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GRAND ROUNDS

Trans-oral approach for the management of a C2 neuroblastoma

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Abstract

Introduction Neuroblastoma is the most common extracranial solid tumour in children. Metastasis in children to the upper cervical spine are quite rare.
Case report An 8-year-old boy was referred to our service following a relapse of a right adrenal stage 4 neuroblastoma with a metastatic deposit in C2. This anterior tumour mass was pressing on the spinal cord with increasing pain in the base of skull, but without gross neurological deficit. He underwent urgent MRI and CT scans and then emergent surgery. The first stage was a posterior stabilization from occiput to C5 with a posterior decompression from C1 to C3 followed by a trans-oral approach to resect the main anterior tumour mass and reconstruction.
Conclusion This is the first report of the use of a trans-oral approach to address a neuroblastoma lesion in the axial spine. This approach was used effectively to achieve local tumour clearance confirmed at 1-year follow-up. Pertinent information to the spinal surgeon on neuroblastoma and the use of the trans-oral approach to the axial spine are discussed.

Keywords Neuroblastoma · Axial spine · Trans-oral approach

Case presentation

A 5-year-old boy was diagnosed with stage 4 neuroblastoma with a right adrenal primary in 2009. His treatment included induction chemotherapy, surgical resection of the primary, high-dose chemotherapy with stem cell rescue, radiotherapy, differentiation therapy (retinoic acid) and immunotherapy. Residual tumour necessitated further tumour bed clearance in 2010. Relapse in three paravertebral abdominal lymph nodes in 2011 resulted in additional chemotherapy treatment and resection of the paravertebral abdominal lymph nodes in early 2012. In September 2012, he presented to his oncologist with worsening neck pain and an MRI scan of the cervical spine identified significant destruction of the C2 vertebral body/peg with tumour mass causing cord compression. He was referred promptly to our spinal service. On presentation, he was found to be well nourished with a normal sensory and motor function in the upper and lower limbs, no bowel or

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bladder dysfunction and no upper motor neuron signs in the upper or lower extremities, with the exception of subtle signs of unsteadiness.

Surgery was performed on an urgent basis during the same admission. He initially underwent a posterior occiput to C5 instrumented stabilization and decompression at C1–3, followed by a trans-oral approach to C1/C2 to achieve a partial C2 resection, tumour excision and an anterior reconstruction. Post-operatively, he tolerated solid food on day 2 and went home on day 4. He was seen by the oncologists a few weeks post-operatively and referred for radiotherapy.

Diagnostic imaging section

Cervical spine pre-operative investigations represented in Figs. 1 and 2.

Historical review of the condition, epidemiology, diagnosis, pathology, differential diagnosis

Neuroblastoma is the most common extra-cranial solid tumour in children. Its incidence is 1:7,000 in the developed world with the highest prevalence in children younger than 4 years (85 %) and adrenal Neuroblastoma accounting for 45 % of the cases [1]. In neuroblastoma, the differentiation of neuroblastic cells into mature neural tissue does not take place or is reversed resulting in small round blue cells with neuritic processes [1]. Despite its limitations in guiding decision-making pre-operatively, the International Neuroblastoma Staging System (INSS) [2] is a widely accepted classification system based on operative findings (Table 1). More recently, the International Neuroblastoma Risk Group produced a staging system (INRGSS) to help evaluate the tumour resectability based on diagnostic imaging using CT scan or MRI paired with histologic confirmation of neuroblastoma, a bone marrow biopsy for all children older than 6 months and a metaiodobenzylguanidine (MIBG) scan [3]. MYCN genomic amplification and DNA ploidy are biologic markers that indicate the aggressiveness of a tumour and serve as poor prognostic factors [4].

