Case Report **Open Access**

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An uncommon case of arterial aneurysms association with high plasma levels of Matrix Metalloproteinase-9 and Neutrophil Gelatinase-Associated Lipocalin

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Abstract: The association of an axillary artery aneurysm and an abdominal aortic aneurysm is extremely rare. In this study, we describe this association in a 69 year-old-man. We measured this patient's metalloproteinases (MMPs) and Neutrophil Gelatinase – Associated Lipocalin (NGAL) levels over a three years period before the abdominal aortic aneurysm rupture. We speculate that high serium levels of MMPs and NGAL may have a prognostic role and may predict aneurysm rupture in patients with an uncommon association of arterial aneurysms.

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1 Introduction

True aneurysms of the axillary artery are extremely uncommon [1-2] and even more uncommon when associated with abdominal aortic aneurysms. In fact, to the best of our knowledge no similar cases are reported in the current literature. Metalloproteinases (MMPs) are enzymes that regulate extracellular structural proteins and consequent tissue remodeling and seem to be involved in several vascular diseases [3]. Neutrophil gelatinase-associated lipocalin (NGAL) is a protein belonging to the lipocalin family and is expressed by activated neutrophils. It has the ability to positively modulate the activity of MMP-9 in particular by forming the NGAL/MMP-9 complex. This complex formation protects MMP-9 from proteolytic degradation [4]. We describe a 69-year-old-male with a concomitant sub-renal abdominal aortic aneurysm (AAA) and a large right axillary artery aneurysm who was admitted for surgical treatment of both the aneurysms in which high plasma levels of MMP-9 and NGAL were detected (Fig. 2).

2 Case Report

A 69 year-old-man with history of sub-renal abdominal aortic aneurysm (30 x 45 mm), hypertension, dyslipidemia, chronic obstructive pulmonary disease (COPD) and cardiomyopathy evaluated for the past three years in our operative unit through clinical and laboratory tests

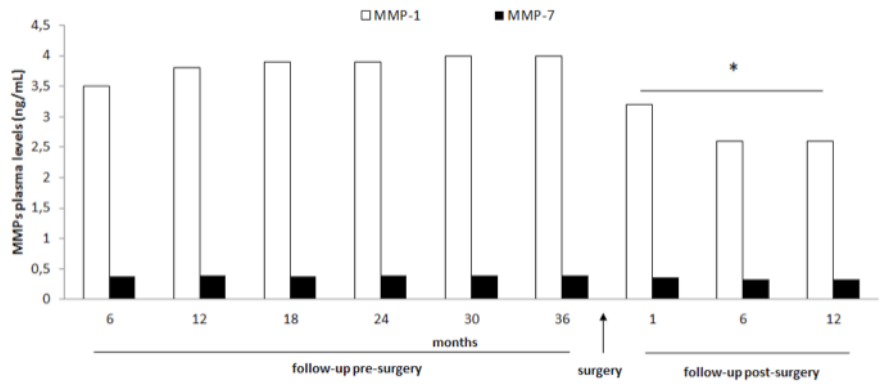

Figure1: Plasma levels of MMP-1 and MMP-7, measured through ELISA test in patients during the follow-up before and after the surgery. *P<0.01 post-surgery vs pre-surgery.

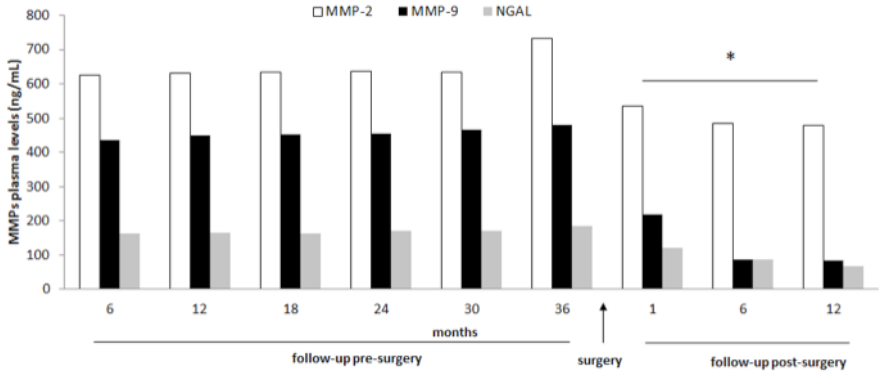

Figure 2: Plasma levels of MMP-2, MMP-9 and NGAL, measured through ELISA test in patients during the follow-up before and after the surgery. *P<0.01 post-surgery vs pre-surgery.

