melanomas demonstrated noncomplex MCPs. The pre-treatment tumour thickness ranged from 5.1-8.0 mm (mean: 6.4 mm). After therapy (Ruthenium-106 in 3, Ruthenium-106 with TTT in 9, and Iodine-125 in 5 cases) the average reduction of tumour thickness in this group was only 27.2%.

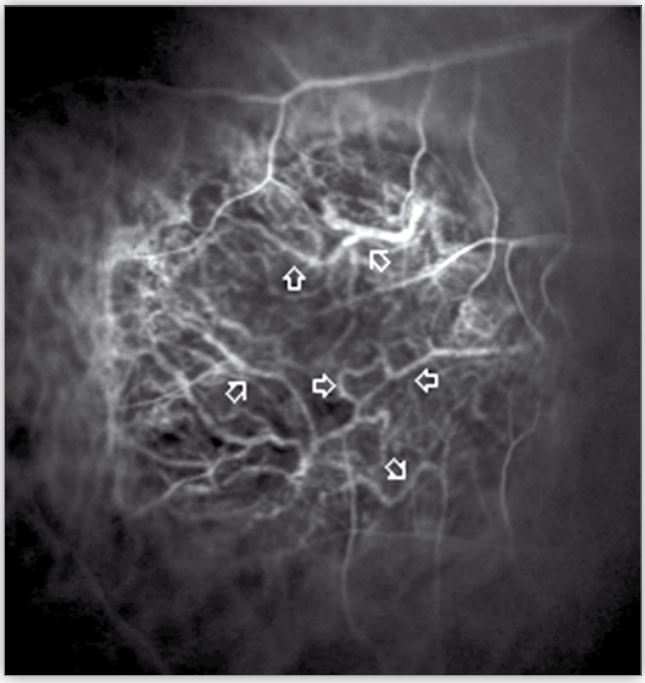

Fig. 1a. Indocyanine green angiography showing choroidal melanoma with complex microcirculation patterns; arcs with branching, loops, networks (arrows).

Ryc. 1a. Angiografia indocyjaninowa – obraz czerniaka naczyniówki ze złożonymi wzorami mikrokrążenia (widoczne łuki z odgałęzieniami, pętle, sieci naczyniowe – strzałki).

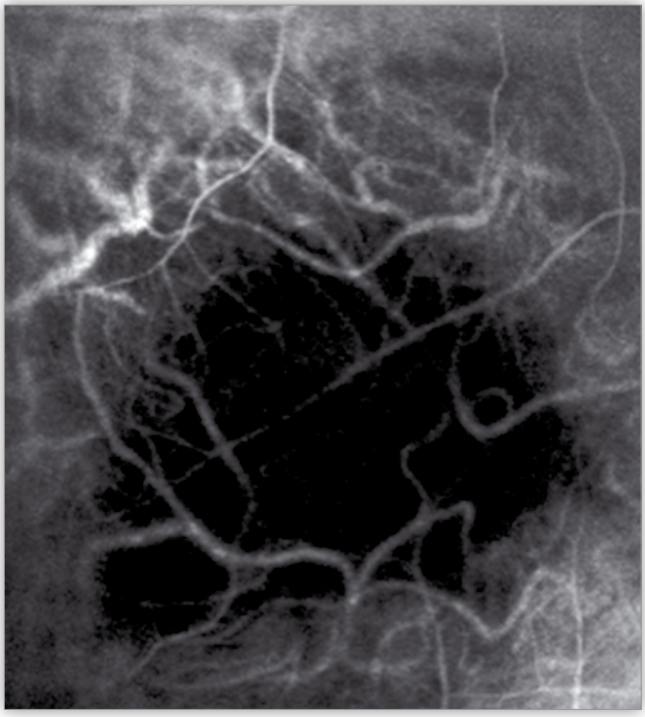

Fig. 1b. The same tumour 12 months after Ruthenium-106 plaque therapy demonstrating regression of microcirculation patterns on indocyanine green angiography.

