

Pathology Section

Malakoplakia of Bone Presenting as Bilateral Septic Arthritis: A Case Report

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ABSTRACT

Malakoplakia is an uncommon chronic inflammatory disorder that usually involves an abnormal immunological response to underlying infection. Though it is reported in almost every organ system, involvement of bone is extremely rare, where it usually presents as a solitary lytic lesion. We report a case of bilateral knee swelling in a 58-year-old woman yielding pus on aspirate due to *Proteus* and *Citrobacter* infection with osteolytic lesions of adjacent bones. As the disease was refractory to antibiotics, a biopsy was taken, which revealed malakoplakia. The aim of this article is to present a unique first case of malakoplakia involving joints. The patient was diabetic and had recently recovered from nephrotic syndrome. Detailed discussion of the case along with characteristic histopathological features, challenge in diagnosis and management with review of the literature of bony malakoplakia is presented.

Keywords: Histiocytes, Malakoplakia, Osteolytic lesion, Nephrotic syndrome, Septic arthritis

CASE REPORT

A 58-year-old woman presented with complaints of bilateral knee joint swelling, pain and foul-smelling discharge during the past three months. Since then, she has had multiple aspirations for her knee joints. She was diagnosed with minimal change disease of the kidney one year ago, for which she had taken steroids for six months. The patient also had a history of colloid cyst of the thyroid and had been diabetic on medication for two years. Currently, her renal function tests and Glycosylated Haemoglobin (HbA1c) are within normal limits.

Physical examination and imaging revealed features suggestive of septic arthritis of bilateral knee joints with chronic osteomyelitis of the distal ends of both femurs and proximal ends of both tibiae. Her Blood Pressure (BP) was 110/70 mmHg, and pulse 114 beats per minute. Ultrasonography (USG) abdomen revealed no abnormality in the kidneys or urinary tract, but showed grade 1 fatty liver. Laboratory tests revealed leucocytosis with raised C-Reactive Protein (CRP) and serum alkaline phosphatase [Table/Fig-1]. The blood culture was negative and the pus culture from the right knee joint revealed growth of *Proteus vulgaris*, which was resistant to Ampicillin, Cefazolin, Cefotaxime, Amoxicillin-Clavulanate, Piperacillin, Tazobactam, Gentamicin, Ciprofloxacin, Imipenem, Meropenem, and Levofloxacin.

An initial scanty biopsy received from the right knee showed acute suppurative inflammation with necrosis and was negative for acid-fast bacilli. Further follow-up investigations revealed Haemoglobin (Hb)- 11.8 g/dL, Total Leukocyte Count (TLC)- 22,300/cumm, platelets- 2.6 lakhs with Prothrombin Time (PT)- 26.4 sec, Activated Partial Thromboplastin Time (APTT)- 59 sec, and C-Reactive Protein (CRP)- 90 mg/dL. The pus drained from both knee joints after a week revealed growth of *Citrobacter koseri*, which showed resistance to Ampicillin, Cefazolin, Cefotaxime, Amoxicillin-Clavulanate, Piperacillin Tazobactam, Ciprofloxacin, Trimethoprim Sulfamethoxazole and sensitive to Imipenem and Meropenem. A bilateral knee arthrotomy with bilateral sequestrectomy and antibiotic bead cement placement was done with high-risk consent. Inj. Vancomycin 1 g intravenously was given pre-operatively. Additionally, Inj. Amikacin 250 mg i.v. and Inj. Meropenem 1 g i.v. were given. Oral salt was given to correct the hyponatraemia.

Histopathological specimen consisted of irregular soft tissue and bony fragments together measuring -2.5x2x1.5 cm. Haematoxylin and Eosin stained 3-micron thin sections of paraffin-embedded tissue revealed fragments of granulation tissue, degenerated bone [Table/Fig-2], areas of necrosis, calcification and large sheets of histiocytes with abundant eosinophilic cytoplasm and round, regular nuclei. The histiocytes contained cytoplasmic targetoid structures with central basophilic spherules {Michaelis-Gutmann (MG) bodies} surrounded by a halo [Table/Fig-3]. Special stains for Perl's Prussian blue [Table/Fig-4] and von-Kossa [Table/Fig-5] were positive for deposits of iron and calcium, respectively, and Periodic Acid Schiff (PAS) stain [Table/Fig-6] showed positive granules in the cytoplasm of histiocytes. Gomori Methanamine Silver stain [Table/Fig-7] was negative for fungi. A diagnosis of malakoplakia of bone was made.

