




A Rare Case of Primary Hyperparathyroidism Presenting as a C2 Brown Tumor-Plain Radiography Has yet again Proved Indispensable in Clinching the Diagnosis

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Abstract

Keywords

- primary hyperparathyroidism
- brown tumor
- plain radiograph
- C2 vertebra
- axis vertebra

A brown tumor is one of the manifestations of hyperparathyroidism. It is a rare type of bone lesion that most often occurs in mandible, ribs, and large bones. Spinal involvement is extremely rare. We report an unusual case of a brown tumor of the axis vertebra in a 33-year-old male who presented to the orthopaedic clinic with posttraumatic C2 vertebra fracture and myelopathy. To plan further fixation and stabilization of C2 fracture, the patient underwent a plain radiograph and magnetic resonance imaging (MRI) of the cervical spine. The available routine chest radiograph at the time of MRI reporting clinched the diagnosis of primary hyperparathyroidism with a brown tumor of the axis vertebra. Thus, familiarity with subtle radiographic findings of this condition not only led to early diagnosis and appropriate treatment but also avoided unnecessary C2 biopsy and hardware fixation.

Introduction

Brown tumor is an uncommon nonneoplastic osseous lesion that develops secondary to bone resorption caused by an elevated level of serum parathyroid hormone (PTH) in patients with primary or secondary or tertiary hyperparathyroidism (HPT).¹ The prevalence of brown tumors is low with a slightly greater frequency in primary than in secondary HPT (3 versus 2%).² However, secondary HPT is much more common than primary; therefore, most brown tumors are seen associated with secondary HPT with a reported incidence of 13%.^{3–5} Although brown tumors can occur in any

location, the most commonly involved sites are facial bones including maxilla and mandible, skull, metacarpals, phalanges, ribs, clavicle, and pelvis.^{1,6,7} The spinal involvement is rare, and occurrence in the cervical spine is exceedingly rare^{4,6} with only a handful of cases previously reported in the literature.^{6–14} Brown tumors involving the axis, the second cervical vertebra, are extremely unusual, and only two cases have been reported so far and both are in patients with primary HPT.^{6,7} We report the third case of axis brown tumor as an initial manifestation of primary HPT. When brown tumors are seen as an initial presentation in patients with nondiagnosed HPT, it can mimic bone tumors like

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metastasis, leukemia, histiocytosis, and primary malignant tumors because of the single or multifocal expansile osteolytic nature of the lesion demonstrating a varying degree of bone destruction with or without pathological fracture.^{1,6,15–19} However, careful examination of other radiographs can aid in diagnosis and avoid the more aggressive surgical intervention of the lesion.

The purpose of our paper is to report a rare case of the brown tumor of the axis, the second cervical vertebra, due to primary HPT, and more importantly, to highlight the significance of subtle radiographic findings on routine radiographs leading to early diagnosis and treatment, preclude the complex spine surgery, and thus, reduce the morbidity due to skeletal-related events.

Case Report

A 33-year-old male patient was referred to our institution to the orthopaedic spine clinic for the further management of posttraumatic C2 vertebrae fracture. A history of cervical spine injury following a fall from a motorbike 6 months back was documented, which was managed conservatively. Following the fall, progressive worsening of difficulty in walking and weakness of lower limbs were noted. Additionally, a history of generalized ache and pain in both the legs for the previous one and half years was confirmed, reported to aggravate by walking and relieved by rest. A history of tingling or numbness over hands or feet or bowel or bladder incontinence was denied. Apart from restricted cervical spine movement, variable weakness in all four limbs (upper limbs: 3/5; lower limbs: proximal 2/5 and distal 4/5) and pitting pedal edema were also noted on clinical examination. Sensations and reflexes were intact. There were no comorbidities except for a recently diagnosed hypertension. There was no significant family history.