Ryc. 1b. Ten sam guz 12 miesięcy po brachyterapii z zastosowaniem płytki rutenowej (106 Ru) z regresją mikrokrążenia widoczną w badaniu angiografii indocyjaninowej.

The mean regression rates on ultrasonography in tumours with complex MCPs and noncomplex MCPs were 57.4% and 36.2%, respectively. A statistically significant association was identified between the echographic tumours regression rates and the various MCPs: parallel with cross-linking ($p = 0.001$), arcs with branching, loops and networks (for all $p<0.001$), straight, parallel without cross-linking and arcs without branching (for each $p = 0.01$). There was no difference between the tumour regression rate as measured on ultrasonography and performed treatment but we found a significant correlation between the type of therapy and the degree of MCPs changes. Twelve months after primary therapy, 18 melanomas treated with "sandwich method" demonstrated slight or no changes in MCPs, while tumours treated with Ruthenium-106 and Iodine-125 showed a significant MCPs changes ($p<0.001$). A significant correlation was found between the baseline types of MCPs and the degree of MCPs changes after treatment; the tumours with networks, loops, arcs with branching and parallel with cross-linking showed a significant MCPs changes (all $p<0.001$) as well as the tumours with arcs without branching ($p = 0.01$) as compared to other MCPs: straight and parallel without cross-linking (for both $p = 0.1$).

In our study the persistence of unchanged microcirculation after primary therapy was an indication to perform additional treatments in 17 cases: with Ruthenium-106 in 3, with Ruthenium-106 plus TTT in 2, and TTT alone in 12 cases (Fig. 2a, b, c).

Control ICG angiography, performed 6-10 months after the re-treatment, demonstrated a subsequent obliteration in 7 cases and thinning and/or distortion of persistent MCPs in 10 tumours. In all of these melanomas we found a significant ultrasonographic decrease in height which ranged from 35-78.5% (mean regression rate – 51.3%).

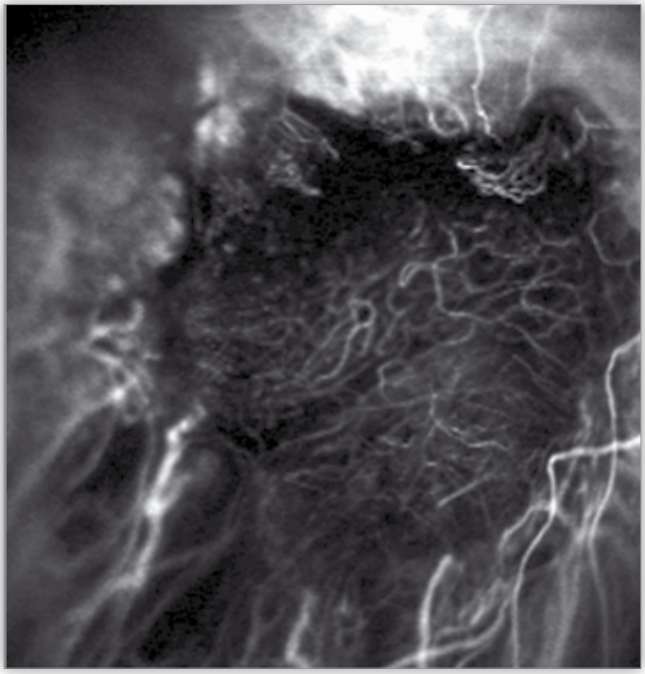

Fig. 2a. Indocyanine green angiography showing choroidal melanoma with complex microcirculation patterns; arcs with branching, loops, networks presented mainly in the central zone of the lesion.

Ryc. 2a. Angiografia indocyjaninowa – obraz czerniaka naczyniówki ze złożonymi wzorami mikrokrążenia (widoczne głównie w centralnej części guza łuki z odgałęzieniami, pętle, sieci naczyniowe).

