SUMMARY

Background:
The aim of this article was an evaluation of the Health Related Quality of Life (HRQL) of a patient with Takayasu’s arteritis complications before and after endovascular treatment. I would have hypothesized that there would be a good response to this treatment in the reduction of stroke symptoms, that is right side paresis and mild aphasia and therefore patients’ quality of life.

Case study:
A 19-year-old female patient developed, at the age of 17, a left hemisphere stroke, right side paresis and mild aphasia. On examination, she was diagnosed as having Takayasu’s Arteritis (TA). MR-Angiography showed severe stenosis of the left common carotid artery (LCCA) at the site of origin, the left subclavian artery (LSA), the brachiocephalic artery (BCA), and a minimal narrowing of the left vertebral artery (LVA) at the site of the origin of LSA. The angioplasty of LSA with stent implanting was done with slight neurological improvement. Two years later she had another stroke caused by restenosis of the LSA with right side paresis, mild aphasia. Another angioplasty of LSA with stent implanting was carried out. The neurological symptoms diminished, which was connected with an improvement in her quality of life.

As hypothesized, there was a good response to both revascularization procedures, which was connected with the reduction of stroke symptoms (right side paresis and mild aphasia) and subsequently, the patient’s quality of life.

Key words: vasculitis, hemiparesis, aphasia, extracranial revascularization
INTRODUCTION

Takayasu’s arteritis (TA) also known as "aortic arch syndrome", "nonspecific aortoarteritis" and the "pulseless disease", [James et al. 2006] is a form of large vessel granulomatous vasculitis [Perera et al. 2013] with massive intimal fibrosis and vascular narrowing. [Kazibudzki et al 2016]

Rokushu Yamamoto from Japan, published the first description of arteritis in 1830, later called Takayasu’s arteritis, following the first scientific presentation of this illness in 1905 by Mikito Takayasu, Professor of Ophthalmology at the Annual Meeting of the Japan Ophthalmology Society. [Kakuta 1996] Takayasu described a peculiar "wreathlike" appearance of the blood vessels in the retina. A similar pathology was described also by two other Japanese physicians (Onishi and Kagoshima), which was coexisted in individuals whose wrist pulses were absent. Nowadays we know that the blood vessel malformations in the retina are an angiogenic response to the carotid narrowings and that the absence of the pulse is connected with the narrowing of the subclavian arteries. The eye findings described by Takayasu’s are rarely seen in patients from North America, British Columbia and in Poland (Kerr et al. 1994; Karageorgaki et al. 2009; Park et al 2005; Kazibudzki et al. 2016).

The Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitis defined TA as “granulomatous inflammation of the aorta and its major branches.” [Nastri et al 2004] It is an uncommon disease with a clinical heterogeneity across different ethnic groups. Females are about 8–9 times more likely to be affected than males but we can find description of this disease in men. Takayasu’s disease has been reported in all parts of the world, although it appears to be more prevalent in young or middle-aged Asians. [Karageorgaki et al. 2009; Shivanand et al. 2014]

Takayasu’s disease frequently affects the aorta and its branches, as well as the pulmonary arteries. It is similar to other forms of vasculitis, including giant cell arteritis which typically affects older individuals. [Perera et al. 2013] Manfrini et al. (2006) reported severe stenosis of the left common carotid artery, the left subclavian artery, the right brachiocephalic artery (BCA). Hotchi et al (1992), found in his group of patients that the most commonly affected branches are the subclavian artery and the common carotid artery.

Due to obstruction of the main branches of the aorta, including the LCCA, the BCA and the LSA, Takayasu’s arteritis can be manifested as a weakness of arms, hands, and wrists with weak or absent pulses. [Ishikawa K, Maetani 1994; Kerr et al 1994] The involvement of renal arteries may lead to renovascular hypertension. Takayasu’s arteritis can manifest itself as an isolated, atypical, and/or catastrophic disease. It can involve any or all of the major organ systems. [Quartuccio et al 2014]

The angiographic classification of Takayasu’s Arteritis based on the localization of angiographic involvement (see: Table 1) divides this illness into the 6 following types [Moriwaki et al 1997].
The most common however are the type I, IIa and IIb.

