

ISSN: 2325-7075 Volume 7, Number 8, August 2018



Case Reports in Clinical Medicine



ISSN: 2325-7075



9 772325 707001 08

www.scirp.org/journal/crcm

Journal Editorial Board

ISSN Print: 2325-7075 ISSN Online: 2325-7083

<http://www.scirp.org/journal/crcm>

Editor-in-Chief

Prof. Shang I Brian Jiang University of California, USA

Editorial Board

Prof. Marcelo Rodrigues Azenha University of Sao Paulo, Brazil
Prof. Carmen Cuffari The Johns Hopkins University, USA
Dr. Christina Ellervik University of Copenhagen, Denmark
Prof. Stephen A. Felt Stanford University, USA
Dr. Ankur Girdhar Peninsula Regional Medical Center, USA
Dr. William F. Kern University of Oklahoma Health Sciences Center, USA
Dr. Chong Tae Kim University of Pennsylvania, USA
Dr. Xiaoqi Lin Feinberg School of Medicine, Northwestern University, USA
Prof. Gary E. Meyerrose Texas Tech University Health Sciences Center, USA
Prof. Michael L. Moritz University of Pittsburgh, USA
Prof. John M. Morton Stanford University School of Medicine, USA
Dr. Yannis Mantas Paulus Wilmer Eye Institute, Johns Hopkins University, USA
Prof. Vinicio A. de Jesus Perez Stanford University, USA
Prof. Phuong-Chi Pham Olive View-UCLA Medical Center, USA
Prof. Ali Rezaie University of Calgary, Canada
Dr. Gabriel C. Tender Louisiana State University Health Sciences Center, USA
Prof. Ted Tewfik McGill University, Canada
Dr. Elena Trombini University of Bologna, Italy
Dr. Roxana Ursea University of Arizona, USA
Prof. Paul J. Zhang University of Pennsylvania, USA

Table of Contents

Volume 7 Number 8

August 2018

An Unusual Case of a Pulmonary-Renal Syndrome with Negative Anti-GBM and ANCA Antibodies

F. M. Webber, E. Ricardo Junior, M. B. L. Morillo, E. M. Webber.....461

Eruptive Keratoacanthomas within a Red Ink Tattoo: A Case Report

B. Healey, W. Galbraith, Y. M. Sammour, D. Baird.....470

Right Atrial Giant Myxoma Occupying the Right Ventricular Cavity

A. Heidari, M. Nourizadeh, M. H. Najafi, S. Nourizadeh, N. Assadinia.....476

Case Reports in Clinical Medicine (CRCM)

Journal Information

SUBSCRIPTIONS

The *Case Reports in Clinical Medicine* (Online at Scientific Research Publishing, www.SciRP.org) is published monthly by Scientific Research Publishing, Inc., USA.

Subscription rates:

Print: \$59 per issue.

To subscribe, please contact Journals Subscriptions Department, E-mail: sub@scirp.org

SERVICES

Advertisements

Advertisement Sales Department, E-mail: service@scirp.org

Reprints (minimum quantity 100 copies)

Reprints Co-ordinator, Scientific Research Publishing, Inc., USA.

E-mail: sub@scirp.org

COPYRIGHT

Copyright and reuse rights for the front matter of the journal:

Copyright © 2018 by Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY).

<http://creativecommons.org/licenses/by/4.0/>

Copyright for individual papers of the journal:

Copyright © 2018 by author(s) and Scientific Research Publishing Inc.

Reuse rights for individual papers:

Note: At SCIRP authors can choose between CC BY and CC BY-NC. Please consult each paper for its reuse rights.

Disclaimer of liability

Statements and opinions expressed in the articles and communications are those of the individual contributors and not the statements and opinion of Scientific Research Publishing, Inc. We assume no responsibility or liability for any damage or injury to persons or property arising out of the use of any materials, instructions, methods or ideas contained herein. We expressly disclaim any implied warranties of merchantability or fitness for a particular purpose. If expert assistance is required, the services of a competent professional person should be sought.

PRODUCTION INFORMATION

For manuscripts that have been accepted for publication, please contact:

E-mail: crcom@scirp.org

An Unusual Case of a Pulmonary-Renal Syndrome with Negative Anti-GBM and ANCA Antibodies

Fabrício Malaguez Webber^{1*}, Edson Ricardo Junior², Maria Belen López Morillo¹, Emanuel Malaguez Webber³

¹Centro de Especialidades Médicas San Lorenzo, El Salvador, Chile

²Hospital Antônio Prudente, Natal, Brazil

³Hospital Regional Teresinha Gaio Basso, São Miguel do Oeste, Brazil

Email: *FabricioWebber@doctor.com

How to cite this paper: Webber, F.M., Ricardo Junior, E., Morillo, M.B.L. and Webber, E.M. (2018) An Unusual Case of a Pulmonary-Renal Syndrome with Negative Anti-GBM and ANCA Antibodies. *Case Reports in Clinical Medicine*, 7, 461-469. <https://doi.org/10.4236/crcm.2018.78040>

Received: July 13, 2018

Accepted: August 6, 2018

Published: August 9, 2018

Copyright © 2018 by authors and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Pulmonary renal syndrome (PRS) is a high mortality, rare disorder presenting with diffuse alveolar hemorrhage and progressive acute glomerulonephritis. This syndrome is often caused by autoimmune entities, the most frequent being ANCA positive vasculitis and anti-GBM disease. We report a case of a 34-year-old Chilean woman, who initially presents with anemia and after a few days of inpatient management, starts with progressively worsening dyspnea, decrease in renal function and hematuria. The patient is initially diagnosed with pneumonia, but further evaluation using Thorax CT scan and renal biopsy confirms the suspicion of PRS. The case is of particular interest due to the lack of extensive bibliography on anti-GBM and ANCA negative pulmonary-renal syndrome, an uncategorized subtype of this syndrome with unknown optimal management.

Keywords

Pulmonary Renal Syndrome, Goodpasture, ANCA, Anti-GBM

1. Introduction

The Pulmonary-Renal Syndrome (PRS) is a rare syndrome caused by a variety of etiologies. The patient presentation is often confused with pneumonia. However, a proper diagnosis can be achieved if there is a high degree of suspicion by the clinician, with major etiologies being anti-neutrophil cytoplasmic antibody (ANCA) vasculitides and anti-glomerular basement membrane (GBM) disease, accounting for up to 75% of PRS cases in intensive care units (ICU) [1]. That

said, a lesser known and studied subset of PRS may be caused by Systemic Lupus Erythematosus (SLE), cryoglobulinemias and drugs, leading to an even greater diagnosis challenge [2]. The case we present is accompanied by negative ANCA and anti-GBM antibodies. We find it relevant to report this case as we aim to discuss the contradictory findings during this patient workup, while evaluating other causes of PRS, and suggesting a treatment rationale along with a possible novel immunological target for diagnosis.

2. Case Report

A 34-year-old Chilean female presented to our emergency service (04/02/2009) with a chief complaint of increasingly progressive dyspnea and fatigability associated with two episodes of bloody stool and vaginal bleeding. Physical exam shows conjunctival pallor and palpable liver edge with tenderness. No jaundice is observed. Laboratory results revealed anemia (Hemoglobin: 6.3 g/dL) and prothrombin time of 35.9%. The patient is transferred to the inpatient unit for transfusional therapy and further study of her anemia and vaginal bleeding. On the following day, physical exam remains unchanged, gynecological consult is obtained and endometrial disease is discarded as the cause of her bleeding, abdominal ultrasound shows splenomegaly and suggestive signs of liver damage. The patient is kept under inpatient setting for proper correction of the underlying hematological disorders. During the night of the fifth day of admission, the patient presents with chest pain and progressive dyspnea with SpO₂% of 75%. The patient is sent to the regional hospital for admission to the ICU due to acute respiratory failure and endovenous ceftriaxone is initiated due to suspected pneumonia. Thoracic computed tomography shows a clear interstitial pattern while laboratory exams show an increase in creatinine levels (2.87 mg/dL) and macroscopic hematuria. A pulmonary-renal syndrome is suspected and methylprednisolone is initiated along with mechanical ventilation due to worsening respiratory failure, with progressively decreasing PaO₂/FiO₂, getting as low as 79 mmHg. The patient is transferred to a higher complexity hospital in Santiago via air ambulance. On arrival, patient SpO₂ is 55% and orotracheal tube aspiration shows multiple blood clots.

