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Non-neoplastic adrenal pseudocysts: A clinicopathologic study of 44 cases with potential insights into pathogenesis



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RTICLE INFO	A B S T R A C T				
words: enal cysts enal pseudocysts cular cysts 1-neoplastic adrenal lesions	Background: Literature on non-neoplastic adrenal pseudocysts (NNAPC) remains limited and to date no large series have been reported. The pathogenesis of these lesions remains poorly defined, however a vascular origin is most often suggested in the literature. We aimed to evaluate the clinicopathological features and the spectrum of vascular changes within NNAPC, in order to better understand the mechanisms and circumstances of their pathogenesis.				
	<i>Methods and results:</i> We reviewed 44 cases of surgically resected NNAPC. There were 30 females and 14 males ranging from 23 to 82 years (median, 53 years). On the basis of histopathologic and immunohistochemical analysis of the vascular changes the following types were defined: pseudocysts with lymphatic-related changes (type 1, n = 16), pseudocysts with large vein-related changes (type 2, n = 15) and pseudocysts with blood vessel microvasculature-related changes (type 3, n = 13). The median patient age of the latter group was higher than that of type 1 and 2 (64 years versus 51 and 50 years, respectively; $p = 0.0002$). Type 3 pseudocysts were more frequently associated with a history of systemic vascular and vascular-related disorders than type 1 and type 2 pseudocysts (92% versus 33% and 64%, respectively; $p = 0.008$). Type 1 pseudocysts were more frequently connected with a history of previous intra-abdominal surgical procedures than type 2 and 3 pseudocysts (60% versus 7% and 25%, respectively; $p = 0.0079$).				
	Conclusions: NNAPC are clinically neterogenous and can arise on a background of various vascular changes. They may represent end-stage processes related to lymphangiomatous lesions, changes in adrenal venous structures or microvasculature.				

1. Introduction

Adrenal cystic lesions are a rare heterogenous group of lesions which have conventionally been divided into four categories: pseudocysts, endothelial, epithelial and parasitic cysts [1]. Adrenal pseudocysts are the most commonly identified adrenal cystic lesions in surgical series [2-4]. They occur within the adrenal cortex or medulla, are unilocular lesions filled with bloody or yellow-brown amorphous material and are enclosed by a fibrous connective tissue wall generally lacking a recognizable layer of lining cells [4, 5]. Adrenal pseudocysts are thought to result from hemorrhage into adrenal neoplasms or normal adrenal tissue [1]. The latter situation is considerably more common, for example out of 32 pseudocysts reviewed by Erickson et al. 26 cases (81%) occurred in normal adrenal tissue, and only 6 cases were associated with an adrenal neoplasm [3]. While the formation of pseudocysts within adrenal neoplasms can be explained as degenerative changes of the pathological tissue of a tumor, the pathogenesis of pseudocysts in non-neoplastic adrenal tissue appears to be more

complex and not as clear. It is thought that these types of lesions may occur due to organization of a traumatic hematoma or in the course of toxic or infectious processes [2, 4, 6]. However, in the literature, the most common theory suggests that adrenal pseudocysts may have a vascular origin. Several studies postulated a close association between adrenal pseudocysts and endothelial cysts, and both these groups were considered variants of vascular adrenal cysts [5, 7-10]. There was also a suggestion that adrenal pseudocysts represent a posthemorrhagic process related to adrenal venous structures [11]. A significant limitation of previous studies are the relatively small groups, which did not allow for statistical analysis of clinical and morphological parameters, and a lack of immunohistochemical studies with a wide panel of vascular markers including lymphatic endothelium specific antibodies.

In order to investigate the possible vascular origin of adrenal pseudocysts we performed a study of surgically treated cases focusing on the analysis of vascular changes within these lesions. Next, we characterised and grouped the different types of vascular lesions observed in adrenal pseudocysts and correlated them with clinical

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Table 1

Clinicopathological characteristics of types of adrenal pseudocysts associated with vascular changes.

