CLINICAL NEUROSCIENCES

Transient Neurological Deterioration Following Anterior Cervical Discectomy and Fusion

Saisunder Shashank Chaganty[1], Himanshu Sharma[2]

(1) Peninsula Medical School, University of Plymouth, Plymouth, UK
(2) University Hospitals Plymouth NHS Trust, Plymouth, UK

ABSTRACT

AIM OF THE STUDY: To present an example and discuss the current understanding of aetiology, pathogenesis, and management of neurological deterioration following anterior cervical discectomy and fusion (ACDF).
BACKGROUND: Single-level ACDF is a relatively straightforward procedure commonly indicated for symptomatic cervical myelo-radiculopathy. Transient neurological deterioration (TND) is sometimes observed post-operatively. This is poorly understood in literature.
CASE REPORT: A 44-year-old male presented with a 5 months' history of progressive neck pain, left arm pain & paraesthesia along with weakness affecting left upper and lower limb. MRI revealed C5/C6 disc prolapse and an ACDF procedure was performed. Immediately postoperatively, the patient developed left-sided loss of sensation and hemiparesis. Emergent postoperative MRI work-up revealed T2 hyperintense MRI myelopathy changes with residual spinal cord signals. His TND returned to pre-operative levels in 4 hours. He was discharged day 2 post-operatively. At 6 months review, the patient achieved excellent improvement in clinico-symptomatology.
WHAT THIS STUDY ADDS: Our recommendation to manage TND after ACDF is non-surgical. This includes regular 15 min neuro-charting, rapid MR imaging, and a short course of glucocorticosteroids. In case of rapid deterioration in neurology, return to theatre without imaging may be justified.

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Corresponding author:
Saisunder S. Chaganty
saisunder.chaganty@students.plymouth.ac.uk

INTRODUCTION

Degenerative cervical spine pathology, such as spondylosis, posterior longitudinal ligament hypertrophy and cervical disc prolapse are harbingers of cervical myeloradiculopathy. There is a clinical consensus that single-level ACDF is favourable to conservative management in cervical myeloradiculopathy (Buttermann et al., 2018). Compared to measures such as physiotherapy or cervical spine immobilisation, ACDF offers quicker pain relief and better long-term functional improvement (Matz et al., 2009; Yuen et al., 2017).

However, ACDF is not without side effects. Common complications include dysphagia, recurrent laryngeal nerve palsy and dural perforation (Yuen et al., 2017). Transient neurological deterioration (TND) can also manifest, albeit rarely (0.2-2%) (Yuen et al., 2017; Rath et al., 2017; Tasiou et al., 2017).

The purpose of this report is to validate existing literary opinion on the aetiology, pathogenesis and management of post-ACDF transient neurological deterioration.

HOFFMAN'S TEST examines the integrity of corticospinal tract.

Loosely hold the middle finger and flick the fingernail downwards, allowing the middle finger to flick back up. Normal response is a flexion and adduction of the thumb on the same hand.

Hoffman's test is often considered to be a Babinski sign equivalent for the upper limb.

CASE PRESENTATION

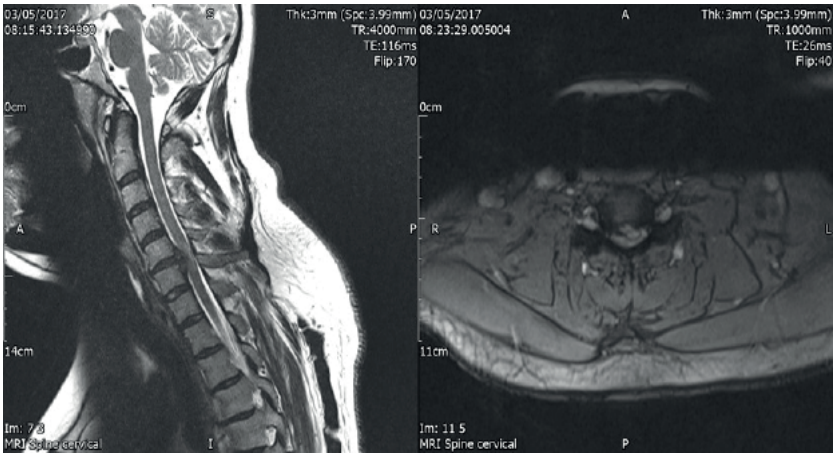
A 44-year-old gentleman presented with a 5 months' history of progressive pain in the neck and left arm. His symptoms also included paraesthesia associated with weakness (Medical Research Council Muscle scale (MRC) 4 out of 5) affecting left upper and left lower limb. The symptoms caused him difficulty maintaining balance and performing dexterous hand movements. There were no red flags such as bladder or bowel symptoms.