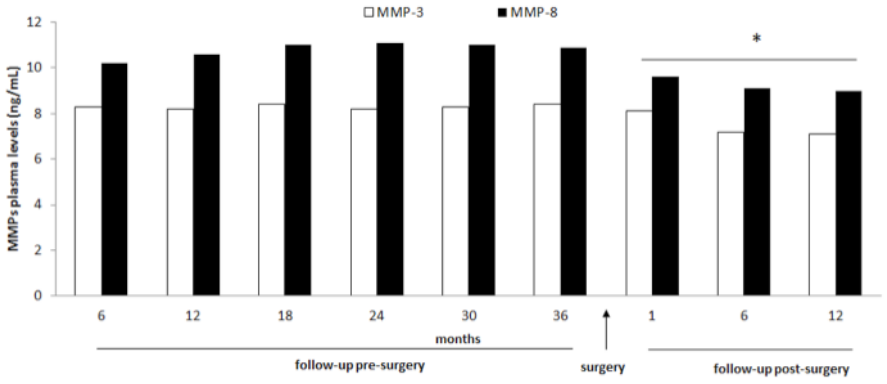

Figure 3: Plasma levels of MMP-3 and MMP-8, measured through ELISA test in patients during the follow-up before and after the surgery. *P<0.01 post-surgery vs pre-surgery.

(MMPs and NGAL plasma evaluation;Fig 1-3) complained of an acute abdominal pain (Visual Analogical Scale score - VAS: 8). Computed tomography (CT) scan with contrast revealed the presence of a ruptured infrarenal abdominal aortic aneurysm (63 x 70 mm) and a right axillary artery (43 x 60 mm) aneurysm with intraluminal thrombus. Clinical evaluation revealed the presence of a solid, palpable pulsating mass in the right axillary fossa. Motility and sensibility of the right hand was normal and the radial pulse was present. Ultrasound examination of

the upper limbs showed a right axillary artery aneurysm (40 x 60 mm). Brachial, radial and ulnar arteries were normal and patent. Ultrasound examination of the lower limbs showed normal and patent arteries. No sign of vasculitis or connective tissue disease (e.g. hyperelastic skin, hypermobile joints, or marfanoid habitus) was present. Laboratory tests including erythrocyte sedimentation rate, C reactive protein, complete blood count, serological test for syphilis, rheumatoid factor, antinuclear antibody, antithrombin III, protein C, and protein S were normal. In contrast, higher plasma levels of MMP-9 and NGAL were detected (Fig. 2). The axillary artery aneurysm was considered unsuitable for endovascular intervention due to tortuosity of the artery. A contemporaneous surgical treatment of both aneurysms was proposed in order to avoid repeated general anesthesia in a patient affected by chronic obstructive pulmonary disease.

Surgical repair of the aortic aneurysm (Fig. 4) was performed using an aorta-aortic bypass with Dacron 18 mm (Vascutek Ltd., Renfrewshire, Scotland, UK) through a median laparotomy and a sample of aneurysmal tissues was taken.

Then, open repair of the right axillary artery aneurysm (Fig. 5) was performed by ligation of the aneurysm followed by a bypass with an 8-mm Propaten polytetrafluoroethylene (PTFE) graft (WL Gore & Associates, Newark, Delaware).

Immunoblotting test performed on aneurysmal tissues from the axillary and abdominal aortic arteries taken at the time of the surgery (described in our previous study [5]) showed increased activation of both MMP-9 and NGAL in the aortic aneurysm tissue and of all MMPs and NGAL in the axillary artery aneurysm tissue with respect to normal tissue (healthy segments of aneurysmatic vessel) (Figs 6,7). The post-surgical period was uneventful: neurological examination of the right upper arm was normal and radial pulse was present. Seven days post-surgery, the patient was discharged on antiplatelet therapy (aspirin 100 mg/day). During follow-up visits at 1, 3, 6, 9 and 12 months, the prosthetic bypass of the right upper arm was patent and no post-surgical complications were seen. Moreover, during this time a significant decrease in plasma levels of MMPs and NGAL was recorded (Figs 1-3).

