Tumours of the Cervical Spine

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Introduction

The most common tumours that affect the spine are metastatic in origin. Roughly 7500 primary spinal tumours are detected annually in the USA and account for less than 10% of all spinal neoplasms among people of all age groups [1]. The estimated prevalence of spinal tumours is reported to be 3.6 out of 100,000 people [2]. However, benign lesions are predominant in the first two decades of life. Benign tumours of the cervical spine are less common than their malignant counterparts from the third decade onwards. Metastatic lesions in children are most commonly haematological malignancies (i.e. leukaemia, etc.). Spinal neoplasms may remain entirely intraosseous or affect the paraspinal soft tissues or the dura/thecal sac and neural structures. The tumours affecting the cervical spine in the paediatric age group could be broadly classified into:

- Benign
- Malignant

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The benign tumours are further classified into:

- Bony
- Cartilaginous
- Vascular

Those which affect the neural elements/dura are further classified into:

- Intradural—meningioma, astrocytoma, etc.
- Extradural—neurofibroma, schwannoma, paraganglioma, etc.

The common primary spinal tumours (both benign and malignant) to affect the paediatric cervical spine across different age groups (i.e. <5 years/5–15 years/>15 years) are summarized in Table 8.1 [3].

Some lesions have a predilection to affect the posterior elements (i.e. lamina, pedicle, spinous process), while others tend to affect or involve anterior elements (vertebral body). Haemangioma of the bone and GCT predominantly affect the anterior elements. There exists a wide spectrum of pathological behaviour by benign neoplasms ranging from latent/asymptomatic lesions that are detected incidentally to locally aggressive ones with destructive pattern, and pathological fractures that can potentially cause spinal instability and/or neurological deficit. Yet, these benign neoplasms share a common, clinical presentation, and a majority of patients present with

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Table 8.1 Common musculoskeletal tumours affecting children's cervical spine

Age (years)	Benign	Malignant
0–5	Langerhans cell histiocytosis	Ewing sarcoma Leukaemia Neuroblastoma (metastatic) Wilm tumour (metastatic) Rhabdomyosarcoma
5–10	Langerhans cell histiocytosis Aneurysmal bone cyst Osteoblastoma Osteoid osteoma	Ewing sarcoma
10–20	Aneurysmal bone cyst Giant cell tumour Osteochondroma Osteoid osteoma Haemangioma Fibrous dysplasia	Ewing sarcoma Osteosarcoma Leukaemia
>20	Giant cell tumour Haemangioma Fibrous dysplasia	

pain localized to the area of involvement. This chapter reviews the principles of diagnosis, staging, treatment with case examples, and outcomes for common benign and malignant tumours of the cervical spine in the paediatric age group.

Clinical Examination and Preoperative Workup

The common presentations for tumours of the musculoskeletal system in children are:

- Pain
- Imminent fracture on X-ray or oedema/hyperintense lesion on MRI scan
- Pathological fracture
- Soft tissue mass

However, the most common presentation is pain, and it is present in 76% of benign and 95% of all patients with malignant lesions in the vertebral column [4]. Night pain is characteristic of certain pathologies (i.e. osteoid osteoma and osteoblastoma), and 30–80% of those may also have a co-existent torticollis and radicular pain (instead of a scoliotic list, which is seen with a thoracic or lumbar osteoid osteoma). Torticollis is due to a protective paraspinal muscle spasm, and it resolves with a definitive treatment of the lesion and with time [5]. The incidence of radicular pain varies from 20% to 40% in published literature [6]. Significant relief with an intake of prostaglandin inhibitors like acetylsalicylic acid (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs) is pathognomonic of osteoid osteoma. Pain relief in up to 70% of osteoblastomas was found to be refractory to NSAIDs in one reported series [7]. The pain of malignant lesions can be acute and severe, with rapid onset of symptoms accompanied by soft tissue involvement or swelling, unlike benign pathologies that are chronic and indolent and are of mild to moderate pain severity without any soft tissue mass. Pathological fractures are uncommon in benign conditions, though their presence may cause instability and/or neurological deficit. The periosteum is highly innervated by nociceptors and has the lowest pain threshold of all the deep sensate structures. The initial evaluation of any child's cervical spine lesion should include:

- Detailed history and physical examination
- Plain X-rays: AP/lateral and open-mouth views (for odontoid peg)
- Dynamic X-rays: Cervical spine lateral in flexion and extension (supervised by a physician)

- Special imaging studies, viz.,
  - Computed tomography (CT)
  - Magnetic resonance imaging (MRI)
  - Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) scans
  - Nuclear medicine (NM) bone scans

History and Physical Examination

A detailed history and physical examination is of paramount importance in all patients. A thorough neurological examination and evaluation of sphincteric function (i.e. the bladder and bowel) is vital and has prognostic significance. Meticulous palpation for any soft tissue mass over the spinous processes, paraspinal area, and front and back of the neck and evaluation for pressure effects on the vital structures (i.e. trachea, oesophagus, and carotid bundle) need to be undertaken. Elicitation of power, tone, and deep tendon reflexes and an assessment of gait are mandatory, and any pathological findings (i.e. upgoing Babinski's sign, exaggerated deep tendon reflexes, clonus or Hoffman's sign) must be recorded diligently. A palpable bony lesion was seen or felt in only 6% of primary benign bone tumours, in comparison to up to 47% of malignant neoplasms [8]. Roughly 1/5 (19%) of all cervical spine tumours are referred to oncologists as soft tissue masses or abnormal swellings. Locally aggressive lesions can cause myelopathy with canal encroachment, as observed with an ABC (aneurysmal bone cyst), GCT (giant cell tumour), and osteoblastoma.

Imaging Studies

The initial method of investigation is always good quality, plain X-rays (anteroposterior and lateral views) with adequate exposure (i.e. covering O–C_1 junction to C_7–T_1 disc space). In a series of 127 consecutive patients with suspected cervical spine pathology, 98% had abnormal radiographs [9]. The most commonly observed findings were:

Table 8.2 Common paediatric cervical spine tumours affecting anterior and posterior elements

Anterior elements	Posterior elements
Langerhans cell histiocytoses (LCH)	Aneurysmal bone cyst
Haemangioma	Osteoid osteoma
Giant cell tumour	Osteoblastoma
Aneurysmal bone cyst	Osteochondroma
Gorham disease	Metastatic lesions
Leukaemia	
Metastatic lesions	

- Presence of a soft tissue shadow
- Destruction of a pedicle—*winking owl* sign

A small subset of patients (especially those with osteoid osteoma) may have normal plain radiographs. The most common region of involvement (i.e. anterior vs. posterior elements) for common paediatric bone tumours of the cervical spine on plain radiographs is summarized in Table 8.2 [10]. The specific radiological features, as well as some unique attributes/characteristics and their significance, are discussed in greater depth under individual pathologies. The dynamic radiographs (i.e. lateral views in flexion and extension) demonstrate spinal instability and the need for MRI-compatible spinal instrumentation at the time of definitive stabilization surgery.

Magnetic resonance imaging (MRI) facilitates an excellent visualization of the soft tissues and the extent or evidence of neural involvement. Their role in evaluation of intradural/extradural and intramedullary tumours cannot be underestimated. MRI scans are the investigation tool of choice in the evaluation of compartmental containment vs. extracompartmental spread. It provides accurate staging, especially in primary malignant neoplasms (i.e. Ewing sarcoma) presenting with soft tissue mass. It is widely used in the preoperative planning of surgical excision, assessment of response to chemo- and/or radiotherapy, as well as monitoring for recurrence. The greatest advantage lies in its noninvasive method of investigation, unlike angiography or myelography, but it requires a great deal of competence in interpreting them. They are also helpful in differentiating pathological fractures

from compressive fractures (hyper intense on T_2 and STIR images).

Computed tomography (CT) scans are especially helpful in early detection of lesions when plain X-rays are normal, as up to 40% of the trabecular bone must be destroyed for X-rays to be abnormal. The central nidus and peripheral sclerosis of osteoid osteoma are well demonstrated on CT (2 mm fine-cut axial bone window). The CT, in addition, would also give a wealth of information regarding the involvement of the neurovascular structures (i.e. vertebral/carotid vessels and nerve roots/spinal cord). The corduroy pattern of haemangioma in the vertebral body and granular ossification in lytic areas of osteoblastoma is well demonstrated on CT scans.

A nuclear bone scan is of great value in detecting the tumour activity and ruling out infections. The old adage *biopsy all infections and culture all tumours* cannot be overemphasized. Infections form the number one differential diagnosis for musculoskeletal neoplasms, especially in the paediatric age group. The most common benign neoplasm that may be picked up on a bone scan and may get missed on plain rays is *osteoid osteoma*. The only benign cervical spine neoplasm that may not exhibit any tumour activity on a bone scan may be *Langerhans cell histiocytosis (LCH)*. Though a bone scan is sensitive, it is not specific enough for a diagnosis of neoplasms, as any condition that affects the metabolic activity or turnover may have increased uptake (i.e. infections, osteoarthritis, fractures, etc.). The predictive value of bone scans for metastasis appears almost 100% [11].