Bronchoalveolar lavage is performed and diffuse alveolar hemorrhage is confirmed, while samples were submitted for the following microbiological tests: Gram stain and bacterial cultures; Kinyoun stain and mycobacterial cultures; Calcofluor-white stain and fungi cultures; polymerase chain reaction for *P. jiroveci*; respiratory viral panel. All the performed microbiological tests were negative.

Rheumatologic studies results show the following: ANA 1/320, normal C3 levels, low C4 levels, anti-Ro positive and Anti-La positive. Anti-DNA negative, anti-DNA (Farr assay) negative, PR3-ANCA negative, MPO-ANCA negative, Anti-GBM negative and antiphospholipids negatives. Coombs test is positive with low haptoglobin.

Figure 1 allows for a summary of the clinical evolution and interventions performed.

Patient alveolar hemorrhage was successfully treated with methylprednisolone pulses (3 grams), plasmapheresis (10 sessions) and two pulses of cyclophosphamide 500 mg. However, despite pulmonary improvement, during ICU stay the patient progressed with a persistent decrease in hematocrit and platelets, being interpreted as hemolytic anemia, thus being treated with two additional methylprednisolone pulses (totaling 5 grams). After initial stabilization, the patient presented with melena and a further decrease in hematocrit with normal LDH and haptoglobin. Upper gastrointestinal endoscopy and further analysis were compatible with upper gastrointestinal bleeding due to portal hypertensive gastropathy. There was also an inappropriate bone marrow response to the anemia with normal-to-low erythropoietin levels, requiring its administration, which was attributed to antibiotics and the concurrent systemic inflammation.

Renal biopsy was positive for crescentic pauci-immune glomerulonephritis with 35% presence of tubular atrophy and interstitial fibrosis. The rapid progression of the renal failure was managed with transitory dialysis, allowing to keep stationary creatinine levels around 1.2 to 1.4 mg/dL.

Even though the patient was under evaluation for possible autoimmune hepatitis, no autoimmune hepatitis markers were found elevated during hospitalization; Anti-LKM, Anti-AMA, ASMA and anti-tissue transglutaminase were all found to be negative. Antibodies against viral hepatitis were also found to be negative.

The last rheumatological markers before discharge and their levels in the following years are summarized in **Table 1**. Worthy of notice was the normalization of Anti-La antibodies (10.8 U/mL, reference range 0 - 20) in December/2010, while keeping a slightly elevated Anti-Ro antibody that normalized by May/2011 (from 22.8 to 18.1 U/mL, reference range 0 - 20).

The patient maintained a stable regimen with prednisolone 8 mg/day, hydroxychloroquine 200 mg/day and mycophenolate 2 grams/day, not presenting further disease exacerbations or loss of renal function until May/2016, when the patient is evaluated for chronic diarrhea. Mycophenolate was removed due to gastrointestinal side effects, and chronic diarrhea subsides with relative normalization of renal function to previous levels. Hydroxychloroquine use had to be discontinued due to the appearance of retinopathy.

The patient, up to the date of publication, has not had any new PRS crisis. However, her renal failure has continued to progress and the patient is currently on peritoneal dialysis due to end-stage-renal-disease (ESRD). A trial of Rituximab was administered on two occasions, yielding no improvement of renal function and causing acute avascular necrosis of the patella during the two infusions. Currently, the patient's only immunomodulatory therapy is methylprednisolone 8 mg/day as other therapies have produced adverse events or are contraindicated due to ESRD.

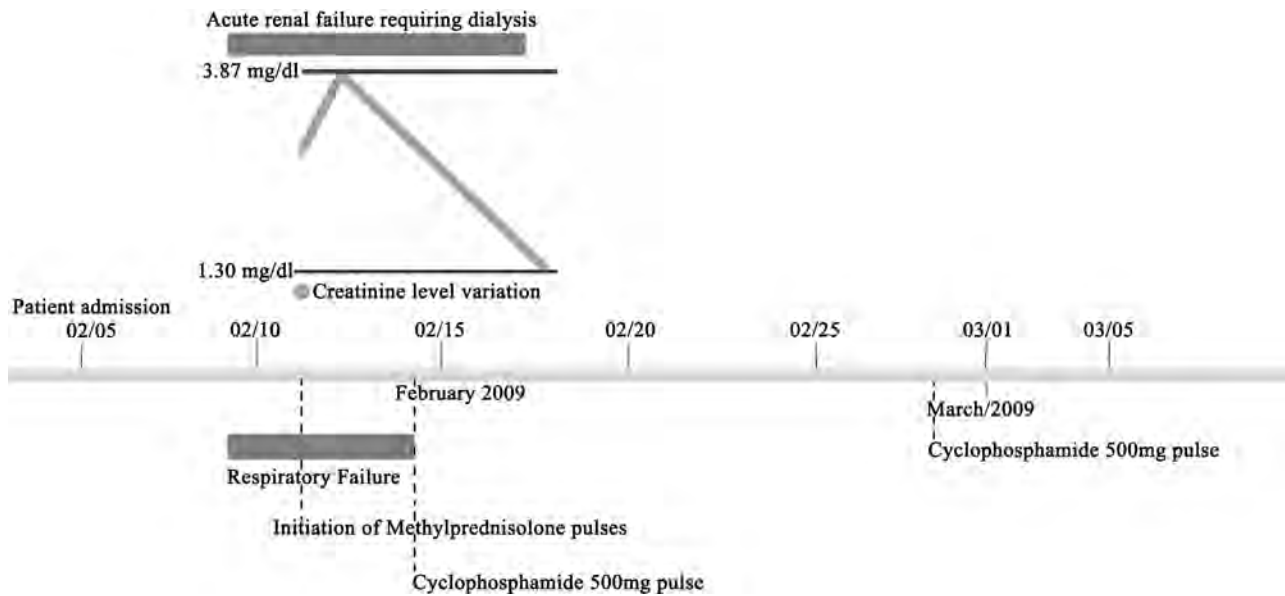


Figure 1. Timeline of patient clinical during hospitalization.

Table 1. Patient serological progression over time.

Antibody essay	Result at discharge	Result on follow-up
ANA (IFI)	1/320	1/320
Anti B2 glycoprotein	Negative	Negative
Anti Ro	Positive	Positive, then negativization
Anti La	Positive	Negative
Anti RNP	Negative	Negative
Anti Smith	Negative	Negative
Anti-DNA	Negative	Negative
Cryoglobulins	Negative	Negative
Antimitochondrial antibodies	Negative	Negative
Anti Ribosomal P Protein	Negative	Negative
Anti Smooth Muscle Antibody	Negative	Negative
Antiphospholipids	Negative	Negative
Lupic anticoagulant	Negative	Negative
Antineutrophil Cytoplasmic Antibody (MPO and PR3)	Negative	Negative
Anti glomerular basal membrane	Negative	Negative

3. Discussion

PRS is a rare disorder caused by heterogeneous pathological entities with the common symptom presentation of diffuse alveolar hemorrhage and progressive acute glomerulonephritis. The etiologies for such syndrome are diverse but usually derive from an autoimmune vascular insult with inflammation and ne-

crisis of blood vessels and the glomeruli, ranging from the most common causal agents such as ANCA positive small vessel vasculitis (such as granulomatosis with polyangiitis, microscopic polyangiitis), anti-GBM disease and systemic erythematous lupus to less frequent causative agents, such as drug-induced vasculitis (e.g., penicillamine, propylthiouracil), mixed cryoglobulinemia and the idiopathic form, to name a few [2].

The PRS has a high mortality rate, which seems to present in a bimodal fashion; During the acute phase a catastrophic clinical debut can present as diffuse alveolar hemorrhage causing airway obstruction and sudden onset of acute respiratory insufficiency. Even more, due to the low frequency of the disease, it can be inadvertently misdiagnosed as pneumonia and delay appropriate therapy, as some patients may present only with pulmonary infiltrates, dyspnea and fever.

