原文題目(出處)：	Clinical and radiological findings of autosomal dominant osteopetrosis type II: A case report. Case Rep Dent 2013, Article ID707343
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報告日期：	102/11/11

內文：

Introduction:

1. Osteopetrosis 又被稱為 “marble bone disease” and “Albers-Sch¨onberg disease” 具有臨床與遺傳異質性(clinically and genetically heterogeneous)，X 光片上會顯示增加的骨頭密度，骨密度增加來自於 osteoclast 分化或功能出現異常。
2. 健康的骨頭是 osteoblasts 與 osteoclast 達到穩定平衡，而功能失調的 osteoclast 會在 Osteopetrosis 中發現，使得骨頭過度生長，且異常密集且脆，而這來自於 Osteopetrosis 不釋放骨吸收所需 lysosomal enzymes 到 extracellular space。
3. Osteopetrosis 表現由不同的基因缺陷造成，至少 10 個基因突變在人類身上被確認，近來 **immune response** 已經被猜測造成 metabolic bone diseases，包括 Osteopetrosis。
4. cytotoxic Tlymphocyte-associated antigen 4 和一種新發現的免疫調節受體 programmed death-1，一直負調控免疫反應和影響 osteoclastogenesis 和 bone remodeling。

5.本病的三個臨床形式：

Autosomal	Recessive (ARO)	Dominant (ADO)	Recessive intermediate
Manifestations	Malignant infantile	Benign/adult	Similar to malignant
	Poor prognosis	Fewer symptoms	
Incidence rate	1/250,000births	1/20,000 live births	lowest

6. **Adult dominant osteopetrosis (ADO):**
   (1) Common type of osteopetrosis
   (2) Benign osteopetrosis
   (3) Approximately 40%: asymptomatic
   (4) Most of patients are diagnosed only when osteomyelitis occurs in the mandible
   (5) Marrow failure: rare
   (6) Other symptoms: bone pain, recurrent fractures, back pain, and degenerative arthritis

   a. **Subtypes: ADO type I**
   (1) Mild with a diffuse sclerosis without alterations in the bone turnover
   (2) Genetic mutations of low-density lipoprotein receptor related protein 5 gene: 骨形成增加，而不是減少骨吸收
   (3) X 光片顯示硬化的頭骨，其中主要在顱頂的厚度的增加的結果，脊椎並沒有表現出很大的硬化。Cranial nerve compression 是常見的 I 型

b. **Subtypes: ADO type II**
   (1) First type of osteopetrosis recognized and described
   (2) 75% of the cases, CLC7 gene mutation: clinical manifestations

(3) The most common form
(4) Extremely heterogeneous: from an asymptomatic to a severe phenotype
(5) Early death is rare
(6) Clinical manifestations:
1. 75 %有或無創傷的患者:由軟骨下骨(subchondral bone)引起的髖關節炎(hiposteoarthritis),面部神經麻痺(facial nerve palsy), 齲齒和膿腫造成的下頜骨骨髓炎(mandibular osteomyelitis),長骨骨折(long-bones)
2. 20%–40%: asymptomatic
3. <5% : 聽力減退，視力喪失
4. Rare: Cranial nerve compression

(7) Radiographs : dramatic skeletal alterations->容易診斷
1. Spine (vertebralend-plate thickening, or Rugger-Jersey spine)
2. Pelvis ("bone-within-bone" structures), and the cranial base.
3. Erlenmeyer-shaped femoral metaphysis and transverse bands in the long bones

Case Report:

(1) 35 歲的女病人主訴有 6-7 個月的 deposits on teeth，過去三年中後腰間歇輕微疼痛，兩側下肢有輻射痛，身體無任何外傷和骨折歷史
(2) General examination:身材矮小，身材瘦削與正常的皮膚和步態，眼瞼的結膜，指甲和手掌蒼白
(3) Etraoral examination: 眼球過距(hypertelorism), 眼球突出(exophthalmos), depressed nasal bridge, broad face, 和下顎前突(prognathic mandible)
(4) Intraoral examination: generalised gingival inflammation, generalised shallow pockets, and gingival recession with lower anterior teeth. No caries, mobility, attrition, abrasion, and so forth were noted in any of the teeth.
(5) Provisional diagnosis: chronic generalized periodontitis was made.
(6) Panoramic radiograph:早期牙周炎的跡象，具有廣泛輕度至中度周圍骨質流失，廣泛的骨密度增加，牙齒缺乏 distinct lamina dura，粗糙、密集且數目增加的 trabecular pattern 出現在 both jaws。右側下顎顯示閉塞的 inferior alveolar canal,下顎右角有 cotton wool。左側顯示出增加骨質密度，但無 cotton wool 與閉塞 inferior alveolar canal，trabecular 密集在兩側上頜骨，the zygomatic complex appeared hyper dense on both the sides, and the maxillary sinus was hypoplastic bilaterally。

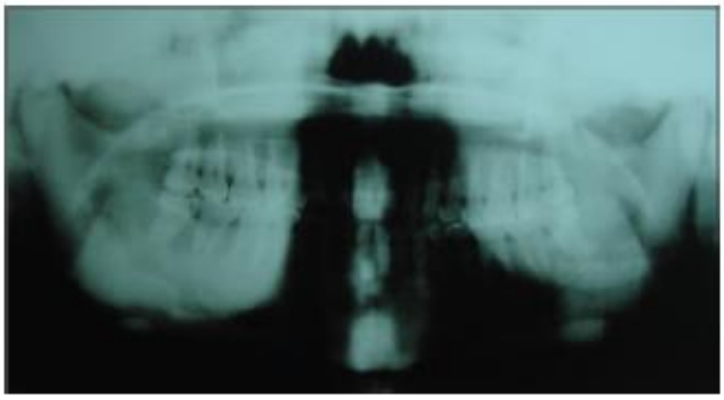

Fig.1 Panoramic radiograph showing signs of early periodontitis and sclerosis of the mandible and maxilla