Pre-operative investigations include urine catecholamines and its metabolites (Vanillylmandelic acid and homovanillic acid) which should be measured as part of a standard retroperitoneal mass assessment. CT and MRI scans are excellent diagnostic modalities giving information on the tumour anatomy, local invasion and metastasis. 123I-MIBG and 131I-MIBG scans have a prodigious affinity for neuroblastoma with uptake in 90 % of cases resulting in concentration in primary/metastatic foci and useful in following treatment response [5]. In its differential diagnosis, Wilms tumour and rhabdomyosarcoma should be considered. Survival in neuroblastoma is inversely proportional to age and stage.

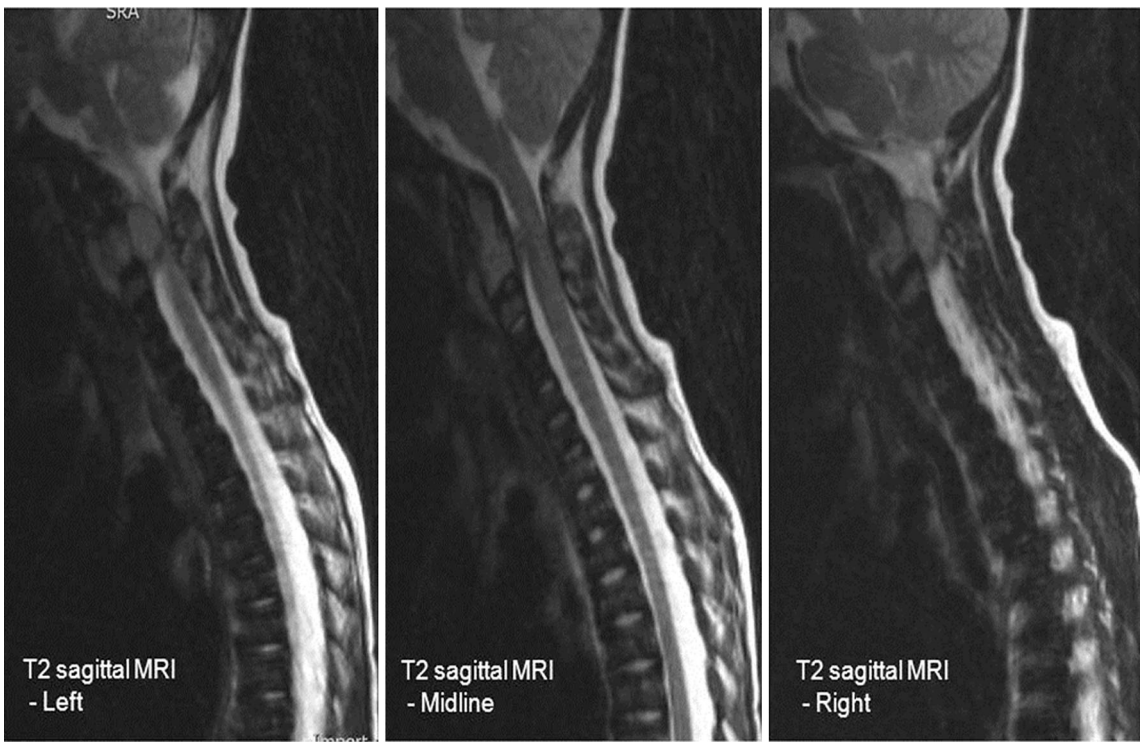

Fig. 1 Pre-operative T2-weighted sagittal images showing severe spinal cord compression by neuroblastoma at C2