The increased mortality in the chronic phase of the disorder could be attributed to potential adverse effects of the therapy, a progressively declining renal function or, even the management of the complex multisystemic disorders underlying this syndrome [3].

No current clinical criteria or score has been developed for rapidly assessing the probability of PRS. *Papiris et al.* (2007) have suggested considering this diagnosis in the presence of pulmonary infiltrates along with following findings: hemoglobin decrease, rapidly progressing renal failure, sinusitis, mononeuritis multiplex, polyarthralgia, severe asthma attack, pericarditis, cerebral ischemia, purpura or congestive heart failure [1]. We suggest that further suspicion should be raised in the presence of any immunological marker or personal history of autoimmune diseases.

Once a syndromic diagnosis is established, the question of the underlying etiology remains unresolved, which we try to explore next.

Systemic Erythematous Lupus (SLE) is one cause of PRS with the frequency of such presentation being as low as 2% in SLE patients. However, this clinical presentation is rarely the first manifestation of the disease [4]. More importantly, the presence of pauci-immune glomerulonephritis in the context of an SLE associated PRS would be, although possible [5] [6], a very unlikely presentation of the disease, as the SLE glomerular disease commonly occurs as a result of a type III hypersensitivity with antibody-deposition being the primary pathogenic insult [7]. Even though these two findings are suggestive of another etiology for the PRS presented in our patient, we find it relevant to point out that this patient fills the Systemic Lupus Collaborating Clinics (SLICC) criteria for SLE [8] (Table 2) and it is worthwhile to notice the transitory elevation of the Anti-Ro antibody which also points towards the possible SLE diagnosis.

Another possibility that has been explored was the Mixed Connective-Tissue Disease (MCTD), due to its extensive clinical presentations including alveolar hemorrhage [9]. Although a possibility, MCTD is not a likely diagnosis for our patient, as she lacks the hallmark positive anti-RNP findings, required in both Alarcon-Segovia and Kahn's criteria, currently the most accurate criteria for

Table 2. Patient presentation and criteria met according to ACR SLE criteria and the newer SLICC criteria. SLICC criteria requires the presence of 4 of the findings, being at least one immunological and one clinical. It is also noteworthy that this criterion mandates that if the patient presents two highly correlated findings, such as a positive Coombs, and hemolytic anemia, only one of these findings should be counted [8].

Patient presentation according to different SLE criteria			
SLICC Criteria		American College of Rheumatology (ACR) SLE criteria	
Acute Cutaneous Lupus	×	Malar Rash	×
Chronic Cutaneous Lupus	×	Discoid Rash	×
Oral/Nasal Ulcers	×	Photosensitivity	×
Non-scarring alopecia	×	Oral Ulcers	×
Arthritis	×	Nonerosive Arthritis	×
Serositis	×	Serositis	×
Renal	✓	Renal	✓
Neurologic	×	Neurologic	×
Hemolytic anemia	✓	Hematologic	✓
Leukopenia	×		
Thrombocytopenia	✓		
ANA	✓	Immunologic	×
Anti-DNA	×	ANA	✓
Anti-Sm	×		
Antiphospholipid Ab	×		
Low complement (C ₃ , C ₄ , CH ₅₀)	✓		
Direct Coombs test	×		

MCTD [10]. Moreover, the presence of renal complications which, even though they have been described, are uncommon in MCTD [11]. Common MCTD clinical features (including the ones used as diagnostic criteria), such as hand edema, synovitis, myositis, Raynaud phenomenon, and acrosclerosis, were all absent in the course of patient's disease. Thus, other differential diagnoses ought to be investigated.

Finally, other important etiologies to be considered in a patient with PRS are the ANCA-positive vasculitides. The ANCA-positive vasculitides are conformed by three major clinical syndromes; microscopic polyangiitis (MPA), Churg-Strauss syndrome and Granulomatosis with Polyangiitis (GPA). As the name suggests, in these three etiologies, there is a well-characterized role of ANCA antibodies, specifically, antibodies directed against myeloperoxidase (MPO) and proteinase 3 (PR3) proteins in neutrophils cytoplasm, in the pathogenesis of these diseases and the expression of PRS [12].

Although it is possible to have GPA with negative ANCA antibodies, this unusual presentation is usually associated with a decreased likelihood of renal

compromise [13]. Meanwhile, the lack of eosinophilia in the absence of use of glucocorticoids in the initial laboratory findings, as the lack of asthma-like symptoms, steer the diagnosis away from a possible Churg-Strauss syndrome. Lastly, the low C4 complement levels make the MPA diagnosis, as well as other vasculitides, less likely since low C4 levels would be expected in non-ANCA related disorders, as ANCA-positive vasculitides obey an alternative pathway activation [14] with increased to normal C4 levels [15] physiopathogenesis.

Thus, due to the lack of supportive findings towards the previously mentioned etiologies, we classified our patient entity as undefined PRS. While most of the patients in this category may have other described etiologies, the contradictory findings of our case and lack of serological markers led us to further search for possible novel immunological markers. Not tested in this case, and a possible marker for undefined pulmonary-renal syndrome is the anti-endothelial cell antibodies, shown to be linked to ANCA-negative pauciimmune glomerulonephritis [16] [17], propylthiouracil-induced ANCA positive vasculitis [18] and antibody-mediated microvascular insult in idiopathic pulmonary fibrosis [19]. Further studies are required to explore this possible marker in this subset of PRS patients.

From the treatment standpoint, once the undefined PRS diagnosis has been achieved, due to the high mortality rate of this syndrome [3], treatment must be initiated as soon as possible. A review in the current literature yields reports in Japan [20], Germany [21], United States [22] with interesting similarities, and an american series report of patients with diffuse alveolar hemorrhage (20 patients), where one of them presented with ANCA negative serology [23], relevant to our case. Common to all these and our case is the improvement of the patient condition with the use of plasmapheresis and immunosuppression, both by corticosteroids pulses only or combined with cyclophosphamide pulses. Stemming from these case reports outcomes, our own experience, and based on the rationale of the autoimmune origin of these insults, a more aggressive therapeutic regimen based on early plasmapheresis, corticosteroid pulses and cyclophosphamide pulses seems to be an appropriate therapy for this subset of PRS patients.

4. Conclusion

The PRS, being a rare disease, presents itself as a significant diagnostic challenge to the clinician. Even when there is clinical suspicion of this syndrome, less common etiologies may present and generate further doubt regarding the diagnosis and proper patient work-up. ANCA positive vasculitides and anti-GBM disease are responsible for the majority of the PRS in ICUs [1]. The data regarding undefined PRS presenting negative ANCA and anti-GBM negative serology is limited. However, we suggest based on similar reports that the approach of combining corticosteroids and cyclophosphamide pulses, along with plasmapheresis, to be considered as a therapeutic strategy. Further studies are yet required to explore novel immunological markers, therapeutic options and proto-

cols in this subset of PRS patients, hopefully shedding light for physicians facing a high mortality disease where the lack of expected immunological findings may delay this difficult diagnosis.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interests

No conflict of interests are reported by any of the authors.