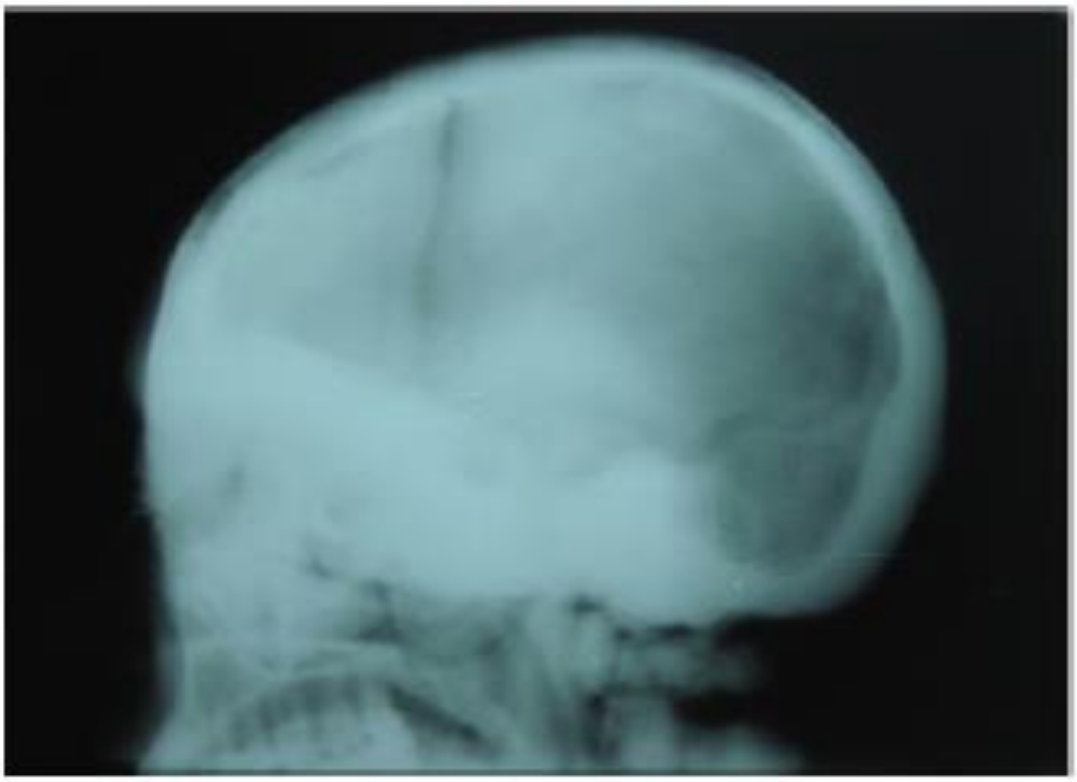

Fig. 2 Lateral skull view showing thickening of the inner and outer cortical tables and widening of the diploic space.