SPECT and PET scans are usually used for the staging of newly diagnosed malignant tumours and to evaluate the response to treatment. The areas of increased glucose uptake in tumour areas are monitored by a positron-emitting radionuclide tracer introduced into the body on fluorodeoxyglucose. A recent study found PET to be a very accurate screening test in diagnosis for all vertebral metastasis in patients with cancer and particularly accurate especially for patients harbouring a non-selective vertebral lesion [12].

Histological Diagnosis: Biopsy

The biopsy provides a definitive diagnosis of a lesion with histological confirmation. However, it is not without complications and should never be taken lightly (including benign pathologies). The key principles one should always adhere to when performing a biopsy are as follows:

- To be performed by a surgeon who will eventually carry out a definitive surgery.
- Direct approach to the lesion with violation of least number of compartments to avoid seedling of tumour cells that would make definitive surgery difficult.
- When using a drain (in open biopsies), the drain should exit in close proximity to the main biopsy surgical incision, which could be included in the final surgical incision at the time of definitive surgery.
- Obtain adequate tissue for frozen section, immunohistochemistry/special stains, and microbiological cultures.
- Secure adequate haemostasis and ideally have a frozen section result before the patient leaves the OR (operating room).

The above generic criteria for musculoskeletal biopsies may be difficult to adhere to in spinal neoplasms, owing to the vital neurovascular structures in the neck. Fortunately, benign lesions of the cervical spine are forgiving to these violations, and malignant ones are very rare, few, and far between! A needle biopsy, either by fine-needle aspiration cytology (FNAC) or core biopsy, can be undertaken and be performed by anterior or posterior approaches. It can be clubbed with definitive excision (especially with benign lesions) as a therapeutic procedure and is called an excisional biopsy.

When performing a needle biopsy, a CT-guided biopsy may provide an accurate representation of the area of interest and reduces false-negative rates. The biopsy could be performed for both anterior and posterior lesions in the neck. For anterior lesions located in the upper cervical spine, the biopsy can be performed through the

thyroid gland, and for lower cervical spine lesions, it is usually performed posterior to the sternocleidomastoid muscle. The success rate of such needle biopsies vary from 50% to 90%. The most common cause of failure in getting a definitive diagnosis with needle biopsies is obtaining (i) nonrepresentative and (ii) non-diagnostic tissue. The use of CT fluoroscopy reduced the operative time in obtaining a biopsy by 50% compared to a conventional CT [13]. More recently, the use of intraoperative 3D fluoro-navigation (O-arm image intensifier) technology has reduced the recurrence rate and allows the confirmation of complete excision of nidus in small lesions (i.e. osteoid osteoma).

Oncological Staging and Treatment Principles

The staging of any neoplasm helps in defining the extent of involvement or spread and in planning treatment options. It is based on histological grade, size, degree of metastasis, and the local spread of the lesion. The Enneking staging system is most commonly used in musculoskeletal oncology and is non-specific to spinal neoplasms. Separate staging systems exist for benign and malignant tumours [14].

The benign tumours are classified into three categories by the Enneking staging system, and their recommended treatments with examples are as follows:

- Inactive (latent): treated by observation (haemangioma of the bone)
- Active: treated by intralesional excision (osteoblastoma)
- Locally aggressive: treated by excision with wide margins (aneurysmal bone cyst)

Most benign tumours are treated by either observation or intralesional excision (i.e. excision through the pseudocapsule and macroscopic tumour residues left behind). The tumour edges are treated with a high-speed burr, electrocautery, dilute 5% phenol (as a chemical cauterization agent), and/or cryotherapy to reduce the risk of tumour recurrence [15]. Utmost care to prevent their contact with the neural tissues (i.e. the dura/nerve root and spinal cord) should be taken to minimize iatrogenic neurodeficit. When a spinal instability is created as a part of the surgical resection of a lesion, MRI-compatible spinal instrumentation and reconstruction of the anterior/posterior column are undertaken to optimize function and outcome [16]. In general, when more than 50% of the facet joints are sacrificed at a single level or when a unilateral facet joint is sacrificed to facilitate the clearance of a tumour mass, posterior instrumented fixation is highly recommended to prevent the development of deformity, secondary to segmental instability. Similarly, laminectomy, especially in children, is notorious for the development of post-laminectomy kyphosis, and instrumented spinal fusion is recommended [17].

Anterior column reconstruction is recommended when more than 50% of the vertebral body is either resected or destroyed by the lesion. Strut grafts (tricortical iliac crest/fibula autografts or allografts) and/or commercially available metallic/carbon cages are routinely used in the reconstruction of the anterior column, supplemented with plate-screw fixation. An external orthosis may be advocated for 6 weeks to 3 months until solid arthrodesis occurs. The surgical stabilization is also influenced by other intrinsic factors like the bone quality, location of the lesion (occipitocervical junction vs. lower cervical spine), and individualization, driven by the patients' unique characteristics and functional needs. Intralesional excision is always preferred over wide excision with the risk of potential instability for all benign neoplasms, except with recurrent giant cell tumours (GCT) and aneurysmal bone cysts (ABC).

An en bloc resection technique may be required for malignant neoplasms (e.g. Ewing and osteosarcoma) [18]. A multidisciplinary, dedicated, paediatric oncology team comprised of medical oncologists and surgeons, coupled with neoadjuvant chemo−/radiotherapy, is a prerequisite for surgical success. An open and

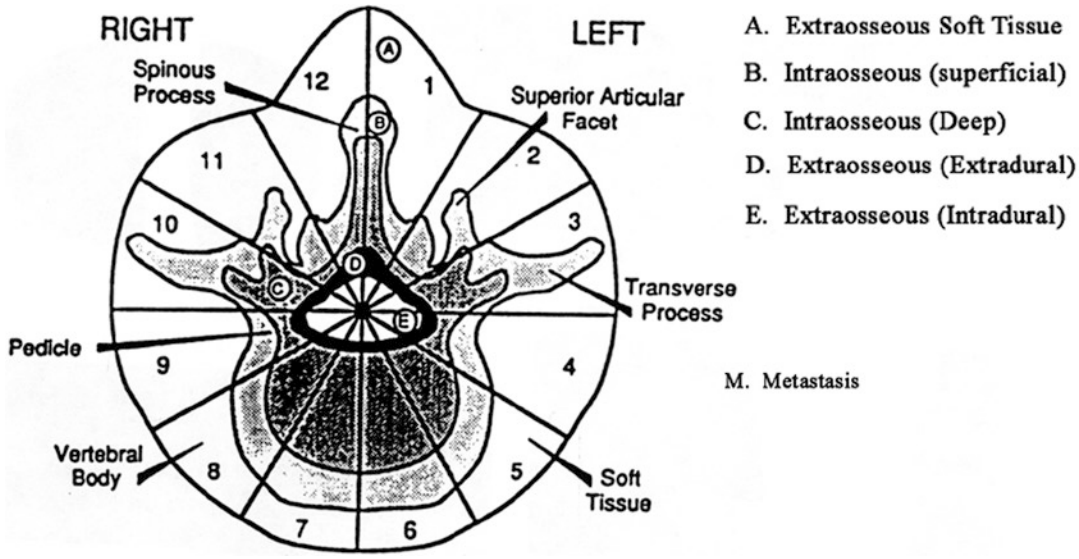

Fig. 8.1 The Weinstein, Boriani, and Biagini (WBB) staging system and representation of 12 transverse zones of a vertebra on axial plane

honest discussion with the parents or guardians about the potential risks, complications, alternative treatment options, and the natural history of the underlying complex pathology is of paramount importance in having realistic expectations and optimizing the patient's experience.

The Weinstein, Boriani, and Biagini (WBB) staging system divides the vertebra on an axial plane into 12 zones that are used to define the borders of a tumour (Fig. 8.1) [6]. This also provides guidelines for the approach and recommendation on the type of reconstruction following surgical excision of the tumour. Lesions involving anterior areas (i.e. zones 4–8 and 5–9) require a vertebrectomy, and those affecting the posterior areas (i.e. zones 10–12 and 1–3) require a posterior approach and the removal of posterior elements. Lesions affecting zones 2–5 or 7–11 would warrant removal of half of the vertebra (i.e. hemivertebrectomy).

Tomita et al. have proposed a two-part numeric classification to accurately express the location of a tumour in the spine, along with the extent of vertebral involvement [19]. It is a refinement and builds on the existing Enneking classification by incorporating a description of affected anatomic site and extent of metastatic involvement. The first set of numbers ranges from 1 to 5 with 1 representing vertebral body and 5 paravertebral area. The second set of numbers ranges from 1 to 7 with lesions 1–3 being intracompartmental, 4–6 being extracompartmental, and subtype 7 representing multiple/noncontiguous/skip lesions (Fig. 8.2) [19]. The main purpose of Tomita classification was to help the treating surgeon in planning curative vs. palliative resection options. More recently, the Tomita classification is incorporated into the Tokuhashi scoring system to form a new algorithm that predicts life expectancy following surgical management in the metastatic disease of the spine [20].