Post-surgery, the patient developed hypotension with decreasing oxygen saturation. There was an increase in the N-terminal prohormone of Brain Natriuretic Peptide (NT-pro BNP) and D-dimer levels (788 pg/mL and 988.90 ng/mL, respectively). Blood lactate

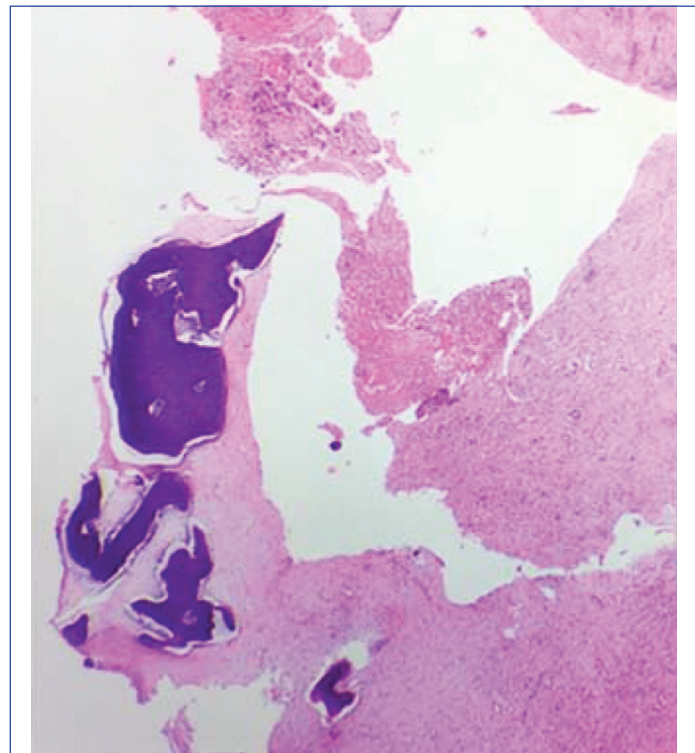
Investigation parameter	Value	Biological reference interval
Haemoglobin (g/dL)	11.5	12-15
Total leukocyte count (cells/cumm)	17700	4000-10000
Platelets (lacs/cumm)	4.42	1.5-4.5
ESR (mm/1st hour)	42	0-20
PT (s)	16.5	11-16
APTT (s)	40.1	30.3-38.6
Serum creatinine (mg/dL)	0.85	0.6-1.2
CRP (mg/L)	50	<5
RBS (mg/dL)	140	70-140
AST (U/L)	41	10-30
ALT (U/L)	21	10-40
Alkaline phosphatase (U/L)	419	30-120
Serum albumin (g/dL)	2.3	3.5-5
Serum sodium (mEq/l)	130	136-142l
Serum potassium (mEq/l)	4.7	3.5-5.0
Serum chloride (mEq/l)	95	96-106
Serum uric acid (mg/dL)	4.8	2.7-7.3
Serum IgE (IU/mL)	>1500	1.5-144

[Table/Fig-1]: Laboratory investigations.
ESR: Erythrocyte sedimentation rate; PT: Prothrombin time; APTT: Activated partial thromboplastin time; CRP: C-reactive protein; RBS: Random blood sugar; AST: Aspartate transaminase; ALT: Alanine transaminase

