

Spinal neurobrucellosis is an unusual cause of nontraumatic paraplegia in Zaria, Northern Nigeria: A report of 3 cases and review of current literature.

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ABSTRACT (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

Introduction: Brucellosis is a zoonotic febrile infection common among farmers or herdsmen who come into contact with animals or animal products. Neurological complications are uncommon, but when they occur can be confused with other neurological diseases, particularly those due to tuberculosis (TB).

Aim: This report is intended to remind health workers and people living in Brucella endemic communities that spinal neurobrucellosis can mimic Potts' disease as the cause of nontraumatic paraparesis or paraplegia.

Study design: longitudinal case series

Methodology: We report the cases of three patients who presented with paraplegia following months of constitutional symptoms of fever, headache, malaise and weight loss. All were exposed to cows, goats and sheep. One patient had received antituberculous therapy for 18 months with minimal recovery. Serology and neuroimaging were used to confirm the diagnosis.

Results: All patients recovered within 6 to 12 weeks of rifampicin, doxycycline, trimethoprim-sulfamethoxazole or streptomycin, but with residual paraparesis.

Conclusion: spinal neurobrucellosis can be confused with Pott's disease (TB of the

spine) with consequent poor treatment outcome.

Keywords: spinal neurobrucellosis, zoonosis, paraplegia, serology, neuroimaging

Introduction

Brucellosis, also called Malta fever or Mediterranean fever (it was first described in Malta in the Mediterranean region) is caused by intracellular gram-negative bacteria of the genus *Brucella*. It is the most common zoonosis in the world, accounting for the annual occurrence of more than 500,000 cases [1]. All *Brucella* infections are caused by direct or indirect exposure to animals or animal products (e.g., milk, milk products and raw meat), although possibility of aerosolized person to person transmission exists. Human disease is caused by any of four species: *Brucella melitensis* (affecting goats, sheep, camel); *Brucella abortus* (cattle); *Brucella suis* (pigs, hogs) and *Brucella canis* (dog) [2]. Symptoms are variable and non specific because any organ or system in the human body can be affected, but the main features are remittent fever which can be intermittent, relapsing and undulant in nature. Others are somatic symptoms of headache, body pains, night sweats, anorexia, fatigue, malaise, weight loss, and depression [2].

Neurobrucellosis is a rare complication of Brucellosis [3, 4], in which any part of the neuraxis may be involved. Chronic spinal localization is a rare but well documented event, and spinal cord compression can simulate Pott's disease [3, 5]. Sometimes the patients receive antituberculous drugs with some recovery [3].

In endemic area we advise screening for TB, brucellosis, typhoid and paratyphoid infections. This paper presents some difficulties in the diagnosis and management of neurobrucellosis.

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46 **Case Reports**

47 1. A.R, a 15 year old Fulani milkmaid, who also ingested unpasteurized milk
48 regularly, developed intermittent fever of 5-7days intervals, profuse night sweats,
49 anorexia, fatigue, malaise and hearing loss for 8 weeks. At the 7th week she
50 developed insidious non- radiating band-like, low back pain, and progressive lower
51 limb weakness culminating in paraplegia and double incontinence at the 8th week.
52 She therefore became bedbound leading to development of multiple gluteal sores
53 and anterior right thigh abscess. At 10th week, she presented to our centre when
54 she developed severe tetanus of one day duration.

55 On examination, she was chronically ill-looking, asthenic, conscious, but febrile
56 (temperature 38.7 °C), diaphoretic and pale. She had multiple gluteal and
57 trochanteric ulcers discharging cheesy/putrid materials; and episodic titanic spasms
58 with locked-jaw, trismus, opisthotonus and rigidity. She also had spastic paraplegia,
59 bilateral extensor plantar reflexes, and sensory loss at level T12, but no obvious
60 vertebral deformity or gibbus. She was incontinent of both faeces and urine, and
61 had a diaper on. X-rays of the spine, pelvis and hips did not reveal abnormalities.