Complications

The salient complications that can occur in cervical spine tumour surgeries are:

- Missed/incorrect diagnosis
- Undertreatment/overtreatment
- Infection
- Recurrence
- Development of post-operative deformity (especially post-laminectomy kyphosis)
- Development of post-operative instability

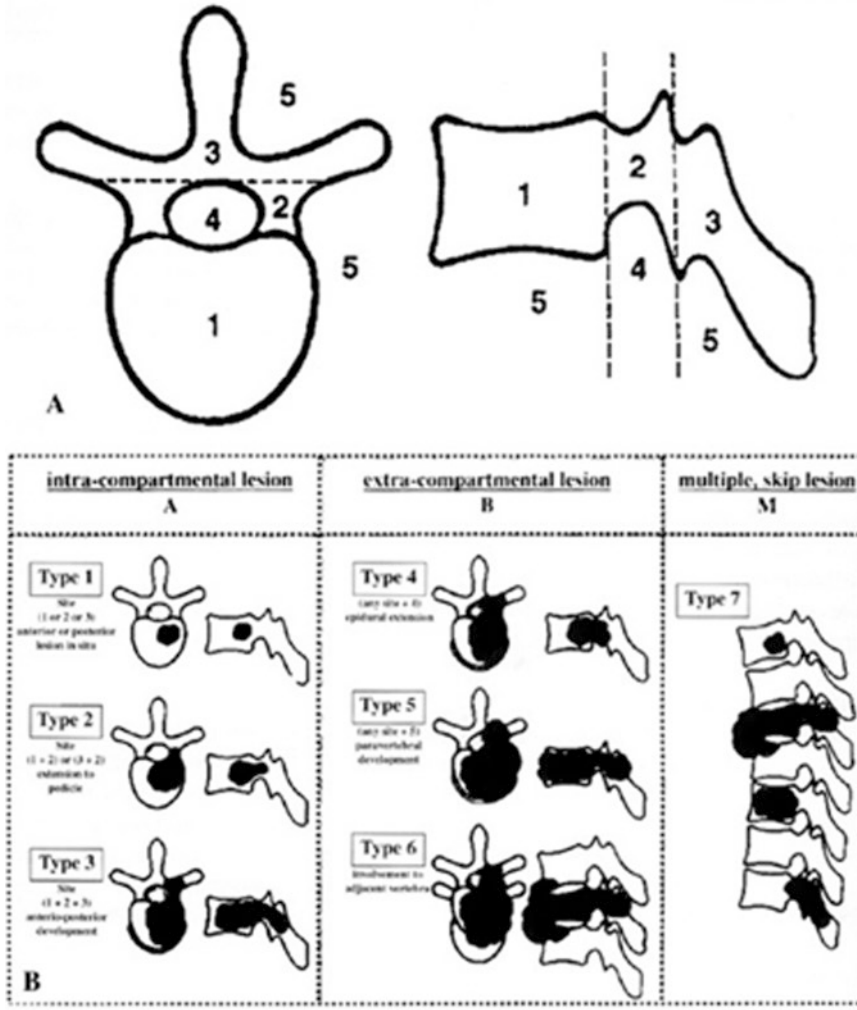

Fig. 8.2 Tomita's two-part numeric classification system with first set of numbers from 1 to 5 and second subset from 1 to 7 (1–3, intracompartmental; 4–6, extracompartmental; and 7, multiple noncontiguous lesions)

The recurrence can be minimized by a multidisciplinary team approach and the judicious use of adjuvant/neoadjuvant treatment (i.e. chemo- and/or radiotherapy). Higher-grade tumours, increased cellular atypia with reactive tumour bed, and intralesional excision are associated with increased recurrence. Irradiated tissues have a risk of undergoing malignant transformation, especially a decade or two after initial treatment, and regular long-term surveillance is mandatory [21].

The overall complication rate reported in literature varies widely from 12% to 92%, and the mortality rate is in range of 2.6–7.7% [22]. Other complications unique to the cervical spine include:

- Airway oedema: treated with definitive airway
- Dysphagia: usually self-limiting and improves in 3–6 months post-op
- Palatal dysfunction
- Injury to vertebral artery
- Risk of dural tear with CSF leak and risk of CSF fistula/secondary infection

Benign Tumours

Osteoid Osteoma

Osteoid osteoma (OO) is the most common benign primary tumour affecting the cervical spine and was seen in 18/41 cases in the series from the Rizzoli Institute (Bologna, Italy) and accounted for 13.5% of all benign lesions of the spine seen at the Mayo clinic [22, 23]. It accounts for up to 9% of primary bone tumours of the spine, and 11–25% of all osteoid osteoma are found in the axial skeleton. It is more common in males, and the mean duration from onset to diagnosis was 19 months in one reported series. The cervical spine is a less common site for OO, in comparison to the thoracic and lumbar spine. OO and osteoblastoma (OB) are histologically identical lesions and have a predilection to affect/involve the posterior elements (i.e. lamina, pedicle, or spinous processes). Often the lesion is characterized by a central nidus surrounded by a sclerotic rim. They are usually ≤15 mm in diameter. OO is at least four times more common than OB, and plain X-rays may be entirely normal. A technetium bone scan is the most sensitive imaging technique in detecting them. Pain is the predominant feature, and torticollis is usually seen when the cervical spine is affected. The involvement of the thoracic/lumbar spine is associated with the development of scoliosis, and OO is usually found in the concavity of the deformity. This torticollis/scoliosis may persist indefinitely despite adequate excision/clearance of nidus, especially when the symptoms are long-standing (i.e. ≥15 months). CT scans are highly diagnostic, and MRI paints an overly aggressive appearance, owing to the surrounding oedema. Night-time pain is also a characteristic feature that can be relieved by intake of NSAIDs/ASA. Histologically, the nidus is composed of a dense layer of osteoblastic cells surrounded by vascular fibrous tissue and ultimately a peripheral layer of mature reactive cortical bone.

The surgical treatment of choice is an intralesional excision of the nidus. The use of intraoperative 3D fluoro-navigation (Iso-C three-dimensional image intensifier) is beneficial to confirm adequate or complete excision [24]. Incomplete excision is associated with recurrence. Kneisl et al. observed that long-term NSAIDs were as effective as a surgical excision of the lesion, though pain relief with NSAIDs was reported to be as low as 30% in one published series [7, 25]. Medical management with NSAIDs is also fraught with the risk of gastric irritation, ulceration, and duodenal perforation. Alcohol, with its vasodilator properties, may precipitate *acute pain crises*. Pain relief is rapid following successful/complete excision of the nidus. Gamma camera scintigraphy facilitates the accurate localization of the nidus, and radiofrequency ablation is also employed in treating OOs. Spontaneous resolution of the nidus over 2–4 years is also reported by some investigators. Figure 8.3a–e depicts an index case of osteoid osteoma arising from right C5 posterior element in an 8-year-old child. The pre- and postoperative axial CT scan images along with histological appearance (in low- and high-power magnification) are shown.

Osteoblastoma

Osteoblastomas (OB) are histologically identical to osteoid osteomas (OO) but are very vascular lesions, and they attain a larger size (i.e. ≥20 mm) [6]. They commonly affect the posterior elements and are less common than OO. The spine is the most common site for OB, and up to 50% of them are found in the lumbar spine. They are equally distributed in the cervical and thoracic spine (i.e. 25%), and they comprise 1% of all spinal neoplasms. They are most commonly seen in children and young adults (i.e. ≤30 years), and they most commonly affect the posterior elements. Vertebral body involvement is rare (<3% of all OBs), and the male/female ratio is 2:1 [4].

Microscopically, the OBs are composed of vascular spindle cell stroma with abundant irregular spicules of the osteoid and mineralized bone, with areas of cystic degeneration or haemorrhage. The features overlap with those of an aneurysmal bone cyst (ABC). However, ABCs may also affects anterior elements (i.e. vertebral body) as

