

*Case Report*

# Heerfordt Syndrome Complicated by Bilateral Simultaneous Facial Palsy, PTH-Independent Hypercalcemia, and Bilateral Obstructive Acute Kidney Injury in the Absence of Thoracic Disease: A Case Report and Narrative Review

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## Abstract

**Background and Clinical Significance:** Heerfordt syndrome (uveoparotid fever) is an uncommon extrapulmonary expression of sarcoidosis defined by parotid enlargement, uveitis, low-grade fever, and facial nerve palsy. It is identified in fewer than 1% of patients with biopsy-confirmed sarcoidosis, and the co-occurrence of bilateral seventh-nerve palsy with calcitriol-driven obstructive kidney injury has been reported only sporadically. Recognizing this metabolic-renal phenotype is clinically important because it is readily reversible yet easily missed when the chest radiograph is normal. **Case Presentation:** A 30-year-old man presented with four months of progressive bilateral parotid swelling, sicca symptoms, and intermittent blurred vision, preceded by a self-limited episode of bilateral simultaneous peripheral facial weakness; renal colic developed one month before admission. Evaluation showed parathyroid-hormone-independent hypercalcemia (peak corrected calcium 13.1 mg/dL), a serum angiotensin-converting enzyme level above 100 U/L, and acute kidney injury (creatinine 2.1 mg/dL) caused by bilateral upper-ureteric calculi with hydronephrosis. Posterior uveitis was confirmed ophthalmologically. Chest radiography and high-resolution thoracic computed tomography were unremarkable, with no hilar lymphadenopathy. Parotid gland biopsy demonstrated non-caseating epithelioid granulomas. Bilateral ureteric stenting and oral prednisolone 40 mg daily produced rapid normalization of serum calcium, recovery of renal function, and regression of parotid enlargement. **Conclusions:** This report characterizes a phenotype that combines bilateral simultaneous facial-nerve involvement, calcitriol-mediated hypercalcemia, and obstructive nephrolithiasis without coexistent pulmonary disease. It argues for early consideration of sarcoidosis whenever hypercalcemia, parotid enlargement, and cranial neuropathy occur together, and reinforces the reversibility of sarcoidosis-related renal injury when corticosteroids are introduced promptly.

**Keywords:** sarcoidosis; Heerfordt syndrome; uveoparotid fever; hypercalcemia; obstructive uropathy; acute kidney injury; bilateral facial palsy; calcitriol; case report



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## 1. Introduction and Clinical Significance

Sarcoidosis is a granulomatous disorder of unknown etiology in which dysregulated cellular immunity drives the formation of compact, non-caseating epithelioid granulomas across multiple organs. The lungs and intrathoracic lymph nodes are involved in roughly 90% of patients, but virtually any tissue can be affected, and the clinical phenotype varies widely between geographic regions and ethnic groups. Reported incidence estimates range from 3 to 50 per 100,000 person-years, with the highest figures coming from northern European and African American populations [1,2].

Christian Frederik Heerfordt described the constellation of febrile parotid enlargement, uveitis, and facial nerve palsy in 1909, more than a decade before sarcoidosis was conceptualized as a unifying disease entity. Waldenström subsequently linked the syndrome to the wider spectrum of sarcoidosis, and the eponym “Heerfordt–Waldenström syndrome” remains in use [3,4]. In contemporary case series the complete tetrad—fever, parotid enlargement, uveitis, and facial-nerve palsy—is encountered in only about 10–15% of patients presenting with Heerfordt syndrome, corresponding to well under 1% of all sarcoidosis cohorts; the true frequency is almost certainly higher because incomplete or sequential presentations are easily overlooked [4]. Facial nerve palsy occurs in about 5% of sarcoidosis cases overall and is the most common cranial neuropathy in neurosarcoidosis [5].

Renal manifestations of sarcoidosis cluster into three broad categories: disorders of calcium homeostasis (hypercalcemia, hypercalciuria, nephrolithiasis, and nephrocalcinosis), granulomatous interstitial nephritis, and, less commonly, glomerular or vascular disease. Subclinical kidney involvement may be present in up to half of patients with chronic disease, although overt renal failure is far less common [6,7]. Hypercalcemia in sarcoidosis is driven by extrarenal conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by 1 $\alpha$ -hydroxylase (CYP27B1) expressed in granuloma-resident macrophages. Unlike the renal isoform, this enzyme escapes the normal negative feedback exerted by parathyroid hormone, calcium, and fibroblast growth factor-23, and the resulting calcitriol surge enhances intestinal calcium absorption and bone resorption [8,9].

We describe a young man whose presentation of Heerfordt syndrome was dominated by metabolic and renal complications rather than pulmonary disease, including bilateral simultaneous facial palsy and acute kidney injury from bilateral stone-related ureteric obstruction. The case is accompanied by a focused narrative review of the clinical phenotypes, differential diagnosis, and therapeutic considerations relevant to this rare overlap.