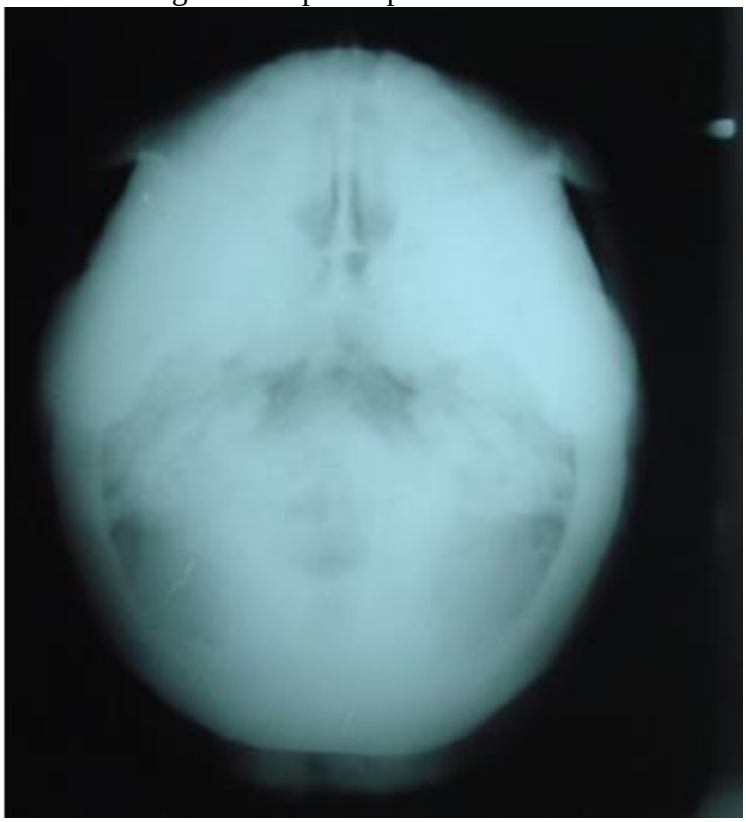

Fig. 3 顱底出現高度 radiodense 與喪失骨小樑圖案，並有枕骨大孔發育不全，及其他椎間孔消失

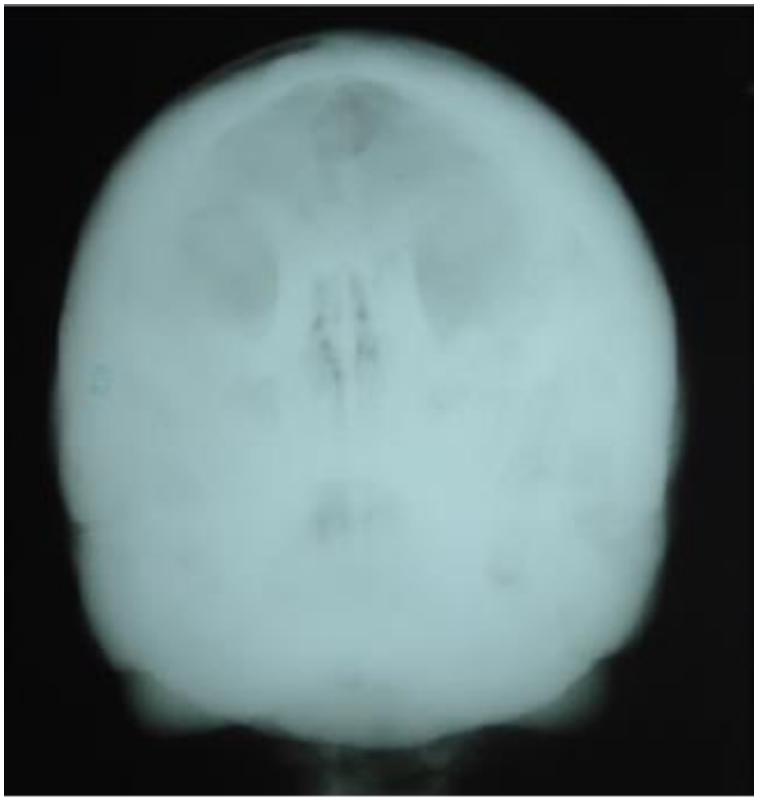

Fig. 4 鼻腔和鼻竇發育不全並顯示高度 radiodensity 區域

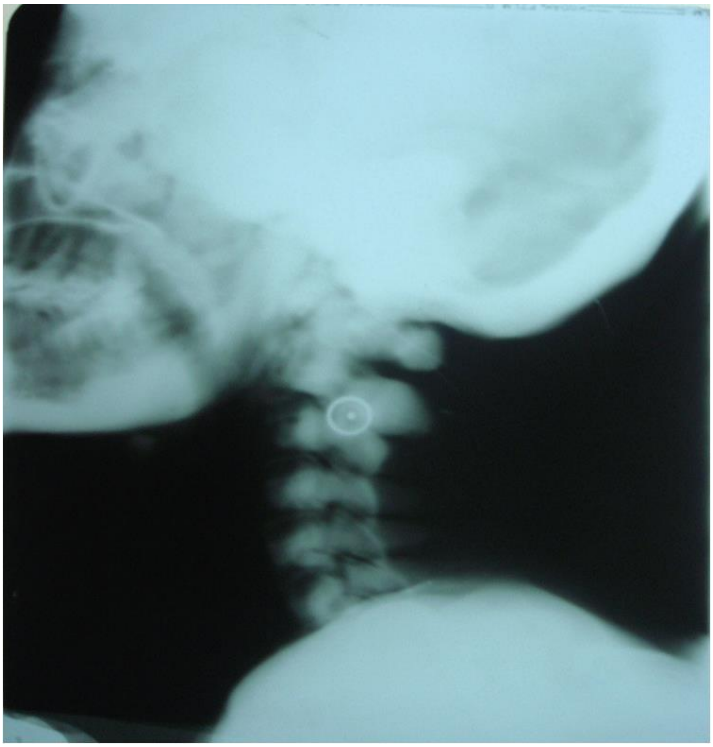

Fig. 5 頸椎的前後視圖顯示，所有的頸椎的 radiodensity 增加

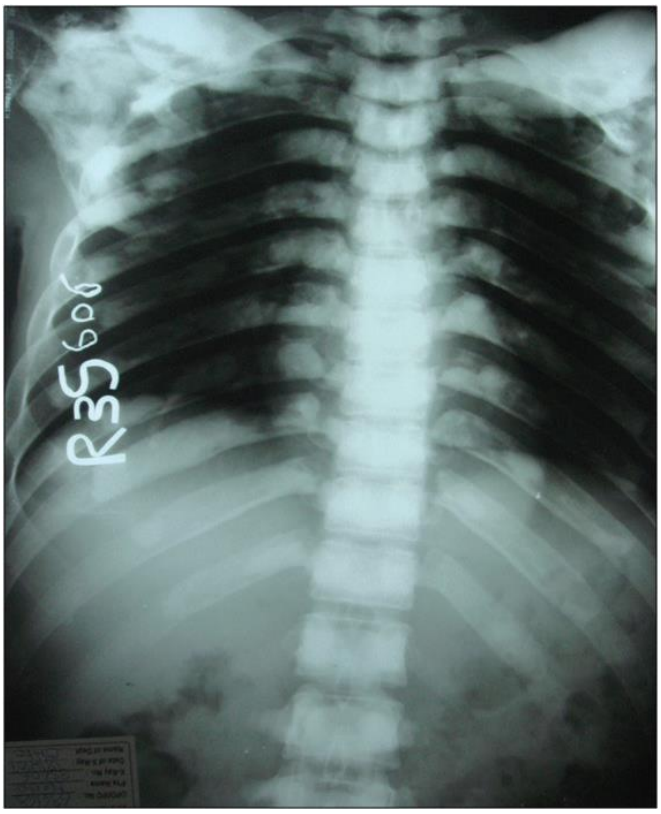

Fig. 6 胸部 PA X 光片顯示一個廣泛的增加骨密度 遍及整個胸廓和兩個鎖骨骨頭

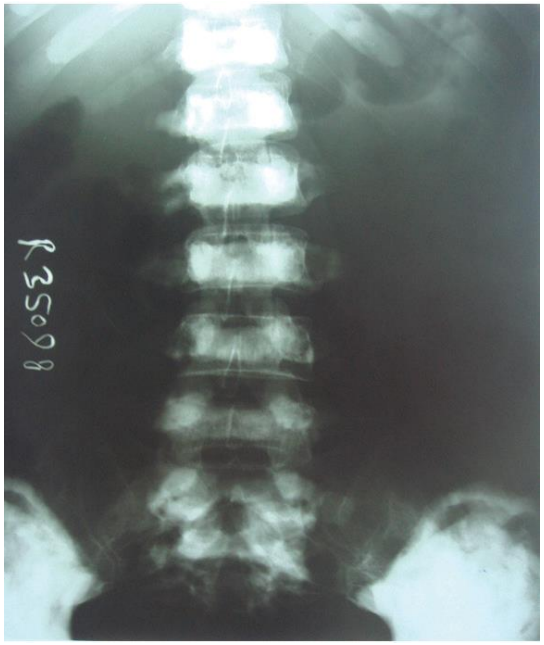

Fig. 7 Anteroposterior view lumbar spine showing sclerosis at all the levels and "bone-in-bone appearance.