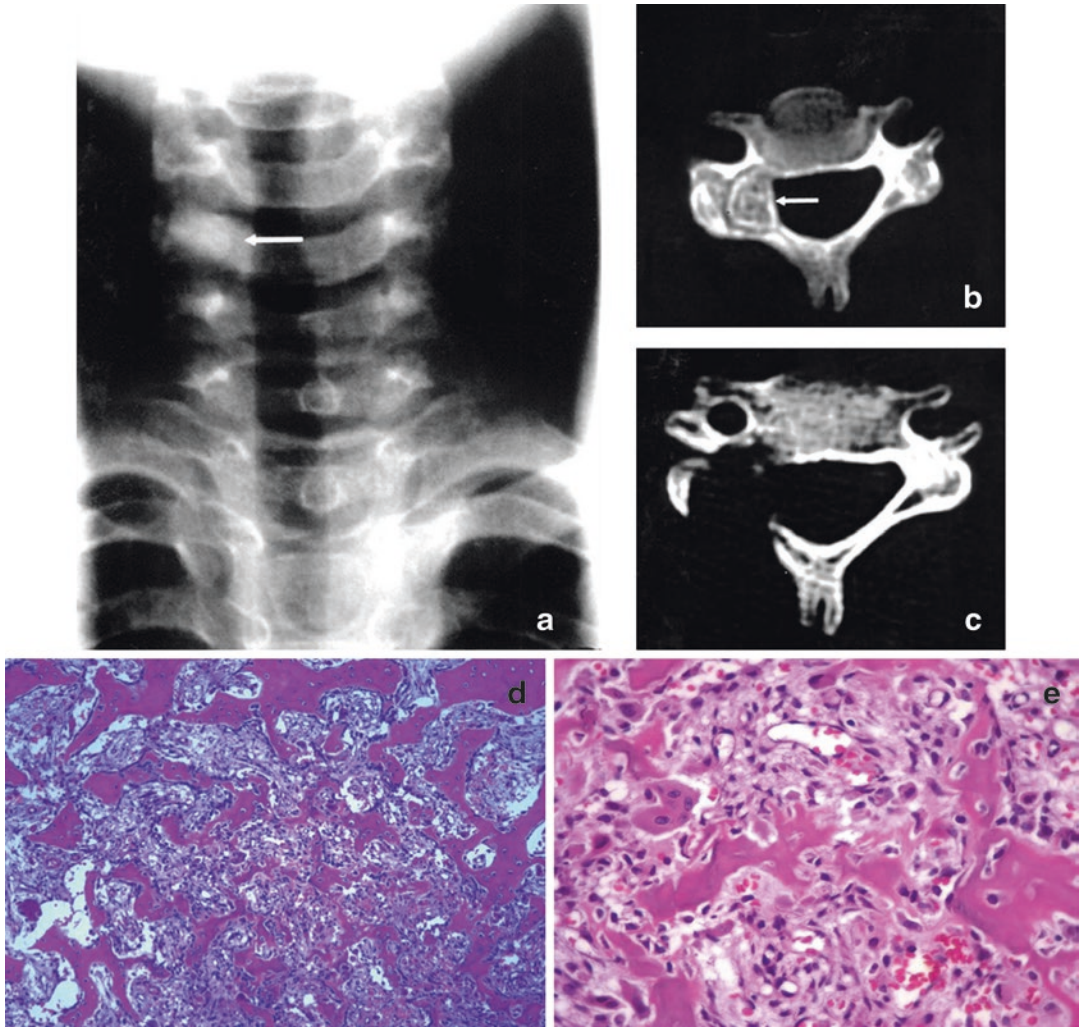

Fig. 8.3 (**a**–**e**) Osteoid osteoma of right C5 posterior elements (lamina-lateral mass junction). (**a**) AP X-ray. (**b**, **c**) Axial CT images before and after resection of the lesion. (**d**, **e**) Low- and high-power magnification views of histology showing osteoid matrix and osteoblastic cells

eccentric, expansile, locally aggressive lesions with cortical destruction and multiple fluid-filled levels. OBs can also be locally aggressive lesions with cortical penetration and adjacent soft tissue involvement. Finally OBs should predominantly contain osteoid elements/cells, and the presence of cartilage cells (i.e. chondroid matrix/chondrocytes) should raise suspicion of malignant transformation into osteosarcoma.

The predominant clinical feature is pain, and its response to NSAID intake is variable and unpredictable. OBs can also cause neurological compression, with local spread into the epidural space by canal encroachment of the neoplastic mass. Plain X-rays may reveal a destructive expansile lesion with a central hyperdense nidus. The destruction is best seen on a CT scan, and an MRI may reveal any impingement of the thecal sac or nerve root.

En masse surgical excision or extended curettage/resection of the lesion is the treatment of choice, and it often warrants spinal instrumentation because facet joints/lamina may need to be sacrificed to facilitate tumour removal [26].

MRI-compatible spinal instrumentation by lateral mass screws and rods is recommended to prevent post-laminectomy kyphosis and/or postoperative instability [16, 17]. Complete excision may not always be possible, owing to the proximity of the OB to the vital structures, and an intralesional excision is fraught with recurrence. Surveillance MRI scans are recommended to monitor for any recurrence. OBs are very vascular tumours, and preoperative embolization of the main/feeder blood vessel is recommended prior to surgical excision [27]. The Rizzoli Institute had one mortality due to excessive haemorrhage in their series of 41 patients with benign cervical spine neoplasms, 38 of whom were treated by surgical excision [23]. The risk of recurrence is strongly correlated with the grade of the lesion. Aggressive high-grade OBs have a 50% risk of recurrence, as opposed to a 10–15% risk for low-grade OBs. Post-op adjuvant radiotherapy, though advocated by some, has not been shown to reduce the risk of recurrence and, therefore, should be used very judiciously. Brachytherapy is recommended for multifocal recurrences [6].

Osteochondroma

Osteochondromas are the most common primary bone tumours in children and adolescents. They constitute 8% of all bone tumours and 35% of all benign bone tumours [1]. They are also referred as osteocartilaginous exostosis, and they most commonly affect the appendicular skeleton. Only 2.5% of OCs are found in the spine [28]. They are hamartomas that develop from aberrant germ cells of the feotal cartilage. They can be either solitary or multiple and sessile or pedunculated. Both males and females are affected equally. They can be a part of multiple hereditary exostosis (MHE), and co-existent exostosis in the appendicular and axial skeleton is common [29]. A majority of OCs in the axial skeleton are asymptomatic and are detected incidentally on a workup for MHEs. They become symptomatic by causing compression on the thecal sac or by causing nerve root pressure/mass effect, and in general, they are usually painless lesions. OCs are most common in the cervical spine, and Dahlin et al. found only eight cervical OCs in a series of 615 patients with exostosis [30]. They most commonly arise from posterior elements but could also affect the anterior elements (i.e. arise from the anterior or anterolateral aspect of the vertebral body). Axial skeletal OCs should be suspected strongly and actively looked for in a patient with MHE presenting with neurological signs or symptoms.

The natural history of OCs is usually growth until skeletal maturity, followed by either a plateau phase or minor regression with time. Spontaneous regression during pubertal growth and adolescence has also been described. They are capped by cartilage cells from the growth plates that are left on the surface of the bone. Rapid increase in the size of an OC with a significant increase in the thickness of the cartilage cap (esp. >20 mm) and acute onset of pain is usually suggestive of a malignant transformation into chondrosarcoma [6]. The presence of calcification in the cartilage cap is suggestive of malignancy. Such a malignant transformation is rare (i.e. <1%) and usually happens in the background of MHE, where the tumour acquires a cauliflower appearance. Acute precipitation of pain may also be seen in stalk fractures of pedunculated OCs.

Asymptomatic OCs do not require any treatment. Surgical excision (intralesional or marginal) is recommended for symptomatic OC, and a complete removal of the cartilage cap is desired to reduce the risk of recurrence. Figure 8.4a–d represents a giant osteochondroma arising from posterior elements of C2. The clinical photograph, sagittal, and axial MRI images, along with histological appearance postexcision, are shown. The perichondrium covers the cartilage cap overlying on the osteoid matrix. Rose et al. have reported an OC of the odontoid peg that caused sudden death by a partial transection of the spinal cord [31].

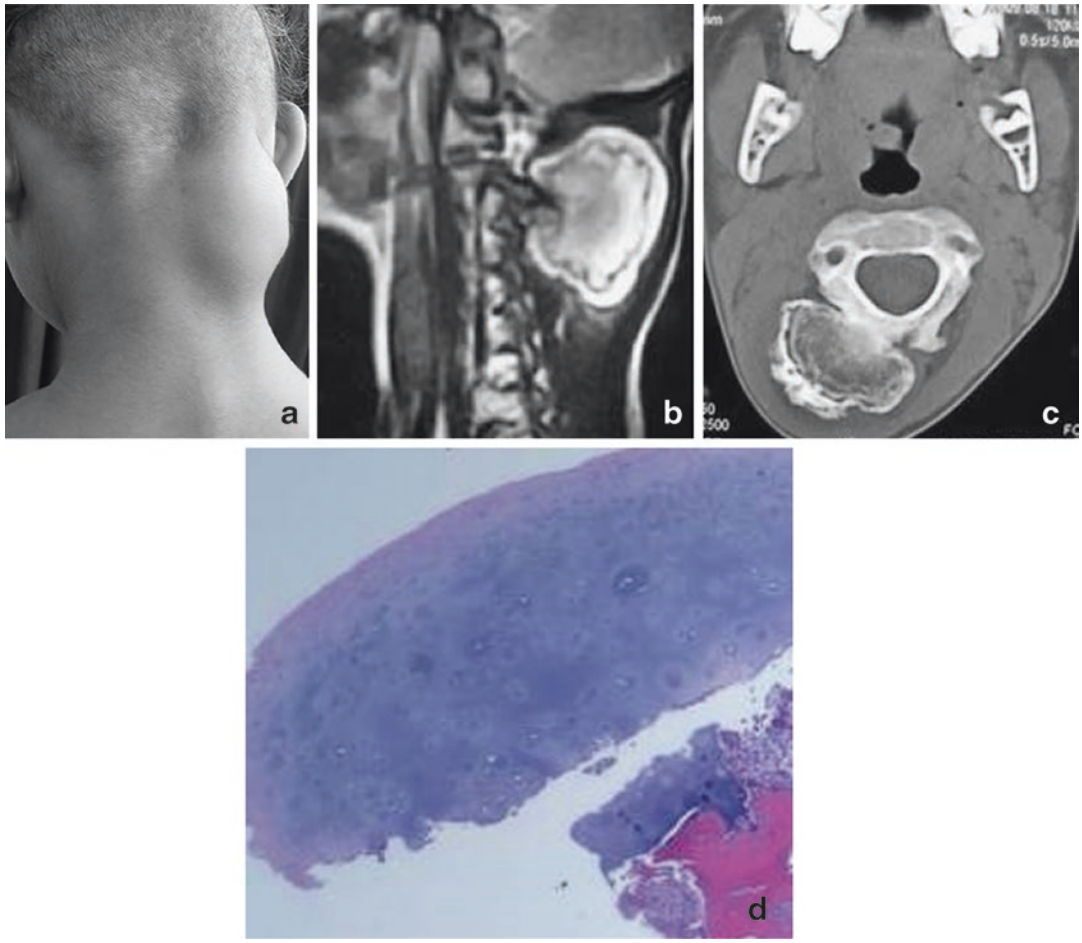

Fig. 8.4 (**a**–**d**) Osteochondroma arising from right-sided lamina of C2 (*axis*) vertebra in a patient with MHE (multiple hereditary exostosis). (**a**) Clinical photograph; (**b**, **c**) MRI sagittal and axial images; and (**d**) histology showing osteoid matrix covered by bluish cartilage cap