62 She was treated with intravenous human tetanus immunoglobulins 10,000
63 international units (I.U) stat after a test dose, metronidazole infusions 500 mg 8
64 hourly, and intermittent diazepam 20-40 mg in 5% dextrose saline 8-12 hours until
65 spasm free. She received 3 pints of packed cells blood transfusion, and recovered
66 from tetanus within 2 weeks of admission. She was also investigated for brucellosis,
67 found positive and was treated with antibiotics. She recovered and was discharged

68 home with residual paraparesis at 12th week of admission. The results of laboratory
69 investigations, drug regimen and outcome of treatment are summarized in table 1.

70 2. J.N, a 13 year old student developed intermittent fever of 5-7 days intervals,
71 headache, neck pain and loss of consciousness for 2 weeks. He was treated for
72 possible pyogenic meningitis with parenteral ceftriaxole at a private hospital where
73 he first presented; and regained consciousness after 10 days. However, the fever
74 continued and he developed paraplegia, urinary retention and incontinence within 4
75 weeks of illness. There was no history of antecedent diarrhea, upper respiratory
76 tract infection, or recent vaccination. Eight weeks later, he developed a sinus above
77 the gluteal cleft which discharged a cheesy material. He worked in his father's
78 animal farm which consisted of pigs, goats and sheep, but did not ingest
79 unpasteurized milk.

80 On examination, he was fully conscious, febrile (temperature 37.6° C), pale and
81 dehydrated. He also had nuchal rigidity with positive Brudzinski and Kernig's signs,
82 flaccid paraplegia, and loss of sensation below the knee joints (L 4 and below).

83 There was a sinus which was discharging cheesy material from a slit-like opening
84 above the gluteal cleft on the midline. He was incontinent of urine, but not of faeces,
85 and there was no obvious vertebral deformity or no gibbus.

86 He was investigated for brucellosis, found positive and treated with antibiotics.

87 Constitutional symptoms of brucellosis resolved within 2 weeks of treatment as
88 shown by the pattern of fever at presentation and 15 days after (in figures I and II
89 respectively), but his neurologic deficit persisted. He was instructed to continue his
90 drug regimen for 16- 24 weeks but was discharged on request with residual

91 paraparesis at 12th week of therapy. He was lost to follow-up. The results of his
92 laboratory tests, drug regimen and outcome of treatment are summarized in table 1.
93 3. M.D, a 56 year old man who worked as a veterinary health extension worker in
94 Kaduna State Ministry of Agriculture and Animal resources presented with 2 years
95 history of headache, anorexia, weight loss, fatigue and progressive lower limb
96 weakness resulting in paraplegia and urinary incontinence. He had completed 18
97 months course of antituberculous therapy for suspected Pott's disease with minimal
98 improvement. His daily routine of more than two decades was vaccination of herds
99 of cows, sheep, goats and pigs. He never ingested unpasteurized milk. On
100 examination, he was fully conscious, pale, afebrile and mildly wasted. He had
101 spastic paraplegia, bilateral extensor plantar reflexes, sensory loss at level T10, and
102 urinary incontinence. There were multiple vertebral deformities and gibbus.
103 He was put on anti-brucella therapy after investigations, and within 12 weeks
104 muscle power in his lower limbs improved from 0/5 to 3/5. He was instructed to
105 continue his drug regimen for 16-24 weeks, but was also lost to follow-up due to
106 loss of job (income) and spouse. The details of his laboratory results, drug regimen
107 and outcome of treatment are summarized in table 1.

108 Discussion

109 Northern Nigeria is indigenous to herdsmen and cultures engaged in animal
110 husbandry; and since the risk of brucellosis is proportional to the degree of contact
111 with Brucella-infected animals, their excreta, or their edible byproducts; the disease
112 is expected to be endemic in our environment [5]. Prolonged contact with animals
113 and their edible byproducts were main risk factors for the disease in our patients.