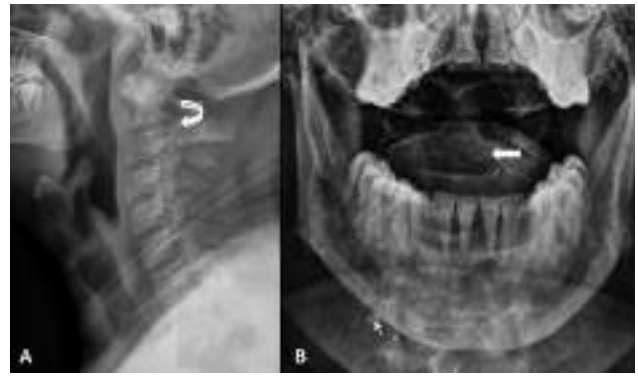


Fig. 1 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. (A) Lateral and (B) open mouth odontoid radiographs of the cervical spine showing a mildly expansile well-defined radiolucent lesion within the body of C2 vertebra (straight arrow) extending into the posterior arch (curved arrow).

No prior imaging was made available at the time of presentation to our institution. Hence, the spinal surgeon requested radiographs and magnetic resonance imaging (MRI) of the cervical spine to look for the current status of C2 vertebra fracture and the presence and extent of mass effect on the spinal cord. Radiographs of the cervical spine showed a mildly expansile well-defined radiolucent lesion involving the body of C2 vertebra (►Fig. 1). MRI confirmed the lesion of the axis vertebra, which appeared hypointense in all pulse sequences, with a mild mass effect on the ventral surface of the adjacent spinal cord (►Fig. 2). At the time of MR reporting, the routine chest radiograph was available to the radiologist. Chest radiograph depicted subchondral and subligamentous resorption of the distal clavicle and insufficiency fractures of the right scapula and ribs on the background of diffuse heterogeneous bone density. Based on the subtle radiographic features on the chest radiograph (►Fig. 3), a musculoskeletal radiologist made the diagnosis

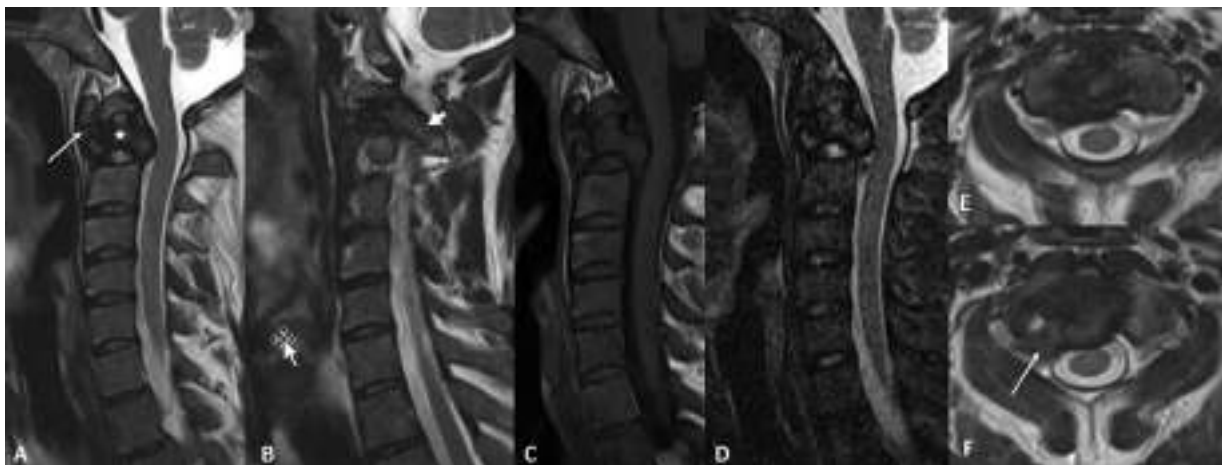


Fig. 2 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. (A and B) T2-W FSE, (C) T1-W SE, (D) T2 STIR sagittal, and (E and F) T2-W FSE axial images show abnormal T1- and T2-W hypointense marrow lesion of C2 vertebral body (star) extends into the posterior arch (short arrow) and causing mild expansion and partial collapse of C2. Associated hypointense extraosseous small soft tissue component (long arrows) around the C2 was observed. The posteriorly bulged C2 causing effacement of anterior CSF space and mild flattening of the anterior surface of the spinal cord without cord signal changes. Note the diffuse low signal intensity of the marrow within the rest of the visualized vertebrae and clivus likely to suggest hematopoietic marrow. CSF, cerebrospinal fluid; FSE, fast spin echo; STIR, short tau inversion recovery.