Haemangioma

Most haemangiomas are incidental findings detected or observed on evaluation for other pathologies. The axial skeleton (i.e. spine) is the most common site for haemangiomas, and 28% of all haemangiomas are located in the spine [32]. They are most common in the thoracic spine and least common in the cervical spine. They can be broadly categorized into three types:

- Asymptomatic
- Symptomatic
- Aggressive/compressive

From a pathological perspective, haemangiomas of the spine can be of three types:

- Capillary
- Venous
- Cavernous

They differ from aneurysmal bone cysts (ABC) by having an endothelial lining of their walls. A majority of haemangiomas are asymptomatic (>99%), and they most commonly affect the anterior elements (i.e. vertebral body). They were found in as many as 10–12% of people in a cadaveric dissection/autopsy study [4]. Though they

affect males and females equally, the incidence of symptomatic haemangiomas (which are less than 1% of all haemangiomas) is more common in females. Up to 20% of patients may have multifocal, noncontiguous haemangiomas elsewhere in the axial skeleton [23]. In a series of 148 symptomatic haemangiomas, Nyugen et al. found ten of them in the cervical spine [33]. Aggressive haemangiomas were most commonly found to involve the T3–T9 vertebrae.

The symptoms are usually either due to a localized haematoma formation/mass effect or a pathological fracture of the expanded trabeculae. They most commonly present with pain localized to the area of the underlying haemangioma. Neurological symptoms are rare and can be seen when there is compression of anterior radiculomedullary artery, epidural haematoma, or/and expansion of the vascular bone. The senior author (JPD) has reported a case of an aggressive haemangioma presenting as acute cauda equina syndrome in an adolescent [34]. Plain X-rays demonstrate characteristic trabecular striations and are colloquially referred to as *honeycomb* or *corduroy* in appearance. On CT scans, they have a characteristic *polka dot* (i.e. stippled) appearance. The characteristic appearance on an MRI is a hyperintense lesion on both a T_1- and T_2-weighted image, owing to the high water and fat content in the tumour (Fig. 8.5). Aggressive lesions may have an expanded or poorly defined cortex with a soft tissue component.

Asymptomatic haemangiomas do not require any treatment. The natural history of an untreated haemangioma is that of ossification of the affected vertebra. Treatment is recommended only for symptomatic or painful lesions. Treatment options include:

- Vertebroplasty
- Radiotherapy
- Surgical stabilization (for aggressive lesions)

Vertebroplasty provides marked to complete pain relief in most of the patients and has the added advantage of reinforcing the structural integrity of vertebra, preventing collapse. Selective arterial embolization of the feeding vessel can also be undertaken and provides consistent pain relief. Radiotherapy at a dose of 20–30 Gy resulted in complete pain relief in a majority of haemangiomas [35]. Corpectomy with anterior column reconstruction using a strut graft/cage, augmented by anterior plate or screw fixation, may be needed for aggressive haemangiomas causing neural compression. Preoperative embolization of the main feeder vessel is recommended prior to surgical fixation to minimize intraoperative blood loss.

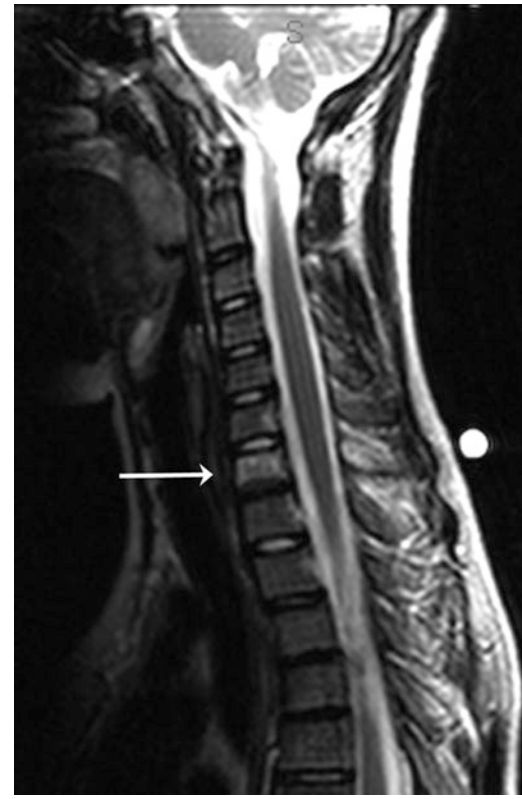

Fig. 8.5 Haemangioma of C7 vertebral body. Haemangiomas are hyperintense on both T_1- and T_2-weighted MRI sequences

Langerhans Cell Histiocytoses (LCH)

LCH is the most well-known childhood histiocytoses and was previously known as *Histiocytoses X*. The hallmark in all three forms of LCH is the presence of a clonal proliferation of cells from

monocyte-macrophage lineage containing Langerhans cells. 10–20% of children with LCH will have vertebral involvement at a mean age of 8 years [36, 37]. LCH constitutes class I histiocytoses and is comprised of a spectrum of three main clinical entities:

- Eosinophilic granuloma
- Hand-Schüller-Christian disease
- Letterer-Siwe disease

Eosinophilic granuloma is a self-limiting condition associated with a focal destruction of the bone and may be either monostotic or polyostotic. Extra-skeletal involvement is not seen in EG, unlike in the other two variants of LCH, and carries the best prognosis. It most commonly affects males aged 5–10 years. Skull bones are most commonly affected. There exists some controversy as to the commonest region in the spine to be affected by LCH, with some studies reporting cervical vs. others as thoracic. Multiple vertebrae in the spine can be involved, and usually a technetium bone scan and/or a skeletal survey are performed to identify other involved sites.

It commonly presents with pain and a local rise in temperature. It most commonly affects the anterior elements and is the most common cause of *vertebra plana*. The vertebra plana is either a partial or complete collapse of the vertebra with a *coin on edge* appearance. The natural history of LCH is that of a complete resolution by conservative management (i.e. watchful observation and symptomatic therapy). However, a biopsy should be performed to confirm diagnosis and rule out other sinister pathologies (mainly Ewing sarcoma and lymphoma). The pathognomonic feature on histology is the presence of *Birbeck granules*. They are tennis racquet-shaped bilamellar granules seen in the cytoplasm of lesional cells (i.e. Langerhans giant cells). Other features on histology include coffee bean-appearing liquid containing histiocytes of the reticuloendothelial system and eosinophils, in addition to Langerhans cells. Letterer-Siwe disease represents the acute disseminated form of LCH with visceral involvement and carries a poor prognosis.

In a series of 26 LCH patients treated by the senior author (JPD), three grades of vertebral collapse were observed: [37]

- Grade I <50% of collapse
- Grade II 51–100% of collapse
- Grade III with Grade II plus involvement of posterior elements

Each grade was further subdivided into two subtypes: (a) symmetric and (b) asymmetric. Grades Ib and IIb (i.e. those with asymmetric collapse) may manifest with spinal deformity (i.e. scoliosis/kyphosis/both), and 4/26 patients did develop one. Neurological involvement in the form of radicular pain in the upper extremities was seen in 3/26 patients, and all three of them had a cervical spine lesion.

The treatment of symptomatic LCH lesions manifesting with persistent pain, and/or spinal instability, includes intralesional curettage with bone grafting with, or without, instrumentation. External immobilization, in the form of a hard cervical collar or custom made cervicothoracic orthosis (CTO), may be needed for 6–12 weeks until sound arthrodesis occurs. There exists no evidence to support that intralesional steroids change or alter the natural history of LCH. Recurrence is rare, and radiotherapy is not recommended for solitary lesions. Systemic multiagent chemotherapy may be needed for disseminated forms of LCH and may also be combined with low-dose radiotherapy (5–10 Gy) for better efficacy. Figure 8.6a is an index case of *vertebra plana* of C3 vertebra in a 9-year-old child. The reconstituted vertebra at 6 years post-op is shown in Fig. 8.6b. The histological features and immunohistochemistry are depicted in Fig 8.6c, d. Birbeck granules are as shown in Fig 8.6e.