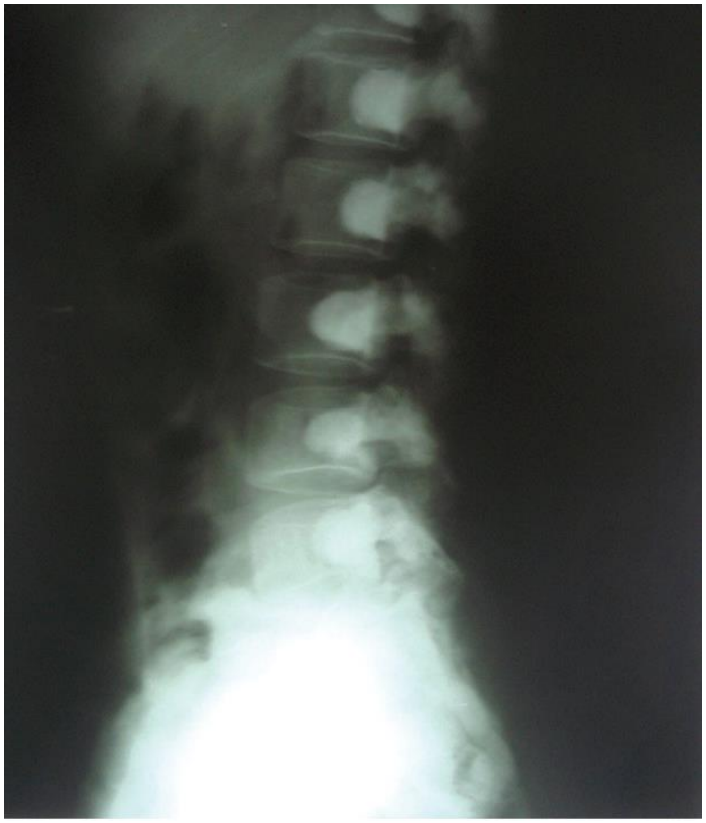

Fig. 8 ”Lateral view of the lumbar spine showing “bone-within bone appearance.”

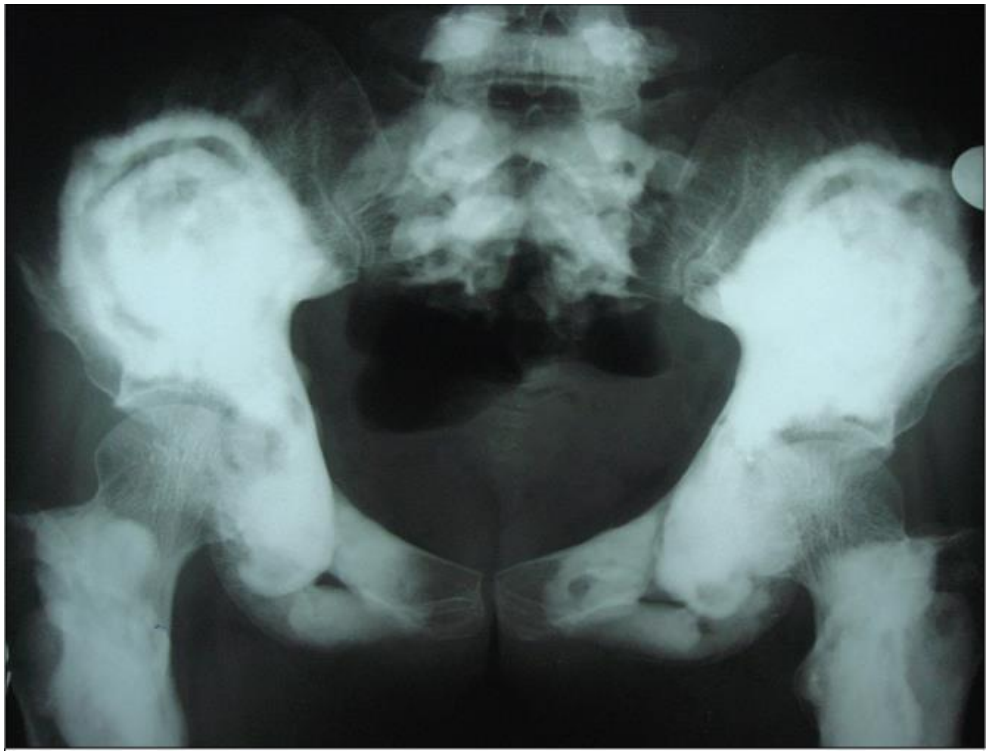

Fig. 9 Radiograph of the pelvis showed expanding osteosclerosis of the pelvic bone and the iliac wings