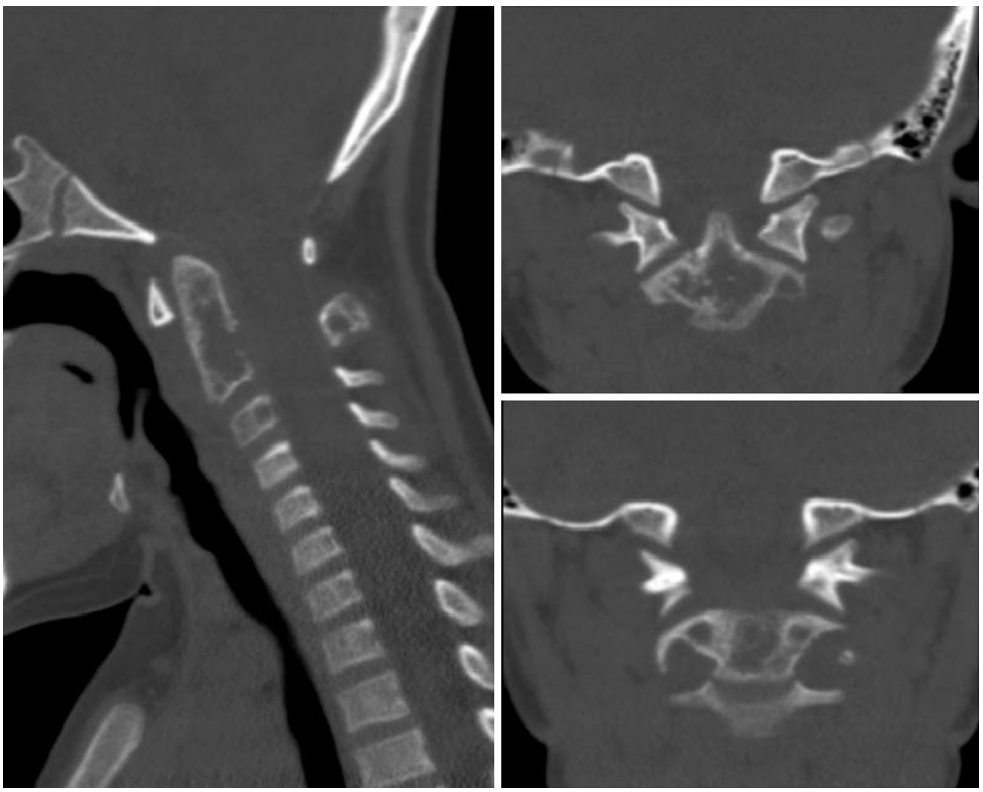

Fig. 2 Pre-operative cervical spine CT scan sagittal and coronal views showing extensive destruction of the C2 body and posterior elements

Table 1 The International Neuroblastoma Staging System (INSS)

Stage	Description
1	Localised tumour with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumour microscopically
2A	Localised tumour with incomplete gross excision; representative ipsilateral non-adherent lymph nodes negative for tumour microscopically
2B	Localised tumour with or without complete gross excision, with ipsilateral non-adherent lymph nodes positive for tumour. Enlarged contralateral lymph nodes must be negative microscopically
3	Unresectable unilateral tumour infiltrating across the midline, with or without regional lymph node involvement; or localised unilateral tumour with contralateral regional lymph node involvement. The midline is defined as the vertebral column
4	Any primary tumour with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs
4S	Localised primary tumour (as defined for stage 1, 2A, or 2B), with dissemination limited to skin, liver, and/or bone marrow (limited to infants younger than 1 year). Marrow involvement should be minimal (<10 % of total nucleated CELLS identified as malignant by bone Biopsy or by bone marrow aspirate). More extensive bone marrow involvement would be considered to be a stage 4 disease. The results of the MIBG (Meta-ldo-Benzyl-Guanidine) scan (if performed) should be negative for disease in the bone marrow

Rationale for treatment and evidence-based literature

As with any tumour excision and complex reconstruction in a child, it is necessary to have a detailed discussion between the patient, family, oncologist and spinal surgeon. It is paramount that all parties understand the complexities of surgery, risks and complications as well as the rarity of the diagnosis in this case. The oncologist is central to guiding the family (and spinal surgeon) with regards to prognosis which would then direct the extent of surgery that can be offered. In this young patient with a grumbling disease pattern, no other symptoms of disease and a well-motivated and informed family, it was deemed important to achieve satisfactory tumour clearance and good functional outcome. Combined posterior and anterior trans-oral approaches have not been previously reported for such a tumour.