Aneurysmal Bone Cyst (ABC)

An ABC is a misnomer, as there is nothing aneurysmal about them. ABCs represent 1.4% of all primary bone tumours, and 5–20% of them are located in the spine [38]. The prevalence of ABC is 1.4 per million population, and they are rare

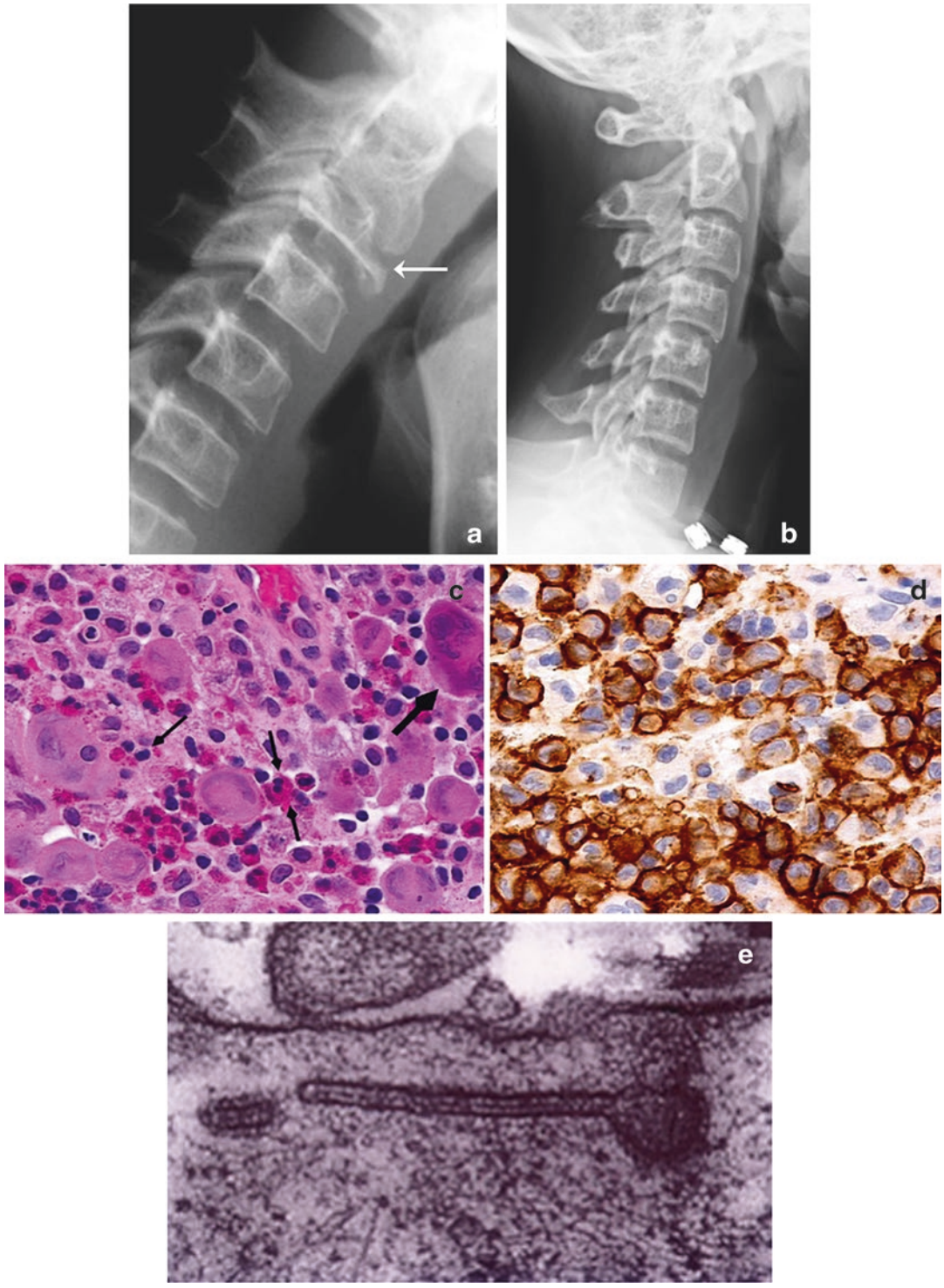

Fig. 8.6 (**a**–**e**) Langerhans cell histiocytoses: plain radiographs of cervical spine lateral view in a child with *vertebra plana* of C2 vertebra. (**a**) Before biopsy; (**b**) 6 years after biopsy showing complete reconstitution; (**c**, **d**) histology showing coffee bean liquid containing histiocytes and immunohistochemistry showing CD1a positivity; and (**e**) characteristic *Birbeck* granule

after the third decade of life. The most commonly affected vertebrae are thoracic. They are locally aggressive pseudotumourous lesions that predominantly affect the posterior elements (in 60–70% of instances) causing eccentric vertebral expansion and cortical destruction with soft tissue involvement [4, 6, 23].

ABCs may affect contiguous 2–3 vertebrae spanning intervertebral discs and may cause regional instability. Unilateral pedicle destruction produces a *winking owl* sign and may potentially cause spinal instability. An MRI scan reveals a characteristic multiloculated, septated, expansile lesion with fluid-fluid levels that produce low intensity on T1-weighted and high intensity on T2-weighted images. The cyst walls lack endothelial lining, in contrast to haemangiomas. Biopsy with an intraoperative frozen section would confirm haemorrhagic fluid with haemosiderin laden macrophages. A CT scan would delineate the accurate extent of vertebral involvement. ABCs may co-exist with other conditions, namely chondromyxoid fibroma (CMF), Langerhans cell histiocytoses (LCH), giant cell tumour (GCT), and chondroblastoma. The solid variant of ABCs does not have a fluid-filled cavity and consists of spindle cells. Both the solid variant and the conventional ABCs can also co-exist together. The soft tissue variant of ABCs does not have osseous involvement, and there are sporadic case reports published of such lesions affecting the appendicular skeleton. However, such soft tissue variant ABCs have not been observed in the axial skeleton/spine. ABCs are characterized by three distinct stages/phases: [4]

1. Growth phase: associated with bony destruction and subperiosteal blowout pattern
2. Stabilization phase: characterized by a distinct peripheral bony shell with an internal bony septa and trabecular meshwork imparting a *soap bubble* appearance
3. Mature phase: bony healing with progressive calcification/ossification of cyst

ABCs are usually symptomatic, causing localized pain either due to a pathological fracture or spinal instability. Neurological symptoms are seen in up to 40% of all patients with ABCs. Historically they were treated by intralesional curettage and the bone grafting. However, this technique is fraught with an increased incidence of recurrence. The senior author's (JPD) four-step approach is comprised of: [15]

1. Aggressive intralesional curettage
2. High-speed diamond burr and electrocauterization of cyst wall
3. 5% dilute phenol application to cyst wall lining (chemical cauterization)
4. Bone grafting (synthetic osteoconductive bone graft substitutes)

This approach was not associated with any evidence of recurrence at a minimum follow-up of 1 year (0/8 recurrence with 4-step approach vs. 4/4 recurrence with mere intralesional curettage and bone grafting) [15]. As ABCs are vascular, preoperative selective arterial embolization is beneficial in keeping intraoperative blood losses to a minimum [39]. An index case of ABC affecting C7 vertebra treated by the four-step approach and combined anterior + posterior spinal stabilization, along with gross macroscopic appearance of excised lesion and histological appearance, is shown in Fig. 8.7a–g.

Calcitonin is also found to be effective in suppressing osteoclastic activity and stimulating trabecular bone formation within the fibrous septa of an ABC [40]. However, external beam irradiation was found to be associated with a risk of recurrence (at least 25%), in addition to the risk of sarcomatous transformation and is currently not advocated for the management of ABCs [41].

