Published in final edited form as:

J Clin Urol. 2018 May ; 11(3): 226–228. doi:10.1177/2051415817716014.

Characterization of the Macrophage Infiltrate in a Case of Xanthogranulomatous Pyelonephritis

Jelani C. Zarif, Heather J. Chalfin, Phillip M. Pierorazio, and Michael A. Gorin

The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine Baltimore, MD 21287

Introduction

Xanthogranulomatous pyelonephritis (XGP) is a rare chronic infectious process of the kidney that results in diffuse destruction of the renal parenchyma [1,2]. The majority of cases of XGP occur in the setting of obstructing nephrolithiasis and are histologically characterized by the presence of lipid-laden foamy macrophages. To date, little is known regarding the molecular and functional phenotype of the infiltrating macrophages observed in cases of XGP.

Human CD14+ monocytes can differentiate into macrophages and then become polarized towards two distinct phenotypes [3–5]. Classically activated (also known as M1) macrophages have the ability to secrete pro-inflammatory cytokines such as IFN- γ , IL-2, and TNF- α . Conversely, alternatively activated (also known as M2) macrophages secrete anti-inflammatory cytokines such as IL-10, IL-23, and VEGF. Characterization of the immune infiltrate in cases of XGP is necessary for understanding the pathogenesis of this disease process. Moreover, this knowledge may form the basis of future non-invasive treatment strategies for XGP. Herein, we report the phenotypic characterization of the macrophage infiltrate in a case of XGP.

Case Report

The patient is a 63-year-old female who presented to an outside hospital with a one-week history of malaise, right upper quadrant pain, low-grade fevers, and dysuria. Her past medical history is notable for morbid obesity, hypertension, gastric reflux, and frequent urinary tract infections. On presentation, she was tachycardic and her labwork was remarkable for an elevated white blood cell (WBC) count (20×10^3 cells/mm²) as well as a urinalysis with too numerous to count WBCs and many bacteria. X-ray computed tomography scan revealed a right kidney with a staghorn calculus and the classic “bear paw”

Correspondence: Michael A. Gorin, M.D., 600 North Wolfe Street, Park 213, Baltimore, MD 21287, Phone: (410) 614-8151, Fax: (844) 330-1544, mgorin1@jhmi.edu.

Contributorship: All authors contributed equally to this work.

Conflicting interests: The Authors report no conflicts of interest.

Informed consent: Written informed consent was obtained from the patient.

Ethical approval: The Johns Hopkins Institutional Review Board approved the protocol for tissue collection.

Guarantor: M.A.G. takes full responsibility for the article, including for the accuracy and appropriateness of the reference list.

sign of XGP (Figure 1). The patient was managed with fluids, broad spectrum antibiotics, and right nephrostomy tube placement. Within 36 hours of initial presentation she was transferred to our center where her WBC count was 16×10^3 cells/mm² and she remained hemodynamically stable. Approximately 48 hours later she underwent an elective simple nephrectomy which led to resolution of her symptoms along with normalization of her WBC count.

Routine pathologic evaluation of the patient's kidney revealed XGP with a classic appearing dense inflammatory infiltrate. To further investigate the phenotype of these cells, immunohistochemistry for previously described M1 and M2 markers [4] was performed using excised XGP and normal appearing renal tissue. In brief, tissues were stained with primary antibodies against the M1 markers iNOS (Thermo Fisher Rockford, IL 1:300) and IFN- γ (Abcam Cambridge, MA 1:600) as well as the M2 markers CD163 (Abcam Cambridge, MA 1:600) and CD206 (LSBIO, Seattle, WA 1:400). Slides were then incubated with PowerVision+ Poly-HRP anti-mouse IgG (Leica Biosystems, Buffalo Grove, IL). Evaluation of the slides revealed positive staining for both M1 and M2 markers within the diseased renal parenchyma and an absence of these markers in the nearby normal kidney (Figures 2 and 3).