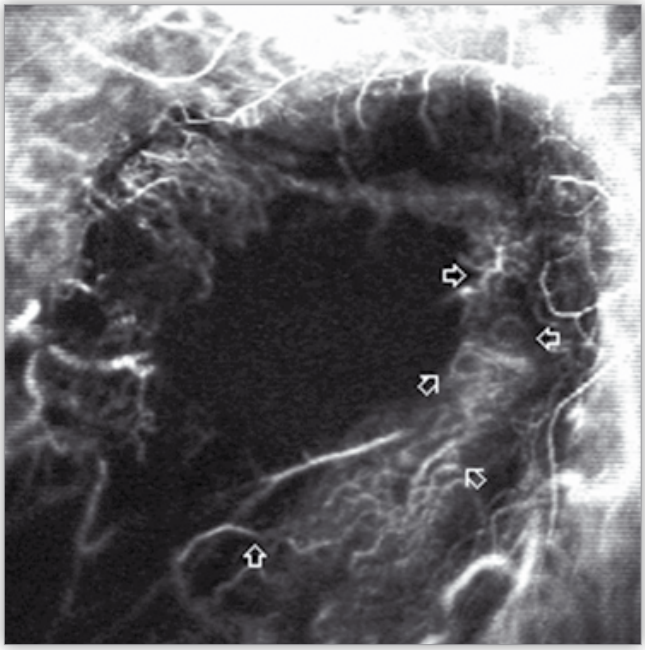

Fig. 2b. The same tumour 8 months after Ruthenium-106 plaque therapy presenting partial regression of microcirculation patterns on indocyanine green angiography; the pathological vessels are still present at the margins of the lesion (arrows).

Ryc. 2b. Ten sam guz 8 miesięcy po brachyterapii z zastosowaniem płytki rutenowej (106 Ru) – widoczna w badaniu angiografii indocyjaninowej regresja mikrokrążenia, patologiczne naczynia widoczne jedynie w obwodowej części guza (strzałki).

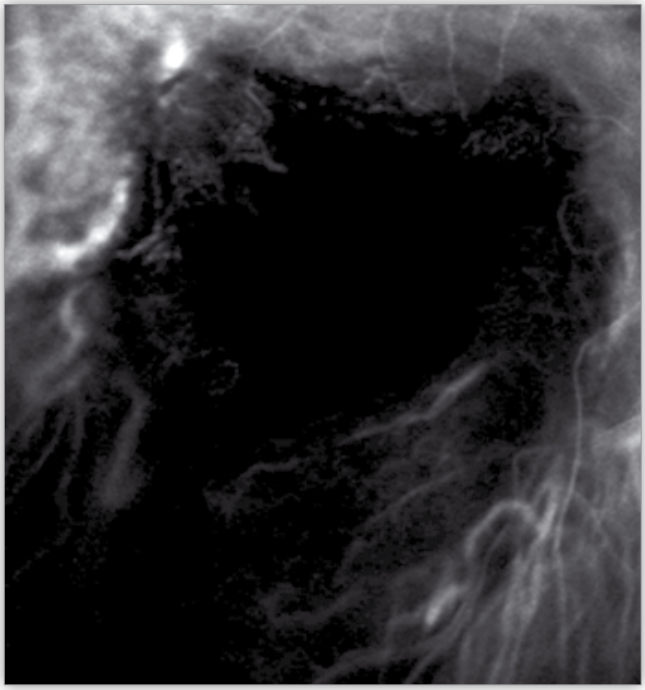

Fig. 2c. The same tumour six months after the "sandwich method" (TTT + 106 Ru) was applied showing total regression of the microcirculation.

Ryc. 2c. Ten sam guz 6 miesięcy po leczeniu „metodą kanapki" (TTT + 106 Ru) – całkowita regresja patologicznego unaczynienia.