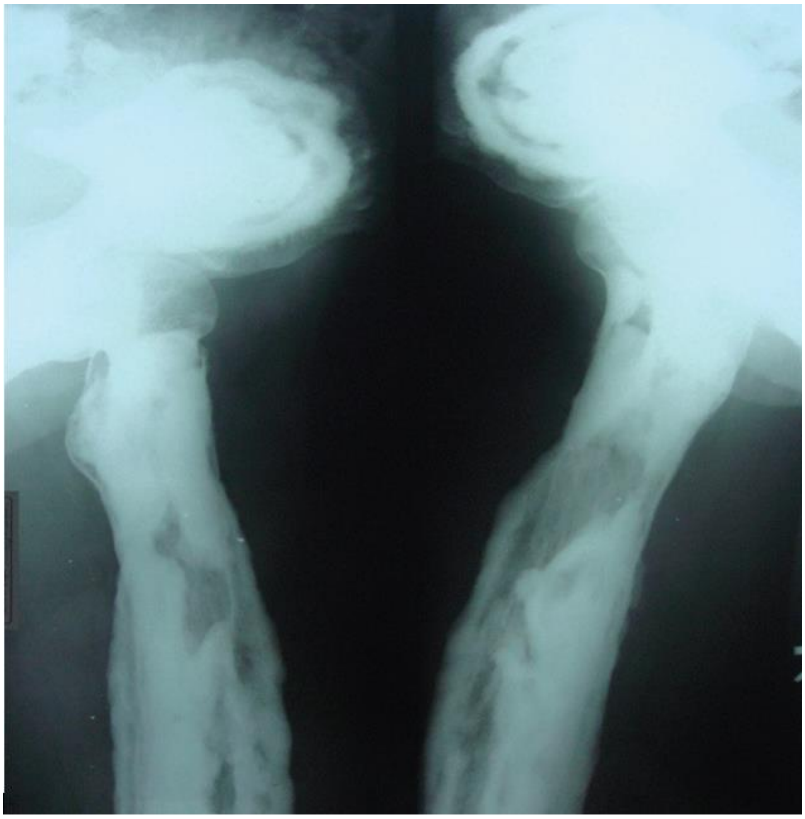

Fig. 10 髖關節呈 generalised sclerosis 的 pelvic rami 和 femur bone

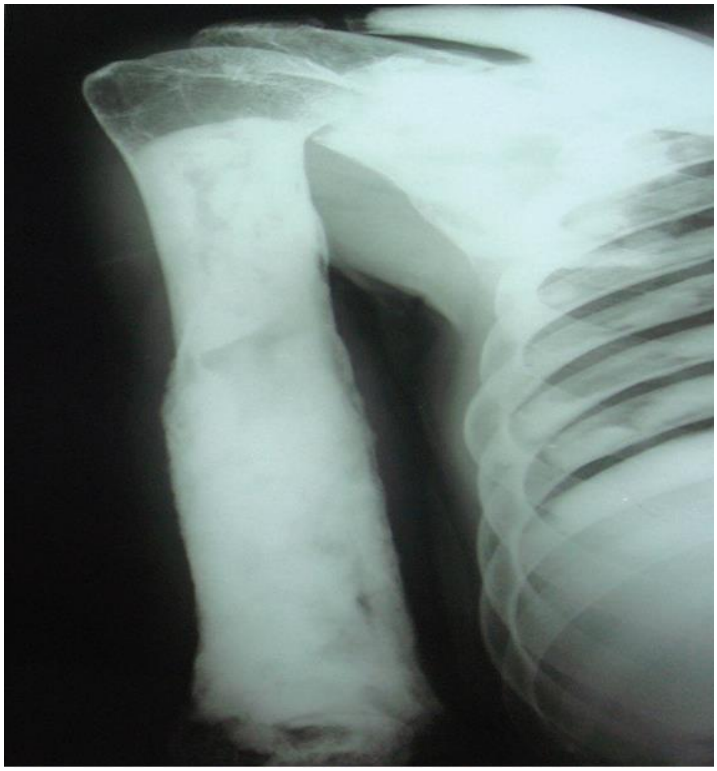

Fig. 11 緻密的硬化的肱骨(humerus)和肩胛骨 (scapula) “funnel-like appearance”的肱骨

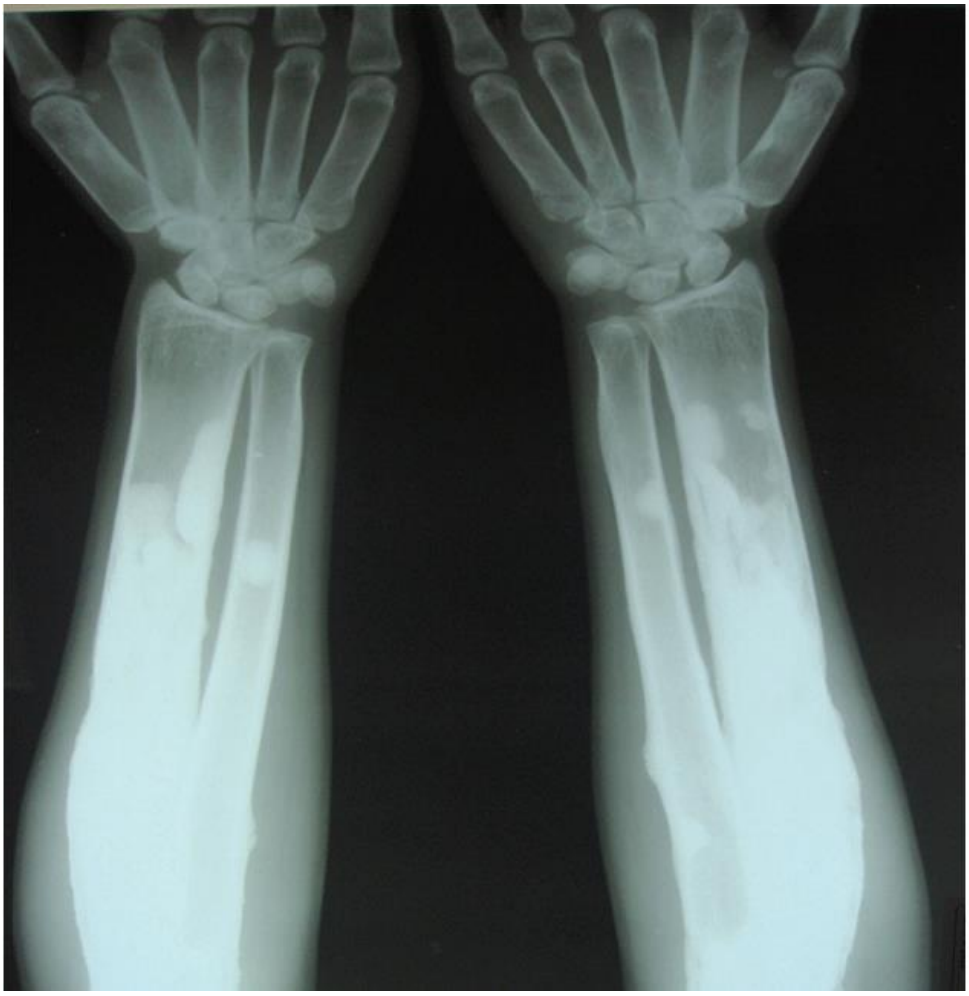

Fig. 12 AP view radius and ulna showing increased radiodensity in all the bones, smoothening of the bone surfaces, and cylindrical appearance of the metacarpals

