Co-Existing Metallosis in Patients with Periprosthetic Joint Infection After Total Hip Arthroplasty Results in Delayed Diagnosis and Worse Post-Operative Outcomes

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INTRODUCTION: Metallosis is a rare complication after total hip arthroplasty (THA) that occurs due to the release of metal ions into the joint. On the contrary, prosthetic joint infection (PJI) is a common reason of implant revision and is associated with poor outcomes if not treated appropriately. While co-existing metallosis and PJI has been associated with worse post-operative outcomes, literature is limited to small series without a control group. This study sought to compare the outcomes of THA patients with co-existing metallosis and PJI to THA patients with PJI alone, specifically evaluating if the presence of metallosis at the time of revision was associated with delayed PJI diagnosis and if metallosis impacted post-operative outcomes.

METHODS: A retrospective review of prospectively collected data from two large, tertiary-care academic centers was conducted. Patients who underwent revision THA between 2009 and 2019 with a concomitant diagnosis of metallosis and PJI were included (metallosis/PJI group). Metallosis was diagnosed based on the intraoperative findings documented in the surgeon's operative report coupled with serum cobalt and chromium levels. Nine of 13 patients in the metallosis/PJI group were tested for serum cobalt and chromium pre-operatively. Diagnosis of PJI was made using the 2011 Musculoskeletal Infection Society criteria. The metallosis/PJI group was matched to a cohort of patients with PJI alone after THA (PJI alone group). A two-to-one propensity-score matching based on age, sex, and type of revision surgery (one-stage vs. two-stage) was conducted. The primary outcomes of interest were time to PJI diagnosis, and reoperation- and revision-free survival. Survival analysis was performed using the Kaplan-Meier method.

RESULTS: There were 13 patients in the metallosis/PJI group, and 26 patients in the PJI alone group. The mean age for the metallosis/PJI and the PJI alone groups were 64 and 66, respectively (Table 1). Mean serum cobalt and chromium levels in the metallosis/PJI group were 9.6 nmol/L (range 0.5 to 35) and 7.16 nmol/L (range 0.1 to 42.6), respectively. Positive cultures were obtained in 62% of patients with metallosis/PJI, and 81% of those with PJI alone. Mean time from symptom onset to positive culture was 1 day in the PJI alone group, and 38 days in the metallosis/PJI group (p=0.008). Gram-positive microorganisms grew in 88% of metallosis and PJI, and 86% of PJI alone cultures, respectively (Table 2). Polymicrobial infections were more common in patients with metallosis/PJI (38%) than those with PJI alone (5%) (p=0.02). One- and two-stage revision were performed in 69% and 31% of cases in both groups (Table 3). Post-operative complications occurred in 8% of metallosis/PJI patients, and 35% of PJI alone patients (p=0.07). Revision after initial PJI index surgery was performed in 46% of patients with metallosis/PJI, and 27% of those with PJI alone (p=0.04). For the entire cohort, 2-year revision-free survival was lower in the metallosis/PJI group compared to the PJI group (34.9% vs, 86.9%, p=0.03) (Table 4 and Figure 1). Within the two-stage revision subgroup, patients with metallosis/PJI exhibited lower one-year reoperation- (50% vs. 100%, p=0.03) and revision-free (50% vs. 100%, p=0.03) survival compared to PJI alone patients (Table 4 and Figure 2)

DISCUSSION AND CONCLUSION: In our study, co-existence of metallosis and PJI resulted in prolonged time to diagnosis due to delayed positive culture along with lower revision-free survival. In the setting of metallosis, surgeons should have a higher index of suspicion for occult PJIs and not necessarily rule them out based on negative culture growth. Future studies should combine data from multiple institutions to further investigate the effect of metallosis on standard PJI diagnostic tests.

Figure 1. Revision-free survival of the entire cohort.

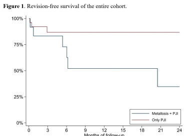

Figure 2. (A) Reoperation- and (B) revision-free survival in patients treated with two-stage revision.

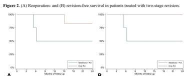

Table 1. Baseline characteristics of the included cohort.