Giant Cell Tumour (GCT)

GCTs represent 5% of all primary bone lesions, and vertebral lesions, especially in children, are rare. They are twice as common as ABCs and have a predilection to affect females (the male/female ratio being 1:2) [42]. They tend to predominantly affect the anterior elements (i.e. vertebral body) and are locally aggressive (especially recurrent GCTs) [4, 23]. They are less common

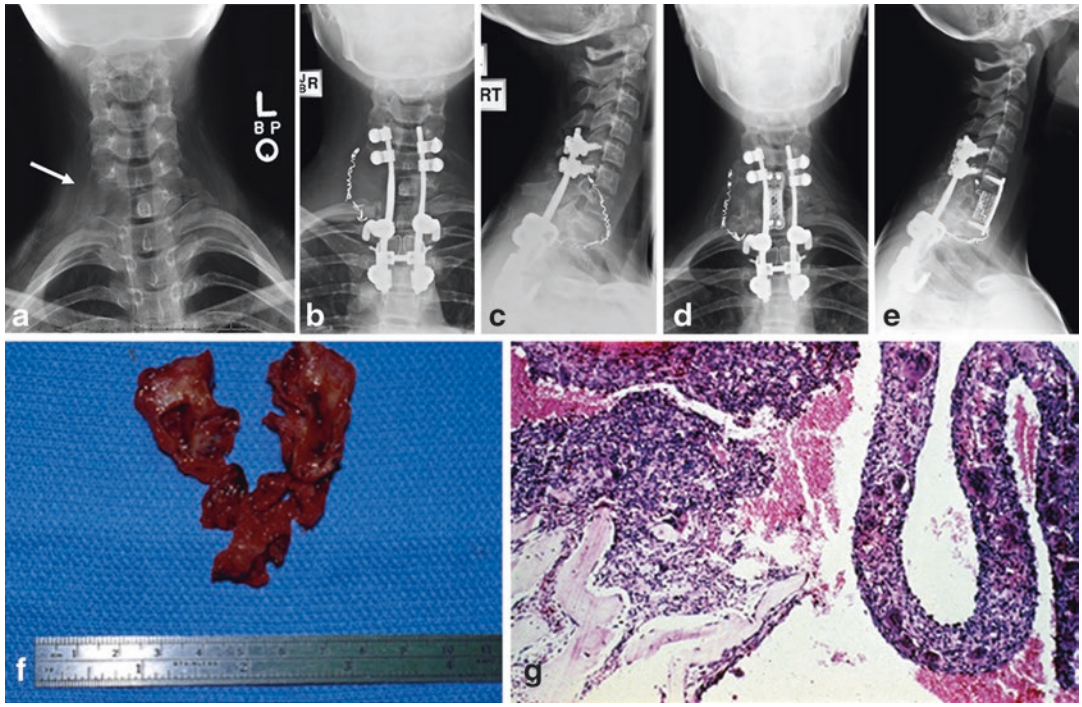

Fig. 8.7 (**a**–**g**) Radiographs of recurrent aneurysmal bone cyst (ABC) with soft tissue mass arising from C7 vertebra. (**a**) AP X-ray showing destruction of right-sided pedicle; (**b**, **c**) AP and lateral X-rays of posterior tension-band fixation following selective arterial embolization of thyrocervical trunk; (**d**, **e**) AP and lateral X-rays following anterior corpectomy, reconstruction of anterior column, and plate/screw fixation; (**f**) macroscopic appearance of cyst wall lining; (**g**) histology showing numerous hemosiderin laden macrophages

in skeletally immature individuals, and they most commonly affect young adults and the middle aged (third–fifth decades). Spinal GCTs account for roughly 15% of all GCTs and are most commonly found in the sacrum. Cervical spine involvement is less common, and the characteristic radiological appearance is that of an expansile lytic cavity in the vertebral body without septation or a mineralized matrix surrounded by the reactive bone. A CT scan accurately delineates cortical destruction or thinning. A co-existent soft tissue mass may be present in many of the GCTs. The characteristic feature on histology is the presence of multinucleated giant cells within the tumour mass, found by the fusion of mononuclear cells. Giant cells are not pathognomonic of GCTs and are also found in other lesions (ABCs, non-ossifying fibroma, chondroblastoma, and osteosarcoma).

Staging of GCTs is done by using a combination of X-rays, bone scans, CT, and MRI scans. Stage II (active) lesions are best treated by intralesional excision and curettage with adjunct therapy, using phenol, liquid nitrogen, and/or methyl methacrylate, whereas stage III (locally aggressive) lesions may need marginal or en bloc resections. Mere intralesional excision without any adjunct treatment is associated with a recurrence of at least 50% and is not recommended. Wide excision is associated with a significant reduction in incidence of recurrence to $\leq$10%. GCTs of the cervical spine are treated by wide excision with corpectomy and anterior + posterior spinal stabilization, using MRI-compatible titanium implants. Selective preoperative embolization of the feeder vessel is desired, as GCTs are highly vascular tumours. Radiotherapy is reserved for unresectable sacral, and/or recurrent, lesions.

Advances in the molecular and cellular biology of GCTs have led to an identification of RANKL (a nuclear factor required for osteoclast formation and expressed by a variety of GCTs). Denosumab, a monoclonal antibody to RANKL, has promising early results in the treatment of GCTs [43].

The biological behaviour of GCTs is unpredictable, and the transformation of stage II and III lesions to overt malignancy is also observed (5–15%). Rapid malignant transformation may cause a pathological fracture with cord or nerve root compression. Pulmonary metastasis, up to 10%, is reported with GCTs, and a high degree of suspicion is needed in detecting them [44]. A CT scan of the chest is the investigation of choice in ruling out the lung involvement.

Recurrent lesions that are not amenable for surgery are treated by:

- Cryosurgery
- Regular/repeated embolization
- Use of interferons
- Bisphosphonate infusion
- High-dose radiotherapy (25–45 Gy).

Miscellaneous Lesions

Gorham Disease It is an extremely rare benign condition characterized by massive regional osteolysis with a proliferation of capillaries. It is a slowly progressive and self-limiting pathology occurring commonly in children and arrests spontaneously by 2 years [6]. It predominantly affects the anterior elements, and the diagnosis is confirmed by histological evaluation. Less than 20 cases are reported in English literature to this day, and the end result is partial restitution with incomplete fusion. The pathogenesis is unknown, and treatment is usually conservative with a halo-vest or collar immobilization. Close monitoring and supervision are needed during the active phase to evaluate for instability and/or new neurology.

Fibrous Dysplasia It is a hamartomatous condition characterized by a *ground-glass appearance* of the affected skeleton on plain X-rays. It could be monostotic (i.e. solitary involvement) or polyostotic. They are largely asymptomatic (i.e. stage I) lesions and are discovered incidentally. Neck pain and torticollis with spasm is the main symptom, owing to the weakening of the trabecular architecture and vertebral collapse. Intense lytic process in stage II and III lesions (i.e. active and locally aggressive forms) may mimic the *vertebra plana* of eosinophilic granuloma. Spinal stabilization is needed when mechanical failure occurs or is impending. Fibrous dysplasia in children is particularly notorious for recurrence, and a bone graft may get resorbed [44].

Malignant Tumours

Primary malignant tumours of the cervical spine are uncommon in children and have a distinct male preponderance, with the male/female ratio being 3.2:1 [6]. The most common tumour is Ewing sarcoma, which is characterized by the presence of numerous small, round blue cells on histology. C2 and C5 appear to be the most commonly affected vertebrae, though chondrosarcoma most commonly affects the C6 and C7 vertebrae [6]. Other lesions that can potentially affect the cervical spine are:

- Osteosarcoma
- Chondrosarcoma
- Metastasis from leukaemia and Wilm tumour neuroblastoma (i.e. PNET family)

Lymphoma and metastasis are also uncommon in children. Chordoma of the craniovertebral junction and sacrum usually occurs in adulthood, though some sporadic cases in the second decade of life (i.e. adolescence) are also reported.

The WBB (Weinstein, Boriani and Biagini) staging system is helpful in describing the zones of involvement and planning surgical resection or spinal stabilization [6]. En bloc resection is the most commonly exercised option in a selective group of patients whose lesions are amenable for surgery. As these are very rare tumours, their diagnosis, preoperative workup, and management

are best performed in tertiary centres with dedicated multidisciplinary oncology teams for surgical success and tumour-free survival. Surgery is often combined with adjuvant/neoadjuvant chemo- and/or radiotherapy, to optimize patient outcomes. A tissue biopsy and a histological confirmation of the underlying pathology are mandatory prior to any definitive en bloc resection. The potential risk of iatrogenic injury to vital structures includes:

- Spinal cord
- Sympathetic trunk
- Vertebral artery and carotid vessels

Ewing Sarcoma (ES)

Of all cases of Ewing sarcoma, 3.5–10% originate in the spine, and up to 75% of all ES occur between 5 and 15 years of age. The average age of ES in the axial skeleton is 16.5 years. ES of the cervical spine is rare, and it most commonly affects the sacrum [4]. Cytogenetic studies typically reveal a translocation of chromosome 11 and 22. ES forms one part of a large family of primitive neuro-ectodermal tumours (PNET), comprising of lymphoma, rhabdomyosarcoma, etc. The mRNA transcript and expression of proto-oncogene '*dbl*' are helpful in distinguishing ES from other PNETs [4].

The most common presentation in symptomatic individuals is pain (seen in 90% of affected individuals), and torticollis, muscular spasms, and a soft tissue mass are usually present. It usually manifests as a painless soft tissue mass with no obvious neurodeficit to begin with (91%), and neurological involvement was reported in only 9% of 344 cases of ES, as reported by Venkateswaran et al. [45]. Another series has reported the incidence of neurological involvement to be 58–64% at the time of diagnosis [4, 6]. Some may have constitutional symptoms in the form of fever, weight loss, and raised biochemical inflammatory markers (i.e. ESR and CRP). An elevated lactate dehydrogenase (i.e. LDH) is a useful blood marker and indicator of the tumour load during follow-up.

The plain X-rays reveal a big soft tissue mass in addition to *moth-eaten appearance* with a permeative pattern of destruction and an aggressive periosteal reaction with a wide zone of transition. Two characteristic of radiological appearance patterns observed were:

(i) Ivory vertebra: Sclerotic appearance with periosteal reaction
(ii) Vertebra plana: Variable osteolysis from focal lesion to complete collapse

The MRI is very sensitive in evaluating soft tissue involvement and neural canal compromise. Metastatic ES is seen in roughly 25% of children, and they most commonly metastasize to the lungs. Other areas of dissemination include the viscera, lymph nodes, brain, and other long bones.