114 Cases of acute uncomplicated brucellosis are not commonly reported in our
115 hospitals, either because health workers are unfamiliar with the infection, or the
116 similarities of its acute constitutional symptoms are confused with those of other
117 tropical infectious diseases particularly malaria fever, typhoid fever and tuberculosis
118 [6]. This may explain why all 3 patients were misdiagnosed at the peripheral
119 hospitals where they first presented before they were referred to us because of the
120 complications they developed.

121 In Nigeria it is common practice for primary physicians to put most nontraumatic
122 paraparesis or paraplegic patients on empiric anti tuberculous therapy with variable
123 outcome [5]. This is borne out of the belief that Pott's disease is the commonest
124 cause of nontraumatic compressive myelopathy because of high prevalence of TB
125 infection in the country [7]. This common management error must be discouraged.

126 Neurobrucellosis affecting the central (CNS) or peripheral nervous system (PNS)
127 has been described in 3–5% of patients, with a variety of clinical manifestations and
128 imaging abnormalities that mimic other neurologic diseases [3, 5]. Although our
129 patients had similar constitutional symptoms and neurological signs, the patterns
130 and extent of spinal cord damage were different. Acute and chronic spinal

131 neurobrucellosis (myelopathy) may result from several mechanisms such as acute
132 transverse myelitis, spinal cord infarction, adhesive arachnoiditis, compression from
133 epidural abscess, brucella spondylitis, and/or vertebral erosion and collapse [8, 9].

134 Diagnostic confusion may occur with lumbar disc protrusion and tuberculous
135 spondylitis [8]. Cervico-brachial plexopathies, and lumbo-sacral plexo-
136 radiculopathies, mononeuritis multiplex and peripheral neuropathies have been
137 described [7]. In the first and second patients (case 1 and 2), paraplegia was due to

138 inflammatory changes in the spinal cord (myelitis & demyelination of white matter),
139 and spinal cord and nerve roots (myelitis, demyelination of white matter &
140 polyradiculitis) respectively; in the third patient (case 3), osteospondylitic extraaxial
141 compression of the spinal cord (by granulomas or abscess formation) was probably
142 responsible. These lesions are said to result from direct or indirect immunological
143 processes involving cytotoxic T lymphocytes, microglia and humoral immune
144 activation leading. Therefore spinal neuroimaging may show normal architecture (if
145 lesion is early and mild), or abnormal enhancement (for inflammatory changes and
146 demyelinating lesions) [5].

147 An understanding of the behavior of the humoral immune system is important in the
148 diagnosis of brucellosis. The level of immunoglobulin M (IgM) antibodies begins to
149 rise at the end of the first week of infection, peaks at about one month, and will
150 remain elevated for years; even in the absence of active infection. IgA antibodies
151 are elaborated late but may also persist for years. On the other hand, IgG
152 antibodies begin to appear at approximately one month of infection, and begin to
153 disappear thereafter. Therefore, persistent elevation of IgG antibodies is an
154 indication of chronic active infection, or a relapse of the illness [10, 11]. In our
155 centre, we test the sera of our patients against the IgG antibodies of *B melitensis*
156 because this organism is the most common cause of human brucellosis globally.

157 Recovery of *Brucella* organisms from cultures of CSF or blood is usually very low in
158 neurobrucellosis because the organisms are chiefly intracellular in locations,
159 although the CSF may exhibit pleocytosis, hypoglycorrhachia, and elevation of
160 protein concentration. The CSF findings of this disease can thus mimic those of
161 other intracellular organisms such as mycobacteria, fungi and toxoplasma [12].