<table-container>Advance Markangene Markang</table-container>		All PC (n = 44)	PC with lymphatic-related changes (n = 16)	PC with large vein related changes (n = 15)	PC with BV microvasculature related changes (n = 13)	p value
<table-container>Index of the set of the set</table-container>	Age (years)					
GenderUS 100 100 100 100 100 100 100 100 100 10	Median (range)	53 (23-82)	51 (23-62)	50 (31-82)	64 (53–79)	0.0002^{a}
Pende Male90/44 (68%)10/16 (68%)10/15 (63%)7/13 (64%)0.089Mate Mato714 (61%)716 (13%)716 (13%)713 (54%)<	Gender					
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<table-container>IA. India9.19.19.19.19.19.1Clinical constraints10.410.110.</table-container>	Left	9/44 (20%)	3/16 (19%)	3/15 (20%)	3/13 (23%)	
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Residual adventa tissuesUse of the second tissue of the second t	Median (range)	5.8 (1,5–19)	4.8 (1,5–13)	9.0 (1,5–19)	4.5 (3–9)	0.022^{b}
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Normal 21/44 (50%) 12/16 (75%) 5/15 (33,%) 5/13 (38%) NAH 21/44 (30%) 3/16 (19%) 5/15 (33,%) 8/13 (62%) Kornal 21/44 (30%) 3/16 (31%) 10/15 (67%) 8/13 (62%) 0.004 Blood and fibrin 27/44 (61%) 5/16 (31%) 10/15 (67%) 12/13 (92%) 0.004 Fluid/bloody fluid 8/44 (18%) 4/16 (25%) 4/15 (26%) 1/13 (8%) 0.004 Fluid/bloody fluid 8/44 (18%) 7/16 (44%) 1/15 (7%) 8/13 (62%) 0.004 Ves 29/44 (66%) 12/16 (75%) 9/15 (60%) 8/13 (62%) 0.627 No 3/44 (30%) 12/16 (75%) 9/15 (60%) 8/13 (62%) <0.001 No 3/44 (20%) 10/16 (0%) 1/15 (7%) 8/13 (62%) <0.001 No 3/44 (41%) 1/16 (25%) 1/15 (7%) 13/13 (100%) <0.001 No 3/44 (47%) 1/16 (0%) 1/15 (7%) 13/13 (10%) <0.005 No 3/44 (7%) 16/16 (100%) 1/15 (3%	Atrophic	6/44 (14%)	1/16 (6%)	5/15 (33,3%)	0/13 (0%)	0.009
NAH 16/44 (36%) 3/16 (19%) 5/15 (33,3%) 8/13 (62%) Contert U Blood and fibrin 2/744 (61%) 5/16 (31%) 10/15 (67%) 12/13 (92%) 0.004 Fibrin 9/44 (21%) 4/16 (25%) 4/15 (26%) 1/13 (8%) 0.014 Fibrin 9/44 (21%) 4/16 (25%) 4/15 (26%) 1/13 (8%) 0.024 Calcification U U U 0.015 (00%) 8/13 (62%) 0.627 No 15/44 (34%) 1/15 (75%) 9/15 (60%) 8/13 (62%) 0.627 No 15/44 (34%) 1/15 (75%) 6/13 (62%) 0.627 0.627 VET V V V V V V 0.627 No 5/44 (65%) 10/16 (0%) 1/15 (75%) 8/13 (62%) <0.001 0.005 No 18/44 (41%) 14/16 (88%) 1/15 (75%) 1/31 (30%) <0.001 No 18/44 (47%) 1/16 (0%) 1/15 (75%) 1/13 (30%) <0.005 N	Normal	22/44 (50%)	12/16 (75%)	5/15 (33,3%)	5/13 (38%)	
Content Blood and fibrin 27/44 (21%) 5/16 (31%) 10/15 (67%) 2/13 (28%) 0.004 Fibrin 9/44 (13%) 4/16 (25%) 4/15 (26%) 1/13 (3%) Blood and fibrin 8/44 (18%) 7/16 (44%) 1/15 (7%) 0/13 (0%) Califications Yes 29/44 (66%) 1/216 (75%) 6/15 (0%) 8/13 (36%) Yes 29/44 (63%) 1/16 (7%) 6/15 (0%) 8/13 (38%) Yes 29/44 (63%) 1/16 (0%) 1/15 (7%) 8/13 (32%) Yes 3/44 (0%) 0/16 (0%) 1/15 (7%) 8/13 (10%) Yes 1/24 (14%) 2/16 (12%) 1/1/15 (7%) 3/13 (10%) 2/0001 No 1/24 (14%) 1/16 (0%) 1/15 (7%) 3/13 (10%) 2/0001 Yes 1/24 (42%) 1/16 (0%) 1/15 (7%) 1/13 (3%) 2/0001 <t< td=""><td>NAH</td><td>16/44 (36%)</td><td>3/16 (19%)</td><td>5/15 (33,3%)</td><td>8/13 (62%)</td><td></td></t<>	NAH	16/44 (36%)	3/16 (19%)	5/15 (33,3%)	8/13 (62%)	