It is worth pointing out that Takayasu’s disorder can be classified not only into the five types presented in Table 1 on the basis of angiographic findings but also clinically into four groups on the basis of complications. Ishikawa defined the four most important complications of TA as being retinopathy, secondary hypertension, aortic regurgitation, and aneurysm formation, each graded as mild, moderate, or severe. [Ishikawa 1978]

From the histopathological point of view, in TA we can find the adventitial thickening, focal lymphocytic infiltration of the tunica media degeneration presents as aneurysmal dilatation. [Perera et al. 2013]

Clinical symptoms arise from systemic inflammation and local vascular complications [Kazibudzki et al. 2016]. The neurological manifestation of the disease includes headaches, dizziness, visual disturbances, transient ischemic attacks (TIA), and strokes [Quartuccio et al. 2012].

The etiology of Takayasu’s arteritis remains poorly understood, but genetic contribution to the disease pathogenesis is supported by the genetic association with HLA-B*52. [Saruhan-Direskeneli et al. 2013] genotyped ~200,000 genetic variants in two ethnically divergent Takayasu’s arteritis cohorts from Turkey and North America by using a custom-designed genotyping platform (Immunochip). Additional genetic variants and the classical HLA alleles were imputed and analyzed. The authors identified and confirmed two independent susceptibility loci within the HLA region (r(2) < 0.2): HLA-B/MICA (rs12524487, OR = 3.29, p = 5.57 × 10(-16)) and HLA-DQB1/HLA-DRB1 (rs113452171, OR = 2.34, p = 3.74 × 10(-9); and rs189754752, OR = 2.47, p = 4.22 × 10(-9)). In addition, there was found and confirmed a genetic association between Takayasu arteritis and the FCGR2A/FCGR3A locus on chromosome 1 (rs10919543, OR = 1.81, p = 5.89 × 10(-12)). The risk allele in this locus results in increased mRNA expression of FCGR2A. The genetic association between IL12B and Takayasu arteritis (rs56167332, OR = 1.54, p = 2.18 × 10(-8)) was also established.

Arterial inflammation leads to stenotic or occlusive arterial lesions, predisposing to symptomatic endorgan ischemia. Less commonly, more acute inflammation leads to medial degeneration in the arterial wall resulting in aneurysmal dilatation [Numano & Kobayashi, 1999].

In the world subject literature we can find many descriptions of TA complications. One of the most comprehensive lists of complications of Takayasu’s arteritis was compiled by Park et al. 2005. It includes the following:

<table>
<thead>
<tr>
<th>Type</th>
<th>Localization of angiographic involvement</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Branches of the aortic arch</td>
</tr>
<tr>
<td>IIa</td>
<td>Ascending aorta, aortic arch, and its branches</td>
</tr>
<tr>
<td>IIb</td>
<td>Type IIa region + thoracic descending aorta</td>
</tr>
<tr>
<td>III</td>
<td>Thoracic descending aorta, abdominal aorta, renal arteries, or a combination</td>
</tr>
<tr>
<td>IV</td>
<td>Abdominal aorta, renal arteries, or both</td>
</tr>
<tr>
<td>V</td>
<td>Entire aorta and its branch</td>
</tr>
</tbody>
</table>
1. Congestive heart failure due to aortic insufficiency, myocarditis, and/or hypertension
2. Aortic aneurysms, thrombus formation, and rupture
3. Ischemic stroke
4. Myocardial infarction
5. Hypertension
6. Clinically silent progressive disease (despite normal acute phase reactants)
7. Morbidity resulting from treatment medications – this must be considered in planning long-term treatment