References

- [1] Papiris, S., Manali, E., Kalomenidis, I., Kapotsis, G., Karakatsani, A. and Roussos, C. (2007) Bench-to-Bedside Review: Pulmonary-Renal Syndromes—An Update for the Intensivist. *Critical Care*, **11**, 213. <https://doi.org/10.1186/cc5778>
- [2] McCabe, C., Jones, Q., Nikolopoulou, A., Wathen, C. and Luqmani, R. (2011) Pulmonary-Renal Syndromes: An Update for Respiratory Physicians. *Respiratory Medicine*, **105**, 1413-1421. <https://doi.org/10.1016/j.rmed.2011.05.012>
- [3] Gallagher, H., Kwan, J.T.C. and Jayne, D.R.W. (2002) Pulmonary Renal Syndrome: A 4-Year, Single-Center Experience. *American Journal of Kidney Diseases*, **39**, 42-47. <https://doi.org/10.1053/ajkd.2002.29876>
- [4] Keane, M. and Lynch, J. (2000) Pleuropulmonary Manifestations of Systemic Lupus Erythematosus. *Thorax*, **55**, 159-166. <https://doi.org/10.1136/thorax.55.2.159>
- [5] Uskudar Cansu, D., Temiz, G., Acikalin, M. and Korkmaz, C. (2017) Pauci-Immune Lupus Nephritis: Possibility or Co-Incidence? *European Journal of Rheumatology*, **4**, 73-75. <https://doi.org/10.5152/eurjrheum.2016.013>
- [6] Fayaz, A., Pirson, Y., Cosyns, J., Yango, J. and Lambert, M. (2008) Pauci-Immune Necrotizing and Crescentic Glomerulonephritis in a Patient with Systemic Lupus Erythematosus. *Clinical Nephrology*, **69**, 290-293. <https://doi.org/10.5414/CNP69290>
- [7] Lech, M. and Anders, H. (2013) The Pathogenesis of Lupus Nephritis. *Journal of the American Society of Nephrology*, **24**, 1357-1366. <https://doi.org/10.1681/ASN.2013010026>
- [8] Petri, M., Orbai, A.-M., Alarcon, G.S., *et al.* (2012) Derivation and Validation of the Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus. *Arthritis & Rheumatism*, **64**, 2677-2686. <https://doi.org/10.1002/art.34473>
- [9] Bull, T., Fagan, K. and Badesch, D. (2005) Pulmonary Vascular Manifestations of Mixed Connective Tissue Disease. *Rheumatic Disease Clinics of North America*, **31**, 451-464. <https://doi.org/10.1016/j.rdc.2005.04.010>
- [10] Alarcón-Segovia, D. and Cardiel, M. (1989) Comparison between 3 Diagnostic Criteria for Mixed Connective Tissue Disease. Study of 593 Patients. *The Journal of Rheumatology*, **16**, 328-34.
- [11] Lundberg, I. (2005) The Prognosis of Mixed Connective Tissue Disease. *Rheumatic Disease Clinics of North America*, **31**, 535-547. <https://doi.org/10.1016/j.rdc.2005.04.005>

- [12] Jennette, J. (2006) Pathogenesis of Vascular Inflammation by Anti-Neutrophil Cytoplasmic Antibodies. *Journal of the American Society of Nephrology*, **17**, 1235-1242. <https://doi.org/10.1681/ASN.2005101048>
- [13] Miloslavsky, E., Lu, N., Unizony, S., *et al.* (2016) Myeloperoxidase-Antineutrophil Cytoplasmic Antibody (ANCA)-Positive and ANCA-Negative Patients with Granulomatosis with Polyangiitis (Wegener's): Distinct Patient Subsets. *Arthritis & Rheumatology*, **68**, 2945-2952. <https://doi.org/10.1002/art.39812>
- [14] Xiao, H., Schreiber, A., Heeringa, P., Falk, R. and Jennette, J. (2007) Alternative Complement Pathway in the Pathogenesis of Disease Mediated by Anti-Neutrophil Cytoplasmic Autoantibodies. *The American Journal of Pathology*, **170**, 52-64. <https://doi.org/10.2353/ajpath.2007.060573>
- [15] Deshayes, S., Aouba, A., Khoy, K., Mariotte, D., Lobbedez, T. and Martin Silva, N. (2018) Hypocomplementemia Is Associated with Worse Renal Survival in ANCA-Positive Granulomatosis with Polyangiitis and Microscopic Polyangiitis. *PLoS ONE*, **13**, e0195680. <https://doi.org/10.1371/journal.pone.0195680>
- [16] Sampathkumar, K., Ramakrishnan, M., Sah, A., Gowtham, S. and Ajeshkumar, R. (2010) ANCA Negative Pauci-Immune Glomerulonephritis with Systemic Involvement. *Indian Journal of Nephrology*, **20**, 43. <https://doi.org/10.4103/0971-4065.62096>
- [17] Cong, M., Chen, M., Zhang, J., Hu, Z. and Zhao, M. (2008) Anti-Endothelial Cell Antibodies in Antineutrophil Cytoplasmic Antibodies Negative Pauci-Immune Crescentic Glomerulonephritis. *Nephrology*, **13**, 228-234. <https://doi.org/10.1111/j.1440-1797.2007.00894.x>
- [18] Yu, F., Zhao, M., Zhang, Y., Zhang, Y. and Wang, H. (2005) Anti-Endothelial Cell Antibodies (AECA) in Patients with Propylthiouracil (PTU)-Induced ANCA Positive Vasculitis Are Associated with Disease Activity. *Clinical & Experimental Immunology*, **139**, 569-574. <https://doi.org/10.1111/j.1365-2249.2005.02725.x>
- [19] Magro, C., Waldman, W., Knight, D., *et al.* (2006) Idiopathic Pulmonary Fibrosis Related to Endothelial Injury and Antiendothelial Cell Antibodies. *Human Immunology*, **67**, 284-297. <https://doi.org/10.1016/j.humimm.2006.02.026>
- [20] Yamaguchi, H., Shirakami, A., Haku, T., *et al.* (2013) Pulmonary-Renal Syndrome with Negative ANCAs and Anti-GBM Antibody. *Case Reports in Nephrology*, **2013**, Article ID: 434531. <https://doi.org/10.1155/2013/434531>
- [21] Fröhlich-Gildhoff, M., Jabs, W., Berhold, C., *et al.* (2016) A Rare Clinical Course of Seronegative Pulmonary-Renal Syndrome. *Case Reports in Critical Care*, **2016**, Article ID: 4893496. <https://doi.org/10.1155/2016/4893496>
- [22] Saladi, L., Shaikh, D., Saad, M., Cancio-Rodriguez, E., *et al.* (2018) Renal Syndrome: A Case Report of Diffuse Alveolar Hemorrhage in Association with ANCA Negative Pauci-Immune Glomerulonephritis. *Medicine*, **97**, e10954. <https://doi.org/10.1097/MD.0000000000010954>
- [23] Klemmer, P., Chalermkulrat, W., Reif, M., Hogan, S., Henke, D. and Falk, R. (2003) Plasmapheresis Therapy for Diffuse Alveolar Hemorrhage in Patients with Small-Vessel Vasculitis. *American Journal of Kidney Diseases*, **42**, 1149-1153. <https://doi.org/10.1053/j.ajkd.2003.08.015>

Eruptive Keratoacanthomas within a Red Ink Tattoo: A Case Report

Brayden Healey^{1*}, William Galbraith¹, Yasser M. Sammour², Diane Baird³

¹Western University of Health Sciences College of Osteopathic Medicine of the Pacific-Northwest, Lebanon, USA

²Cleveland Clinic, Cleveland, USA

³Diane Baird Dermatology, Eugene, USA

Email: *bhealey@westernu.edu

How to cite this paper: Healey, B., Galbraith, W., Sammour, Y.M. and Baird, D. (2018) Eruptive Keratoacanthomas within a Red Ink Tattoo: A Case Report. *Case Reports in Clinical Medicine*, 7, 470-475. <https://doi.org/10.4236/crcm.2018.78041>

Received: July 9, 2018

Accepted: August 10, 2018

Published: August 13, 2018

Copyright © 2018 by authors and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: There has been a longstanding debate regarding whether keratoacanthomas (KAs) are neoplastic or reactive/inflammatory lesions. **Aim:** The aim of this case report is to, within the aforementioned debate, offer support in favor of the potential reactive nature of keratoacanthomas. **Case Presentation:** A 64-year-old male presented with an eruption of 25 keratoacanthomas within a red ink tattoo. Eruptions were partially resolved over a matter of months, and completely resolved with treatment using oral Acitretin therapy. We believe this to be the third such reported case of eruptive KAs within only the red ink portions of a tattoo. Prior cases involved 2 and 8 KAs each. **Discussion:** Multiple studies suggest that KAs are neoplastic in nature and very distinct from cutaneous squamous cell carcinoma. Especially interesting is the finding that KAs have increased expression of apoptotic genes; this is particularly notable because of the tendency for these lesions to spontaneously involute. Skin tumorigenesis can occur in predisposed individuals after carcinogen exposure, thus red ink possesses theoretical potential as a carcinogen. KAs could be seen in this case as in fact a reactive neoplasm.