## 2. Case Presentation

### 2.1. History

A 30-year-old man with a childhood diagnosis of eczema and no history of tobacco use, occupational dust exposure, recent travel, or known autoimmune illness was referred to our internal medicine service. He had experienced painful bilateral parotid swelling for four months, with no improvement after two short courses of empirical antibiotics, accompanied by xerostomia, ocular dryness, and intermittent blurred vision. Two months before admission he had a self-limited, roughly two-week episode of bilateral simultaneous peripheral facial weakness with incomplete eye closure, drooling, and loss of forehead furrowing on both sides; the weakness resolved spontaneously before referral. One month before admission he developed bilateral flank pain, intermittent colicky discomfort, and dysuria without gross hematuria. There was no fever, weight loss, night sweats, arthralgia, skin lesions, productive cough, exertional dyspnea, or gastrointestinal symptom. His father had advanced diabetic–hypertensive kidney disease requiring hemodialysis; there was no family history of sarcoidosis, autoimmunity, or nephrolithiasis.

## 2.2. Physical Examination

On admission the patient was alert, oriented, and hemodynamically stable. Both parotid glands were diffusely enlarged, firm, and tender, with mild overlying erythema; there was no fluctuation, and no discharge could be expressed from the Stensen ducts. There was no peripheral lymphadenopathy, hepatosplenomegaly, peripheral edema, or cutaneous involvement (no erythema nodosum, lupus pernio, or plaque lesions). Cranial-nerve examination was normal, the antecedent facial weakness having resolved, and the remainder of the neurological examination, including reflexes and sensation, was unremarkable. Cardiac, respiratory, and abdominal examinations were normal.

## 2.3. Laboratory Findings

Initial biochemistry revealed acute kidney injury (serum creatinine 2.1 mg/dL; urea 64 mg/dL) and severe hypercalcemia, peaking at 13.1 mg/dL with normal serum albumin. Intact parathyroid hormone was suppressed at 3.4 pg/mL. Serum angiotensin-converting enzyme exceeded the upper detection limit of the assay (>100 U/L; reference 8–52 U/L). 25-hydroxyvitamin D was insufficient at 22 ng/mL; the 1,25-dihydroxyvitamin D assay was unavailable at our institution during the admission, which we acknowledge as a limitation. Inflammatory markers were mildly elevated (ESR 19 mm/h, CRP 10 mg/L). A full autoimmune panel (antinuclear antibodies, anti-Ro/SSA, anti-La/SSB, c-ANCA, and p-ANCA) was uniformly negative. Complement (C3, C4) and immunoglobulin G were within reference limits. Screening for human immunodeficiency virus, hepatitis B surface antigen, and hepatitis C antibody was non-reactive, as was an interferon-gamma release assay for *Mycobacterium tuberculosis*. Urinalysis showed sterile pyuria (>100 leukocytes per high-power field, with negative cultures on four separate occasions), microscopic hematuria, dipstick proteinuria, and hyaline casts; quantified 24 h urinary protein excretion was 595.9 mg. Complete laboratory results are summarized in Tables 1 and 2.

**Table 1.** Biochemistry, renal function, and metabolic panel at admission.

| Parameter                      | Result          | Reference Range | Interpretation      |
|--------------------------------|-----------------|-----------------|---------------------|
| Creatinine (admission)         | 2.1 mg/dL       | 0.67–1.17 mg/dL | Elevated (AKI)      |
| Creatinine (post-treatment)    | 1.21 mg/dL      | 0.67–1.17 mg/dL | Improving           |
| Urea                           | 64 mg/dL        | 19–44 mg/dL     | Elevated            |
| Uric acid                      | 9.9 mg/dL       | 3.4–7.0 mg/dL   | Elevated            |
| Total calcium (admission)      | 13.1 mg/dL      | 8.6–10.2 mg/dL  | Severely elevated   |
| Total calcium (post-treatment) | 9.4 mg/dL       | 8.6–10.2 mg/dL  | Normal              |
| Phosphate                      | 4.40 mg/dL      | 2.5–4.5 mg/dL   | Normal              |
| Magnesium                      | 1.90 mg/dL      | 1.7–2.2 mg/dL   | Normal              |
| Intact PTH                     | 3.4 pg/mL       | 15–65 pg/mL     | Suppressed          |
| 25-hydroxyvitamin D            | 22 ng/mL        | 30–100 ng/mL    | Insufficient        |
| 1,25-dihydroxyvitamin D        | Not assayed     | —               | Unavailable at site |
| Angiotensin-converting enzyme  | >100 U/L        | 8–52 U/L        | Elevated            |
| TSH/free T4                    | Within range    | —               | Euthyroid           |
| Albumin                        | 4.7 g/dL        | 3.5–5.2 g/dL    | Normal              |
| Total protein                  | 7.4 g/dL        | 6.0–8.0 g/dL    | Normal              |
| AST/ALT/ALP/GGT                | Within range    | —               | Normal liver panel  |
| Sodium                         | 138 mmol/L      | 136–145 mmol/L  | Normal              |
| Potassium                      | 4.63 mmol/L     | 3.5–5.0 mmol/L  | Normal              |
| Chloride                       | 108 mmol/L      | 98–106 mmol/L   | Mildly elevated     |
| Fasting glucose/HbA1c          | 76 mg/dL/4.97%  | —               | Normal              |
| Lipid panel                    | LDL 112, HDL 29 | —               | Low HDL             |
| LDH                            | 172 U/L         | 140–280 U/L     | Normal              |

Abbreviations: AKI, acute kidney injury; PTH, parathyroid hormone; TSH, thyroid-stimulating hormone.