	All (N = 39)	Metallosis + PJI (n = 13)	PJI Alone (n = 26)	p-value
Age +	65 ± 9	64 ± 9	66 ± 9	0.71
Female sex	18 (46%)	6 (46%)	12 (46%)	0.99
Race				0.65
White	36 (92%)	13 (100%)	23 (88%)	
Black	1 (3%)	0 (0%)	1 (4%)	
Asian	1 (3%)	0 (0%)	1 (4%)	
Hispanic	1 (3%)	0 (0%)	1 (4%)	
ASA class				0.33
1	1 (3%)	1 (8%)	0 (0%)	
2	11 (28%)	4 (31%)	7 (27%)	
3	27 (69%)	8 (62%)	19 (73%)	
Clinical symptoms				0.06
No	4 (10%)	3 (23%)	1 (4%)	
Yes	35 (90%)	10 (77%)	25 (96%)	
Culture growth				0.19
No	10 (26%)	5 (38%)	5 (19%)	
Yes	29 (74%)	8 (62%)	21 (81%)	
Days from symptom onset to positive culture +	11 ± 35	38 ± 62	1 ± 3	**0.008**
Sinus tract	3 (8%)	1 (8%)	2 (8%)	0.99
CRP > 10 mg/L	33 (94%)	11 (92%)	22 (96%)	0.63
PMN% > 80%	20 (87%)	4 (67%)	16 (94%)	0.09
WBC count > 3000 (cells/µL)	21 (81%)	5 (71%)	16 (84%)	0.46
Follow-up (months) +	28 ± 37	18 ± 21	34 ± 42	0.22

ASA: American Society of Anesthesiologists; *CRP*: C-reactive protein; *PJI*: periprosthetic joint infection; *PMN%*: polymorphonuclear leukocyte percentage; *WBC*: white blood cell.

+ Values displayed in these rows refer to the mean ± standard deviation.

Table 2. Microbiology of the included cohort.

	All (N = 39)	Metallosis + PJI (n = 13)	PJI Alone (n = 26)	p-value
Gram-positive	25 (86%)	7 (88%)	18 (86%)	0.90
Staphylococcus aureus	13 (46%)	3 (38%)	10 (50%)	0.55
Coagulase-negative Staphylococcus	8 (29%)	4 (50%)	4 (20%)	0.11
Streptococcus spp.	6 (21%)	2 (25%)	4 (20%)	0.77
Gram-negative	5 (17%)	1 (13%)	4 (19%)	0.68
Pseudomonas aeruginosa	2 (7%)	0 (0%)	2 (10%)	0.37
Salmonella spp.	1 (3%)	0 (0%)	1 (5%)	0.53
Morganella morganii	1 (3%)	1 (13%)	0 (0%)	0.10
Escherichia coli	1 (3%)	0 (0%)	1 (5%)	0.53
Fungal	1 (3%)	1 (13%)	0 (0%)	0.10
Polymicrobial	4 (14%)	3 (38%)	1 (5%)	**0.02**

PJI: periprosthetic joint infection.

Table 3. Treatment and post-operative outcomes.

	All (N = 39	Metallosis + PJI (n = 13)	PJI Alone (n = 26)	p-value
PJI index surgery				1.00
One-stage revision	27 (69%)	9 (69%)	18 (69%)	
Two-stage revision	12 (31%)	4 (31%)	8 (31%)	
Post-operative complications				
No	29 (74%)	12 (92%)	17 (65%)	0.07
Yes	10 (26%)	1 (8%)	9 (35%)	
Reoperation				0.23
No	26 (67%)	7 (54%)	19 (73%)	
Yes	13 (33%)	6 (46%)	7 (27%)	
Time to reoperation (months) +	8 (11)	7 (7)	8 (15)	0.78
Revision				**0.04**
No	29 (74%)	7 (54%)	22 (85%)	
Yes	10 (26%)	6 (46%)	4 (15%)	
Time to revision (months) +	8 (13)	7 (7)	11 (19)	0.63

PJI: periprosthetic joint infection.

+ Values displayed in these rows refer to the mean ± standard deviation

Table 4. Survivorship free of reoperation or revision by group.

		All		One-stage		Two-stage	
		1-year	2-year	1-year	2-year	1-year	2-year
Reoperation	**PJI Alone**	78.9 (56.3 - 90.7)	70.1 (42.6 - 86.3)	68.6 (39.1 - 85.9)	68.6 (39.1 - 85.9)	100 (-)	100 (-)
	Metallosis + PJI	52.1 (19.8 - 76.9)	34.7 (6.6 - 66.2)	56 (14.5 - 84)	28 (1.4 - 68.7)	50 (5.8 - 84.5)	50 (5.8 - 84.5)
	p-value	0.28	0.19	0.88	0.56	**0.03**	0.09
Revision	**PJI Alone**	86.9 (64.2 - 95.7)	86.9 (64.2 - 95.7)	79.7 (48 - 93.2)	79.7 (48 - 93.2)	100 (-)	100 (-)
	Metallosis + PJI	52.3 (19.9 - 77.1)	34.9 (6.7 - 66.4)	56 (14.5 - 84)	28 (1.4 - 68.7)	50 (5.8 - 84.5)	50 (5.8 - 84.5)
	p-value	0.07	**0.03**	0.40	0.21	**0.03**	**0.03**

Values displayed in all rows refer to the survivorship at each point and 95% confidence interval in parenthesis.