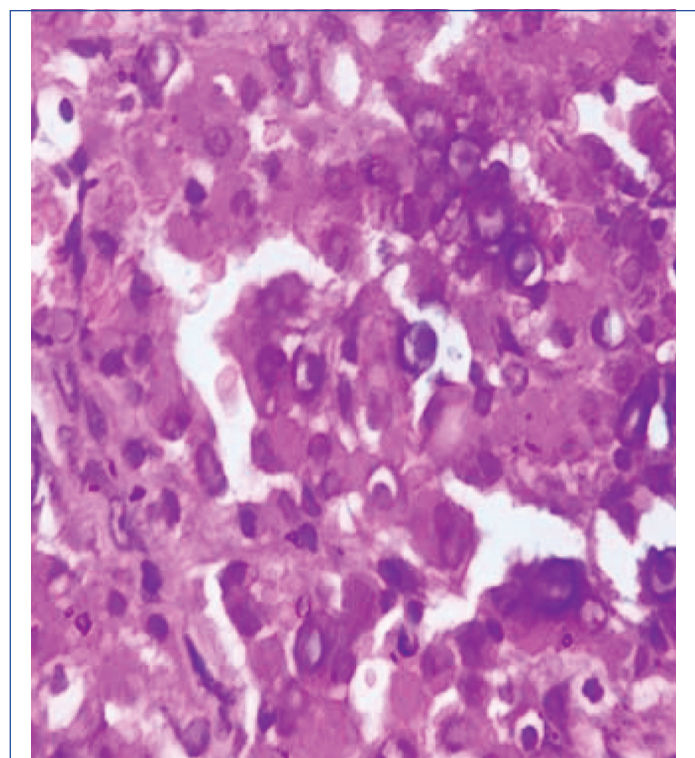
was 7.7 mmol/mL and CRP was 58.1 mg/L. She succumbed to septic shock and multiorgan dysfunction due to septicaemia in spite of efforts to treat with inotropes, antibiotics, analgesics and oxygen support.

DISCUSSION

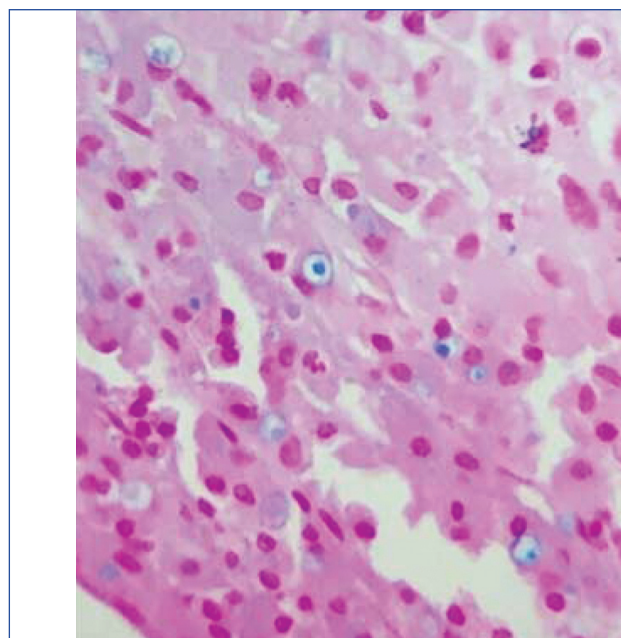
Malakoplakia is a rare chronic inflammatory lesion primarily affecting the genitourinary system, but also involves different organs such as the gastrointestinal system, lungs, and skin [1]. Malakoplakia of the bone is a highly rare entity [2-11]. The first case of malakoplakia of bone was described by Gupta RK et al., [7]. The femur and vertebra are the most common affected sites. Our patient had a



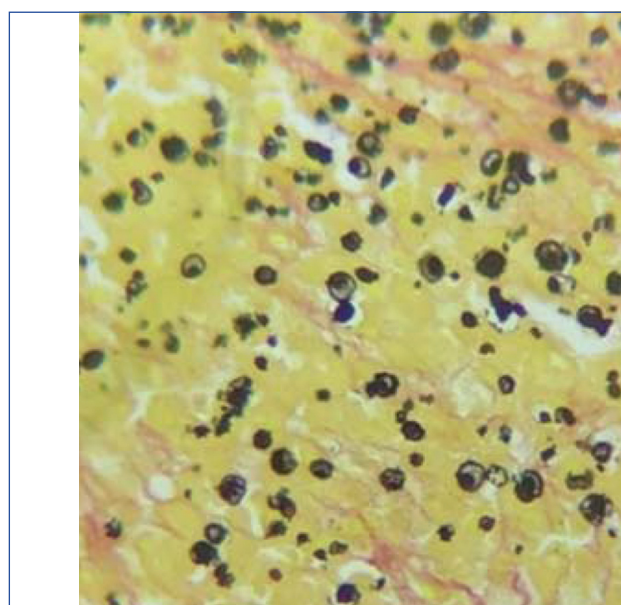
[Table/Fig-2]: a) Photomicrograph of H&E stain 10x showing fragments of bony tissue and inflammatory tissue.