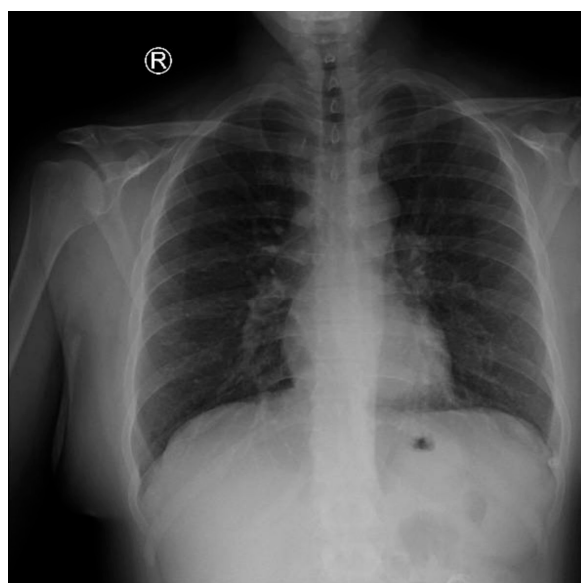
**Table 2.** Hematology, immunology, infectious workup, and urinalysis.

| Parameter                    | Result                                  | Interpretation            |
|------------------------------|-----------------------------------------|---------------------------|
| Hemoglobin/Hematocrit        | 14.2 g/dL/43.6%                         | Normal                    |
| WBC count (differential)     | $8.7 \times 10^9$ /L; lymphocytes 12.8% | Lymphopenia               |
| Platelets                    | $418 \times 10^9$ /L                    | Mild thrombocytosis       |
| PT/INR/APTT                  | Within range                            | Normal                    |
| ESR/CRP                      | 19 mm/h/10 mg/L                         | Mildly elevated           |
| C3/C4                        | 1.61 g/L/0.332 g/L                      | Normal                    |
| IgG                          | 12.20 g/L                               | Normal                    |
| ANA/c-ANCA/p-ANCA            | Negative                                | Negative                  |
| Anti-Ro (SSA)/Anti-La (SSB)  | Negative                                | Negative                  |
| HIV/HBsAg/HCV antibody       | Non-reactive                            | Negative                  |
| IGRA (M. tuberculosis)       | Non-reactive                            | Negative                  |
| 24 h urinary protein         | 595.9 mg/24 h                           | Sub-nephrotic proteinuria |
| Urine leukocytes             | >100/HPF                                | Sterile pyuria            |
| Urine red blood cells        | 3+                                      | Microscopic hematuria     |
| Urine protein (dipstick)     | 2+                                      | Proteinuria               |
| Hyaline casts                | 3+                                      | Present                   |
| Urine culture ( $\times 4$ ) | No growth                               | Sterile                   |

Abbreviations: ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; HPF, high-power field; IGRA, interferon-gamma release assay. Urine findings are reported semi-quantitatively; the plus sign (e.g., 2+, 3+) denotes the dipstick/microscopy grade of positivity.

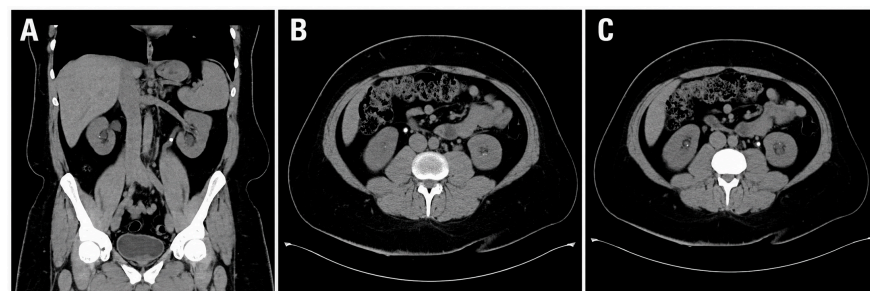
## 2.4. Imaging Studies

Posteroanterior chest radiography demonstrated clear lung fields, a normal cardiome-diastinal silhouette, and no hilar prominence or parenchymal infiltrate (Figure 1). High-resolution thoracic computed tomography was likewise negative for parenchymal disease, mediastinal adenopathy, or bilateral hilar lymphadenopathy. This was a notable finding, given that more than 90% of sarcoidosis cases harbor some thoracic radiographic abnormality at diagnosis.



**Figure 1.** Posteroanterior chest radiograph at presentation. The lung fields are clear bilaterally with no infiltrate, the cardiome-diastinal silhouette is normal, and there is no bilateral hilar lymphadenopathy or parenchymal disease. The absence of any thoracic abnormality, which is uncommon in sarcoidosis, delayed early consideration of the diagnosis and underscores the importance of pursuing extrapulmonary manifestations on their own clinical merits. The circled letter “R” is a radiographic laterality marker denoting the patient’s right side.