Fig. 3 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. The frontal view of the chest radiograph shows diffuse heterogeneous fuzzy bone density. Resorption of the lateral end of the clavicle (*arrowhead*) suggesting subchondral resorption with widening of the left acromioclavicular joint (*curved dash line*), concavity at the inferior surface of the lateral third of the clavicles (*white thick arrows*) in keeping with a subligamentous resorption at the insertion of the coracoclavicular ligament and deformity and lucency suggesting looser zone/insufficiency fracture along the axillary border of the right scapula (*white open arrow*). Note the subtle incomplete or insufficiency fracture of the right first rib (*thin white arrow*), rarefaction with resultant fracture of the right transverse process of C7 vertebra (*black arrow*) and probably T1 and bilateral chest wall deformity and crowding (*elbow arrows*) suggest bone softening.

of primary HPT with a presumed brown tumor of the axis, C2 vertebra seen on MRI. Indeed, once a chest radiograph suggested the diagnosis of HPT, the radiologist made an effort of searching the parathyroid adenoma on available T2-weighted axial images through the cervical spine obtained as a part of routine cervical spine MRI. It showed a well-defined cystic lesion behind the inferior pole of the left lobe of the thyroid (*►Fig. 4*). Further ultrasound of the neck to confirm the left parathyroid adenoma and concerned laboratory parameters were recommended.

On biochemical evaluation, PTH was high at 1,732.2 pg/mL (normal, 8.0–74 pg/mL); calcium level was high at

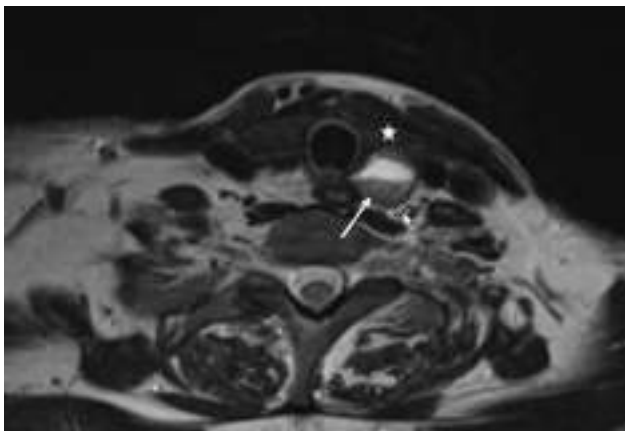


Fig. 4 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. T2-W FSE axial image shows a well-defined lesion with fluid-debris/fluid-blood level (*arrow*) posterior to the lower pole of left lobe of thyroid gland (*star*) suggest parathyroid lesion. FSE, fast spin echo.

14.40 mg% (normal, 8.3–10.4 mg%); serum phosphate was low at 1.8 mg% (normal, 2.5–4.6 mg%); vitamin D level was slightly low at 16.2 ng/mL (normal, >30 ng/mL); alkaline phosphatase was markedly high at 2,042 U/L (normal, 40–136 U/L); and 24-hour urine calcium was high at 596 (normal, <240), while phosphate was within normal limits. His ultrasound neck showed a left inferior parathyroid adenoma (*►Fig. 5*). Further the sestamibi scan (not shown) was concordant with ultrasound findings. Ultrasound abdomen (not shown) demonstrated nonobstructive renal calculi. The renal and adrenal cause of his recent onset of hypertension was excluded, and workup for renal function test, renal artery stenosis, Cushing's disease, and pheochromocytoma was negative. He was started on antihypertensive (tablet cilnidipine and telmisartan) and oral vitamin D supplements.

No active intervention was performed for the presumed brown tumor of the axis. The patient was advised to wear the Philadelphia cervical collar and reevaluation of the C2 lesion after parathyroidectomy. He was referred to our endocrine surgery facility and planned for the removal of parathyroid adenoma. Preoperatively, hypercalcemia was managed by hydration, zoledronic acid injection, and calcitonin nasal spray. He was also started on injectable dexamethasone and later replaced by oral prednisolone for his recent onset neurological deficit developed while he was admitted, and this was presumed to be attributed to spinal cord edema caused by C2 lesion though there was no evidence of edema on MRI done 15 days ago. He underwent focused left inferior parathyroidectomy under general anesthesia, and his postoperative period was uneventful. The diagnosis of parathyroid adenoma was subsequently confirmed on histopathological examination.