The pharmacological treatment used is not always promising, especially in advanced cases. Most people with Takayasu's arteritis respond to steroids such as prednisone. However, long-term high–dose prednisone use might produce significant side effects. [Maksimowicz-McKinnon et al 2007] Mycophenolate, tocilizumab and infliximab are thought to be promising in the reduction of the inflammation process and the reduction of the symptoms. [Salvarani et al 2012] If treatment is not kept to a high standard then long term damage or death can occur. [12] Stress is a major factor that should be avoided at all costs; if this is not taken into account the surge of adrenaline can have a damaging effect on the heart. [Phillip & Luqmani 2008]

If the patient does not respond to steroids treatment surgical options (large vessel reconstructive surgery such as bypass grafting or autologous tissue grafting) may be necessary. [Kim & Kim 2012] Tissue re-perfusion can be achieved, however the results might only be temporary. [Perera et al 2013] The development of endovascular technologies has brought new possibilities, which have led in some cases to spectacular results – improving patients’ health and therefore quality of life. [Quartuccio et al. 2012] Stenting often, unfortunately, needs open surgery, which is much more aggressive. [Qureshi et al 2011] Even though, in the case of complications (tissue ischemia, strokes) we have to decide which method of revascularization should be chosen.

The better option, in the beginning, should be endovascular procedures (balloon angioplasty with or without stents, both plain or coated by antiproliferative drugs), which is less invasive. [Byrne et al. 2014] However, in some cases, restenosis occurs and neurological complications urge us to save the patients’ life using open surgery procedures. [Andrews & Mason 2007; Perera et al 2013].

In a MEDLINE search for the years 2000-2016, there are no articles dealing with the problem of the impact of endovascular surgery on Health Related Quality of Life (HRQOL). There are only a few articles devoted to the impact of pharmacological treatment in patients suffering from Takayasu's arteritis (TA) in relation to the quality of life [Perera et al 2013; Quartuccio et al 2012]. Therefore, the aim of this article was to fill this gap and to evaluate the Health Related Quality of Life (HRQL) of a patient with Takayasu's arteritis complications before and after endovascular treatment.
A 19-year-old female patient developed at the age of 13 (2010), a Langerhans cells histocytosis with the symptoms of strong back and neck pain, complicated by a compressive fracture of the third cervical vertebra (C3). There was no history of a fall or of head injury. She underwent 4-month chemotherapy and finally in August 2010 the symptoms were resolved and she was told she had completely recovered. A few months later she developed severe bone pain, a high temperature, bleeding from the nose, weakness and fainting. She was diagnosed at the Hematology Ward of the Pediatric Institute, Cracow, and later diagnosed and treated at the Rheumatology Clinic. At that time a differential diagnosis was made in relation to the chronic recurrent multifocal osteomyelitis (CRMO).

The next deterioration occurred in autumn 2011. She developed upper and lower intestinal tract bleeding with a loss of weight, weakness and nocturnal sweating. She was diagnosed with Crohn syndrome at the Gastrology Ward of the Pediatric Institute, Cracow. After a few months of steroids and Mesalazine treatment, she developed anemia with fainting. In January 2012, she was admitted to the Cardiology Ward of the Pediatric Institute, Cracow. She was diagnosed with pericarditis and stenosis of the pulmonary trunk. After standard treatment (pericardial sac puncture, antibiotics) and additional steroids, her condition improved.

In August 2013, at the age of 17, she developed vision problem (she saw white spots) and a deficit in the left radial artery pulse. After a few days she had a severe ischemic stroke of the left brain hemisphere with two weeks of unconsciousness, right hemiparesis and aphasia. She was admitted to the Neurological Ward, St. Lucas Hospital in Tarnow.

The Angio-CT examination of the thoracic aorta and its branches revealed a widening of the ascending aorta wall, arch, BCA, LCCA and LSA with the blurring of their contour and occlusion of LCCA and a 4-cm segment of LSA. These findings suggest arteritis and Takayasu's arteritis was finally diagnosed.