Non-contrast computed tomography of the abdomen and pelvis revealed obstructive calculi within the proximal third of both ureters, measuring 8 mm on the right and 6 mm on the left, with mild upstream pelvicalyceal dilatation. Multiple small non-obstructing parenchymal stones (2–4 mm) were present bilaterally (Figure 2). Renal ultrasound corroborated grade II–III hydronephrosis with diffuse parenchymal hyperechogenicity, fair corticomedullary differentiation, and fullness of both collecting systems; an incidental left adrenal nodule (1.3 cm, 4 Hounsfield units) was consistent with a benign, most likely non-functioning adenoma on the basis of its imaging characteristics alone (size and low attenuation of 4 HU); dedicated biochemical screening for hormonal excess (an overnight 1 mg dexamethasone-suppression test and plasma metanephrines) was not pursued, as there were no clinical or biochemical features to suggest a functioning lesion, so the “non-functioning” designation rests on imaging characteristics alone. Neck ultrasound showed diffuse parotid enlargement with heterogeneous echotexture and intraparenchymal lymph nodes, together with subcentimetric cervical and submandibular nodes with preserved fatty hila. Dual-energy X-ray absorptiometry of the lumbar spine and bilateral hips returned T-scores within the normal range, arguing against chronic skeletal calcium mobilization. Ophthalmological assessment identified bilateral posterior uveitis with mild vitritis but no granulomatous keratic precipitates.



**Figure 2.** Non-contrast computed tomography of the abdomen and pelvis. (A) Coronal reconstruction showing both kidneys with bilateral intrarenal calcifications (hyperdense foci within the renal collecting systems) and mild pelvicalyceal fullness. (B,C) Representative axial images demonstrating the bilateral upper-ureteric calculi (8 mm on the right and 6 mm on the left) together with small non-obstructing renal calculi. The radiographic pattern reflects sustained calcitriol-driven hypercalciuria.

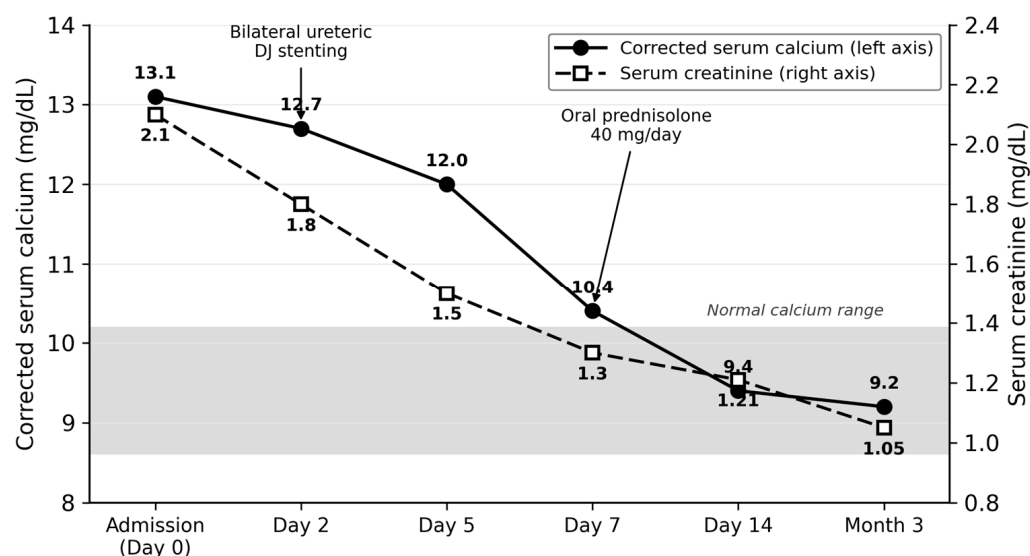
### 2.5. Histopathology

Open biopsy of the right parotid gland was chosen over bronchoscopic or skin biopsy because superficial salivary disease offered an accessible, high-yield target in the absence of radiographic thoracic involvement. Because of the antecedent (albeit resolved) bilateral facial weakness, the specimen was taken from the superficial lobe only through a standard modified Blair approach, with intraoperative identification and preservation of the facial-nerve trunk and its peripheral branches; no new facial weakness followed the procedure. Microscopy demonstrated well-formed, compact, non-caseating epithelioid granulomas with scattered multinucleated giant cells distributed in the interlobular stroma. There was no necrosis, fibrinoid degeneration, or vasculitic change. Special stains for acid-fast bacilli (Ziehl–Neelsen) and fungal elements (Grocott methenamine silver and periodic acid–Schiff) were negative, and tissue culture for mycobacteria and fungi yielded no organisms. In the appropriate clinical setting, and after exclusion of competing granulomatous diseases, this pattern was diagnostic of sarcoid involvement of the parotid gland.

### 2.6. Management and Outcome

Bilateral retrograde double-J ureteric stenting was performed by the urology service for the obstructive component of the renal injury; urine output increased and serum

creatinine declined within the first 48 h. Once histological confirmation was obtained, oral prednisolone was started at 40 mg daily (approximately 0.5 mg/kg/day). Serum calcium reached the normal range within seven days of starting corticosteroids, creatinine settled at 1.21 mg/dL by day fourteen, the parotid glands visibly regressed within two weeks, and serum ACE began to trend downward. The patient was discharged on a tapering steroid regimen with planned nephrology and ophthalmology follow-up. At three-month review he remained in clinical and biochemical remission, with a creatinine of 1.05 mg/dL, normal calcium, and resolution of posterior uveitis. The clinical course is summarized in Figure 3.