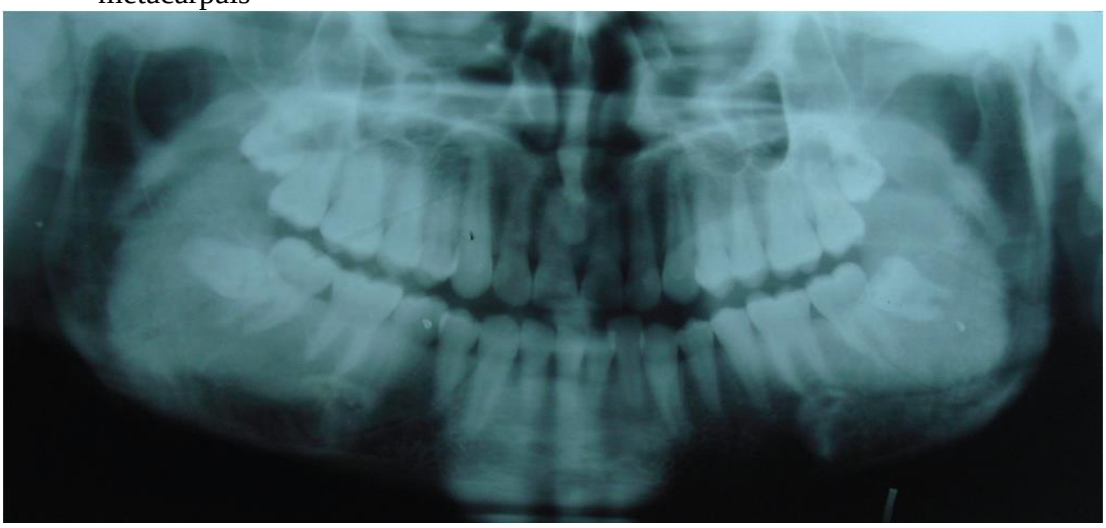

Fig. 13 Panoramic radiograph of the patient's brother

(7) Hematologic investigations: Hb、white blood、platelet count 均正常；Peripheral smear showed normocytic and Normochromic anemia. Red cell indices and iron profile were normal.腎功能和血清電解質在正常範圍內，肝功能檢查均正常。

(8) Final diagnosis : autosomal dominant osteopetrosis type II
(9) Treatment:
➀Supragingival, subgingival scaling, and root planning，每日兩次 0.2% chlorhexidine，局部塗氟
➁ Lower back pain:使用肌肉鬆弛劑
(10) f/u (6 months):病人沒有顯示骨折和骨髓炎影響任何骨頭，沒有任何跡象顱神經牽連，無齲齒和膿腫。

Discussion:

ADO type II:

(1) 77.8%患者有 ClCN7 mutation (Del Fattore et al.)
(2) Most common form of osteopetrosis (1 in 20,000 births.)
(3) Onset: late childhood or adolescence
(4) Gender incidence : male: 55% female:45% (Del Fattore et al.)
Male >female (Waguespack et al.)
(5) Most individuals diagnosed :have an affected parent
(6) Extremely heterogeneous course ranging from an asymptomatic to a severe phenotype
(7) Clinical manifestations: ➀ Main:long-bone fractures
➁ Other : Hip osteoarthritis, scoliosis, andosteomyelitis, particularly affecting the mandible.
➂ Rare: Cranial nerve compression
➃ 40% :diffuse pain(Del Fattore et al)
➄ Fracture: 20%≤3 bones ；10%4–10 bones；15%>10 bones
(8) 最常見的臨床特徵為骨折:
➀ 佔了報告中的 84% (Waguespack et al)
➁ Femur and ribs being the most common (76%)(B´enichou et al)
➂ 62%骨折率(femur most common)(El-Tawil AndStoker)
➃ 67%的骨折最常見於闌尾骨架(Bollerslev and Andersen Jr.)
(9) 視覺障礙和牽涉中樞神經系統是罕見的:19 %的患者有嚴重視力喪失(Waguespack et al)；5%的患者有視力喪失(B´enichou et al)

	This case	ADO type II
Gene	Unclear	Parent
Gender	Female	Male > Female
Fracture	no history of fractures reported in any of the bones	62%-84% fracture
Visual loss	no signs of visual loss and central nervous system involvement	5% (B´enichou et al) 19%(Waguespack et al)
Osteomyelitis	No signs and symptoms of osteomyelitis	11% (B´enichou et al) 13% affecting either the maxilla and or mandible (Waguespack et al)
Other clinical manifestations	Early periodontitis with generalized gingival inflammation, shallow pockets, and gingival recession	disturbance of tooth eruption, hypodontia, malformed teeth, multiple caries, enamel dysplasia, abnormal pulp chambers, and hypercementosis

Radiographs	1. Generalised increase in the bone density 2. Lack of distinct lamina dura, and absence of normal trabecular pattern involving both jaws, obliteration of the inferior alveolar nerve canal, cotton wool 3. Appearance on the right side of the mandible, and bilateral hypoplasia of the maxillary sinus.	1. A generalized increase in radio density of the maxilla and mandible 2. Abnormal trabecular pattern and diminished marrow spaces, constriction of the inferior alveolar nerve canal, and dental pulp canal as well as thickening of the lamina dura 3. Maxillary sinuses also appear hypoplastic
	Our patient had hallmark diffuse sclerosis, affecting the skull, spine, pelvis, and appendicular bones; bone modelling defects at the metaphyses of long bones, such as funnel-like appearance ("Erlenmeyer-flask" deformity), and characteristic lucent bands; **"bone-within-bone"** appearance in the vertebrae	1. Osteosclerosis of the spine predominates, with a "sandwich vertebra" appearance. 2. Most individuals have a **"bone-within-bone"** appearance primarily in the iliac wings, but also in other bones. 3. Transverse bands of sclerosis, perpendicular to the main axis, are often observed in long bones. 4. Increase in the skull base density can also be seen
Differential diagnosis		Sclerosing bone dysplasias, such as pycnodysostosis, craniometaphyseal dysplasia, diaphyseal dysplasia, melorheostosis, osteopoikilosis, and osteopathiastriata. Fluoride poisoning and secondary hyperparathyroidism from renal osteodystrophy also may produce a diffuse osteosclerosis
Hematological system	Our patient hemoglobin was 10.8 g/dL, and white blood cell count and platelet count were in the normal range. Peripheral smear showed normocytic normochromic anemia. Other investigations, that is, renal function test, liver function test, ESR, serumcalcium, and serumphosphorus,were also within the normal limit	Bone marrow function in benign osteopetrosis is not compromised, and the hematological findings are often normal

(10) 骨折和關節炎是常見的，可由經驗豐富的骨科治療外科醫生治療，但由於骨骼的脆性，會相對頻繁發生的繼發性併發症例如延遲癒合或不癒合骨折，骨髓炎。例行的維持口腔清潔可預防骨髓炎，而因為會有明顯的感染風險，biopsy 必