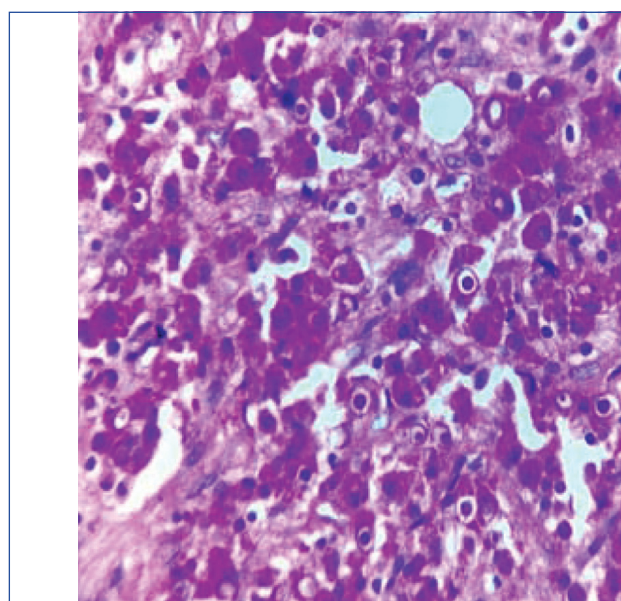
[Table/Fig-3]: H&E stain 40x showing sheets of histiocytes with eosinophilic cytoplasm containing basophilic laminated structures (Michaelis-Gutmann (MG) bodies).



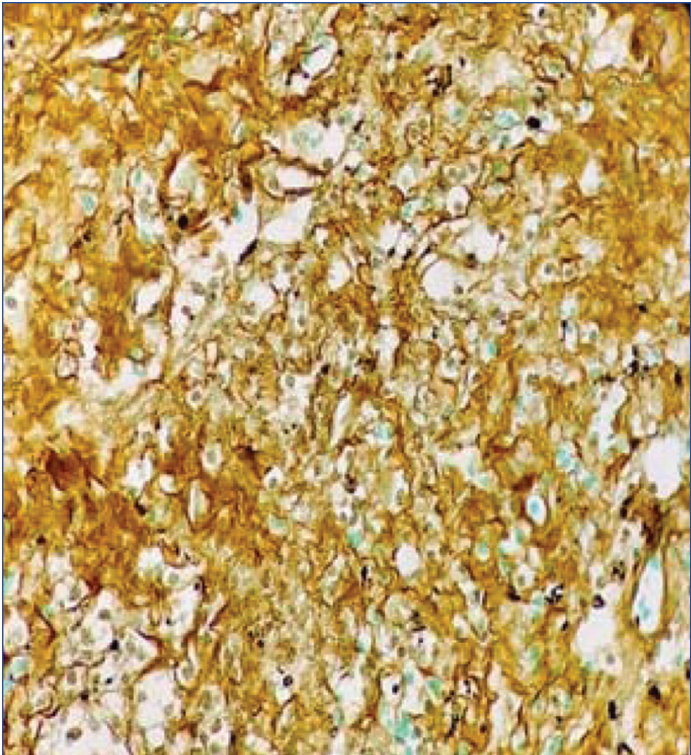
[Table/Fig-4]: Perl's (iron) stain 40x showing histiocytes containing blue coloured targetoid structures (MG bodies).



[Table/Fig-5]: Von Kossa (calcium) stain 40x showing histiocytes with cytoplasmic black coloured laminated structures (MG bodies).



[Table/Fig-6]: PAS stain 40x showing PAS-positive granules in the cytoplasm of histiocytes.



[Table/Fig-7]: Gomorimethanamine silver 10x-negative for fungi.

yet unreported involvement of both knee joints affecting both the distal femur and both proximal tibiae. It can occur at any age with female predilection, as in our patient. In genitourinary malakoplakia female-to-male ratio is 4:1 but it appears to be low (2:1) in bony malakoplakia [11].

Unlike its presentation in other organs, in bone, it presents as a lytic lesion with or without a pathological fracture or as a soft tissue lesion, secondarily eroding the adjacent bones. The patient presented with clinical features of septic arthritis of both the knee joints, with the X-ray and CT scan revealing lytic lesions affecting the lower ends of both tibiae and femurs.