He did not develop features of hypocalcemia postoperatively, and serum calcium came down to 8.5 mg% and PTH level to normal at 14 pg/mL. He was transferred to an endocrine facility for further medical management. Later, the prednisolone tablet was tapered, and he was discharged in a stable condition. The conservative management was continued, and spinal fixation surgery was postponed till the next follow-up.

After 6 weeks, the patient came for follow-up, with improvement in the limb weakness and pain. The follow-up MRI of the cervical spine showed mild interval shrinkage and some healing of C2 vertebral body lesion with improvement in the previously noted mild mass effect on the spinal cord (*►Fig. 6*). He came for the second follow-up after 4 months and showed a significant clinical improvement in the generalized pain and limb weakness and no imaging was done during this follow-up. During a telephonic follow-up call after 9 and 12 months, the patient reported overall remarkable improvement with no significant residual pain and weakness.

Discussion

The most significant point about the index case is that the patient presented with a diagnosis of a traumatic C2 vertebral fracture at the orthopaedic clinic with no clinical hint to

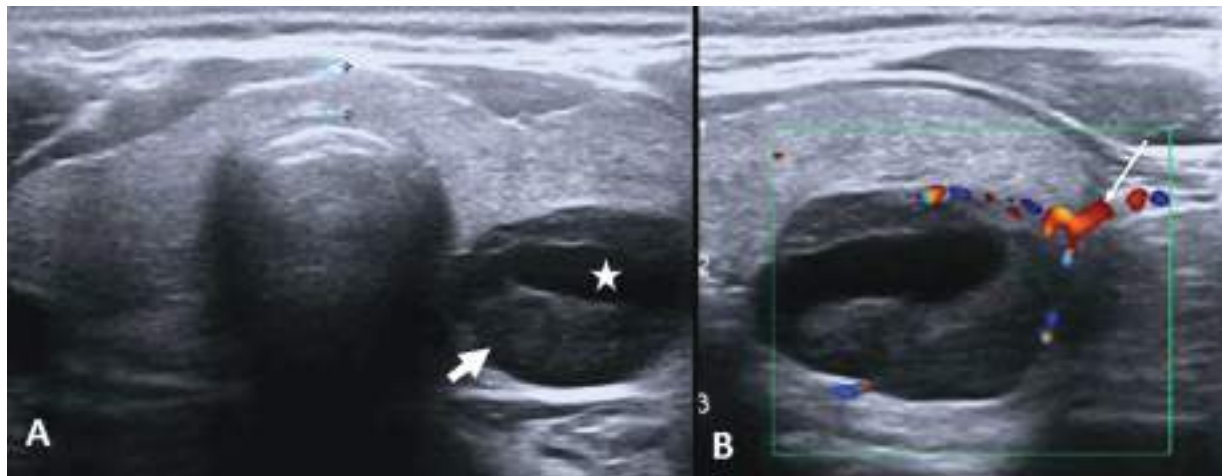


Fig. 5 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. (A) Grayscale and (B) color Doppler transverse images of the ultrasound of the neck show a well-defined hypoechoic mass lesion (*short arrow*) with central cystic change (*star*) posterior to the inferior pole of the left lobe of thyroid, supplied by a polar artery (*thin arrow*) in keeping with a left inferior parathyroid adenoma.

suggest HPT. MRI was ordered to plan for posterior decompression and C2 vertebral fixation. MRI without conventional radiographs would have subjected the patient to unnecessary open biopsy and hardware fixation of the C2 vertebra, and thus, the final diagnosis would have been delayed leading to significant morbidity. This case highlights the

importance of familiarity with subtle plain radiographic findings for the early diagnosis of HPT with a thorough diagnostic workup, including imaging and biochemical markers of bone metabolism.

The emergence of advanced imaging in the field of radiology has overshadowed plain radiography as the first-line