A 'simple trans-oral' approach provides access to the anterior aspect of C0–C3 depending on the inter-dental distance and trajectory. Inter-dental distance should ideally be more than 25 mm, while the trajectory can be affected by the sub-axial cervical kyphosis or basilar invagination [6]. Pre-operatively, a lateral X-ray of the cervical spine in hyperextension and oral swabs to help with antibiotic prophylaxis planning (covering both gram-positive and gram-negative organisms) are advised. The anterior approach can be performed with the assistance of a head

and neck surgeon, although in our case this was not required as the approach was performed entirely by the senior spinal surgeon (NAQ).

For ventilation and to protect the airway, our preference is a tracheostomy with a throat pack and a Trendelenburg position, but an oro- or a naso-tracheal intubation remains an option [7]. We prefer the Crockard trans-oral retractors for exposure, and the soft plate can be displaced with malleable retractor or by suturing or a nasogastric tube passed out through the mouth and retracting the uvula. More exposure can be achieved by splitting the soft plate or even the hard plate [8]. We prefer to maintain the soft plate to reduce risks of swallowing difficulties and nasal regurgitation post-operatively.

As described by Fang and Ong (1962), before incising the mucosa, the anterior tubercle of C1 which lies in the midline should be identified. The incision is made directly down to bone centred 1 cm distal to the tubercle measuring 3–5 cm in length. Sub-periosteal lateral dissection is done to raise a flap to the lateral margin of the lateral masses taking with it the longus colli muscle [9]. This should allow the closure in layers with the longus colli and anterior longitudinal ligament sutured as a deep layer, while the overlying facia and mucosa closed separately as the superficial layer [9].

The vertebral arteries, Eustachian tubes, and hypoglossal nerves are lateral to the incision and the safe zone from midline laterally lies within 11 mm at C0, 24 mm at C1 and 14 mm at the lower border of C2 [10]. The use of the trans-oral approach in children is limited, as evident from the scarcity of publications and the small cohorts within the reported series. Nonetheless, the approach remains a valuable tool in the spine surgeon's armamentarium as a rare adjunct in the management of the craniocervical pathologies in children.

Technically, although the approach in children follows the same steps described for an adult, there are a few considerations that should be kept in mind. In paediatrics, the oral cavity and pharynx are smaller, and forceful retraction can result in a dislocation of the smaller, more mobile temporo-mandibular joint, a problem that should be identified and managed before the end of the procedure [11]. The physiological hypertrophy of the adenoid and tonsils can create difficulty in identifying the midline in an already small oropharynx.

Additional exposure can be achieved through a soft palate with or without hard palate split particularly if the lesion is at the level of or extends above the foramen magnum [11–13]. An extended open-door maxillotomy provides better access to the clivus [8], while median labiomandibular glossotomy can aid in access to more caudal lesions [13].

Over 15 years ago, Tuite et al. [13] reported on their experience over 10 years with the trans-oral approach in 27 paediatric patients with an average follow-up of 5.7 years. Trans-oral surgery was performed for irreducible anterior neuraxial compression at the craniovertebral junction caused by basilar impression (9), atlantoaxial subluxation with pseudotumor (9), atlantoaxial subluxation with Down's syndrome (2), chordoma (6) and in one patient suffering with C2/3 kyphosis. In their series, approach-related complications included cerebro-spinal fluid leak (2) which required a lumboperitoneal shunting to control, two posterior pharyngeal wound infections and 11 patients (40 %) required prolonged enteral feeding. Eight patients requiring a palate split had additional complications including a hard palatal fistula (1) and a soft palate dehiscence (1), both requiring additional surgery. Although monitored, no significant tongue swelling was noted (mean operative time 1.5 h increasing to 4 h when the hard palate was split). These authors also reported "prolonged ventilation" as a complication due to prolonged laryngeal