Fig. 1. Angio-CT of the aortic arch branches; the LCCA and LSA are occluded (a); clearly visible thickening of the aortic and BCT walls (b)
At the same time a brain MR was conducted, which revealed the results of the LCCA and LICA occlusion due to Takayasu’s arteritis (see: Fig. 2, 3, 4). In the T2 sequence, coronal, sagittal and axial planes it shows a hyperintensive porencephalic lesion in the left temporal lobe (insula and operculum) and frontal lobe (operculum) with a widening of the left ventricle (tissue retraction) – post infarction in the region of the left medial cerebral artery supply; very small left carotid artery, absent left anterior and medial cerebral artery (present on the opposite side).

At the beginning of December 2013 our patient was admitted to the Clinical Ward of the Heart and Vascular Diseases, the John Paul II Hospital, Cracow. The neurological state was stabilized and the patient underwent revascularization procedure – LSA angioplasty with stent implanting (Nefro) which resolved the steal syndrome (Fig. 5).

In June 2014 a steal syndrome of LSA appeared again. She was admitted at the end of October 2014 to the Pediatric Neuroinfection and Neurology Department, the John Paul II Hospital, Cracow. In Angio-CT, in-stent critical restenosis was found. The Drug Coated Balloon (DCB) angioplasty of the LSA was carried out (ADMIRAL, paklitaksel) with good results (Fig. 6).

The next clinical syndrome of restenosis appeared at the beginning of 2015. She was admitted once again in June 2015 to the Clinical Ward of the Heart and
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Fig. 3. Brain MRI, FLAIR T2 sequence, axial planes: hypointensive porencephalic lesion with hyperintensive gliotic rim in the left temporal lobe (insula and operculum) and frontal lobe (operculum) with a widening of the left ventricle (tissue retraction) – post infarction in the region of the left medial cerebral artery supply.

Fig. 4. Brain MRI, 3DTOF angiography sequence, MIP reconstructions in the axial and coronal plane. No blood flow signal in the left carotid artery, discrete signal of blood flow in the M1 portion of the left medial cerebral artery (inflammation of the arteries with thrombus?), stronger flow signal in the left posterior communicating artery.
Vascular Diseases, the John Paul II Hospital, Cracow. A procedure of the Drug Coated Balloon (DCB) angioplasty of the LSA was carried out (Biopath, coated with Paclitaxel) with a pleasing result (Fig 7).

Fig. 5. LSA angioplasty with stent implanting (Nefro). Following stages; (a) initial LSA angiography; (b) balloon predilatation; (c) stent placing; (d) final angiography

Fig. 6. LSA with in-stent restenosis: Initial angiography (a); the Drug Coated Balloon (DCB) angioplasty of LSA (ADMIRAL, paclitaxel) (b); final angiography (c)
At the beginning of 2016 the symptoms of LSA restenosis appeared once again. She was admitted in March 2016 to the Department of Vascular Surgery and Endovascular Interventions, the John Paul II Hospital, Cracow. Angioplasty of the LSA with implantation of the self-expanding Drug Eluting Stent (Stentys 3.5-4.5x22mm, covered with Paclitaxel) with balloon post-dilatation (NC Quantum 5x20mm, 14-18Atm) was carried out with good clinical results (Fig. 8).

After this (last) procedure the Steal Syndrome disappeared and the patient was discharged from the Hospital with no symptoms. She took part in a comprehensive rehabilitation program for stroke patients (Physiotherapy, speech ther-
apy, neuropsychological rehabilitation with neurofeedback). Her quality of life, as she put it, was improved.

DISCUSSION

Diagnosis of Takayasu Disease is not easy and patients are often misdiagnosed or diagnosis is delayed. The main reason for this is connected with the coexistence of other auto-immunological diseases. This state led to a considerable delay in the diagnosis of our patient, as in another described case of TA, which may partially reflect a failure to recognize a rare disease (Nastri et al. 2014).

