Connections between renovascular hypertension and nephrectomy

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Abstract
Renovascular hypertension (RVH) is very often an under-diagnosed condition, being discovered incidentally, at a routine medical check-up or during a medical examination for another disease. A number of 217 biological samples (kidney and renal pelvis) resulting from the nephrectomies performed during the period 2008–2009 in the Urology Clinic of Oradea County Hospital have been taken into study. These samples were processed in the Pathology Laboratory of the same hospital. The distribution of nephrectomies according to the urological diagnosis has shown that 38.2% of the patients underwent surgical procedure for renal parenchymal malignant tumor (Grawitz tumor). Out of the 83 nephrectomies caused by renal tumor, in eight cases, benign and malignant angiosclerosis histological changes were seen, which demonstrates a long evolution of hypertension. Its clinical symptoms were masked by those triggered by the tumor. Histopathological changes of benign nephroangiosclerosis with arteriolar vasospasm associated with edema of the wall and/or hypertrophy of the intima with the formation of hyaline deposits were found in three nephrectomies due to hydrenephrosis. The pathological study carried on samples obtained from nephrectomies showed that the symptoms of RVH are hidden or accompanied by clinical manifestations of a surgical disease. The percentage of 8.0% of the patients that had histopathologic changes or malignant of benign nephroangiosclerosis and suffered nephrectomies for a surgical disease is quite small compared to the large number of nephrectomies. It is imperative to identify in due time the secondary mechanism of hypertension in order to perform the surgical intervention which saves the kidney or prevents the extension to other organs. Although no special investigations were performed showing a possible preoperative RVH, it can be stated that the renal origin of the arterial hypertension can be established retrospectively, after nephrectomy. The monitoring of blood pressure values during several years is extremely important for establishing the etiology of renal hypertension.

Keywords: renovascular hypertension, nephrectomy.

Introduction
The term RVH, highlighting a particular form of arterial hypertension, has grown steadily, especially in the last decades, because it refers to the arterial hypertension caused by the decrease of renal irrigation by a local mechanism. It has clinical characteristics, which set it apart from the big group of essential hypertension. RVH is that type of hypertension caused by the partial or total unilateral or bilateral stenosis of the renal artery, which is potentially curable by surgical intervention (vascular reconstruction surgery or nephrectomy). A part of the hypertensions considered as essential are actually secondary to well-defined, most of the times renal injuries; the kidney can become a victim or a cause of hypertension. The timely detection of the secondary mechanism of arterial hypertension is required for the surgery that saves the kidney or prevents the elevation of pressure values. It is true that the number of RVH cases is relatively low, in comparison with the alarming high frequency of essential hypertensions, but their interest resides in the fact that they are curable, a fact which gives them a special status [1, 2]. RVH is frequently an under-diagnosed condition, being discovered incidentally, at a routine medical check-up or during a medical examination for another disease, because many of the patients do not know that they are hypertensive [3, 4].

Nephrectomy is always executed in diffuse parenchymal lesions which have irreversibly compromised the renal parenchyma: unilateral chronic pyelonephritis, renal tumor, hydrenephrosis, etc. Simple nephrectomy performed in extracapsular manner is recommended in some renal artery lesions such as: large obstructive lesions, muscular hyperplasia with lesions that have spread on the branches of the main trunk of the vessel but also in the malformed, hyperplastic or ectopic kidney [5].

Materials and Methods
A number of 217 biological samples (kidney and renal pelvis) resulting from nephrectomies performed during the period 2008–2009 in the Urology Clinic of Oradea County Hospital have been taken into study. These samples were processed in the Pathology Laboratory of the same hospital. We would like to state the fact that the nephrectomized patients underwent the surgery for a urological problem and not for the treatment of a possible secondary arterial hypertension of renal cause.

The study consisted of macroscopic examination of the removed kidneys and the microscopic examination of biological samples. In order to detect microscopic structures, for the achievement of good quality histological samples, we decided that the collection should
be made with extreme caution. Thus, the tissue samples were collected by trained personnel required for such operations (urologist and pathologist) and with the appropriate tools to eliminate brutal tractions, excessive compression or laceration that would change the histological architecture of the biological material. The sampling of the biological material for the microscopy was performed in the Pathology Laboratory of Oradea County Hospital. It was an essential step for the histological and pathological study. A suitable microclimate (light, ventilation, water source) was provided for a good sampling.

After studying the external configuration, we prepared the renal vessels as deep as possible in renal sinus. We divided the kidney into two halves connected at the medial edge through a section from the convex to the concave edge. The interior portion of the renal pelvis was highlighted by cutting the hind lip of the surface of the kidney; the major calyx was prepared. Tissue containing kidney parenchyma, renal pelvis and calyces and blood vessels was harvested.

