CASE REPORT

Acute myeloid leukaemia presenting as a rapidly progressive polyradiculoneuropathy

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SUMMARY

Neurological involvement at onset in acute myeloid leukaemia (AML) is rare, with only a few isolated case reports. We present the case of a 46-year-old man with rapidly progressive polyradiculoneuropathy as the presenting feature of AML. The proposed mechanism for this is postulated to be direct intraneural infiltration, although a paraneoplastic, autoimmune-related phenomenon could be possible. Despite chemotherapeutic intervention, the patient died 1 month after initial presentation. Although rare, neurological manifestations of AML do occur and it is important to include haematological malignancies in the differential diagnosis in patients presenting with neurological symptoms.

BACKGROUND

Neurological involvement at onset in patients with acute myeloid leukaemia (AML) is infrequent, with only a few isolated case reports.^{1–6} Central nervous system (CNS) involvement in AML, including raised intracranial pressure, cranial nerve palsies, spinal cord compression or intracerebral haemorrhage, has been reported, although it has decreased in frequency since the introduction of cytarabine. We describe a case of AML presenting with normocytic anaemia and rapidly progressive polyradiculoneuropathy; it has only been reported once previously.⁴ The mechanism for this is postulated to be infiltration by malignant cells, although a paraneoplastic, autoimmune phenomenon could also be possible. We believe this case to be important, as it highlights the necessity of recognising haematological malignancies in the differential diagnosis of acute neurological presentations.

CASE PRESENTATION

A 46-year-old man presented following a 3-week history of feeling non-specifically unwell. A week prior to presentation, he developed lower abdominal and flank pain, and an intense, painful itching sensation affecting his legs, abdomen and lower back. In addition, he had experienced excessive sweating though he denied weight loss. Neurologically, he described left leg weakness and numbness causing him to get a catch in his toes when walking. His symptoms deteriorated and he subsequently developed painful urinary retention requiring urinary catheterisation with a residual volume of 800 mL. His only medical history was urticaria, for which he took desloratadine. He smoked 20 cigarettes per day and drank 36 units of alcohol per week. He was unemployed.

On initial examination by the admitting surgical team, the only neurological deficits recorded were mild weakness of left hip and knee flexion, reduced reflexes throughout his lower limbs and reduced sensation to pin prick 'in the distribution of L2/3 on the left'. Initial blood results demonstrated normocytic anaemia, borderline low neutrophils and platelets, and no blasts (haemoglobin 75 g/L, white cell count $3.1 \times 10^9/L$, platelets $146 \times 10^9/L$, neutrophilia of $1.6 \times 10^9/L$). Sodium was low at 116 mmol/L (diagnosed as syndrome of inappropriate ADH secretion after review by endocrinology) and erythrocyte sedimentation rate (ESR) was elevated at 40 mm/h. Over a few days, the patient's leg weakness worsened and he developed left facial weakness. He was started on prednisolone 40 mg daily for a presumed diagnosis of Bell's palsy and referred for a neurological assessment.

On neurological review, the cranial nerves were normal except for a left lower motor neurone facial palsy. The patient had mild weakness of elbow extension bilaterally and left finger extensors (Medical Research Council, MRC grade 4/5), though tone and reflexes, and sensory examination, were normal in the upper limbs. In the lower limbs there was mild weakness of right hip and knee flexion (MRC grade 4/5) in addition to the previous left hip flexion (MRC grade 2/5) and left knee flexion (MRC grade 3/5) weakness described earlier. Tone was normal and reflexes were absent. He had reduced joint position sense distally and a patchy distal reduction in pin prick sensation, more on the left than the right. It was also noted that he had discrete, pigmented, dusky purple nodules over the right shoulder and abdomen (figure 1).

INVESTIGATIONS

MRI of the spine was unremarkable except for mild cervical spondylotic change. CT of the head was normal and CT of the thorax, abdomen and

Figure 1 Leukaemia cutis. Pigmented nodules over the thorax and abdomen.

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Table 1 Nerve conduction studies and electromyography

Motor nerves	Latency (ms)	Amplitude (mV)	Conduction velocity (m/s)
Right median			
Wrist—APB	3.2	4.4	
Elb—wrist	7.9	2.7	52.8
Right ulnar			
Wrist—ADM	4.0	0.4	
Ab Elb—wrist	8.9	0.3	54.1
Right tibial			
Ankle—AH	Absent	Absent	

Sensory nerves	Latency (ms)	Amplitude (uV)	Conduction velocity (m/s)
Right radial			
Forearm—1st Web	1.85	4.6	55.1
Right sural			
Midcalf—ankle	Absent	Absent	

Muscle	Interpretation	Fib	PSW	IP
Right FDI	Active denervation	8/10	8/10	0 act.
Right EDC	Active denervation	8/10	8/10	0 act.
Right tibialis anterior	Active denervation	8/10	8/10	0 act.
Right gastrocnemius	Active denervation	8/10	8/10	0 act.

APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor hallucis; FDI, first dorsal interosseous; EDC, extensor digitorum communis.

pelvis revealed a few prominent axillary and inguinal lymph nodes; none were considered to be pathological, with the largest measuring 1 cm in diameter. There was no radiological evidence of a haematological or abdominal malignancy. A lumbar puncture demonstrated clear and colourless cerebrospinal fluid containing three white cell count, protein 0.89 g/L and glucose 4.4 mmol/L (paired plasma glucose 8.4 mmol/L). Nerve conduction studies showed evidence of acute motor and postganglionic sensory axonal damage present in upper and lower limbs though most marked in the lower limbs (table 1).

DIFFERENTIAL DIAGNOSIS

Given the development of a subacute, asymmetric painful neuropathy with raised ESR and systemic features, vasculitis was suspected, and the patient was started on intravenous methylprednisolone 1 g per day for 5 days. Unfortunately, there was no clinical response and he continued to decline. His legs became profoundly weak over the course of the following week, and he developed progressive weakness of both upper limbs and right facial weakness. Pain was a prominent feature and he required oramorph to control this.

A vasculitic screen was negative, as were tests for hepatitis, HIV and syphilis. Serum protein electrophoresis, B12 and

ferritin were normal with folate slightly low. Lactate dehydrogenase was raised at 696 U/L (normal 200–500 U/L). One week following admission, the patient's white cells increased to $8.2 \times 10^9/L$ and the blood film now showed dysplastic myeloid features and blasts. Immunophenotyping of peripheral blood demonstrated positive expression for CD11c, CD13, CD56, CD15, CD33, CD64, CD117 and HLADR, which, along with bone marrow morphology, confirmed acute monoblastic leukaemia (figure 2), and the white cell count now increased rapidly. Dermatology review considered the skin lesions to be leukaemia cutis—cutaneous infiltration by neoplastic leucocytes.⁷

OUTCOME AND FOLLOW-UP

The patient later became feverish with raised C reactive protein, and was started on meropenem. In view of his general condition, intensive chemotherapy was not possible and initial cytoreduction with oral hydroxycarbamide was implemented. Following his first dose of hydroxycarbamide, he deteriorated and developed type II respiratory failure requiring intensive care; blood cultures grew *Staphylococcus aureus*. Neurologically, he continued to deteriorate, developing a flaccid quadriplegia, bulbar impairment, bilateral facial weakness and ophthalmoplegia. In particular, there was impaired adduction, upgaze and downgaze, with minimal abduction.

Sodium spontaneously corrected from 116 to 148 mmol/L over 17 days, so the possibility of central pontine myelinolysis was considered, but MRI of the brain only showed mucus in the frontal sinuses and mastoid air cells. The patient developed multiorgan failure requiring inotropic support, and died 1 month after initial presentation.

DISCUSSION

Neurological presentations of AML in adults are rare and only a few case reports exist in the literature. These mainly relate to granulocytic sarcomas, rare myeloblastic tumours that can develop in AML. Granulocytic sarcomas have been reported at initial presentation to cause facial nerve palsy,¹ facial nerve palsy and paraplegia,³ and epidural compression.^{5 6} Cranial neuropathy at initial presentation has also been reported.² Ascending sensory motor polyradiculoneuropathy with cranial nerve involvement has been reported in a few cases of AML in adults following chemotherapy⁸ and only once previously as the presenting feature of AML.⁴ A further case report of a patient with rapidly progressive painful neuropathy with symmetric sensorimotor and autonomic involvement occurring postchemotherapy showed intraneural leukaemic infiltrates on sural nerve biopsy.⁹ Similarly, an infiltrative polyneuropathy has also been described in a patient with AML in remission, who had undergone systemic and intrathecal chemotherapy.¹⁰ A larger study of neurological involvement in AML showed a presentation rate of 0.4%

Figure 2 Bone marrow histology. Densely hypercellular bone marrow with very scanty fat spaces. The marrow spaces are packed with immature myeloid cells and other mononuclear cells consistent with monocytic precursors. Occasional megakaryocytes are seen.

with symptoms including headache, cranial nerve palsies and motor deficit.¹¹

Other neurological manifestations reported in patients with an established diagnosis of AML include brachial plexopathy,¹² myeloid sarcoma of temporal bone¹³ and facial palsy.¹⁴

Although rare, neurological manifestations of AML do occur and it is important to include haematological malignancies in the differential diagnosis in patients presenting with neurological symptoms. As reported previously, it is probable that the polyradiculoneuropathy was secondary to neural infiltration by leukaemic cells, although a postmortem was not performed to confirm this.

Learning points

- ▶ Although rare, neurological presentations of haematological malignancies do occur.
- ▶ Haematological malignancies should be considered in the differential diagnosis of all patients with acute neurological presentations.
- ▶ Early diagnosis is of paramount importance in order to treat quickly and effectively.

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