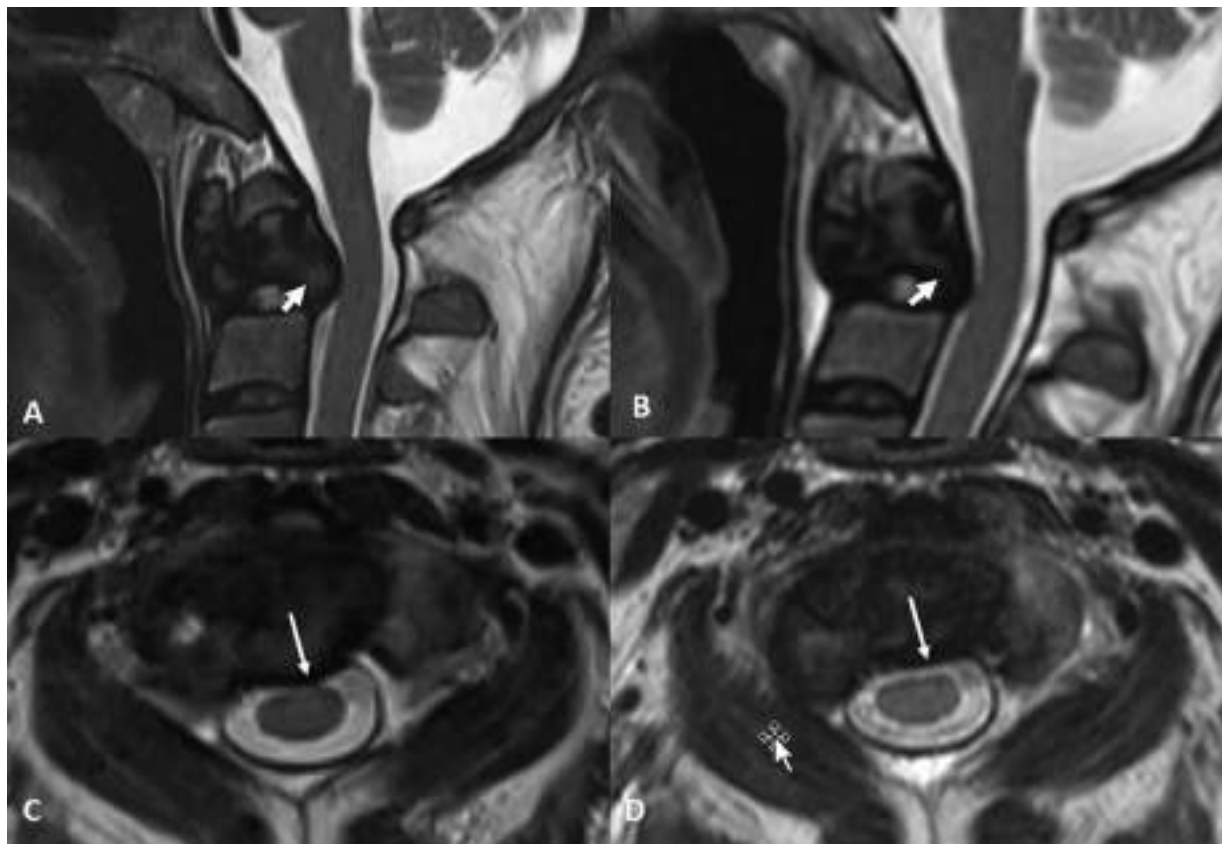


Fig. 6 A 33-year-old man with primary hyperparathyroidism and brown tumor of C2 vertebra. Pre- and postparathyroidectomy 2 months follow-up MRI of the cervical spine. (A) Pre- and (B) postparathyroid adenoma resection T2-W FSE sagittal images show appreciable interval decrease in the size of C2 vertebra lesion particularly of posterior component (*short arrows*) with improvement in the mass effect on the ventral surface of the spinal cord. (C) Corresponding pre- and (D) postresection T2-W FSE axial images depict the interval reduction in mass effect on the anterior surface of the spinal cord (*long arrows*). FSE, fast spin echo.

imaging modality. Over the years, there has been widespread use of high-end modalities such as MRI without baseline plain radiography in developing nations where the health care sector is not well structured and patients contribute to the health care needs. Hence, advanced expensive imaging is commonly ordered for investigation. Interpretation of cross-sectional imaging including MRI or computed tomography (CT) without diligent perusal and review of the accompanying conventional radiographs often masks important hints that might lead to the diagnosis of the particular bone condition. This case draws the attention of radiologists, general physicians, orthopedists, and endocrinologists, whose attention and opinion for the plain radiography and correlating radiographic features with advanced cross-sectional imaging like MRI/CT can be vital for early diagnosis of bone conditions especially metabolic bone diseases like HPT. As with timely diagnosis, treatment can be started early in the disease course that can prevent significant morbidity, which may result if left untreated.