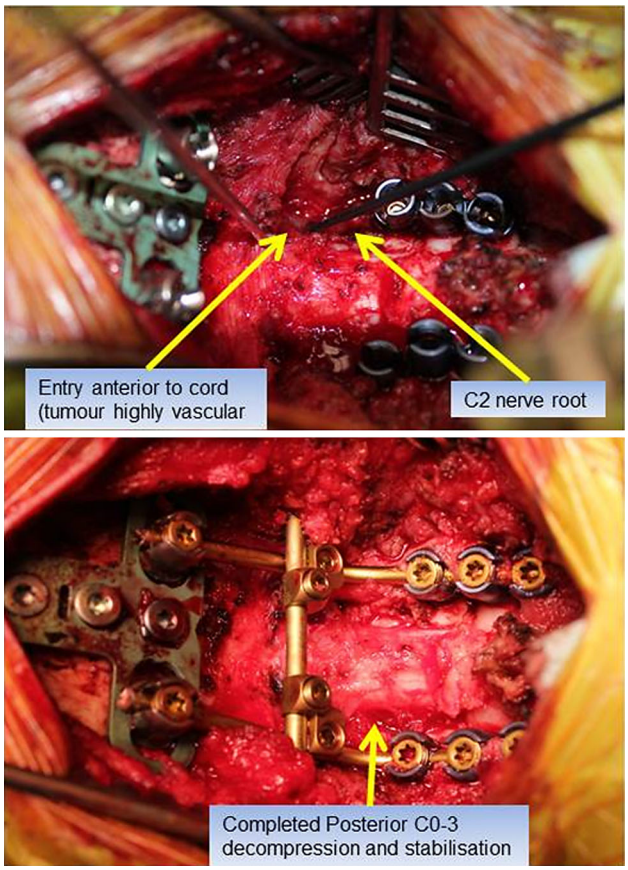

Fig. 3 This intra-operative photograph is taken from the first stage—posterior C1–3 decompression and stabilization from occiput to C5

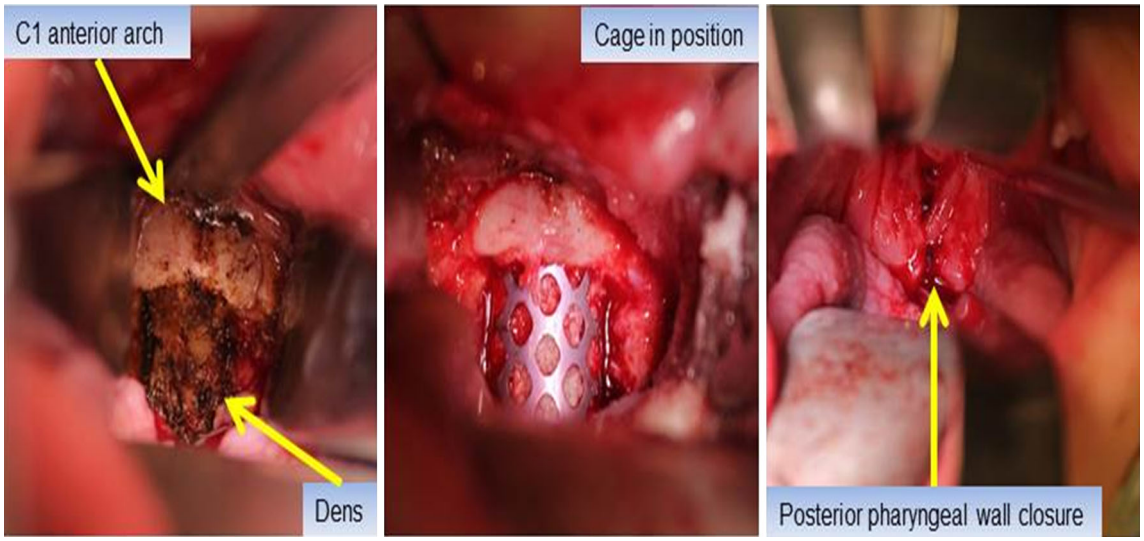

Fig. 4 These intra-operative photographs from the second stage show the trans-oral approach—identification of the dens, excision with replacement using a cage and final closure of the posterior pharyngeal wall