Keywords

Keratoacanthoma, Squamous Cell Carcinoma, Tattoo, Red Ink, Acitretin

1. Introduction

Keratoacanthomas (KAs) are squamous cell variant neoplastic lesions frequently encountered in clinical dermatology [1] [2]. Their exact etiology is yet to be clearly understood, though most recently the literature suggests they are a folli-

cular variant of cutaneous squamous cell carcinoma (SCC). Nevertheless, KAs have been shown to react differently than most cutaneous neoplasms [3]. Clinically, they present distinctly as rapidly progressing erythematous papules and nodules that evolve to contain a hyperkeratotic, crateriform central crust. They often progress rapidly and have potential for spontaneous involution [4]. Despite this, KAs are often treated clinically as SCC and excised before spontaneous involution occurs. This is due to the clinical and histopathologic difficulty in distinguishing the two. Various exposures and risk factors have been associated with the development of KAs, though typically the lesions are spontaneous [3]. Multiple genetic syndromes have been described in which the eruption of multiple KAs can occur, however in non-syndromal patients eruptive lesions is rare. In certain case reports, various traumatic insults have been suggested to cause KAs to occur, potentiating a reactive or koebnerization-like tendency of KAs. The potential for tattoo ink to act as one such inciting insult has not been well described, despite the multiple other diseases known to be associated with tattoos. A total of 17 cases have been reported in which a KA has occurred within the red ink areas of cutaneous tattoos [5]. We report a case of eruptive KAs occurring entirely within red ink portions of a tattoo.

2. Case Presentation

A 64 year-old male presented to a dermatology clinic with multiple lesions that developed over the past 6 weeks with no prior treatment or evaluation. Sixteen months prior, the patient had obtained a solid black full sleeve tattoo with a 3-inch thick red circumferential band just above the elbow. The original red portion was inked with Lipstick Red ink by Eternal. This tattoo healed entirely as expected. Four months prior to presentation, the red band was re-inked with Dark Red ink, also by Eternal. Three days later, the patient began to notice a deep, burning sensation within the red band; this progressed to the development of painful, draining pustules and papules, which waxed and waned but progressed overall for the next 8 weeks until presentation. Upon presentation, he was found to have approximately 25 tender, well-circumscribed papules, some with hyperkeratotic, crusted centers, located entirely within the red-ink band (**Figure 1**). Two punch biopsies were obtained. Pathological evaluation showed results of invasive, well-differentiated squamous cell carcinoma in both samples. Appearing pathologically as SCC (**Figure 2**) and clinically as eruptive KAs, oral Acitretin 10 mg daily was prescribed. The patient did not start the medication until his next office visit eight weeks later. Interestingly, at that follow up with no treatment as of yet, some improvement of lesions was noted on exam. Ten weeks later, he followed up with near complete resolution of the lesions after using Acitretin 10 mg daily (**Figure 3**). Nearly one year later, the patient continues to have nearly full resolution and has developed any new lesions since the initial eruption. The patient gave full consent for the case as well as photos to be published.



Figure 1. Seen entirely within the red portions of this sleeve tattoo are multiple crusted, crateriform papules clinically representative of keratoacanthomas. This image was taken at the time of biopsy.

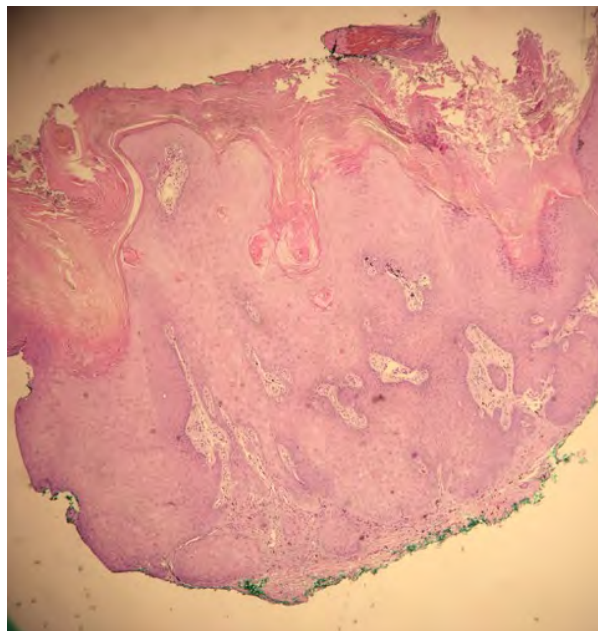


Figure 2. H & E stained sections of the specimen show a punch biopsy of skin with acanthosis, hyperkeratosis and parakeratosis. A central, endophytic squamous proliferation is present with dyskeratosis and cytologic atypia. Associated tattoo pigment is present in the interstitium with solar elastosis and chronic inflammation.



Figure 3. After ten weeks on Acitretin therapy, the lesions had fully regressed and all that remained in their place were a few small crateriform or papular scars without loss of tattoo pigment.

3. Discussion

KAs are most frequently recognized as a variant of follicular SCC [6]. They have a tendency to develop quickly and clinically present as solitary papules ranging from 0.5 to 2 cm in diameter. Maturity of the lesion leads to a pink-red nodule with a crateriform, hyperkeratotic center. Differentiation from SCC, amelanotic melanoma, and basal cell carcinoma is often not possible with physical examination alone. Growth typically continues for months and is often followed by involution over the same time span. Notwithstanding, many lesions are treated before spontaneous involution due to the difficulty in differentiation from other neoplasms [7].

Much debate has been had in classifying KAs as neoplastic or reactive. They have been found to occur in areas of trauma, surgery, chemical irritation, and UV exposure [3]. Most commonly, however, they are found to be isolated and apparently spontaneous. Rare cases of eruptive lesions are encountered mainly with genetic syndromes [6]. The appearance of eruptive KAs confined to a red ink tattoo is inconsistent with these known syndromes.

The etiology of KAs remains unclear. In many instances, as in this case, pathologists do not differentiate KAs from SCC, or label KAs as subtypes of SCC. Recent studies have suggested that both molecularly and clinically, KAs are distinct from SCC and should be treated accordingly. A clinical systematic review argues strongly for the benign nature of the lesions, citing that of 445 cases studied over time, zero cases of metastasis were reported and no deaths occurred at the hand of the disease. To the contrary, 5.6% of SCCs directly resulted in death [8].

Despite their low metastatic potential and distinctness from SCC, KAs are pathogenetically neoplastic. Ra *et al.* studied the molecular profiles of KAs in comparison to both regular skin and SCCs and found highly varied expression profiles; 1449 genes were expressed differently between the two diseases. This is compared to actinic keratosis, a purported pre-cursor to SCC, which only varied from SCCs by only 9 genes [9]. Likewise, other studies have supported molecular differentiation between the two in pathways ranging from growth to cellular maturation and apoptosis. Interestingly, many of the genetic derangements identified lead to increased apoptotic signaling, a potential cause of spontaneous involution.

The finding that skin tumors can be induced by exposure to a carcinogen in those with an oncogenic predisposition has been demonstrated [9]. HPV is one such potential carcinogen that has been associated with KAs. The potential for tattoo ink in this case to act as a carcinogen in KAs has not been proven but is theoretically within reason.

Tattoos have been known to cause a variety of dermatologic complications, albeit rarely. Most adverse reactions are infectious or allergic. Autoimmune reactions to various ink components are also described. One small trial estimated that 2.1% of tattoos develop infectious, allergic or granulomatous reactions [10]. However, the incidence of tumorous reactions within tattoos is so rare that it is not currently described. Less than 50 cases of skin cancer occurring within a tattoo, including melanoma, basal cell carcinoma, SCC and KAs have been reported. Of all reported cases, 28 were associated with red ink, 17 of these being KAs; only two of these cases described eruptive or multiple KAs arising solely within red ink portions of the tattoos [5]. Thus, while an association with red ink can be proposed, the tendency for eruptive KAs to occur within red ink is exceedingly rare.