The diagnosis of malakoplakia is usually an incidental finding on biopsy and rarely on cytology [4,12,13]. Biopsy findings demonstrate a special type of Von Hanseman histiocytes containing diagnostic cytoplasmic calcospherites called MG bodies, which reflect defective phagolysosomal activity leading to iron and calcium deposition in the residual glycolipid of partially digested bacteria [14-16]. The current case demonstrated plenty of such macrophages with MG bodies [Table/Fig-2,3]. These MG bodies showed positivity for iron [Table/Fig-4], calcium [Table/Fig-5] and glycolipid [Table/Fig-6]. On electron microscopy, the lysosomes within the histiocytes contain laminated material with myelin structures and electron-dense calcifications. The cytoplasm shows plenty of coarse endoplasmic reticulum and glycogen granules [9].

Malakoplakia is usually associated with immunosuppressive conditions such as malignancy, diabetes mellitus, HIV infection and steroid therapy, predisposing to bacterial infection, commonly *Escherichia coli* in bony malakoplakia [17,18]. In our patient, *Proteus* and *Citrobacter* were isolated from cultures of pus from the joints.

Differential diagnoses of bony malakoplakia include Brodie's abscess, tuberculosis, fungal infection, osteomyelitis, aneurysmal bone cyst, giant cell tumour, chondroblastoma and metastases [2,19]. In our patient, as joint effusion was aspirated several times with pus, septic arthritis was implicated but unresponsive to antibiotics, with osteolytic lesions of adjacent bones, who later underwent surgical debridement. The literature regarding malakoplakia is sparse [Table/Fig-8] [2-11,20]. Coates M et al., mentioned the utility of long-term combination antibiotics for more than 30 days, including cotrimoxazole and quinolones, due to their good intracellular penetration, along with surgical treatment [17]. Excision

Authors & year	Age/Sex of patient	Site	Clinical presentation
Gupta RK et al., 1972 [7]	61/F	Vertebra	Bladder & renal malakoplakia with direct extension to bone
Van den bout AH and Dreyer L 1981 [9]	47/F	Femur	Pain in the right thigh with a lytic lesion in a renal transplant patient
Weisenburger DD et al., 1985 [6]	68/F	Femur	Pathological fracture with lytic lesion in a patient with lymphoma on chemotherapy
Nayar RC et al 1991[8]	9 m/M	Temporal bone	Aural polyp eroding bone
Tyagi N et al., 1994 [5]	54/M	Femur	Pathological fracture with lytic lesion
Choudhury M et al., 2001 [4]	3/F	Pelvis	FNA diagnosis of Gluteal painful swelling
Bansal SS et al., 2014 [2]	24/F	Tibia	Pain in the knee with a lytic lesion
Land DD et al., 2014 [10]	6/ F	Tibia	Knee pain with permeative lesion
Xu AL et al., 2021 [3]	66/F	Vertebra L2-L4	Lytic lesion in a patient with polymyositis
Roark SC et al., 2024 [11]	66/M	Maxilla	Radiolucent lesion in a liver transplant patient
Toubes-Klingler E et al., [20]	41/M	Cranium	In advanced HIV infection

[Table/Fig-8]: Review of literature of published bony malakoplakia of different clinical presentations [2-11, 20].

with antibiotics achieved a better result compared to debridement with antibiotics. Bethanechol chloride was also tried along with antibiotics to increase cyclic GMP level in the histiocytes, enhancing bactericidal effect [21]. In renal transplant-associated malakoplakia cases, Abbasi AB et al., observed better improvement of lesions without surgical intervention (94%) than with surgical resection (50%) [22]. Toubes-Klingler E et al., demonstrated a good outcome with resection of the lesion, antibiotic therapy, along with treating underlying HIV infection, whereas the patients of Chaudhary N et al., and of Wong SH et al., had a malignant outcome [20,23,24]. The disease is also known for recurrence when it occurs as a mass lesion [25]. The present patient was resistant to several antibiotics, including sulphonamides and succumbed to septic shock even with surgical debridement. The nephrotic syndrome, diabetes mellitus and steroids might have contributed as predisposing factors for malakoplakia in our patient infected by uncommon drug-resistant Gram-negative organisms. Malakoplakia is usually associated with a favourable prognosis, but can be fatal if diagnosed late.

CONCLUSION(S)

Malakoplakia of bone is a rare entity, especially presenting as septic arthritis of large joints with *Proteus* and *Citrobacter* infection. The lesion should be considered in patients with immunosuppression, osteolytic lesions and bacterial infection unresponsive to routine antibiotics. Histopathologic examination is the gold standard for its diagnosis with pathognomonic MG bodies. Early diagnosis with timely proper management is pivotal for patient care.

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