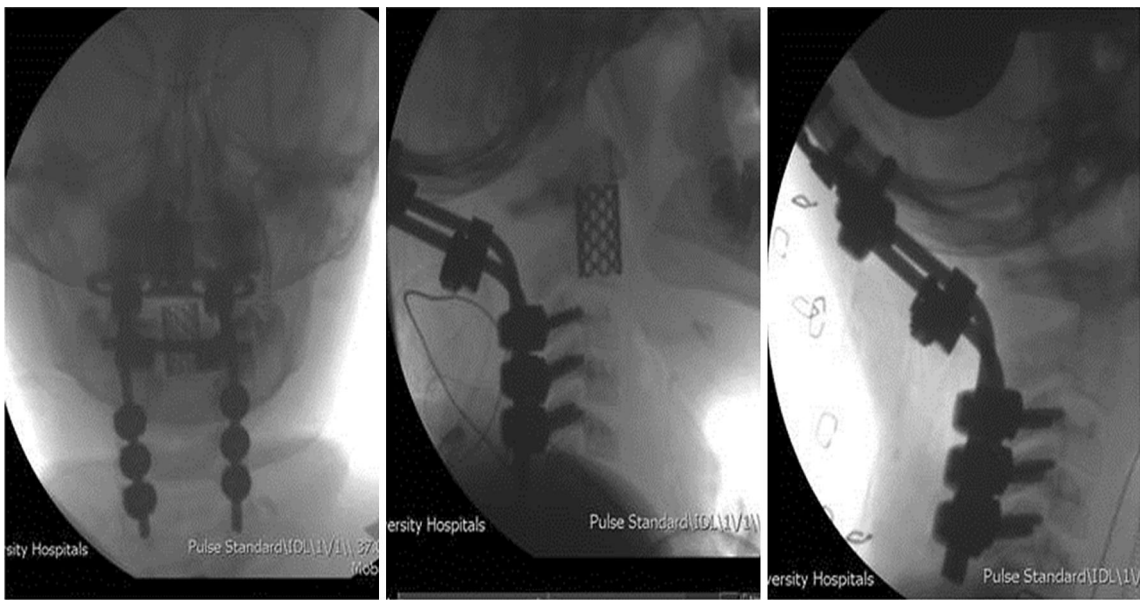

Fig. 5 Post-operative image intensifier X-rays

oedema in the one patient and neurologic decline in three patients [13].

Procedure (surgery, intervention)

Under image guidance and spinal cord monitoring and following a general anaesthetic (endotracheal (ET) intubation), a posterior approach to the cervical spine was performed to carry out an occiput to C5 instrumented stabilization and a decompression from C1 to C3 (Fig. 3). The posterior elements were removed in an 'en bloc' fashion using a 3-mm diamond burr and rongeurs. Tumour was carefully dissected off the vertebral arteries bilaterally, preserving the C2 nerve roots. On entering, the C2 vertebral body posteriorly, the tumour was found to be fairly vascular [Surgical time 2 h 30 min; Estimated Blood Loss (EBL) 400 mls]. The patient was then positioned supine, and a tracheostomy was performed to replace the ET tube and facilitate access. A Crockard retractor was used to