This case appears to highlight much of this information. The patient appears to have had a reaction to the red ink used to re-ink his tattoo band. In concert with the findings of Ra, *et al.* it seems that this ink may have acted as a carcinogen. It is unknown what phenotypical characteristics make up a predisposed individual for KAs, though this patient's Fitzpatrick 1 skin type does predispose him to non-melanoma skin cancers such as basal cell carcinoma and SCC. The eruption is inconsistent with syndromal KAs based upon the localized nature of the lesions. Clinically, the lesions were perfectly consistent with typical KA le-

sions. Interestingly, they also followed the pattern of spontaneous involution as the patients saw some improvement over the course of eight weeks without treatment. Acitretin therapy appears to have been successful in obtaining near clearance with successful eradication at one-year follow-up.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Sullivan, J.J. (1997) Keratoacanthoma: The Australian Experience. *The Australasian Journal of Dermatology*, **38**, S36-S39. <https://doi.org/10.1111/j.1440-0960.1997.tb01007.x>
- [2] Reizner, G.T., Chuang, T.Y., Elpern, D.J., Stone, J.L. and Farmer, E.R. (1993) Basal Cell Carcinoma and Keratoacanthoma in Hawaiians: An Incidence Report. *Journal of the American Academy of Dermatology*, **29**, 780-782. [https://doi.org/10.1016/S0190-9622\(08\)81701-X](https://doi.org/10.1016/S0190-9622(08)81701-X)
- [3] Ko, C.J. (2010) Keratoacanthoma: Facts and Controversies. *Clinics in Dermatology*, **28**, 254-261. <https://doi.org/10.1016/j.clindermatol.2009.06.010>
- [4] Ko, C.J., McNiff, J.M., Bosenberg, M. and Choate, K.A. (n.d) Keratoacanthoma: Clinical and Histopathologic Features of Regression. *Journal of the American Academy of Dermatology*, **67**, 1008-1012. <https://doi.org/10.1016/j.jaad.2012.02.041>
- [5] Kluger, N. (2010) Issues with Keratoacanthoma, Pseudoepitheliomatous Hyperplasia and Squamous Cell Carcinoma within Tattoos: A Clinical Point of View. *Journal of Cutaneous Pathology*, **37**, 812-813. <https://doi.org/10.1111/j.1600-0560.2009.01375.x>
- [6] Kwiek, B. and Schwartz, R.A. (2016) Review: Keratoacanthoma (KA): An Update and Review. *Journal of the American Academy of Dermatology*, **74**, 1220-1233.
- [7] Cavicchini, S., Tournalaki, A., Lunardon, L., Boneschi, V. and Gianotti, R. (2013) Amelanotic Melanoma Mimicking Keratoacanthoma: The Diagnostic Role of Dermoscopy. *International Journal of Dermatology*, **52**, 1023-1024. <https://doi.org/10.1111/j.1365-4632.2011.05025.x>
- [8] Savage, J.A. and Maize, J.C. (n.d) Keratoacanthoma Clinical Behavior: A Systematic Review. *American Journal of Dermatopathology*, **36**, 422-429.
- [9] Ra, S.H., Su, A., Li, X., Zhou, J., Cochran, A.J., Kulkarni, R.P. and Binder, S.W. (2015) Keratoacanthoma and Squamous Cell Carcinoma Are Distinct from a Molecular Perspective. *Modern Pathology*, **28**, 799-806. <https://doi.org/10.1038/modpathol.2015.5>
- [10] Kazandjieva, J. and Tsankov, N. (2007) Tattoos: Dermatological Complications. *Clinics in Dermatology*, **25**, 375-382. <https://doi.org/10.1016/j.clindermatol.2007.05.012>

Right Atrial Giant Myxoma Occupying the Right Ventricular Cavity

Amanollah Heidari^{1*}, Mohammad Nourizadeh¹, Mohammad Hossein Najafi¹, Sara Nourizadeh², Najmeh Assadinia³

¹Atherosclerosis Research Center, Joundishapour University, Ahwaz, Iran

²Department of Cell & Molecular Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

³Department of Pathology, Shahidbeheshti Medical University, Tehran, Iran

Email: *heidari_a@ajums.ac.ir

How to cite this paper: Heidari, A., Nourizadeh, M., Najafi, M.H., Nourizadeh, S. and Assadinia, N. (2018) Right Atrial Giant Myxoma Occupying the Right Ventricular Cavity. *Case Reports in Clinical Medicine*, 7, 476-481.

<https://doi.org/10.4236/crcm.2018.78042>

Received: June 10, 2018

Accepted: August 18, 2018

Published: August 21, 2018

Copyright © 2018 by authors and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Introduction: Atrial myxomas are the most common primary heart tumors. Because of nonspecific symptoms, early diagnosis may be a challenge [1] [2]. Left atrial myxoma may or may not produce characteristic findings on auscultation. Two-dimensional echocardiography is the diagnostic procedure of choice. Most atrial myxomas are benign and can be removed by surgical resection. Cardiac myxoma is located mostly in left atrium [3]. This was amazing huge mass of cardiac myxoma in unusual part of the heart with the patient showed significant response to anticoagulation after presumed recurrence of tumor. **Case Presentation:** A case of giant right atrial myxoma mimicking the right ventricular tumor is described. Surgery was performed in 41 years old female and the fist like tumor with its stalk was excised. Surprisingly it recurred after 2 month as the smaller tumor was completely resolved with anticoagulation therapy. In addition because of previous normal echocardiography that was done for another reasons, we estimated the speed of tumor's growth (3 millimeter/month). **Conclusion:** To sum up a very large myxoma in right ventricle may only present with occasional dyspnea and we can diagnose it with precise evaluation and with performing on time echocardiography.

Keywords

Giant Myxoma, Right Atrial, Right Ventricular

1. Introduction

Intracardiac myxoma with an estimated incidence of 0.5 - 1 per million per annum constitute about 60% of all primary heart tumor. Approximately 90% occur

in the left atrial cavity, and the right atrium is an unusual location. Right atrial myxomas rarely produce symptoms until they are huge [4] [5]. Our case is of special interest because of its big size and the recurrence after 2 month. We had this opportunity to estimate tumor's growth rate because of serial normal echocardiograms that were performed for another non-cardiac reasons.

We presented this case to introduce the patient with atypical symptom of cardiac myxoma and unusual size and unusual response to treatment

2. Case Presentation

A 41 year-old woman complained of exertional dyspnea and cough 2 month prior to the admission. Electrocardiography was nonspecific but she had a systolic murmur in physical examination. A transthoracic 2D echocardiogram showed a large right atrial mass through the tricuspid valve (**Figures 1-3**). The contrast computerized tomographic scan showed an abnormal shadow defect in the right ventricle. The coronary angiography was normal. We diagnosed it as a right ventricular tumor.

The patient undergone surgery using Median sternotomy, after cardiac arrest by ante grade blood cardioplegia, a right atriotomy was done. Most of the mass was in the right ventricle of the tricuspid valve. The tumor was excised along with the stalk. Tricuspid valve repaired after that.

On gross inspection, the tumor was a soft, lobulated mass measuring $90 \times 20 \times 60$ mm, histological examination confirmed that it was a myxoma. A transthoracic echocardiogram obtained 5 days post operation that showed no residual tumor and mild tricuspid regurgitation. The patient discharged 5 days after surgery.

She came back 3 month after discharge with some dyspnea. Transthoracic echocardiogram revealed a mobile right atrial tumor measuring 10×6 mm.

Because the patient had nephrolithiasis and for this reason she had serial echo-study for preoperative evaluation the last normal trans-thoracic echocardiogram was 24 month ago (in 29/Jun/2011). The tumor was diagnosed in 19/Jun/2013. It's very striking finding that tumor in 24 month can grow up to the 90 mm length(the mean velocity of growth in length was at least 3.7 mm per month).

The patient rejected admission for another surgery so oral anticoagulation with warfarin started and close contact with patient preserved. Dyspnea gradually disappeared and repeated transthoracic echocardiogram after 2 month showed no tumor in the right atrium (**Figure 4**). The patient evaluated in 3 month by echocardiography and she was normal on 3 occasions.

