Skin nodules and acute renal failure, what is the link?

**Keywords:** cutaneous nodular lesions; granulomatous nephritis; hypercalcaemia; sarcoidosis

**Case**

A 58-year-old woman was referred to the hospital with a 2 months history of anorexia, fatigue, cutaneous nodular swellings, recently developed acute renal failure and hypercalcaemia. On admission, her blood pressure and pulse were normal and physical examination revealed (+) pretibial oedema and reddish nodular swellings on her face, elbows (Figure 1) and legs. Laboratory findings are given in Table 1. Other biochemical parameters and chest X-ray were normal. Immunglobulins, C3 and C4 levels, thyroid function tests were all normal. Protein electrophoresis showed no evidence of a paraprotein. The urine analysis showed a mild proteinuria (800 mg/day). There was no history of tuberculosis in her past and the tuberculin skin test was negative. Her electrocardiogram and echocardiography were normal. Computerized tomography (CT) scan of the thorax and abdomen showed bilateral hilar lymphadenopathies without interstitial abnormality. Ultrasonographic evaluation of the urinary tract was unremarkable. Renal stone and nephrocalcinosis were absent. On the basis of these findings, renal and skin biopsies (Figure 2) were performed.

**Questions**

What is the histopathologic diagnosis of the skin biopsy?

Is there a link between cutaneous nodular lesions and acute renal failure?

What is your diagnosis?

**Table 1.** Laboratory values of the patient

<table>
<thead>
<tr>
<th>Parameters</th>
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</thead>
<tbody>
<tr>
<td>Urea (mmol/l)</td>
<td>9.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Haemoglobin (gr/dl)</td>
<td>9.9</td>
</tr>
<tr>
<td>Serum Creatinine (µmol/l)</td>
<td>150&lt;sup&gt;a&lt;/sup&gt;</td>
<td>White blood cells (&lt;10&lt;sup&gt;9&lt;/sup&gt;/l)</td>
<td>4.7</td>
</tr>
<tr>
<td>Calcium (mmol/l)</td>
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<td>ANA</td>
<td>Negative</td>
</tr>
<tr>
<td>Phosphate (mmol/l)</td>
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<td>ANCA</td>
<td>Negative</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>35.0</td>
<td>Anti-GBM</td>
<td>Negative</td>
</tr>
<tr>
<td>Sedimentation rate (mm/h)</td>
<td>100&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Cryoglobulin</td>
<td>Negative</td>
</tr>
<tr>
<td>CRP (IU/ml, normal range: 0–5)</td>
<td>2.58</td>
<td>Parathyroid hormone (ng/l)</td>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Higher, <sup>b</sup>lower than normal range; CRP, C-reactive protein; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; GBM, glomerular basement membrane antibody.

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**Fig. 1.** Nodular swellings over the elbows.

**Fig. 2.** Light microscopy of skin biopsy (H&E Stain; × 50 objective)
Sarcoidosis was diagnosed on the basis of clinical and biopsy findings. Sarcoidosis is a granulomatous multisystem disorder of an unknown cause and its diagnosis depends on exclusion of other granulomatous disorders. The physician may stop the examination of granulomatous disease when either the radiologist or the pathologist reports the result is being concordant with sarcoidosis [1]. Although, our patient had no history of tuberculosis, bronchoscopic investigation was performed and bronchoalveolar lavage fluid was negative for mycobacterium and fungi. She had no drug history.

There is no specific test for the definitive diagnosis of sarcoidosis; however, serum angiotensin converting enzyme (ACE) activity may add a little diagnostic value. In our patient, serum ACE level was 248 UI/l, which is nearly five times of the upper limit. Unregulated secretion products, like ACE, are synthesized by granulomatous epitheloid cells, and plasma concentration of ACE may reflect the activity of the disease [2]. In addition, the patient had hypercalcaemia and low iPTH levels. Like ACE, granulomatous epitheloid cells can produce calcitriol and cause hypercalcaemia, which suppresses the release of parathyroid hormone and production of calcitriol in the kidney [3]. In the diagnosis, the Kwem-Siltzbach skin test is not well standardized and analysis of the bronchoalveolar lavage fluid, the ratio of CD4 to CD8 cells, are not specific for sarcoidosis [1].

The clinical manifestations of sarcoidosis can be widespread. Pulmonary involvement is the most common [3]. Although the patient had no pulmonary symptoms and had a normal chest roentgenogram, her computerized tomography scan of the thorax showed bilateral hilar lymphadenopathies.

Renal involvement in sarcoidosis is not uncommon but rare. Recently, Robson et al. [4] reported renal limited form of sarcoidosis, which was presented by granulomatous interstitial nephritis. A decrease in renal function occurs in <3% of the patients [4]. Nephrocalcinosis and nephrolithiasis are seen due to hypercalcaemia and hypercalciuria. Membranous nephropathy, minimal change disease, proliferative os crescentic glomerulonephritis and focal glomerulosclerosis have been reported as case presentations [3–5,6], however, granulomatous interstitial nephritis is more common in sarcoidosis [3]. In our case, the renal biopsy showed the replacement of the tubulointerstitial tissue by granuloma with giant cells and scattered lymphocytes, especially in the lower cortex and in the medullary area. There were no significant glomerular and tubulointerstitial immune complex deposition. The characteristic histopathologic features are the presence of noncaseating granulomas which displace and disrupt the normal parenchyma, primarily in the cortex, and sometimes in the capsule and medulla. The lesions are accompanied by an intense lymphocytic infiltrate. Multinucleated giant cells are present in over 90% of biopsy specimens [7].

Twenty-five percent of patients with sarcoidosis have skin manifestations like erythema nodosum, a remarkable array of plaques, subcutaneous nodules, macules and papules. Sometimes occurring in scars and tattoos [1]. In our case, the skin biopsy of the cutaneous nodular lesion showed disseminate replacement of the upper-middermis by granuloma. Some deeply situated nodular lesions were also seen. Non-caseous sarcoid granulomas characterized with well circumscribed collections of epitheloid histiocytes with a sparse infiltrate of lymphocytes were noticed; however, no giant cells were observed (Figure 2).

Alternate day oral corticosteroid treatment is recommended for patients with skin and renal involvement [1–4]. In our case, after the diagnosis, dietary calcium was lowered and prednisone 0.5 mg/kg/day (30 mg/day) was initiated. In the third week of the treatment, the skin lesions disappeared, serum calcium and creatinine levels became normal. Control CT scan of the thorax showed regression of hilar lymphadenopathies, and the serum ACE level decreased to 79 UI/l. Corticosteroid dosage was tapered slowly and discontinued.

References

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