**Figure 3.** Clinical course. Trends in corrected serum calcium (left axis) and serum creatinine (right axis) from admission to the three-month review, with timing of the principal interventions indicated. The shaded band marks the normal calcium reference range (8.6–10.2 mg/dL). Note the rapid biochemical improvement after introduction of oral prednisolone. DJ, double-J ureteric stent.

### 3. Discussion

This patient drew together a striking and uncommon cluster of findings: florid bilateral parotid disease, posterior uveitis, antecedent bilateral simultaneous peripheral facial palsy, calcitriol-driven hypercalcemia with bilateral obstructive nephrolithiasis, and a conspicuously silent chest. Taken together, they illustrate the diagnostic difficulty that extrapulmonary sarcoidosis can pose when the familiar radiographic clues are absent, and they frame the questions this report sets out to address.

#### 3.1. Diagnostic Criteria and Phenotypic Variants of Heerfordt Syndrome

Heerfordt’s original description comprised a low-grade fever, parotid enlargement, anterior uveitis, and cranial neuropathy, most often peripheral facial-nerve palsy [3,4]. Subsequent reviews have made clear that complete forms are the exception rather than the rule, and most authors now accept an “incomplete” diagnosis when two of the four cardinal features coexist with compatible histological evidence of non-caseating granulomas [10]. Our patient fulfilled three of the four classical features (parotid enlargement, uveitis, and facial palsy) without overt fever. The posterior (rather than anterior) pattern of uveitis is somewhat atypical: the pooled case series report anterior involvement in roughly 60–70% of Heerfordt patients [10,11]. The cardinal features and accepted variants are summarized in Table 3. Importantly, IgG4-related disease is a key mimic of this overall presentation, since it can also cause bilateral salivary-gland enlargement, sicca symptoms, and tubulointerstitial renal disease; the finding of well-formed non-caseating granulomas on parotid biopsy—rather than the storiform fibrosis and IgG4-rich plasma-cell infiltrate that characterize IgG4-

related disease—together with a markedly elevated serum ACE and PTH-independent, calcitriol-mediated hypercalcemia, favored sarcoidosis in our patient. Dedicated serum IgG4 measurement and IgG4 immunostaining of the biopsy were not performed during the admission; however, total serum IgG was within the reference range (12.20 g/L), and the biopsy showed well-formed non-caseating granulomas without the storiform fibrosis or obliterative phlebitis that typify IgG4-related disease, arguing against that diagnosis.

**Table 3.** Cardinal features and accepted variants of Heerfordt syndrome.

| Feature             | Classical Description          | Reported Variants                              | Frequency in Published Series |
|---------------------|--------------------------------|------------------------------------------------|-------------------------------|
| Parotid enlargement | Bilateral, painful, persistent | Unilateral; submandibular involvement          | ~80–95%                       |
| Uveitis             | Anterior, granulomatous        | Posterior uveitis; panuveitis; vitritis        | ~70–80%                       |
| Facial nerve palsy  | Unilateral, peripheral         | Bilateral simultaneous; alternating; recurrent | ~50–60%                       |
| Fever               | Low-grade, intermittent        | Absent in up to 40% of contemporary reports    | ~50–60%                       |
| Complete tetrad     | All four features              | Two of four with biopsy support is accepted    | ~10–15%                       |

Reported frequencies are pooled estimates from major case series and reviews [4,10,11]; precise figures vary because of small numbers and selection bias.

3.2. Bilateral Simultaneous Facial Palsy: A Clinical Red Flag

Bilateral simultaneous peripheral facial weakness (diplegia facialis) is uncommon, accounting for fewer than 2% of all lower-motor-neuron facial palsies [12,13]. Unlike unilateral Bell palsy, in which an idiopathic or post-viral etiology can be accepted with reasonable confidence after a brief workup, bilateral involvement carries a narrow but important differential. Leading causes include Lyme borreliosis, Guillain–Barré syndrome (especially the Miller Fisher and pharyngo-cervico-brachial variants), human immunodeficiency virus infection, leukemic or lymphomatous meningeal infiltration, basal meningitis (tuberculous, fungal, or carcinomatous), Möbius syndrome (in younger patients), and, relevant here, neurosarcoidosis [11,13]. Spontaneous recovery, as occurred in our patient, does not absolve the clinician of the obligation to search for an underlying systemic cause. The differential is summarized in Table 4.