3. Discussion

Primary cardiac neoplasms are rare and occur with an estimated incidence of 0.0017% to 0.19%, representing less than 5% of all heart tumors [6] [7]. Myxoma is the most prevalent primary cardiac tumor. The RA is an unusual location and

is the site of 15% to 20% of cases of myxoma. A low incidence of RA myxoma has been reported for decades in several series of autopsy cases. Approximately 70% of affected patients are women [7] [8] predominantly between the third and sixth decades of life [8].

Myxomas are usually polypoid and pedunculated tumors (approximately 83% of cases) [8] [9]. In this report, our patient had a 90 × 20 × 60 mm a soft, lobulated mass.

In a recent publication reporting 19 years of experience with surgical treatment of primary intracardiac myxoma, seven (17%) cases out of 41 originated from the RA [10]. However, in this case report, the mean maximal diameter of the tumors was measuring 90 × 20 × 60 mm. To the best of our knowledge, our case is one of the largest RA myxomas described in the literature.

We report a case of a giant right atrial myxoma occupying the entire right ventricular cavity. Three aspects of this case are of special interest. First, the tumor in this patient is very large 90 × 20 × 60 mm that protruding in the right ventricle (Figure 5).



Figure 1. Myxoma in RA.



Figure 2. Extension of myxoma to RV.

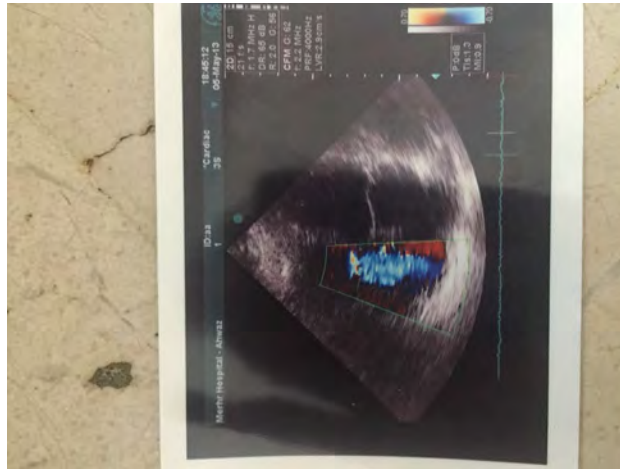


Figure 3. Tricuspid regurgitation due to myxoma.

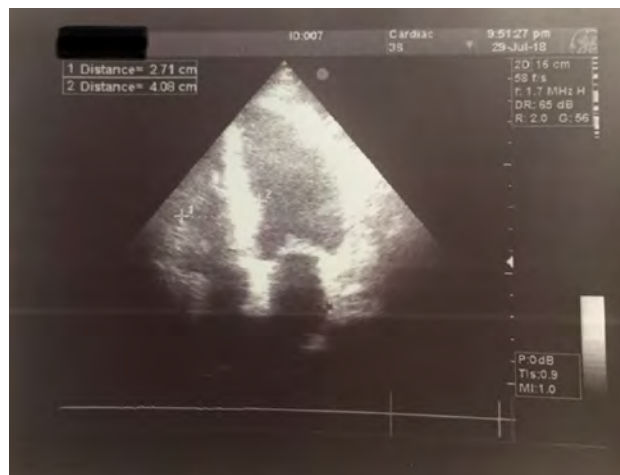


Figure 4. Myxoma is not seen in RA or RV.



Figure 5. Size and shape of tumor in gross pathology.

Symptoms are said to be more variable when a tumor occurs in the right rather than the left atrium. It was, however, a striking feature of this patient's his-

tory, that the symptoms were not only vague but also mild and intermittent. Despite the presence of such a large tumor, one of the largest recorded, she could be free from symptoms for several weeks. Although this tumor is one of the largest myxoma that ever reported, the patients had only a mild dyspnea that it is possible that it was related to reductions in cardiac output to the pulmonary system produced by variable right atrial outflow obstruction. In comparison to the other myxoma this patients was diagnosed sooner because echocardiography performed in the first visit of patient.

Second patients come back with dyspnea again 3 moth after surgery. recurrence occurred in the site of previous tumor that successfully responds to oral anticoagulation therapy. because the shape of tumor is very similar to previous tumor in site of interatrial septum we wanted to excise it again but patient didn't accept surgery and she wanted to continue anticoagulation therapy with warfarin 5 mg daily (The INR between 2 - 3) we surprisingly found that the tumor was resolved completely after 2 month and the patients be free of symptoms again.

So we recommended that if the myxoma like tumor recruited after the first surgery a trial of anticoagulation therapy performed before another surgery.

Third because the patients had normal echocardiography 24 month ago we had this opportunity that calculate the mean velocity of growth of the tumor

The first normal transthoracic echocardiogram was on 14//Jun/2008. Another normal one was on 29/Jun/2011. The first abnormal transthoracic echocardiogram was on 24/Jun/2013, 24 months after last normal echocardiogram. With a simple calculation we can conclude that linear growth of this tumor was at least approximately 3.7 mm/month. Previously reported myxoma have ranged in size from 1.5 to 11 cm [5]. although we didn't have serial echocardiography in these 2 years and the tumor may grow later, this calculation is the least mean velocity estimation and this is the first time that the mean velocity of the growth of myxoma tumor estimated.

4. Conclusions

In summary, this is the rare case report with large and rapid growing tumor in right side of the heart showing that initial intensive treatment with anticoagulation in patient with presumed recurrence of cardiac myxoma before secondary high risk surgery may result in a rapid clinical improvement and disappearing cardiac mass.

On the other hand if we assume another recurrence after previous surgery based on echocardiographic finding alone we should consider anticoagulation trial before performing another surgery.

Acknowledgements

The authors would like to thank Dr. Mohammad Hasan Adel who provided skillful editorial assistance. Financial support for editorial services was provided by Ahwaz Jundishapur research center.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interests

The authors declare that they have no competing interests.

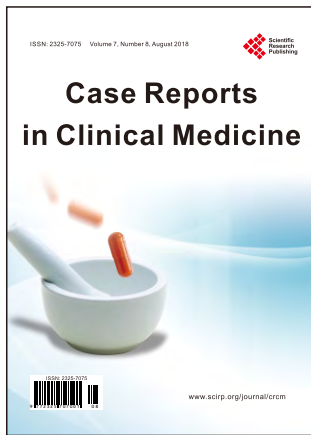
Authors' Contributions

All authors participated in the interpretation of clinical data and writing of this case report. All authors read and approved the final manuscript.

References

- [1] Reynen, K. (1996) Frequency of Primary Tumor of the Heart. *The American Journal of Cardiology*, **17**, 107. [https://doi.org/10.1016/S0002-9149\(97\)89149-7](https://doi.org/10.1016/S0002-9149(97)89149-7)
- [2] Pavlides, G.S., Levin, R.N. and Hauser, A.M. (1989) Left Ventricular Recurrence of a Resected Left Atrial Myxoma. *American Heart Journal*, **117**, 1390-1392. [https://doi.org/10.1016/0002-8703\(89\)90427-4](https://doi.org/10.1016/0002-8703(89)90427-4)
- [3] Fang, B.R., Chang, C.P., Cheng, C.W., et al. (2004) Total Detachment of Cardiac Myxoma Causing Saddle Embolization and Mimicking Aortic Dissection. *Japanese Heart Journal*, **45**, 56-63.
- [4] Bigelow, J.C., Herr, R.H. and Starr, A. (1969) Atrial Myxoma. *Surgery*, **65**, 247-255.
- [5] Bahnson, H.T. and Newman, E.V. (1953) Diagnosis and Surgical Removal of Intracavitary Myxoma of the Right Atrium. *Bulletin of the Johns Hopkins Hospital*, **93**, 150-163.
- [6] Guhathakurta, S. and Riordan, J.P. (2000) Surgical Treatment of Right Atrial Myxoma. *Texas Heart Institute Journal*, **27**, 61-63.
- [7] Azevedo, O., Almeida, J., Nolasco, T., Medeiros, R., Casanova, J., Bartosch, C., Almeida, J. and Pinho, P. (2010) Massive Right Atrial Myxoma Presenting as Syncope and Exertional Dyspnea: Case Report. *Cardiovascular Ultrasound*, **8**, 23. <https://doi.org/10.1186/1476-7120-8-23>
- [8] Manfroi, W., Vieira, S.R., Saadi, E.K., Saadi, J. and Alboim, C. (2001) Multiple Recurrences of Cardiac Myxomas with Acute Tumoral Pulmonary Embolism [in Portuguese]. *Arquivos Brasileiros de Cardiologia*, **77**, 161-163. <https://doi.org/10.1590/S0066-782X2001000800007>
- [9] Ojji, D.B., Ajiduku, S.S., Omonua, O.O., Abdulkareem, L.L. and Parsonage, W. (2008) A Probable Right Atrial Myxoma Prolapsing through the Tricuspid Valve into the Right Ventricle: A Case Report. *Cases Journal*, **1**, 386. <https://doi.org/10.1186/1757-1626-1-386>
- [10] Samanidis, G., Perreas, K., Kalogris, P., Dimitriou, S., Balanika, M., Amanatidis, G., Khoury, M. and Michalis, A. (2011) Surgical Treatment of Primary Intracardiac Myxoma: 19 Years of Experience. *Interactive Cardiovascular and Thoracic Surgery*, **13**, 597-600. <https://doi.org/10.1510/icvts.2011.278705>