Blood and fibrin 27/44 (61%) 5/16 (31%) 10/15 (67%) 12/13 (92%) 0.004 Fibrin 9/44 (21%) 4/16 (25%) 4/15 (26%) 1/13 (8%) 0.004 Fibrin 8/44 (18%) 7/16 (44%) 1/15 (7%) 0/13 (0%) Calcifications Yes 29/44 (66%) 12/16 (75%) 9/15 (60%) 8/13 (62%) 0.627 0.627 No 15/4 (34%) 4/16 (25%) 0/15 (60%) 8/13 (62%) 0.627 0.627 PEH 0.627 No 35/44 (80%) 1/16 (0%) 1/15 (7%) 8/13 (62%) < 0.0001 No 35/44 (80%) 1/61 (610%) 1/15 (7%) 8/13 (10%) < 0.0001 No 18/44 (41%) 1/16 (88%) 1/15 (7%) 13/13 (100%) < 0.0001 No 31/44 (41%) 1/16 (0%) 1/15 (7%) 1/13 (8%)	Content					
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Fluid/bloody fluid 8/44 (18%) 7/16 (44%) 1/15 (7%) 0/13 (0%) Calcifications Yes 9/9/4 (66%) 12/16 (75%) 9/15 (60%) 8/13 (62%) 0.627 No 15/4 (34%) 4/16 (25%) 9/15 (60%) 8/13 (30%) 0.627 PEH Yes 9/44 (20%) 0/16 (0%) 1/15 (7%) 8/13 (62%) No 35/44 (80%) 0/16 (100%) 1/15 (7%) 8/13 (100%) <t< td=""><td>Fibrin</td><td>9/44 (21%)</td><td>4/16 (25%)</td><td>4/15 (26%)</td><td>1/13 (8%)</td><td></td></t<>	Fibrin	9/44 (21%)	4/16 (25%)	4/15 (26%)	1/13 (8%)	
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PEH Yes 9/44 (20%) 0/16 (0%) 1/15 (7%) 8/13 (62%) < 0.0001	No	15/44 (34%)	4/16 (25%)	6/15 (40%)	5/13 (38%)	
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ECC Ves 26/44 (59%) 2/16 (12%) 11/15 (73%) 13/13 (10%) < 0.0001 No 18/44 (41%) 14/16 (88%) 4/15 (27%) 13/13 (0%) < 0.0001	No	35/44 (80%)	16/16 (100%)	14/15 (93%)	5/13 (38%)	
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ICLM Ves 10/44 (23%) 0/16 (0%) 1/15 (7%) 9/13 (69%) < 0.0001 No 3/4/4 (77%) 16/16 (100%) 1/15 (93%) 4/13 (31%) Macrophages V V V V V Yes 21/44 (48%) 4/16 (25%) 6/15 (40%) 11/13 (85%) 0.005 No 23/44 (52%) 12/16 (75%) 9/15 (60%) 2/13 (15%) 0.005 Cholesterol clefts V V V V V Yes 12/44 (27%) 5/16 (31%) 7/15 (47%) 0/13 (0%) 0.02 No 32/44 (73%) 11/16 (69%) 8/15 (53%) 13/13 (100%) V	No	18/44 (41%)	14/16 (88%)	4/15 (27%)	0/13 (0%)	
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No 34/44 (77%) 16/16 (100%) 14/15 (93%) 4/13 (31%) Macrophages	Yes	10/44 (23%)	0/16 (0%)	1/15 (7%)	9/13 (69%)	< 0.0001
Macrophages Yes 21/44 (48%) 4/16 (25%) 6/15 (40%) 11/13 (85%) 0.005 No 21/46 (25%) 12/16 (75%) 9/15 (60%) 2/13 (15%) 0.005 Cholesterol clefts	No	34/44 (77%)	16/16 (100%)	14/15 (93%)	4/13 (31%)	
Yes21/44 (48%)4/16 (25%)6/15 (40%)11/13 (85%)0.005No23/44 (52%)12/16 (75%)9/15 (60%)2/13 (15%)Cholesterol cleftsYes12/44 (27%)5/16 (31%)7/15 (47%)0/13 (0%)0.02No32/44 (73%)11/16 (69%)8/15 (53%)13/13 (100%)	Macrophages					
No 23/44 (52%) 12/16 (75%) 9/15 (60%) 2/13 (15%) Cholesterol clefts <t< td=""><td>Yes</td><td>21/44 (48%)</td><td>4/16 (25%)</td><td>6/15 (40%)</td><td>11/13 (85%)</td><td>0.005</td></t<>	Yes	21/44 (48%)	4/16 (25%)	6/15 (40%)	11/13 (85%)	0.005
Yes 12/44 (27%) 5/16 (31%) 7/15 (47%) 0/13 (0%) 0.02 No 32/44 (73%) 11/16 (69%) 8/15 (53%) 13/13 (100%)	No	23/44 (52%)	12/16 (75%)	9/15 (60%)	2/13 (15%)	
Yes 12/44 (27%) 5/16 (31%) 7/15 (47%) 0/13 (0%) 0.02 No 32/44 (73%) 11/16 (69%) 8/15 (53%) 13/13 (100%) 0.02	Cholesterol clefts					
No 32/44 (73%) 11/16 (69%) 8/15 (53%) 13/13 (100%)	Yes	12/44 (27%)	5/16 (31%)	7/15 (47%)	0/13 (0%)	0.02
	No	32/44 (73%)	11/16 (69%)	8/15 (53%)	13/13 (100%)	