ES is both a radio- and chemo-sensitive tumour, and nonoperative management with these modalities is the first line of treatment. The 3-year survival rate is at least 80% with newer anticancer medications [4]. Local treatment of ES has included high-dose irradiation of the affected area, and the incidence of local recurrence is as high as 25%, despite optimum treatment [46]. The cumulative risk of developing radiation-induced soft tissue sarcoma at 20 years was 42.8% (±17.2%) [47]. En bloc resection is usually advocated for recurrent cases, as survival rates are impressive. Neoadjuvant therapy is usually instituted prior to surgical resection. The prognosis of axial ES is better than its appendicular counterpart. Multiagent chemotherapy has resulted in impressive survival results, and the common agents used include vincristine, actinomycin-D, and cyclophosphamide (VAC) regimen or vincristine, actinomycin-D, cyclophosphamide, and Adriamycin (VAC-A) with, or without ifosfamide/etoposide [48]. Pulmonary irradiation and chemotherapy have markedly reduced the incidence of metastasis to the lungs. Factors associated with poor prognosis include:

- Metastasis at the time of presentation
- Large soft tissue mass/tumour
- High-grade tumour

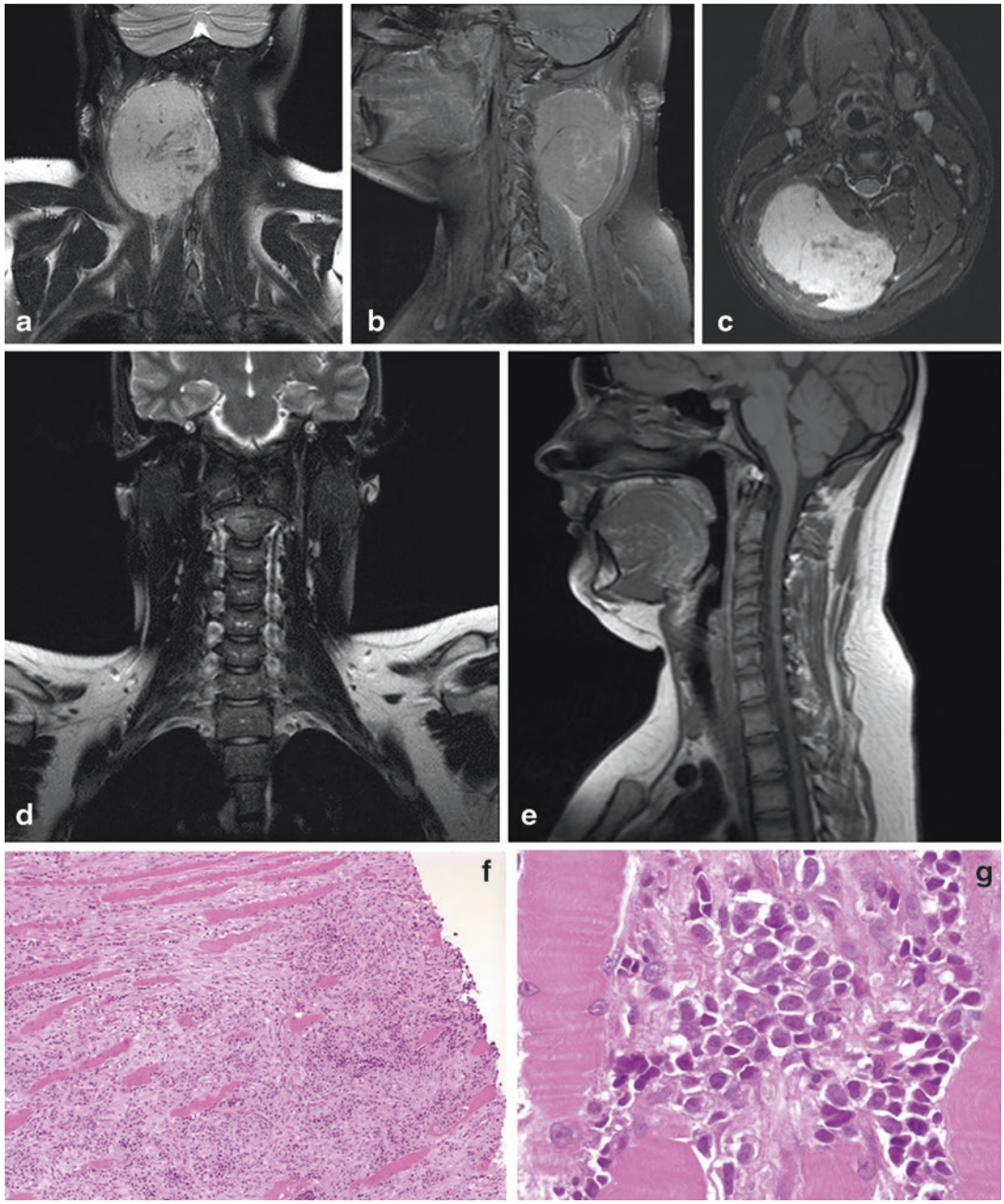

Fig. 8.8 (**a**–**g**) MRI of child with Ewing sarcoma. (**a**, **b**, **c**) Coronal, sagittal, and axial MRI showing isointense T_1 and hyperintense T_2 soft tissue mass arising from right posterior intermediate muscles of the neck; (**d**, **e**) coronal and sagittal post-op MRI following exploration of tumour bed, intraoperative biopsy with frozen section and flap mobilization with closure; (**f**, **g**) histology showing small, round blue cells (low- and high-power magnification)

- Poor response to chemotherapy
- Primary ES arising from epidural space without any osseous involvement (very rare)

An index case of ES of the neck presenting as a soft tissue mass treated by surgical excision and adjuvant chemotherapy by the senior author

(JPD) is depicted in Fig. 8.8a–e. The pathognomonic histological finding is numerous small, round blue cells (Fig. 8.8f, g).

Osteosarcoma (OS)

Though osteosarcoma is the most common primary malignant bone tumour, it is less commonly seen in the axial skeleton and constitutes only 4–5% of all spinal tumours [4]. They are aggressive lesions that cause a permeative pattern of destruction with a wide zone of transition. An abnormal radiodense osteoid matrix is produced by neoplastic cells with periosteal reaction imparting a *sunburst appearance* and causes distant metastases. It is uncommon in children, and most commonly seen in the third decade of life. Neurological abnormality is present in 40%. Mutations in the tumour suppressor gene (*p53*) and retinoblastoma (*Rb*) gene locators on chromosome 17 and 13 are contributory (25–80%). OS commonly occur in families with *Li-Fraumeni* and *Rothmund-Thomson* syndromes. Malignant transformation of the pagetoid bone into OS is uncommon in vertebrae.

An MRI is the investigation tool of choice in the evaluation of OS, and neural encroachment was seen in 84% (i.e. 38/45 patients) in a recently reported series of spinal osteosarcomas [49]. The different histological types/patterns which are reported are:

- Parosteal
- Periosteal
- Telangiectatic
- Dedifferentiated/anaplastic

In a series of 30 cases with the spinal OS by Shives et al., only four were found in the cervical spine [50]. The entire vertebra was affected at the time of diagnosis. En bloc surgical resection is the treatment of choice, and neoadjuvant chemotherapy has eliminated the risk of micrometastasis. The 5-year survival rate with en bloc resection and chemotherapy is 30% [51].

Leukaemia and Haematological Malignancies

The peak incidence of leukaemia is between 2 and 5 years of age, and it is the most common form of cancer to affect young children. The diagnosis is challenging, as the cells are physiologically metastatic from an early phase of the disease process, and surgery has no role in the treatment of leukaemia. Constitutional symptoms are very common, and bone pain is present in up to 25% of affected patients. Peripheral smear, blood tests, and immunohistochemical studies confirm the diagnosis. It is treated by using chemotherapy and radiotherapy.

The vertebral lesions are non-specific and do not help in a definitive diagnosis. Vertebral collapse may be seen in 6% and pathological fractures in 10–15% of affected children [52, 53]. The plain radiographs may show features of osteolysis, osteosclerosis, a permeative pattern of destruction, and a mixed pattern of involvement (i.e. areas of lysis and sclerosis).

Metastasis in Cervical Spine and Miscellaneous Tumours

These include other primitive neuro-ectodermal tumours (i.e. PNET family) which are Wilm tumour, neuroblastoma, lymphoma, and soft tissue sarcoma (e.g. rhabdomyosarcoma and teratoma) [54]. They most commonly present as pathological fractures, and neurological involvement is rare and uncommon. The treatment options are dictated by an underlying diagnosis and are specific to the type of malignancy and stage at the time of diagnosis.

Summary

Tumors of the child's cervical spine are rare and in the first 2 decades of life are usually benign. Metastatic lesions are often part of a hematological disorder. Staging and grading of malignant

tumors follow biopsy and advanced imaging principles as in other tumors. Surgical resection follows principles of anatomical zones.

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