須避免，目前，還沒有有效的治療骨症存在。如果發生骨髓炎，必須考慮手術，因為抗生素不會達到損害區域。

Conclusion

良性骨硬化症是一種罕見的疾病，可能臨床無症狀.適當的臨床和影像學的調查是不可少的準確的診斷。牙科問題，像牙齒 delayed tooth, eruption, ankylosis, abscesses, cysts, and fistulas 是常見的在良性骨硬化症患者。因為骨密度增加閉塞的下牙槽神經管和牙髓管和硬腦膜層增厚，這種情況經常出現在牙科 X 光片。由於高感染風險和增加易感性在頜骨骨折患者中，他們應該得到更多的重視和預防。

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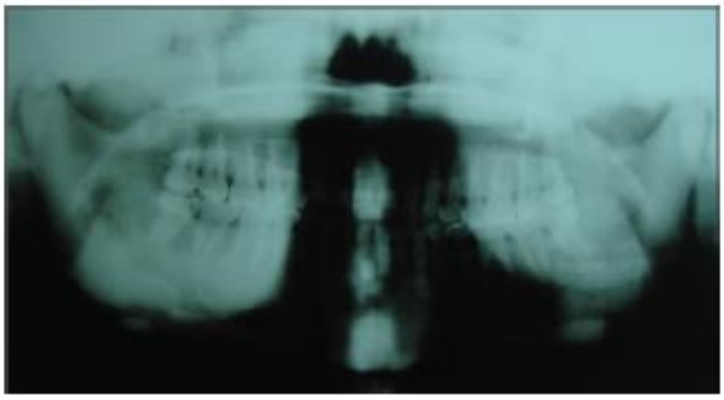

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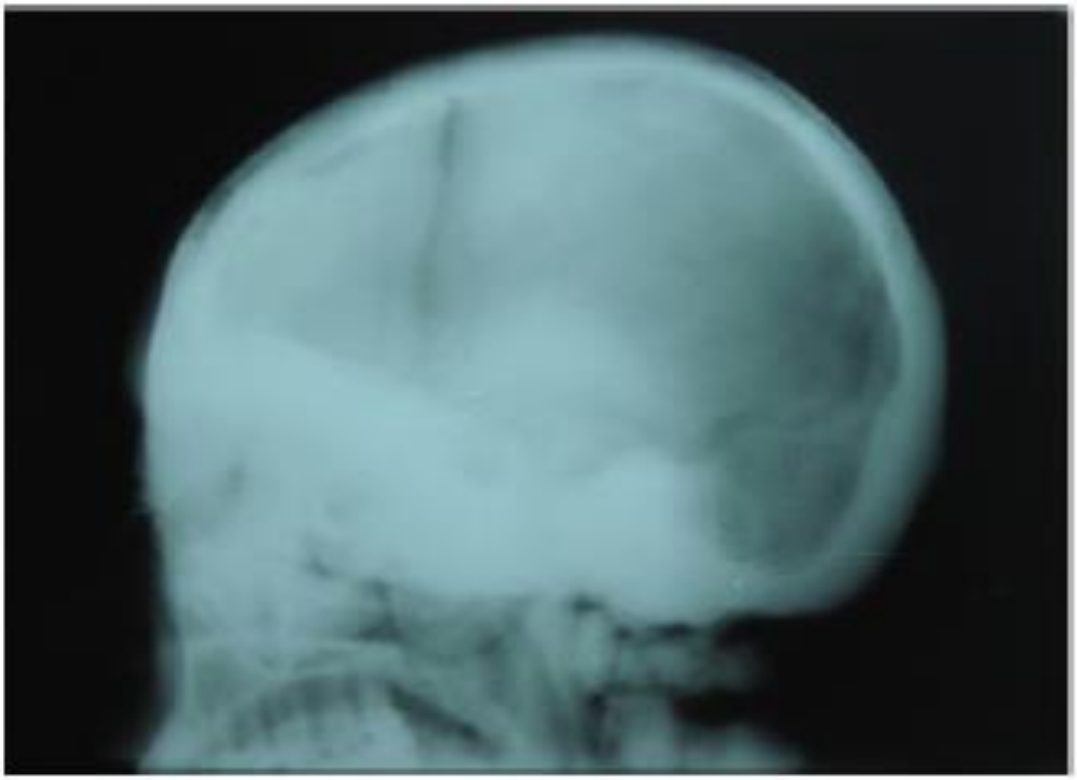

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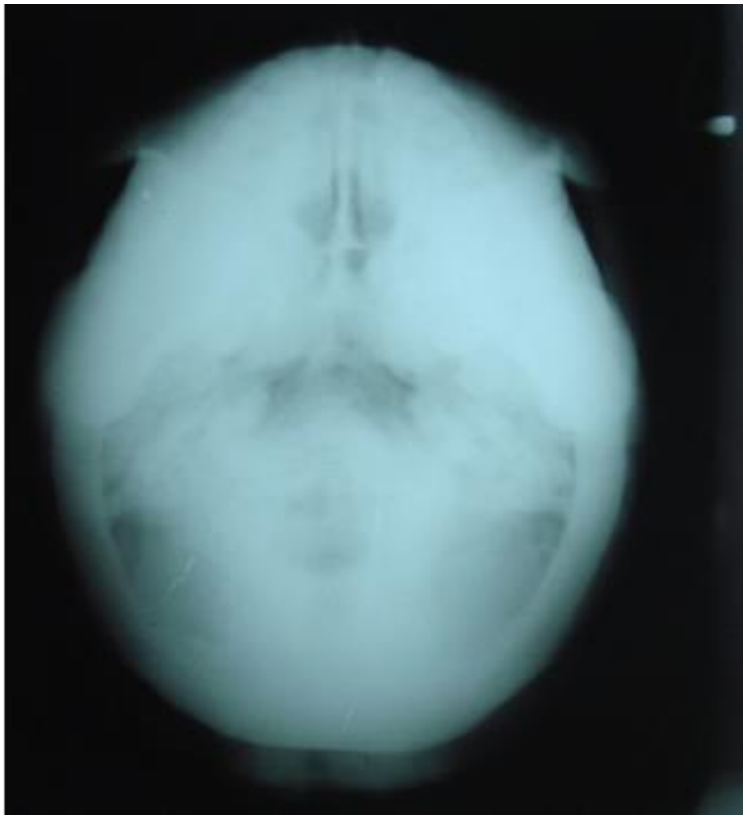