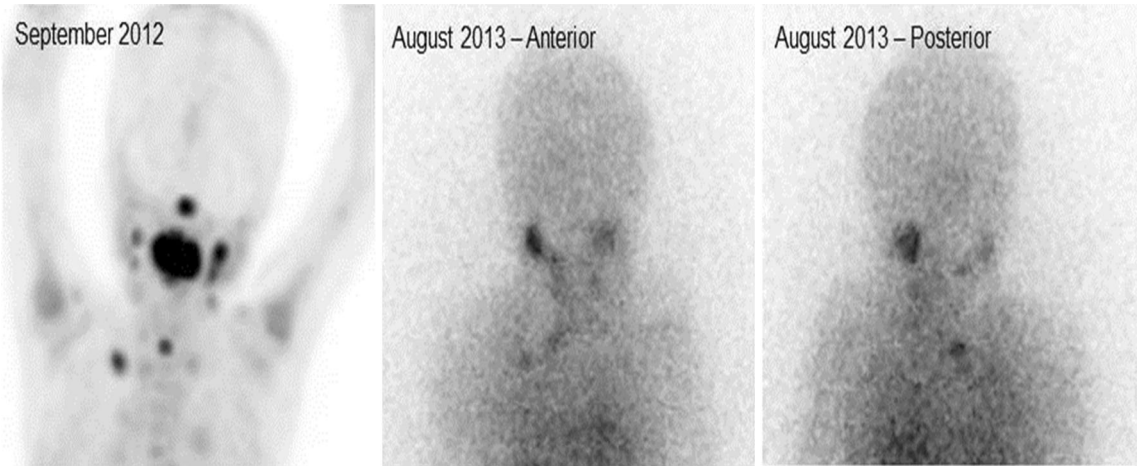

Fig. 6 MIBG scan showing no local recurrence at the site of the axial cervical surgery at 1 year post-operatively

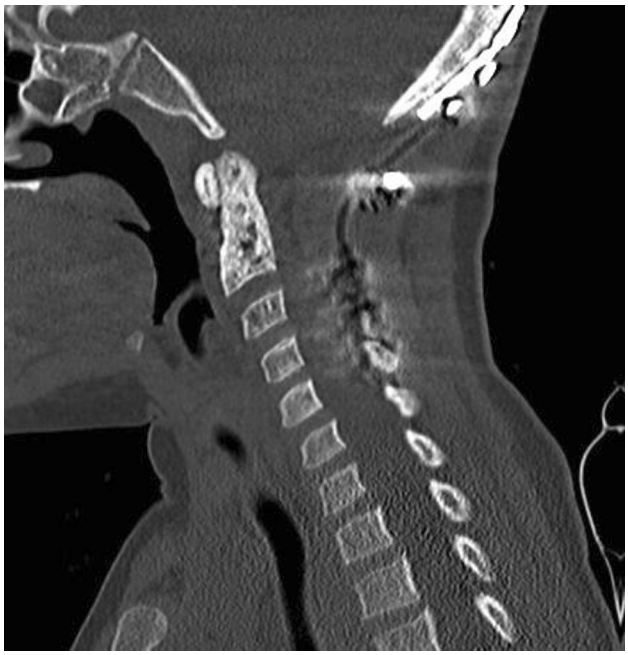

Fig. 7 A sagittal CT scan of the cervical spine 1 year post-operatively showing good fusion through the cage

facilitate the trans-oral approach. The dens was resected below the C1 level and the tumour was removed. Dura was seen from C1 tubercle to the base of C2. A SynMesh® cage (Synthes) was packed with demineralized bone graft/allograft chips, and was "press fit" between C1 and the base of C2. Closure was performed in layers—Figs. 4 and 5 (Surgical time 2 h 30 min; EBL 100 mls).

Procedure imaging section

Intra-operative images are represented in Figs. 3, 4 and 5.

Outcome and follow-up

He was discharged home on day 5 having made a remarkably quick recovery. He has now been followed for 1 year and reports no complaints—he remains independently mobile, has no neck pain and no neurological deficit. At the 1-year follow-up, he remains free of any local recurrence (Fig. 6). A CT scan of the cervical spine demonstrated a satisfactory bony fusion through the cage (Fig. 7).

Conflict of interest None.

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