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

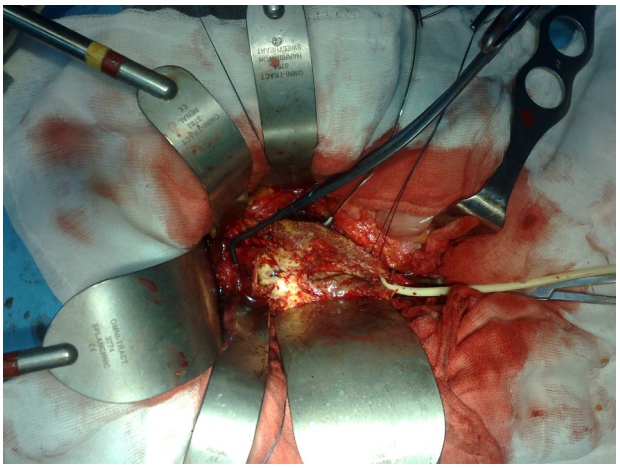

Figure 4: Aortic aneurysm.

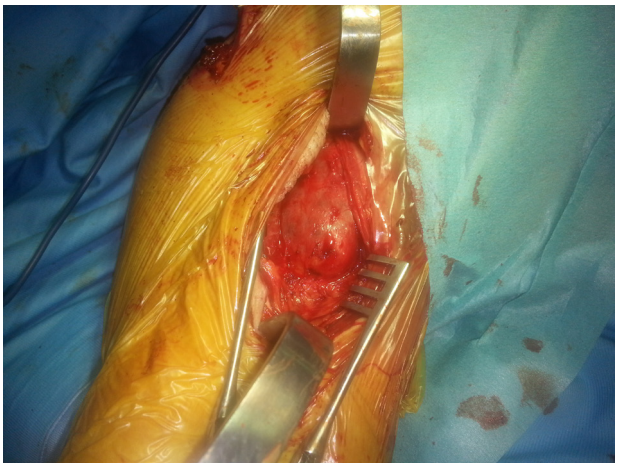

Figure 5: Right axillary artery aneurysm.

3 Discussion

Here, we report a patient admitted to our hospital for surgery of sub-renal AAA and right axillary artery aneurysm. Some authors have previously documented the presence of axillary artery aneurysm [6-11], very few papers have documented an association of abdominal and peripheral aneurysms [12-13]. Tanaka et al., [15] described a patient with multiple atherosclerotic aneurysms of the bilateral subclavian artery, aortic arch and abdominal aorta. Commonly, patients affected by abdominal aortic aneurysms present an aneurysm at the level of the femoral-popliteal segment [13-14].

Using Medline, PubMed, Embase, Cochrane library and Reference lists for articles published up to June 30 2014, we did not find any publications describing a contemporaneous presence of axillary artery aneurysms and with an infrarenal abdominal aortic aneurysm.