162 In endemic areas, isolation of bacteria from serum or cerebrospinal fluid (CSF) is
163 the gold standard diagnostic method, but appropriate serological tests such as IgG
164 agglutination titers of >1:160 in CSF or >1:320 in serum can be diagnostic,
165 particularly if there are rising titers in serial testing [10]. Rapid diagnosis and
166 treatment often leads to prompt and complete recovery in acute infection, but
167 response to appropriate antibiotic is variable in chronic brucellosis [13]. Treatment
168 entails use of triple drugs selected from rifampicin, doxycycline, gentamicin,
169 streptomycin, trimethoprim-sulfamethoxazole and ciprofloxacin, usually for periods
170 of 6 weeks (streptomycin) and 3 months (for others). Standard treatment for adults
171 with acute spinal brucellosis comprises capsule doxycycline 100 mg BD and tablets
172 trimethoprim-sulphamethaxole 960 mg BD, or capsule rifampicin 600 mg for at least
173 12 weeks, combined during the first 3-4 weeks with IM streptomycin. Treatment is
174 prolonged for 18-24 weeks in chronic neurobrucellosis [13]. Clinical improvement as
175 well as improvement in CSF pleocytosis and fall in CSF and blood *Brucella* titers
176 should occur after appropriate treatment. Poor outcomes are associated with
177 complications such as raised intracranial pressure, stroke, endocarditis, intracranial
178 mycotic aneurysm and haemorrhage, and osteospondylitis with compressive
179 myelopathy or radiculopathy [3].

180 In conclusion, neurobrucellosis is a treatable disease with a favorable outcome, but
181 because acute symptoms are similar to many tropical fevers, the infection may be
182 misdiagnosed with dire consequences. Also, the presence of complications like
183 meningoencephalitis and myelopathy worsens the prognosis. Therefore the disease
184 will continue to be an important health problem in developing countries unless
185 certain steps are taken to reduce its incidence. The steps must include avoidance of

186 unpasteurized dairy products, animal contact or improperly cooked meat; regulation
187 of abattoirs; surveillance, culling and vaccination of herds of sheep, goats, cows and
188 pigs.

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222 Table i. Summary of Laboratory test results, drug regimen, duration of therapy and
223 outcome.

224

INVESTIGATIONS	CASE 1	CASE 2	CASE 3
HIV I & II	NEGATIVE	NEGATIVE	NEGATIVE
MANTOUX SKIN REACTION	< 5 MM (NEGATIVE)	< 5 MM (NEGATIVE)	< 5 MM (NEGATIVE)
CHEST X RAY	NORMAL	NORMAL	NORMAL
LEUCOCYTES (NORMAL 2- 11X10 ⁹ /L)	LYMPHOCYTIC PLEOCYTOSIS	LYMPHOCYTIC PLEOCYTOSIS	NORMAL
HEMOGLOBIN (NORMAL 11- 16 G/DL)	6.9 (SEVERE ANEMIA)	10.2 (MILD ANEMIA)	14.0 (NORMAL)
INITIAL BRUCELLA ABORTUS IGG SEROLOGY	1/320	1/320	1/320
BRUCELLA ABORTUS IGG SEROLOGY 4 &	1/16, <1/16	1/16, < 1/16	1/64, 1/16

12 WEEKS

RESPECTIVELY

CSF ANALYSIS	PLEOCYTOSIS, MARKEDLY ELEVATED	LUMBAR
*RELATIVE TO	PROTEIN, LYMPHOCYTOSIS,	PUNCTURE WAS
RANDOM	*HYPOGLYCORRHACHIA	CONSTRAINED
BLOOD SUGAR		BY VERTEBRAL
		SPINE
		DEFORMITIES
CSF CULTURE	NEGATIVE	NEGATIVE
		NOT DONE
HISTOPATHOLOGY	NON CASEATING	NON
OF CHEESY	GRANULOMA	CASEATING
MATERIAL		GRANULOMA
SPINAL MRI	FIGURE III(AREA OF	FIGURE
	HYPER-INTENSITY	IV(AREAS OF
	ON A SEGMENT OF	HYPER-
	SPINAL CORD)	INTENSITIES ON
		MANY
		SEGMENTS OF
		SPINAL CORD &
		SPINAL NERVE
		ROOTS)