Perera et al. 2013 found out that delays in diagnosis might be caused by a lack of awareness about the condition of the illness, due to its rarity, varied presentation, and also the suboptimal methods for assessing disease activity. Nevertheless, Takayasu's arteritis is considered to be a rare, though not infrequent disease as described by Asan et al. (2015), who reported five cases seen over a four year period.

It is worth noting that early diagnosis and treatment of Takayasu's arteritis is necessary to prevent serious complications. One of the most important tools is spin-echo magnetic resonance imaging (MRI). This can depict the early wall thickening of the aorta and significant enhancement in and around the aorta and carotid arteries, which is observed on postcontrast MR images in the acute phase of Takayasu arteritis. In the chronic phase, any contrast enhancement in the aortic wall that is stronger than in the myocardium suggests the activity of the disease. Breath-hold contrast-enhanced three-dimensional MR angiography is very effective in a noninvasive evaluation of the luminal change of the aortitis. Contrast-enhanced MRI and MR angiography play an important role not only in early diagnosis and activity determination but also in the follow-up of Takayasu arteritis.

In clinical practice, this diagnostics tool is not frequently ordered because of the cost and therefore is used only in clear cut indications. It is not used for screening in the case of a lack of TA symptoms, as was the case with our patient. Nevertheless, a lack of the pulse in one or two upper extremities should be more than enough to have the patient sent off for an Angio-MRI examination.

The course of TA has two phases: the initial "inflammatory phase" following by a secondary "pulseless phase". In our patient, we did not observed any of those phases. The patient developed a lack of the pulse in the left upper extremity only a few days before the stroke, so there was no time to conduct an Angio-MRI examination. This constituted the last moment for TA diagnosis, even though we do not know if we could have prevented her from the stroke.

It should be noted, however, that in her history of illness, there was such a time of an increasing of the inflammatory state (probably one to two years earlier).

She developed pericarditis and stenosis of the pulmonary trunk, Crohn Disease and Non-bacterial Multifocal Osteomyelitis, which were concomitant with TA. Retrospectively, it is hard to establish the moment for the beginning of the ‘inflammatory phase,’ because some symptoms of this diseases are similar to TA.
There was also a problem with the diagnosis of the secondary ‘pulseless phase’. Only the onset of the stroke directed her diagnosis, because in a 17-year-old woman we do not observe arteriosclerosis and very rarely arrhythmia. After the stroke, following angio-CT examination, she was finally diagnosed as having Takayasu’s Arteritis.

When the diagnosis of TA was established she was immediately send for revascularization treatment. Occlusion of the LCCA and LICA and the severity of the brain damage excluded the possibility of brain revascularization as it is suggested by Fields et al. (2006).

Some researchers have noted that open surgical treatment remains superior to endovascular intervention in the treatment of TA lesions [Saadoun et al 2012; Fields et al 2006; Min et al 2005]. However, the recent results of endovascular procedures are very encouraging, so we could use it in our patient and reduce the ‘Steal Syndrome’.

Angioplasty of the LSA stenosis was carried out three times. For the first time we used the nitinol stent, for the second the Drug Coated Balloon (DCB) angioplasty and for the third time angioplasty with implanting Drug Eluting Stent (DES) with an antimitotic drug. All procedures were successful and she recovered, however, TA is a fatal illness and has a progressive course. It is important, therefore, to inform the patient about the nature of this disease, the need to take medications and to be systematically diagnosed, to prevent further complications.

It is important to provide individual, patient-orientated, rehabilitation with a team of specialists (physiotherapists, neuropsychologists, logopedists, neurofeedback trainers). Only in such conditions we can improve the Health Related Quality of Life (HRQL) of patients with TA (see also: Pachalska 2008; Pachalska, Kaczmarek, Kropotov 2014).

**CONCLUSIONS**

As hypothesized, there was a good response to all revascularization procedures, which was connected with the reduction of the stroke symptoms (right side paresis and mild aphasia) and subsequently, the patient’s quality of life.

**REFERENCES**


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