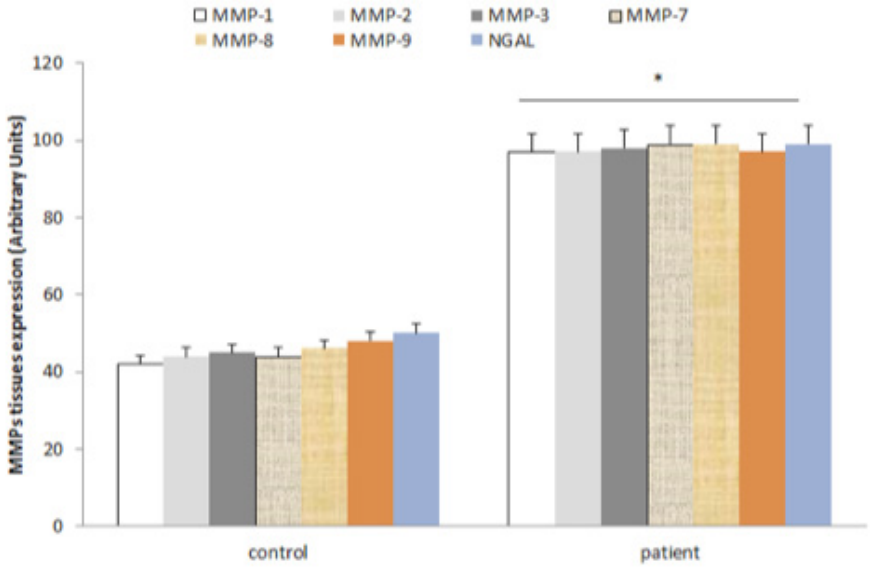

Figure 6: MMP-s and NGAL tissue expression in healthy and in aneurysmatic segments of the patient, measured through western blot analysis on the tissues taken from axillary artery aneurysm at the time of the surgery. *P<0.01.

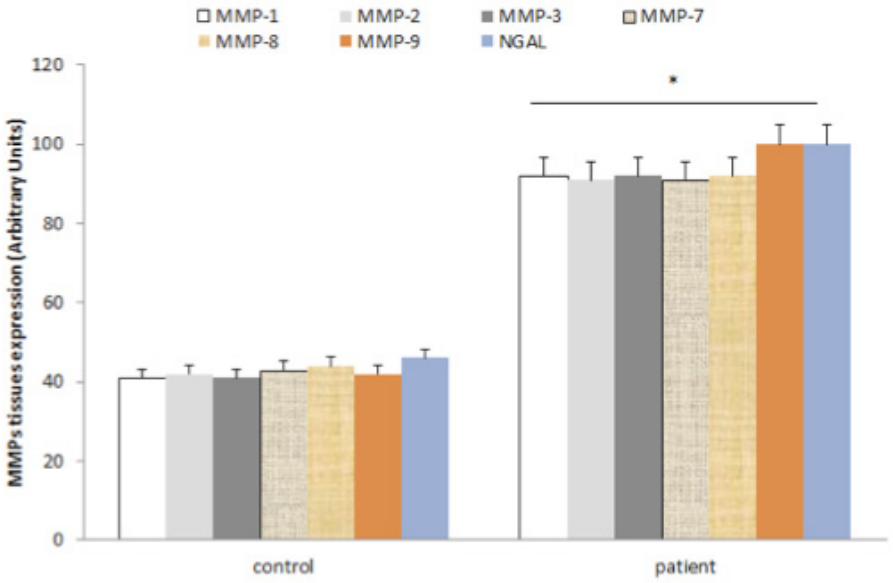

Figure 7: MMP-s and NGAL tissue expression in healthy and in aneurysmatic segments of the patient measured through western blot analysis on the tissues taken from abdominal aortic artery aneurysm at the time of the surgery. *P<0.01.

Both early diagnosis and appropriate treatment are mandatory, in order to avoid major complications, e.g. thrombosis, distal embolization with acute ischemia of the hand and limb loss, compression of adjacent structures and rupture with blood loss that represents a life-threatening event.

Surgery is the gold standard of treatment, while endovascular management is an interesting, less invasive and attractive alternative, but long term results are still unknown [15-16]. A contemporaneous surgical treatment of both aneurysms is feasible, without an increase in local and general complications.

As previously described, MMPs and NGAL play a pivotal role in the pathophysiology of both vascular [17-30] and non-vascular diseases [3]. According to the protocols reported in agreement with literature data [3,14-15] we detected in our patient during follow-up a time-dependent increase of MMP-1, -2, -3, -7, -8, and 9 plasma

levels. Moreover, at the time of the aneurysm rupture, higher levels of MMP-9 and NGAL were detected. Several authors have reported that zymography may also be used to identify both pro-MMPs and MMPs. In our present study, we used Western blot analysis with anti-MMPs able to identify the activated form of MMP;this could represent a limit of this study. However, as reported by Hu and Beeton [31] detection limits for Western Blots are often much lower than those of zymographic gels, potentially leading to false-negative results related to this technique.

In conclusion, in this uncommon case report we confirm the prognostic role of MMPs in the follow-up of patient with aneurysmal artery. Moreover, we can underline the role of MMP-9/NGAL complex during the rupture event.

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The Authors declare no conflict of interest.

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