SPINE	NORMAL	NORMAL	DESTRUCTION
VERTEBRAL			OF
X RAY			INTERVERTEBRAL
			DISCS AND
			VERTEBRAL
			BONES T12, L1,
			L2
DIAGNOSIS	TRANSVERSE	TRANSVERSE	OSTEOSPONDYLITIC
	MYELITIS	MYELITIS AND	EXTRAAXIAL
		POLYRADICULITIS	COMPRESSIVE
			MYELOPATHY
DRUGS AND	12 WEEKS OF CAPS	INTRAMUSCULAR	INTRAMUSCULAR
DURATION OF	RIFAMPICIN 450 MG	STREPTOMYCIN	STREPTOMYCIN
THERAPY	DAILY,	750 MG DAILY	1 GRAM DAILY
	DOXYCYCLINE	FOR 4 WEEKS,	FOR 12 WEEKS,
	100MG BD AND	CAPS	CAPS
	TABS	RIFAMPICIN 450	RIFAMPICIN 600
	TRIMETHOPRIM-	MG DAILY FOR	MG DAILY FOR 24
	SULPHAMETHAXOLE	12 WEEKS, AND	WEEKS, AND
	960 MG BD.	CAPS	CAPS
	TO CONTINUE	DOXYCYCLINE	DOXYCYCLINE
	REGIMEN FOR 16	100 MG BD FOR	100 MG BD FOR
	WEEKS	12 WEEKS.	24 WEEKS.