**Table 4.** Differential diagnosis of bilateral simultaneous peripheral facial palsy.

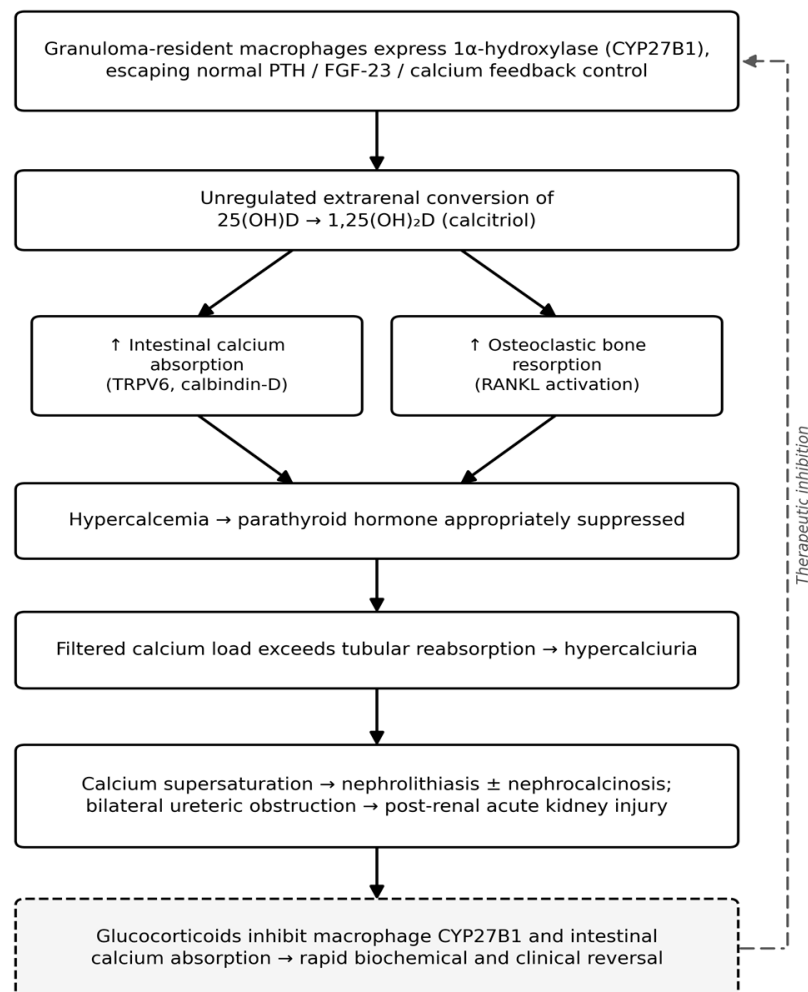
| Category            | Specific Entity                                  | Key Clues/Investigations                      |
|---------------------|--------------------------------------------------|-----------------------------------------------|
| Infectious          | Lyme borreliosis                                 | Erythema migrans; tick exposure; serology     |
| Infectious          | HIV (acute or advanced)                          | Risk factors; ELISA/Western blot              |
| Infectious          | Tuberculous or fungal meningitis                 | Imaging; CSF analysis; cultures               |
| Infectious          | Otitis/parotitis/Ramsay Hunt                     | Local examination; vesicular rash             |
| Inflammatory        | Sarcoidosis (Heerfordt or pure neurosarcoidosis) | ACE; calcium; chest imaging; biopsy           |
| Inflammatory        | Sjögren syndrome                                 | Sicca symptoms; anti-Ro/anti-La               |
| Neurological        | Guillain–Barré (incl. Miller Fisher)             | Areflexia; albumin–cytological dissociation   |
| Neoplastic          | Leukemic/lymphomatous infiltration               | Smear; LDH; bone marrow; CSF cytology         |
| Neoplastic          | Meningeal carcinomatosis                         | MRI with contrast; CSF cytology               |
| Vascular/structural | Brainstem ischemia/pontine lesion                | MRI brain                                     |
| Congenital          | Möbius syndrome                                  | Onset in infancy; abducens involvement        |
| Idiopathic          | Bilateral Bell palsy (diagnosis of exclusion)    | <25% of bilateral cases; exhaustive exclusion |

Adapted from Keane [12] and Jha et al. [13]. ACE, angiotensin-converting enzyme; CSF, cerebrospinal fluid; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging.

3.3. Pathophysiology of Hypercalcemia in Sarcoidosis

Hypercalcemia complicates 5–10% of sarcoidosis cases, and hypercalciuria a considerably higher proportion, up to 40–60% in older biochemical surveys [14,15]. The mechanism is autonomous extrarenal synthesis of 1,25-dihydroxyvitamin D by 1 $\alpha$ -hydroxylase (CYP27B1) expressed in granuloma-resident macrophages. The renal isoform of this enzyme is tightly regulated by PTH and FGF-23 and is suppressed by its own product; the

granuloma-derived isoform behaves quite differently, remaining active even in the face of hypercalcemia and elevated calcitriol and escaping FGF-23 restraint. The result is unrestrained intestinal calcium absorption, mobilization of skeletal calcium, hypercalciuria, and, once the urinary calcium load exceeds tubular capacity, calcium-based nephrolithiasis [8,9]. Plasma PTH is appropriately suppressed, as it was in our patient (3.4 pg/mL). Consistent with substrate consumption by unregulated extrarenal  $1\alpha$ -hydroxylase rather than vitamin D excess, the 25-hydroxyvitamin D level was low-normal (22 ng/mL) despite frank hypercalcemia, and serum phosphate was normal to high-normal (4.40 mg/dL) rather than reduced, further distinguishing this PTH-independent, calcitriol-mediated pattern from PTH-driven hypercalcemia. The pathway is illustrated schematically in Figure 4.



**Figure 4.** Pathophysiology of calcitriol-mediated hypercalcemia in sarcoidosis (schematic). Granuloma-resident macrophages generate 1,25-dihydroxyvitamin D through feedback-independent  $1\alpha$ -hydroxylase activity, driving intestinal calcium absorption and bone resorption; the consequent hypercalcemia and hypercalciuria promote nephrolithiasis, obstruction, and post-renal acute kidney injury. Glucocorticoids inhibit macrophage CYP27B1, accounting for the rapid reversal observed with treatment. Solid arrows indicate the direction of the pathophysiological sequence, and the dashed arrow denotes the site of therapeutic (glucocorticoid) inhibition. 25(OH)D, 25-hydroxyvitamin D; 1,25(OH)<sub>2</sub>D, 1,25-dihydroxyvitamin D (calcitriol); RANKL, receptor activator of nuclear factor- $\kappa$ B ligand; TRPV6, transient receptor potential vanilloid 6.