In the remaining group of 38 melanomas that had demonstrated MCPs and ultrasonographic changes at 12 months after therapy, further follow-up examinations revealed subsequent

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MCPs on ICGA angiography/ Wzory mikrokrążenia w ICGA	No. of tumours (%)/ Liczba guzów (%)	Average ultrasonographic regression rate (%)/ (p value)/ Średnia wartość regresji guza w USG (%) (wartość p)	Percentage of tumours with MCPs obliteration/ (p value)/ Odsetek guzów z zamknięciem MCPs (wartość p)
Straight/ Proste naczynia	22 (40%)	51.2% (p = 0.01)	43.3% (p = 0.1)
Parallel without cross-linking/ Równoległe naczynia bez poprzecznych połączeń	25 (45.4%)	48.6% (p = 0.01)	53% (p = 0.1)
Arcs without branching/ Łuki naczyniowe bez odgałęzień	32 (58.2%)	52.1% (p = 0.01)	67.5% (p = 0.01)
Parallel with cross-linking/ Równoległe naczyniowe z poprzecznymi połączeniami	18 (32.7%)	68.3% (p = 0.001)	83.3% (p<0.001)
Arcs with branching/ Łuki naczyniowe z odgałęzieniami	20 (36.4%)	73.2% (p<0.001)	85% (p<0.001)
Loops/ Pętle naczyniowe	18 (32.7%)	88.6% (p<0.001)	88.9% (p<0.001)
Networks/ Sieci naczyniowe	30 (54.5%)	83.9% (p<0.001)	85.6% (p<0.001)

Tab. I. Correlations between the baseline tumour microcirculation patterns (MCPs) and the average ultrasonographic regression rates and the percentage of tumours with MCPs obliteration at the end of follow-up.

Tab. I. Zależności zachodzące między wyjściowymi wzorami mikrokrążenia guza (MCPs) a średnią wartością regresji guza w badaniu ultrasonograficznym i odsetkiem guzów z regresją MCPs pod koniec okresu obserwacji.

tumour regression in all cases. While obliteration of MCPs was already present in 20 cases at 12 months, it was now seen in 29 cases. Nine tumours demonstrated thinning of MCPs. The tumours appeared as flat or mild elevated lesions on ultrasonography (tumour thickness: 0-2.2 mm; mean – 1.45 mm).

Correlations between the baseline tumour MCPs and the average ultrasonographic regression rates and the percentage of tumours with MCPs obliteration at the end of follow-up are shown in Table I.

During follow-up, metastatic disease (liver and lungs metastases) was diagnosed in 12 cases (21.8%). The tumours of all of these patients had demonstrated complex MCPs (parallel with cross-linking, arcs with branching, loops and networks patterns) on ICG angiography and the melanomas thickness had ranged from 6.2-8.7 mm at the baseline. The tumours of the patients that did not develop metastases had shown complex MCPs in 11 (20%) of the remaining 43 cases.