Brown tumor is a rare benign reactive bone lesion, which occurs only in the setting of HPT due to a long-standing increase in the PTH level.¹ Usually, it is seen as a focal expansile lytic lesion and can mimic expandable lytic primary benign or malignant bone lesions when present as a single lesion and lytic metastasis or multiple myeloma when involving multiple bones in a nondiagnosed case of HPT.^{17–19} Although commonly involves the facial and mandibular bones, it can occur in any bone.^{1,7} The involvement of the spine is a very rare occurrence, and if the vertebral lesion progresses critically, it can require immediate attention and emergency surgery like decompression and/or fusion, to avert serious neurological issues.^{6,7,20} However, in the absence of neuronal compromises like without significant nerve root or spinal cord compression or cord edema, the shrinkage of tumor and regression of clinical symptoms following parathyroidectomy within weeks to months is usual.⁷ The tumor gradually begins to mineralize and demonstrates sclerosis and rapid healing once the underlying metabolic condition is corrected, provided there have been no intratumoral cystic changes.¹ Although in the present scenario, the index patient did have restricted cervical spine mobility and mild-to-moderate limb weakness owing to mild mass effect on the spinal cord, he did not undergo surgical decompression as there were no distressing compressive symptoms or intralesional cystic changes or fluid–fluid level on MRI. Gradually, the tumor regressed and stabilized leading to marked symptomatic improvement with conservative treatment after parathyroidectomy. For this reason, the complete clinico-radiological and biochemical knowledge about this rare disease and a high level of suspicion are essential to reach an early diagnosis and avoid unneeded interventions and complications.¹

Radiographically, these lesions initially present as lytic lesions of the bone with or without pathological fracture.^{1–3,17,19} When it involves the spine, it can mimic other expansile destructive lesions like myeloma, plasmacytoma, metastasis, and giant cell tumor^{1,17–19} and can cause spinal cord compression.⁷ On MRI, the dominant

hypointensity of the lesion on all pulse sequences with or without fluid–fluid level or cystic changes due to hemorrhage and hemosiderin deposition¹⁹ can simulate giant cell or aneurysmal bone tumors or solitary fibrous or fibro-osseous tumors as seen in our case. Further gradient-echo images could confirm the hemosiderin content of the lesion. However, other imaging characteristics would exclude these entities. An additional chest radiograph entirely changed the patient's diagnosis and avoided the needless challenging spinal intervention and biopsy of the C2 vertebra. Therefore, it is crucial to evaluate the available basic radiographs particularly the chest and pelvic radiographs at the time of reading MRI for the subtle important radiographic clues for the early or clinically unsuspected diagnosis of HPT. Even if the plain radiographs are not available, we should always ask them before concluding the final diagnosis of bone condition on cross-sectional imaging and if required a skeletal survey detecting other lesions like the presence of diffuse osteopenia, various resorption (subperiosteal/subchondral/trabecular/subligamentous/subtendinous/intracortical), brown tumors, and chondrocalcinosis would be of value.

Surgical biopsy is a gold standard in the diagnosis of brown tumor,¹⁹ but radiographic findings and biochemical tests, including serum PTH, calcium, phosphate, and vitamin D level, help in making the precise diagnosis of HPT^{1,19} and, upon treatment of the underlying metabolic cause (parathyroidectomy), commonly lead to spontaneous healing with mineralization (increased radiodensity) to complete disappearance of the brown tumor¹ and improved patient outcome as happened in the present case. Hence, the main treatment of these tumors is resection of parathyroid adenoma^{4,10,19} or partial or complete resection of the parathyroid gland given that the patient is neurologically sound or has mild symptoms of compression with the otherwise steady spine. In cases with opted conservative management, close supervision with regular follow-up is required to prevent any neurological complications that may result in a serious outcome.⁷ And that is what we chose for our patient, who showed progressive tremendous improvement in pain and weakness on regular follow-up visits, while he was on conservative management after resection of adenoma. Unprecedented results were obtained after 1 year with profound improvement in the overall condition.

Conclusion

This case highlights the art of plain radiography in clinching the bone condition and prompt final diagnosis even with more promising advanced high-tech imaging which otherwise could have been missed easily and subjected the patient to unwarranted spinal surgery. The quick and timely diagnosis prevents progression and catastrophic neurologic complications.

Conflict of Interest

None declared.

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