On examination, generalised restriction in range of neck movement and pain were elicited upon overhead shoulder abduction. Both Hoffman's and Romberg's test were positive along with hand paraesthesia and hyperreflexia noted on left knee jerk (Bendheim et al., 1937; Lanska et al., 2000). MRI scan confirmed a large C5/C6 prolapse with spinal cord compression and presence of spinal cord signals (Fig.1) (Type 2 MRI hyperintensity) (Epstein et al., 2018). Preoperative Neck Disability Index(R) (NDI) score was 64%, VAS for arm pain was 7/10 and neck pain 9/10 (Vernon et al., 1991).

Subsequently, a C5/C6 ACDF procedure was performed under general anaesthetic. A large sequestrated disc compressing the left antero-lateral spinal cord was removed. A 6mm cage was inserted, reinforced with autogenic bone grafts. Intra-operatively, no surgical or anaesthetic deterioration was noted, including any iatrogenic spinal cord contusion, CSF leak, excessive bleeding or hypotension.

However, immediately following surgery, the patient complained of generalised numbness and weakness. Examination revealed left-sided reduced sensation and hemiparesis (MRC grade 3/5). Despite this, the patient reported no signs of pain and was not in respiratory distress, maintaining a patent airway. Patient was catheterised and nasal cannula was inserted as saturations fell below 93%.

An emergency postoperative MRI imaging was expedited (Fig. 2). Imaging confirmed satisfactory positioning of implant with no protuberant lesion such as haematoma. Two residual changes were demonstrated on MRI: firstly, osteophytes from vertebral end plate seen encroaching into neural foramina contributing to significant degree of bilateral foraminal stenosis at C5/C6 level; secondly, T2-weighted hyperintense myelopathic



↑ **FIGURE 1:** *Preoperative T2 weighted sagittal & axial MRI scan showing C5/C6 disc prolapse and presence of cord signals.*

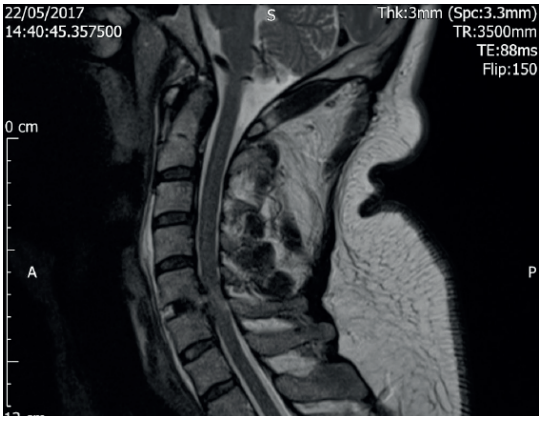
changes (white cord syndrome) visualised as intrinsic to the spinal cord without any compression (Vinodh et al., 2018). No haematoma, pseudo-meningocoele or implant displacement were detected.

Patient was not returned to the operating theatre for re-exploration. Instead, dexamethasone 2mg OD was administered as a 2-day course and the patient underwent extensive neuro observation every 15 minutes. By 4 hours following surgery, the patient reported neurological improvement: sensation consistent with preoperative levels and an increased power. Day 1 post-operatively, left sided hemiparesis had resolved to that of the preoperative baseline. Following satisfactory assessment of neurological and physiotherapy parameters, the patient was discharged day 2 post-op.

At 2 months review, the patient reported moderate improvement in symptoms from his preoperative baseline, including good range of neck movements, hand grip increased from 20% to 80% in MRC muscle scale. The signs of hyperreflexia settled. Cervical spine x-ray revealed 2mm crater at anterior aspect of cage but no evidence of displacement (Fig. 3). Patient was advised to avoid high impact activities until further consolidation of the implant. Upon 6 months review, vast majority of the symptoms had regressed, including weakness, paraesthesia and coordination. The patient's end outcomes regarding surgical treatment using NDI and EQ-5D-5L were: NDI 34%, arm pain 0/10, neck pain 5/10, health 80% (Vernon et al., 1991; EuroQoL Group, 2016).

DISCUSSION

Postoperative neurological dysfunction can arise due



→ **FIGURE 2:** *Immediate postoperative T2 weighted sagittal MRI scan showing residual cord signals at C5/6 level with no haematoma or cage displacement.*

to direct spinal cord insult, including vascular injury, graft displacement, wound haematoma and spinal cord contusion (Fountas et al., 2007; Cheung et al., 2016). Notwithstanding exclusion of these etiologies through our peri-operative workup, our case still experienced neurological deterioration with residual T2 hyperintense MRI postoperatively.