Discussion

XGP was first described in 1916 by Schlagenhauser as a mimicker of other inflammatory renal parenchymal and neoplastic diseases [6]. The current mainstay of therapy for this rare entity is nephrectomy with the loss of the renal uni [1,2]. Previously, others have demonstrated the presence of CD68-positive macrophages in XGP specimens [1,7–9]. However, CD68 is expressed by a number of phagocytic cells and represents a pan-macrophage marker [10]. To shed further light on the underlying pathophysiology of this destructive disease process, we characterized the macrophage infiltrate in a case of XGP by assessing for the presence of inflammatory cytokines and markers expressed on M1 and M2 macrophages. Notably, we found that the stained tissue was positive for markers of both cell populations. Based on this observation, we hypothesize that in cases of XGP, which is a chronic insidious process, the trafficking of M2 macrophages may be a late event after early inflammation driven by the M1 cells. Given the limitations of a single case, additional investigation is required to provide further insight into the role of polarized macrophage subsets in XGP.

In conclusion, we observed positive staining for both M1 and M2 macrophage markers in a case of XGP. The presence of M2 macrophages provides a possible mechanism of tissue repair during the chronic inflammation of XGP. This finding may have implications for medical management of this disease.

Acknowledgments

None

Funding: This study was supported the UNCF/Merck Postdoctoral Science Research Fellowship and Prostate Cancer Foundation Young Investigator award both to J.C.Z.

References

1. Li L, Parwani AV. Xanthogranulomatous pyelonephritis. *Arch Pathol Lab Med*. 2011; 135:671–4. [PubMed: 21526966]
2. Hou J, Herlitz LC. Renal Infections. *Surg Pathol Clin*. 2014; 7:389–408. [PubMed: 26837446]
3. Novak ML, Koh TJ. Macrophage phenotypes during tissue repair. *J Leukoc Biol*. 2013; 93:875–881. [PubMed: 23505314]
4. Mantovani A, Biswas SK, Galdiero MR, Sica A, Locati M. Macrophage plasticity and polarization in tissue repair and remodelling. *J Pathol*. 2013; 229:176–85. [PubMed: 23096265]
5. Sica A, Erreni M, Allavena P, Porta C. Macrophage polarization in pathology. *Cell Mol Life Sci*. 2015; 72:4111–26. [PubMed: 26210152]
6. Schlagenhauer F. Über eigentümlich staphylomykosender neiven und des pararenalen bindegewebes. *Frankfurt Z Pathol*. 1916; 19:139–48.
7. Boulanger V, Merville P, Morel D, Pariente JL, Deminière C, Potaux L. Xanthogranulomatous pyelonephritis in the native kidney of a renal transplant recipient. *Nephrol Dial Transplant*. 1997; 12:831–2. [PubMed: 9141028]
8. Mohanty A, Kim O. Nonfunctional right kidney in a 50-year-old woman. Xanthogranulomatous pyelonephritis. *Arch Pathol Lab Med*. 2005; 129:e209–11. [PubMed: 16332150]
9. Nandedkar SS, Malukani K, Sakhi P. Xanthogranulomatous pyelonephritis masquerading as a tumor in an infant. *Indian J Urol*. 2014; 30:354–6. [PubMed: 25097328]
10. Kunisch E, Fuhrmann R, Roth A, Winter R, Lungershausen W, Kinne RW. Macrophage specificity of three anti-CD68 monoclonal antibodies (KP1, EBM11, and PGM1) widely used for immunohistochemistry and flow cytometry. *Ann Rheum Dis*. 2004; 63:774–84. [PubMed: 15194571]

Figure 1. Image from a coronal CT scan demonstrates an obstructed left kidney with a staghorn calculus (yellow arrow). The dilated pelvises (red arrow) form the classic “bear paw” sign of xanthogranulomatous pyelonephritis.

Figure 2. Immunohistochemical staining of renal parenchyma affected by xanthogranulomatous pyelonephritis demonstrates positivity for the M1 macrophage marker iNOS and secreted cytokine IFN- γ . Cells in the nearby normal renal tissue are negative for these markers.

Figure 3. Immunohistochemical staining of renal parenchyma affected by xanthogranulomatous pyelonephritis demonstrates positivity for the M2 macrophage markers CD163 and CD206. Cells in the nearby normal renal tissue are negative for these markers.