### 3.4. The Renal Phenotype of Sarcoidosis

Renal involvement in sarcoidosis is heterogeneous. The prototypical histological lesion is granulomatous interstitial nephritis (GIN), characterized by non-caseating epithelioid

granulomas with surrounding lymphoplasmacytic infiltration and variable interstitial fibrosis. Other recognized patterns include nephrocalcinosis, nephrolithiasis, distal renal tubular acidosis, nephrogenic diabetes insipidus and, much less often, membranous nephropathy, focal segmental glomerulosclerosis, and IgA nephropathy [6,7,16,17]. Acute kidney injury can arise from any of these mechanisms or their combination [18]. Obstructive uropathy from calcium-based stone disease, as in our patient, is mechanistically distinct from granulomatous inflammation of the interstitium, but the two coexist in a subset of patients [19]. Renal biopsy was deferred here because the metabolic and obstructive substrate adequately accounted for the AKI and the parotid biopsy had already established the underlying disease; subclinical granulomatous nephritis cannot be excluded with certainty, and longer-term renal surveillance is appropriate.

### 3.5. Comparison with Published Cases

A focused literature search of PubMed and Scopus (terms: “Heerfordt syndrome,” “uveoparotid fever,” “sarcoidosis hypercalcemia acute kidney injury,” “sarcoidosis nephrolithiasis”) returned 14 directly relevant English-language reports between 2010 and 2025. We compared our patient with eight of these in which sufficient clinical, biochemical, and outcome detail was available for structured comparison; the remaining six lacked adequate detail (Table 5). Several patterns emerge. First, bilateral simultaneous facial palsy is rare even within the Heerfordt subset; most published cases describe unilateral or sequential (“alternating”) involvement [10,11,20]. Second, hypercalcemia of the severity seen here is more often reported in isolation than as a component of the Heerfordt phenotype [16,17,19]. Third, the complete absence of any pulmonary radiographic finding is unusual: most published cases retain at least mediastinal adenopathy, apical change, or hilar prominence [21]. Fourth, where outcome data are available, the response to corticosteroid monotherapy is uniformly favorable, with renal recovery generally evident within two to four weeks, a pattern mirrored in our patient.

### 3.6. Therapeutic Considerations

Treatment of extrapulmonary sarcoidosis is largely empirical, derived from observational cohorts and expert consensus rather than randomized trials [22,23], and structured guidance specific to renal sarcoidosis remains limited [24]. For neurosarcoidosis or clinically significant renal involvement, oral prednisolone at 0.5–1 mg/kg/day for four to eight weeks, followed by a slow taper over six to twelve months, is widely used; pulse intravenous methylprednisolone is reserved for severe or rapidly progressive disease. Steroid-sparing agents (methotrexate, azathioprine, mycophenolate mofetil, or hydroxychloroquine) are introduced when relapse occurs on taper, when corticosteroid intolerance limits the dose, or when maintenance beyond 12 months is anticipated. Tumor necrosis factor inhibitors (infliximab, adalimumab) are reserved for refractory or organ-threatening disease [22].

In hypercalcemic patients, ultraviolet exposure and dietary calcium and vitamin D supplementation should be limited; bisphosphonates may be considered for severe acute hypercalcemia, but calcitriol-mediated hypercalcemia generally responds rapidly enough to corticosteroids that they are seldom necessary. Mechanical obstruction must be relieved promptly with ureteric stenting or percutaneous nephrostomy. Our patient illustrates this two-pronged approach: stenting addressed the mechanical problem while corticosteroids targeted the granulomatous substrate, and both interventions were needed for the rapid recovery observed.

**Table 5.** Comparison of the present case with published reports of Heerfordt syndrome and sarcoidosis-related hypercalcemia/acute kidney injury.