Call for Papers



Case Reports in Clinical Medicine

ISSN Print: 2325-7075 ISSN Online: 2325-7083

<http://www.scirp.org/journal/crcm>

Case Reports in Clinical Medicine (CRCM) is a monthly open access journal. The goal of this journal is to provide a platform for scientists and academicians all over the world to promote, share, and discuss various new issues and developments by publishing case reports in all aspects of Clinical Medicine.

All manuscripts must be prepared in English, and are subject to a rigorous peer-review process. Accepted papers will immediately appear online followed by printed in hard copy. The areas covered by Case Reports in Clinical Medicine (CRCM) include but are not limited to:

Case Reports in Allergy and Clinical Immunology
Case Reports in Cancer Research and Clinical Oncology
Case Reports in Clinical Anaesthesiology
Case Reports in Clinical Anatomy
Case Reports in Clinical and Applied Thrombosis/Hemostasis
Case Reports in Clinical and Experimental Allergy
Case Reports in Clinical and Experimental Dermatology
Case Reports in Clinical and Experimental Hypertension
Case Reports in Clinical and Experimental Immunology
Case Reports in Clinical and Experimental Medicine
Case Reports in Clinical and Experimental Metastasis
Case Reports in Clinical and Experimental Nephrology
Case Reports in Clinical and Experimental Ophthalmology
Case Reports in Clinical and Experimental Optometry
Case Reports in Clinical and Experimental Otorhinolaryngology
Case Reports in Clinical and Experimental Pathology
Case Reports in Clinical and Experimental Pharmacology and Physiology
Case Reports in Clinical and Molecular Allergy
Case Reports in Clinical and Translational Oncology
Case Reports in Clinical Anesthesia
Case Reports in Clinical Apheresis
Case Reports in Clinical Autonomic Research
Case Reports in Clinical Biochemistry and Nutrition
Case Reports in Clinical Biomechanics
Case Reports in Clinical Cardiology
Case Reports in Clinical Case Studies
Case Reports in Clinical Child Psychology and Psychiatry
Case Reports in Clinical Chiropractic
Case Reports in Clinical Densitometry
Case Reports in Clinical Effectiveness in Nursing
Case Reports in Clinical Endocrinology and Metabolism
Case Reports in Clinical Epidemiology
Case Reports in Clinical Forensic Medicine
Case Reports in Clinical Gastroenterology and Hepatology
Case Reports in Clinical Genetics
Case Reports in Clinical Haematology
Case Reports in Clinical Hypertension
Case Reports in Clinical Imaging
Case Reports in Clinical Immunology
Case Reports in Clinical Implant Dentistry and Related Research
Case Reports in Clinical Interventions in Aging
Case Reports in Clinical Laboratory Analysis
Case Reports in Clinical Linguistics & Phonetics
Case Reports in Clinical Lipidology
Case Reports in Clinical Microbiology and Antimicrobials
Case Reports in Clinical Microbiology and Infection
Case Reports in Clinical Microbiology and Infectious Diseases
Case Reports in Clinical Molecular Pathology
Case Reports in Clinical Monitoring and Computing
Case Reports in Clinical Neurology and Neurosurgery
Case Reports in Clinical Neurophysiology
Case Reports in Clinical Neuropsychology
Case Reports in Clinical Neuroradiology

Case Reports in Clinical Neuroscience
Case Reports in Clinical Nursing
Case Reports in Clinical Nutrition
Case Reports in Clinical Obstetrics and Gynaecology
Case Reports in Clinical Oncology and Cancer Research
Case Reports in Clinical Oral Implants Research
Case Reports in Clinical Oral Investigations
Case Reports in Clinical Orthopaedics and Related Research
Case Reports in Clinical Otolaryngology
Case Reports in Clinical Pathology
Case Reports in Clinical Pediatric Emergency Medicine
Case Reports in Clinical Periodontology
Case Reports in Clinical Pharmacology & Toxicology
Case Reports in Clinical Pharmacy and Therapeutics
Case Reports in Clinical Physiology and Functional Imaging
Case Reports in Clinical Practice and Epidemiology in Mental Health
Case Reports in Clinical Psychology and Psychotherapy
Case Reports in Clinical Psychology in Medical Settings
Case Reports in Clinical Radiology
Case Reports in Clinical Rehabilitation
Case Reports in Clinical Research and Regulatory Affairs
Case Reports in Clinical Research in Cardiology
Case Reports in Clinical Respiratory
Case Reports in Clinical Rheumatology
Case Reports in Clinical Simulation in Nursing
Case Reports in Clinical Sleep Medicine
Case Reports in Clinical Techniques in Small Animal Practice
Case Reports in Clinical Therapeutics
Case Reports in Clinical Toxicology
Case Reports in Clinical Transplantation
Case Reports in Clinical Trials
Case Reports in Clinical Ultrasound
Case Reports in Clinical Virology
Case Reports in Complementary Therapies in Clinical Practice
Case Reports in Consulting and Clinical Psychology
Case Reports in Contemporary Clinical Trials
Case Reports in Controlled Clinical Trials
Case Reports in Diabetes Research and Clinical Practice
Case Reports in Evaluation in Clinical Practice
Case Reports in Fundamental & Clinical Pharmacology
Case Reports in Hematologic Diseases
Case Reports in Hereditary Cancer in Clinical Practice
Case Reports in Human Psychopharmacology: Clinical and Experimental
Case Reports in Innovations in Clinical Neuroscience
Case Reports in Laboratory and Clinical Medicine
Case Reports in Neurophysiologie Clinique/Clinical Neurophysiology
Case Reports in Nutrition in Clinical Practice
Case Reports in Pacing and Clinical Electrophysiology
Case Reports in Psychiatry in Clinical Practice
Case Reports in Therapeutics and Clinical Risk Management
Case Reports in Veterinary Clinical Pathology
Case Reports in Obstetrics and Gynecology

Website and E-Mail

<http://www.scirp.org/journal/crcm>

Email: crcm@scirp.org

What is SCIRP?

Scientific Research Publishing (SCIRP) is one of the largest Open Access journal publishers. It is currently publishing more than 200 open access, online, peer-reviewed journals covering a wide range of academic disciplines. SCIRP serves the worldwide academic communities and contributes to the progress and application of science with its publication.

What is Open Access?

All original research papers published by SCIRP are made freely and permanently accessible online immediately upon publication. To be able to provide open access journals, SCIRP defrays operation costs from authors and subscription charges only for its printed version. Open access publishing allows an immediate, worldwide, barrier-free, open access to the full text of research papers, which is in the best interests of the scientific community.

- High visibility for maximum global exposure with open access publishing model
- Rigorous peer review of research papers
- Prompt faster publication with less cost
- Guaranteed targeted, multidisciplinary audience



**Scientific
Research
Publishing**

Website: <http://www.scirp.org>

Subscription: sub@scirp.org

Advertisement: service@scirp.org