Existing literary opinion on TND immediately following ACDF is despairingly sparse. This phenomenon can be attributed to microvascular transient ischemia-reperfusion injury (IRI) (Vinodh et al., 2018; Chin et al., 2012; Giammalva et al., 2016).

Aetio-pathogenesis

Certain conditions are required for development of IRI: dysfunction of Na/K ATPase pumps leading to intracellular swelling, increased anaerobic respiration rendering an acidic *milieu*, and finally, ribosomal detachment from the rough endoplasmic reticulum, resulting in reduced protein synthesis (Horea et al. 2014; Koekkoek & van Zanten et al., 2016). This proinflammatory environment arises in the context of a generalized ATP and antioxidant deficiency, due to protracted ischaemia, as rendered in our case, through chronic hypoxia at compression point of spinal cord for several months prior to the operation.

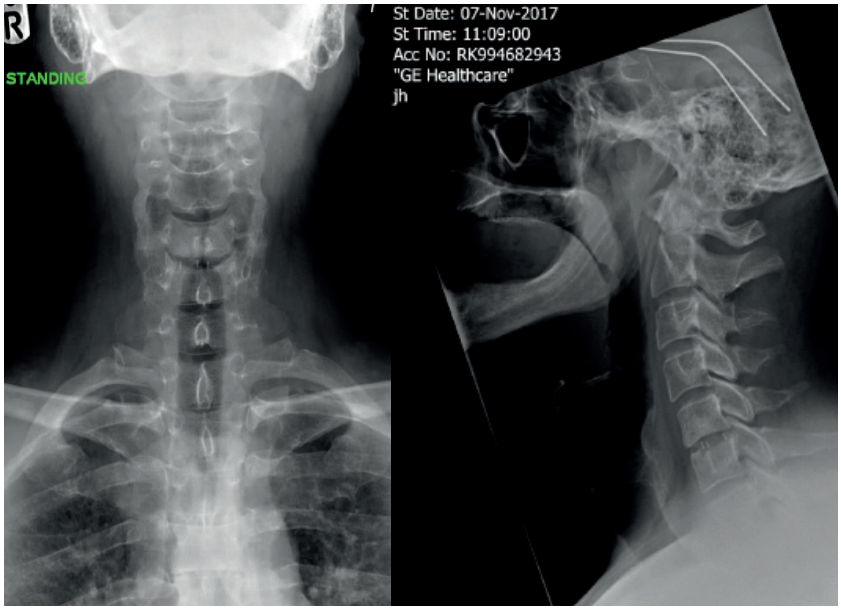
Reperfusion of chronically ischemic tissue is seen to precipitate unbridled production of specific mediators such as oxygen-derived free radicals, mitochondria-dependant apoptosis, platelet activating factor, TNF-α, and complement factors (Bai et al., 2015; Carden et al., 2000). As in our case, these mechanisms collectively induced localised neuropraxia and worsening cord oedema, which manifested clinically with neurological deterioration and radiographically as hyperintensity on sagittal MRI (Fig. 2).

A rat model study was conducted in 2015 by (Wu et al., 2015) to further elucidate the pathophysiology of IRI. The authors micro-surgically implanted different sized polymer sheets (mild to severe compression) under T8-9 laminae of mice. Following decompression, presence of IRI was determined by measuring superoxide dismutase (SOD) level, which is an anti-oxidant compound, and malondialdehyde (MDA) concentration, which is a marker of oxidative stress (Gottfredsen et al., 2013; Horea et al., 2014). In mild compression groups, there was a significant increase in SOD and a reduction in MDA. However, in severe compression groups, there was a marked reduction in SOD and a significant rise in MDA.

These findings suggest clinical efficacy of decompression is limited to cases of mild compression and IRI is likely to arise in chronic severe spinal cord compression.

Similar cases in the literature

Only two other case reports exist describing this phenomenon. First, in 2013, Chin et al reported a 59-year old patient who underwent a double-level ACDF for C5-C6 compression. Postoperatively, the patient developed tetraplegia without any discernible aetiology, a post MRI revealed residual bony compression and white cord syn-



↑ **FIGURE 3:** *: 6 month follow up cervical spine x-ray showing consolidated cage without displacement*

NURICK GRADE
is a system of cervical myelopathy classification it goes from 0 (normal or root symptoms only) to 5 (wheelchair or bedbound)

drome. The patient underwent further decompression and corpectomy at C5.
Despite this, the patient reported a 2 month post op Nurick Grade 4 and partial improvement was 16-months following the operation (Chin et al., 2012).