The microscopic study was performed by sectioning with 4–8 microns thick sections, depending on the analyzed structure. The staining was made with Hematoxylin, but special stains were also used; the staining and the evaluation of the histological samples were conducted in the Pathology Laboratory of Oradea County Hospital.

Results

The biological samples resulted from the nephrectomies from 98 male individuals (45.2%) and 119 females (54.8%), with a female/male ratio of 1.2 to 1. A statistical correlation was not found (Table 1).

Table 1 – Distribution of nephrectomies according to the age of the nephrectomised subjects

<table>
<thead>
<tr>
<th>Age [years]</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>30–40</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>40–50</td>
<td>11</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>50–60</td>
<td>26</td>
<td>26</td>
<td>52</td>
</tr>
<tr>
<td>60–70</td>
<td>31</td>
<td>31</td>
<td>62</td>
</tr>
<tr>
<td>&gt;70</td>
<td>22</td>
<td>22</td>
<td>44</td>
</tr>
</tbody>
</table>

In over 75% of the cases, the nephrectomy was performed in patients over 50-year-old. There are no significant differences between men and women regarding the distribution according to the age criterion (p=0.8499).

The distribution of the nephrectomies according to the urological diagnosis showed that 38.2% of the patients underwent surgical procedure for malignant tumour of the renal parenchyma (Grawitz tumor) (Table 2).

Table 2 – Distribution of nephrectomies according to the urological diagnosis

<table>
<thead>
<tr>
<th>Urological diagnosis</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grawitz tumor</td>
<td>40</td>
<td>43</td>
<td>83</td>
</tr>
<tr>
<td>Pyonephrosis</td>
<td>21</td>
<td>29.4</td>
<td>50</td>
</tr>
</tbody>
</table>

There are no significant differences between men and women regarding the distribution according to gender and urological diagnosis (p=0.9241).

After the macro- and microscopic examination of the renal samples of 19 kidneys (8.8%), the histopathological changes that were seen confirmed the coexistence of arterial hypertension and a urological disorder, of which nine cases in renal tumor (Grawitz) and five cases in pyonephrosis and hydronephrosis (Table 3).

Table 3 – Correlation between urological diagnosis and pathologic lesions due to arterial hypertension

<table>
<thead>
<tr>
<th>Urological diagnosis</th>
<th>Myocardial ischemia</th>
<th>Benign nephroangiosclerosis</th>
<th>Malignant nephroangiosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydronephrosis</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Renal tumor (Grawitz)</td>
<td>1</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Pyonephrosis</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Out of the 83 nephrectomies for renal tumor, histological changes of benign and malignant angiosclerosis were highlighted in eight cases, which show a long evolution of the arterial hypertension with clinical symptoms masked by the tumor ones.

Histopathological changes of benign nephroangiosclerosis with arteriolar vasospasm associated with edema of the wall and/or hypertrophy of the intima with the formation of hyaline deposits were found in three nephrectomies due to hydronephrosis (Figures 1 and 2).

The decrease in volume of the kidneys with fibrosing endarteritis and fibrinoid necrosis with glomerular and tubular lesions – histopathological features of malignant nephroangiosclerosis – were seen in two nephrectomy specimens for hydronephrosis (Figures 3 and 4).

![Figure 1 – Benign nephroangiosclerosis with ischemic glomerular sclerosis of the glomerules located under the renal capsule and partial atrophy of the renal tubes (PAS stain, ×120).](image-url)
Connections between renovascular hypertension and nephrectomy

Figure 2 – Glomerular ischemia with collagen deposits in Bowman’s capsule (PAS stain, ×360).

Figure 3 – Vascular lesions of sclerosis associated with glomerular sclerosis and interstitial fibrosis (HE stain, ×400).

Figure 4 – Malignant nephroangiosclerosis with fibrinoid necrosis of the interlobular arteries and efferent arteries, dead glomerulus and tubular atrophy (HE stain, ×600).

Out of the 56 nephrectomies due to pyonephrosis, changes of benign and malignant nephroangiosclerosis were found in five cases.

Discussion

Nephrectomy represents a method of surgical treatment for renal artery stenosis along with the techniques for renal revascularization such as bypass, dilation (plasty) or stent placement for the renal artery. Khosla S [6] and Textor SC and McKusik MA [7] consider that the choice of nephrectomy, revascularization or medical treatment must be taken in accordance with some elements that are based both on the results reported in the literature and on the pathology of the renal artery stenosis and their evolution in time. Some authors consider that medical treatment with ACE inhibitors (Captopril, Enalapril, Teprotid) is an alternative for the blood pressure decrease through renal and systemic vasodilatation as well as through the increase of natriuresis [8]. Hebert LA et al. recommend three levels of treatment for the renal diseases indicating the revascularization for renovascular hypertension [9].