| Feature             | Present Case           | Chappity et al. [10]  | Sharma et al. [16]    | Sharmeen et al. [17] | Fujiwara et al. [21]  | Denny et al. [20] | Zakharova et al. [19] | Gallo et al. [11]      |
|---------------------|------------------------|-----------------------|-----------------------|----------------------|-----------------------|-------------------|-----------------------|------------------------|
| Age/sex             | 30/M                   | 52/F                  | 61/F                  | 55/M                 | 53/M + 55/F           | 59/F              | Not specified         | 47/F                   |
| Heerfordt syndrome  | Complete (3/4)         | Complete              | Absent                | Absent               | Incomplete + complete | Complete          | Absent                | Partial                |
| Parotid involvement | Bilateral              | Bilateral             | No                    | No                   | Unilateral/bilateral  | Bilateral         | No                    | No                     |
| Facial palsy        | Bilateral simultaneous | Bilateral alternating | No                    | No                   | Unilateral            | Unilateral        | No                    | Bilateral simultaneous |
| Uveitis             | Posterior, bilateral   | Anterior              | No                    | No                   | Absent/present        | Anterior          | No                    | Absent                 |
| Hypercalcemia       | Severe (13.1)          | No                    | Severe                | Severe               | No                    | No                | Severe                | No                     |
| PTH                 | Suppressed (3.4)       | Normal                | Suppressed            | Suppressed           | —                     | —                 | Suppressed            | —                      |
| ACE                 | Elevated (>100)        | Elevated (129)        | Elevated              | Elevated             | Elevated              | Elevated          | Elevated              | Elevated               |
| Renal involvement   | Obstructive AKI        | None                  | AKI                   | GIN + AKI            | None                  | None              | GIN + stones + AKI    | None                   |
| Nephrolithiasis     | Bilateral ureteric     | No                    | No                    | Yes (history)        | No                    | No                | Yes                   | No                     |
| Thoracic imaging    | Normal                 | Mediastinal LAD       | Apical bronchiectasis | Mediastinal LAD      | Mediastinal LAD       | Hilar markings    | Not detailed          | BHL                    |
| Biopsy site         | Parotid                | Parotid               | Marrow + lung         | Kidney (GIN)         | Eyelid + node         | Lymph node        | Kidney                | Lymph node             |
| Dialysis required   | No                     | No                    | No                    | No                   | No                    | No                | Yes (transient)       | No                     |
| Steroid response    | Excellent              | Excellent             | Good                  | Good                 | Excellent             | Excellent         | Good                  | Good                   |

ACE, angiotensin-converting enzyme; AKI, acute kidney injury; BHL, bilateral hilar lymphadenopathy; F, female; GIN, granulomatous interstitial nephritis; LAD, lymphadenopathy; M, male; PTH, parathyroid hormone.

### 3.7. Diagnostic Pitfalls and Learning Points

Several practical lessons deserve emphasis. Sarcoidosis should be considered in any patient with parathyroid-hormone-independent hypercalcemia regardless of the chest film, since exclusively extrathoracic disease accounts for missed or delayed diagnoses in an estimated 10–15% of cases [15]. Parotid biopsy is a high-yield, low-morbidity route to histological confirmation when superficial salivary disease is present, and obviates bronchoscopic sampling when the thorax is radiographically silent. Bilateral simultaneous facial palsy should never be ascribed by default to bilateral Bell palsy; the differential is narrow and warrants a structured workup. Normal serum ACE does not exclude sarcoidosis, but markedly elevated levels in the appropriate clinical setting support the diagnosis and can serve as a coarse marker of disease activity [25]. Finally, the speed of biochemical and clinical response to corticosteroids in sarcoidosis-related AKI argues for early empirical treatment once competing diagnoses, notably tuberculosis and malignancy, have been reasonably excluded.

#### Key Teaching Points

- PTH-independent hypercalcemia with elevated ACE in a young adult should prompt active investigation for sarcoidosis, even when the chest film is normal.
- Bilateral simultaneous peripheral facial palsy is a clinical red flag with a narrow differential; neurosarcoidosis should always be on the list.
- Posterior uveitis can occur in Heerfordt syndrome and does not exclude the diagnosis; anterior involvement is more common but not obligatory.
- Parotid biopsy is high-yield when accessible disease is present and avoids more invasive bronchoscopic sampling in radiographically silent chests.
- Sarcoidosis-related AKI is largely reversible when both the mechanical (stenting) and granulomatous (corticosteroid) substrates are addressed in parallel.
- Calcitriol-mediated hypercalcemia responds to glucocorticoids, which inhibit macrophage  $1\alpha$ -hydroxylase activity; bisphosphonates are seldom required.

### 3.8. Limitations

Several limitations should be acknowledged. Active vitamin D (1,25-dihydroxyvitamin D) could not be measured during admission because the assay was unavailable at our institution, which would have provided direct biochemical confirmation of the proposed mechanism of hypercalcemia. Renal biopsy was not performed, since the obstructive and metabolic substrate accounted for the acute kidney injury and a histological diagnosis had already been secured at the parotid; subclinical granulomatous interstitial nephritis therefore cannot be formally excluded. A 24 h urinary calcium measurement and a spot urine albumin-to-creatinine ratio were not obtained (24 h urinary protein was quantified instead, at 595.9 mg), so the magnitude of hypercalciuria could not be documented directly; serum calcium was used to monitor the metabolic response and normalized within a week of starting corticosteroids, remaining normal at the three-month review. Long-term follow-up beyond three months is ongoing and will be reported separately if clinically meaningful changes arise.

## 4. Conclusions

We have described a young man with Heerfordt syndrome whose clinical picture was dominated by extrathoracic complications: severe parathyroid-hormone-independent hypercalcemia, bilateral upper-ureteric calculi, and obstructive acute kidney injury, all on a background of antecedent bilateral simultaneous peripheral facial palsy and posterior uveitis, all in the absence of radiographic thoracic disease. To our knowledge this particular constellation has not previously been reported. The patient recovered fully after ureteric

decompression and oral corticosteroid therapy. The case argues for an active search for sarcoidosis in patients with otherwise unexplained calcium dysregulation, parotid swelling, or bilateral facial weakness regardless of the chest film, and reinforces that sarcoidosis-related renal injury is largely reversible when treated promptly. Wider clinician familiarity with these less common phenotypes will reduce diagnostic delay and the attendant risk of irreversible end-organ damage.

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