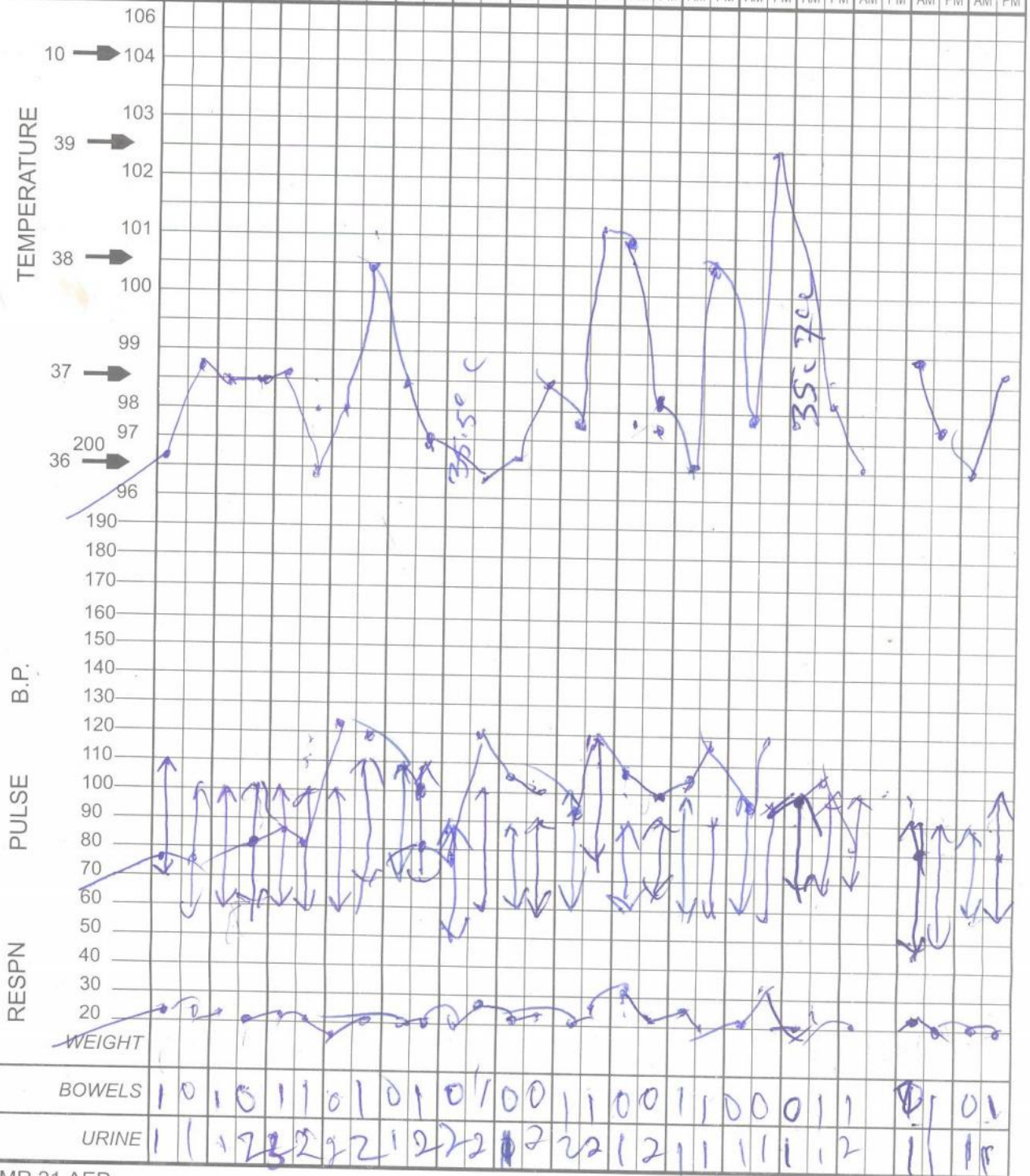
TO
CONTINUE
REGIMEN FOR
16-24 WEEKS

OUTCOME	DISCHARGED HOME ON WALKING FRAME (LOWER LIMBS MUSCLE POWER 4/5) AT 12 WEEKS	DISCHARGED HOME ON WHEELCHAIR (LOWER LIMBS MUSCLE POWER 3/5) AT 12 WEEKS	DISCHARGED HOME ON WHEELCHAIR (LOWER LIMBS MUSCLE POWER 3/5) AT 12 WEEKS
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LEDGER NO.		

NAME Leahigha WARD PMK

LEDGER NO.

[illegible][illegible]

MR 21 AEP

ASOM NIG. ENT.

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229 Figure 1. Undulant and intermittent temperature pattern before treatment (case 2)

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A.B.U HOSPITAL

SHEET NO. (4)

Unit No.

TEMPERATURE CHART

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LEDGER NO.