Discussion

Histopathologically recognized extracellular matrix patterns may play an important role in the biological behaviour of choroidal melanomas (10,16). ICG angiography can be capable of detecting microvasculature patterns of choroidal tumours *in vivo* which show similar patterns and thus, can be a novel clinical predictor of tumour growth and metastatic disease (14,15). ICG angiography can also provide information about tumour microcirculation changes after plaque therapy *in vivo*. However, there is scant information regarding the use of ICG angiography, as there are only a few studies focusing on the use of ICG angiography in the follow-up of choroidal melanomas treated with Ruthenium-106 and Iodine-125 plaques (15,17-19). Amoaku et al. (17) studied the changes of choroidal vasculature in the irradiated peritumoural zone in eyes treated with Ruthenium-106. In this study the authors analyzed the development of radiation choroidopathy, indicating that peritumoural vascular malformations were different in morphology from those within the tumour. Sallet et al. (18) studied tumour microcirculation before and after Ruthenium-106 plaque therapy, indicating that an optimal radiation effect is almost complete with vascular occlusion after only 4 to 6 months. Persistence of the original abnormal intratumoural vessels at 6 months or more after radiotherapy could possibly be a sign of a residual tumour activity, even in spite of a successful clinical and ultrasonographical response to the treatment (18). There are also reports demonstrating that persistent microcirculation may be a sign of bad prognosis for tumour regrowth and metastatic disease (15). It has been documented in literature by Schaller and Sallet that the presence of microcirculation-related patterns: the normal and the parallel without cross-linking are correlated with a favourable prognosis, whereas networks, loops, arcs with branching and the parallel with cross-linking patterns are correlated with high proliferation indices as well as with a high regression of tumour thickness after treatment (15,18). It is noteworthy that melanomas which are shown to be still active on ICG angiography can demonstrate regression on ultrasonography (15,18). An explanation may be that ICG angiography can reveal very early signs of residual tumour activity or tumour regrowth even before it is detectable clinically or on ultrasonography (15,18). According to the findings reported by Bujara et al. (19), Schaller et al. (15) and Sallet et al. (18), the changes in the ultrasonographic dimensions may not necessarily reflect the degree of residual tumour activity. This observation was confirmed in 9 of our patients (16.4%); twelve months after therapy these patients presented a significant decrease of lesion thickness on ultrasonography, while they demonstrated no significant changes in tumour MCPs. Schaller et al. (15) reported the same findings in 3 patients (23%) with choroidal melanomas treated with Ruthenium-106 and Iodine-125 plaques, who showed no changes

of the microcirculation despite a documented tumour regression on ultrasonography.

Schaller et al. (15) presented various types of tumour microcirculation changes after plaque therapy; obliteration, distortion, thinning and thickening. We observed the first three types of these changes, but did not see any thickening, which may have been due to the short time of follow-up in our group of patients. Amoaku et al. (17) observed telangiectasis of the persistent microcirculation on ICG angiography 30-72 months after plaque therapy.

In our group of 17 cases who demonstrated no vascular changes 12 months after primary treatment we decided to use the results of ICG angiography as the main indication for re-treatment. Based on observation of Sallet et al. (18) and Amoaku et al. (17) that the earliest vascular changes are detected between 4 to 6 months after plaque therapy, we decided upon additional therapy in these "non-responding" group of uveal melanomas.

The results of our study show that the type of response to treatment was related to the baseline tumour microcirculation pattern. Generally, we observed a higher diminution of tumour thickness in cases with complex MCPs than in tumours with non-complex MCPs ($p = 0.01$). The same observations were presented by Schaller et al. (20).

The presence of networks on ICG angiography are indicative of a higher regression rate as measured on ultrasonography after plaque therapy. Highly proliferative tumours with the presence of networks are known to be more sensitive to irradiation (20).

In our group of patients, MCPs changes were correlated to the method of treatment. Stoffelns (21) published that in 75% of choroidal melanomas after TTT in the heat-treated areas, tumour microcirculation can still be perfused. In these cases, ICG angiography results suggest that damage of the tumour microcirculation might be less effective and may lead to a higher rate of tumour regrowth (21). In our group of patients, the "sandwich method" was used in 30 cases and in 60% of them no significant regression of microcirculation was noted 12 months after therapy.

It has been documented that tumours with a rapid post-irradiation regression and with complex MCPs are the more aggressive ones with regard to later development of metastases (22). In our group of patients, a systemic metastatic disease was found in 12 cases (21.8%); all of these melanomas demonstrated complex MCPs and the tumour thickness ranged from 6.2 to 8.7 mm at the baseline examination. After primary therapy all of these tumours showed a significant diminution on ultrasonography (mean: 62.4%.). To assess a risk of a systemic metastatic disease the longer time of follow-up is needed.

Conclusions

Our observations suggest that ICG angiography can be helpful in monitoring choroidal melanomas after plaque therapy. The results of our study have shown that the presence of complex MCPs in confocal ICG angiography is associated with a high ultrasonographic regression rate of choroidal melanoma after irradiation. The persistent MCPs could be a pointer of residual tumour activity in spite of ultrasonographic regression.

We will extend our group of patients and continue our study over time to document further observations.

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