A second similar case was reported by Giammalva et al, wherein following a double level ACDF a 64 year old male displayed C6 incomplete tetraplegia. In this case, partial improvement was seen by 7 days with Nurick Grade 4 (Giammalva et al., 2017).

Both authors attribute their case presentation to reperfusion ischaemic injury. As in our patient, there was no worsening of intrinsic cord signals and neurological deterioration was transient. However, the degree of transience was much less with our case (4hours). Chin et al. reported 16 months and Giammalva et al. 7 days.

Residual T2 hyperintense myelopathic changes postoperatively suggests reperfusion ischaemia. However, we cannot confidently rule out the possibility of temporary vasospasm or embolic insult that may be have precipitated a transient ischaemic attack phenomenon. A 60-pack-year smoking history is likely to have put the patient at risk of this. As demonstrated by (Giammalva et al., 2017) intra-operative neurophysiology monitoring would be able to identify such sub-clinical insult.

RECOMMENDATIONS

Following ACDF procedures associated with neurological deterioration, we recommend close neuro charting at 15 min interval, immediate stabilisation of C-spine with cervical collar and an emergent MR imaging to exclude any surgically treatable pathology. Most commonly, this would include aetiology such as graft displacement, wound haematoma, pseudo-meningocoele and residual bony compression, attributable to the symptomatology. Identification of any of these would warrant neurosurgical management to relieve the protuberant lesion on the spinal cord (Villavicenico et al., 2001).`
In absence of such lesions, as in our case, medical management in conjunction with close neuro charting and cervical spine stabilisation would be recommended. Pharmacologically, a short course of dexamethasone for its ability to ameliorate neuroinflammation through treating cord oedema and maintaining cord perfusion has been elucidated.

In case of profound neurological compromise such as tetraparesis with progressive deterioration, return to theatre without imaging could be justified. This would allow for explorative neurosurgery in order to salvage residual neurological function and must be accompanied with dexamethasone or intravenous methylprednisolone.

Our case report serves to increase the awareness of ischaemic reperfusion injury as a complication in patients with chronic compression of the spinal cord undergoing decompression surgery. It is vital that medical staff are aware of this rare yet potentially catastrophic phenomenon and patients are properly counselled pre-operatively.

Alternative treatment options
A myriad of alternative treatments is currently being investigated for attenuating reperfusion injury of the spinal cord, most notably administration of anti-oxidative agents such as vitamins A, C and E (Horea et al., 2014; Koekkoek & van Zanten et al., 2016; Spoelstra-de Man et al., 2018). Vitamin supplementation in IRI seems logical not only in terms of improving oxidative stress but also because of a potential reduction in inflammation and modulation of the immune response. Vitamin E, for instance, is a lipid-soluble antioxidant important for neural tissue integrity and suppressing prostaglandin E2 production (Morsy et al., 2010).

Antioxidant agents that have been thoroughly studied in experimental models and have proven efficacy in terms of reducing oxidative stress (Straaten et al., 2014; Chronidou et al., 2009). However, clinical studies investigating the efficacy of antioxidants have exclusively focused on patients in critical care (Manzanares et al., 2012; Andrews et al., 2011; van Zanten et al., 2014; Heyland et al., 2014). According to (Koekkoek & van Zanten, 2016), these studies show conflicting findings due to lack of methodological uniformity and lack of consensus on what constitutes 'normal' plasma antioxidant levels and targeted outcome. Though there is reasonable evidence base on antioxidant use in critically-ill patients, large randomised controlled trials are needed to corroborate the preliminary experimental findings supporting antioxidant supplementation in ischaemic reperfusion injury.

CONCLUSIONS

We present a rare case of 44 year old male who sustained transient neurological deterioration following single-level ACDF, most likely due to ischemic reperfusion injury of the spinal cord. A pro-inflammatory cascade featuring generalised ATP deficiency and production of reactive oxygen species (ROS) are indicated in the pathogenesis of ischemic reperfusion injury. We recommend C-spine immobilisation, neuro charging, an urgent MR

imaging, and glucocorticoid administration (methylprednisolone or dexamethasone) in the management of post-ACDF TND. Low dose anti-oxidant agents can also be used as adjunct treatment, though ultimately this is yet to be proven to work in larger trials.

The authors declare no conflicts of interest.

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