The results of the surgical treatment can be quantified only during a period of analysis of 10 years, aiming evaluation criteria for complete recovery, improvement or failure [10–12].

Some comparative studies on patients surgically and medically treated revealed that the medical treatment has little or nothing to do with the control of the renovascular hypertension, especially when renovascular hypertension is accompanied by the degradation of the renal function. Moreover, since most of the time the renovascular hypertension is accidentally discovered, after a complex clinical scenario, after a long period of time, as Jaff MR stated, the interventional therapy becomes the preferable option [13, 14]. This conclusion was reached after a long period of research, focusing on the blood pressure, the morbidity, the heart attacks, the evolution of the renal parameters, the life quality of the patients surgically and medically treated [15, 16]. As for the surgical treatment of renovascular hypertension, when choosing the surgical procedure, the degree of renal artery stenosis is very important. In the functionally significant stenosing lesions that induced a prolonged evolution of the hypertension, the nephrectomy on the part of the stenosis can lead to the resection of the best parenchyma leaving in place the non-stenosed kidney, which is altered by the nephroangiosclerosis.

Out of 146 nephrectomies for Grañitz tumor, Proca E identified severe arterial hypertension in only nine patients (5.4%), although there are information indicating a higher percentage (up to 17.5%) [17, 18]. The frequency of histopathological changes is very much reduced, being considered as a complication and not as a sign of hydronephrosis [19]. Some authors report the discovery of other stenoses during routine necropsies, especially since the beginning of the staining for the study of the elastic-connective tissue in the renal artery and the highlighting of renal arterial lesions in live, healthy and normotensive volunteer donors of renal grafts [20, 21].

Conclusions

There are three types of relations between hypertension and renal disease. When hypertension is the cause of renovascular disease the consequence can be benign or malignant nephroangiosclerosis or renovascular hypertension. When hypertension is the cause of some lesions located at the glomerular or interstitial level, the consequence is renoparenchymatous hypertension. Renovascular hypertension is the hypertension determined by unilateral or bilateral, partial or complete stenosis of arterial renal blood vessels, potentially curable by a surgical intervention (reconstructive vascular surgery or nephrectomy). Part of the hypertensions considered essential are in fact secondary to
some well-defined lesions, mostly renal, the kidney being either a victim or a cause of the hypertension.

The 8.8% of the patients that have had histopathologic changes of benign or malignant nephroangiosclerosis and underwent nephrectomy for a surgical disease is quite small compared to the large number of nephrectomies. It is imperative to identify in due time the secondary mechanism of hypertension in order to perform the surgical intervention which saves the kidney or prevents the extension to other organs. Because of this, the hypertension caused by the decrease of renal irrigation through renal mechanism is clearly detached from the big category of essential hypertension. In the case of renovascular hypertension, there are two anatomic manifestations, consequences of stenosis, one of them being the collateral circulation and the other one being the post-stenotic dilatation produced by the post-stenotic systolic flow in an artery with modified elasticity.

Sometimes, the discovery of renovascular hypertension can be made on the basis of some symptoms suggestive for the presence of hypertension, namely cerebral, cardiac, peripheral clinical manifestations and sometimes through the presence of some complications of increased blood pressure values. Most of the times renovascular hypertension is discovered during medical examinations for another condition or during a periodic medical examination. This shows that renovascular hypertension is barely showing, the patient minimizing and neglecting it.

There is no clinical pattern that would allow the individualization of renovascular hypertension from the large group of patients suffering from hypertension. Although there are similarities between the clinical symptoms of renovascular hypertension and the other forms of hypertension, there are some particularities grouped on the four poles: cerebral, cardiac, renal and peripheral.

The pathological study performed on samples obtained from nephrectomies showed that the clinical features of RVH are masked or accompanied by the clinical manifestations of a surgical disease. The data from the literature reveal the discovery of stenosis at routine necropsies, and renal arterial fibro-muscular lesions in voluntary donors of renal grafts in perfect health state and with normal blood pressure.

Although no special preoperative investigations were performed showing a possible RVH, it can be stated that the renal origin of the arterial hypertension can be established retrospectively, after nephrectomy. The monitoring of blood pressure values during several years is extremely important for establishing the etiology of renovascular hypertension.

References


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