NAME

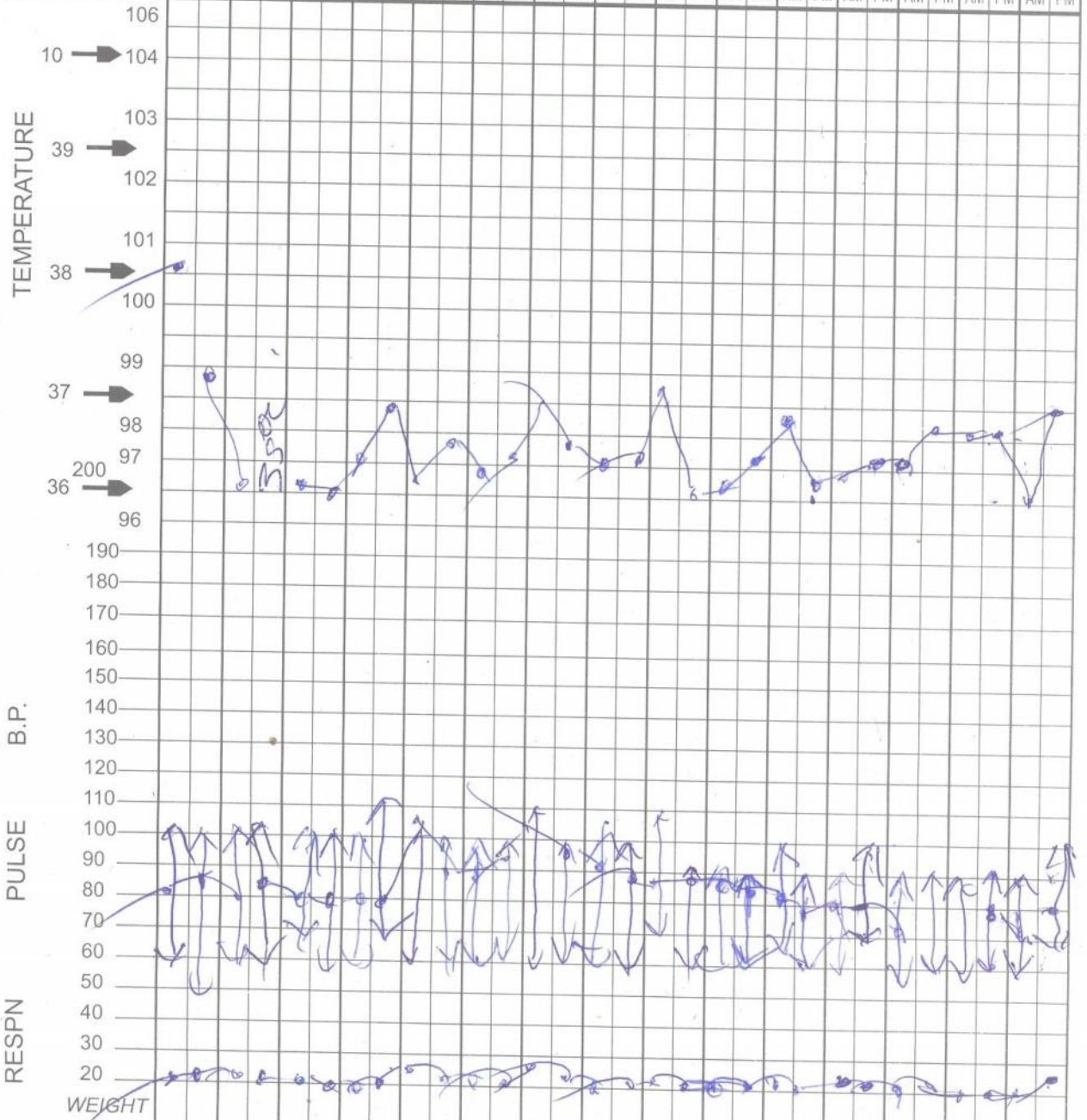
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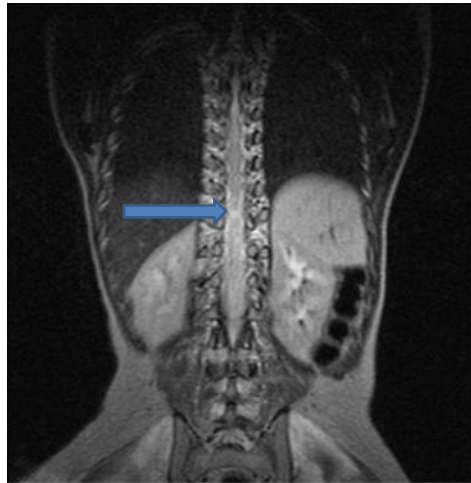
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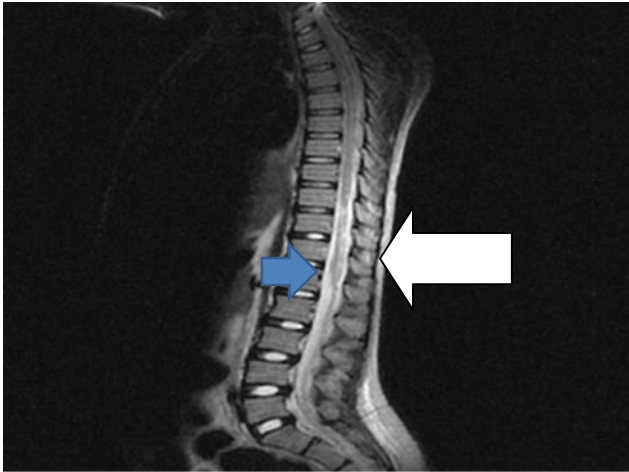
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Figure 2. Normal temperature pattern after 15 days of treatment (case 2)



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Figure 3. Coronal view of T2 weighted spinal MRI showing area of hyperintensity on a segment of the cord.



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243 Figure 4. Sagittal view of T2 weighted spinal MRI showing areas of hyper
244 intensities on many segments of the spinal cord and spinal nerve roots
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