Abbreviations: PC, pseudocysts; BV, blood vessels; F, female; M, male; L, left; R, right; SVD, systemic vascular and vascular-related disorders; PIS, previous intraabdominal surgery; NAH, nodular adrenal hyperplasia; PEH, papillary endothelial hyperplasia; ECC, intracapsular/intracystic entrapped cortical cells; ICLM, intracystic lipomatous metaplasia.

^a Pairwise analysis: group 1 vs 3, p < 0.0001; group 2 vs 3, p = 0.002; group 1 vs 2, p = 0.495.

 $^{\rm b}$ Pairwise analysis: group 1 vs 3, p=0.714; group 2 vs 3, p=0.022; group 1 vs 2, p=0.015.

parameters.

2. Materials and methods

2.1. Patient selection

This retrospective study was approved by the Bioethics Committee at the Medical University of Warsaw (No. 104/17). We searched our database for all cases of surgically treated adrenal pseudocysts without associated adrenal neoplasms since 2001. We identified 51 cases originally diagnosed as "adrenal hemorrhagic pseudocyst" (25 cases) and "adrenal pseudocysts" (26 cases). However in order to avoid qualifying cases of pseudocysts which occurred within adrenocortical adenomas (ACA) and due to the emphasis in the literature on the difficulty of differentiating ACA from diffuse hemorrhage and several non-neoplastic lesions [12], all routinely (H&E) - stained slides were reviewed by the authors (ŁK, BG). After re-evaluation of 51 primarily identified cases 7 were reclassified and excluded from our study. In 6 cases of hemorrhagic-fibrinous masses, expanded residual neoplastic cortical tissue was found and these lesions were reclassified as "hemorrhagic pseudocysts within an adrenocortical adenoma". One case was excluded due to a lack of a fibrous wall surrounding the lesion. Ultimately 44 cases were included in the study. Additionally we retrieved and analyzed the clinical details. Next, representative paraffin blocks were selected for additional immunohistochemical and histochemical studies.

2.2. Immunohistochemistry and histochemistry

Immunohistochemical studies were performed using formalin-fixed, paraffin-embedded (FFPE) 4 µm tissue sections and the following antibodies from Dako (Denmark) were used: against CD34 (QBEnd10), Download English Version:

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