Fig. 3 顱底出現高度 radiodense 與喪失骨小樑圖案，並有枕骨大孔發育不全，及其他椎間孔消失

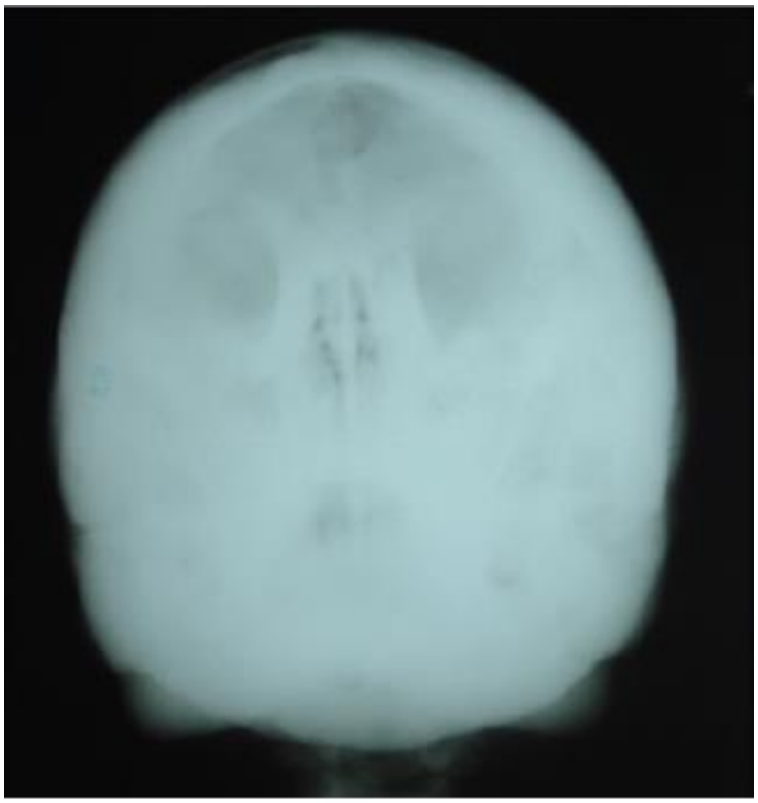

Fig. 4 鼻腔和鼻竇發育不全並顯示高度 radiodensity 區域

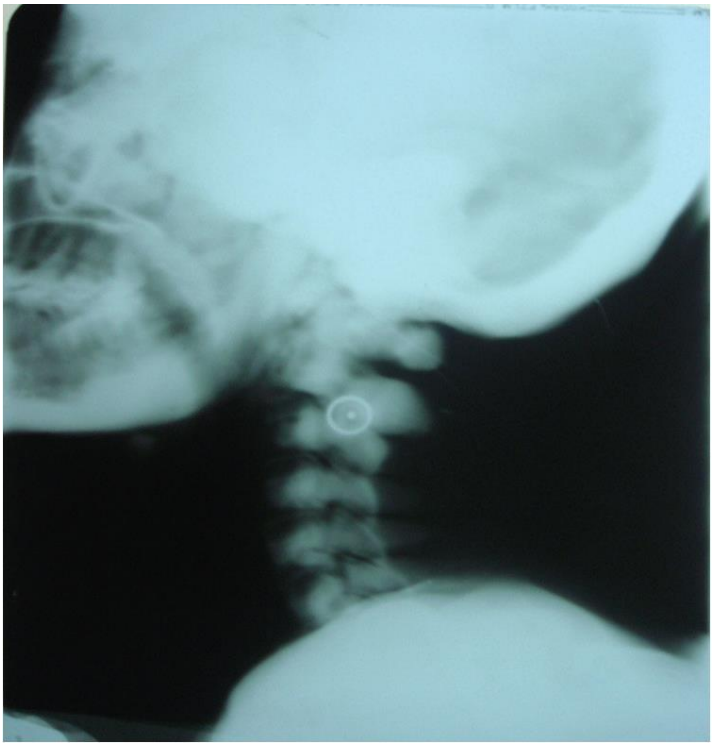

Fig. 5 頸椎的前後視圖顯示，所有的頸椎的 radiodensity 增加

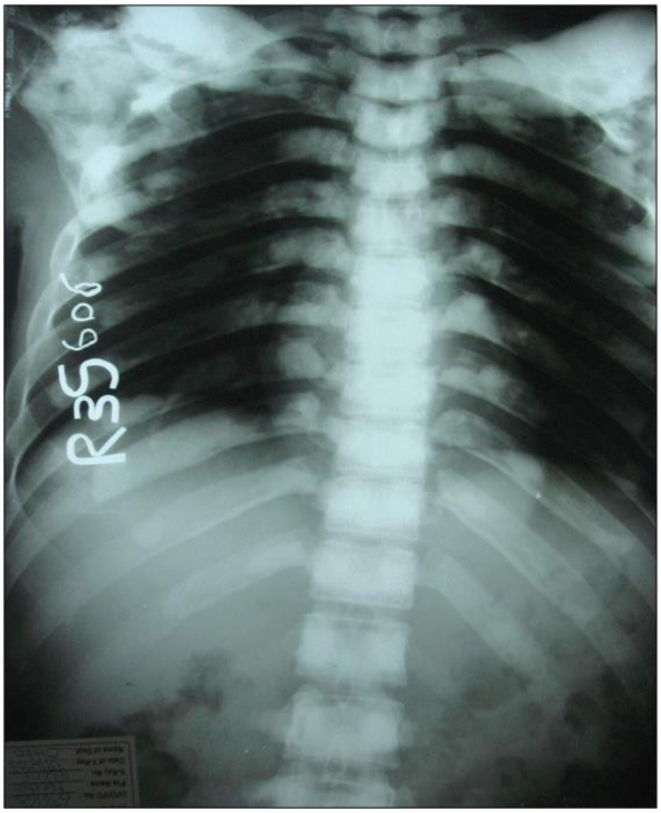

Fig. 6 胸部 PA X 光片顯示一個廣泛的增加骨密度 遍及整個胸廓和兩個鎖骨骨頭

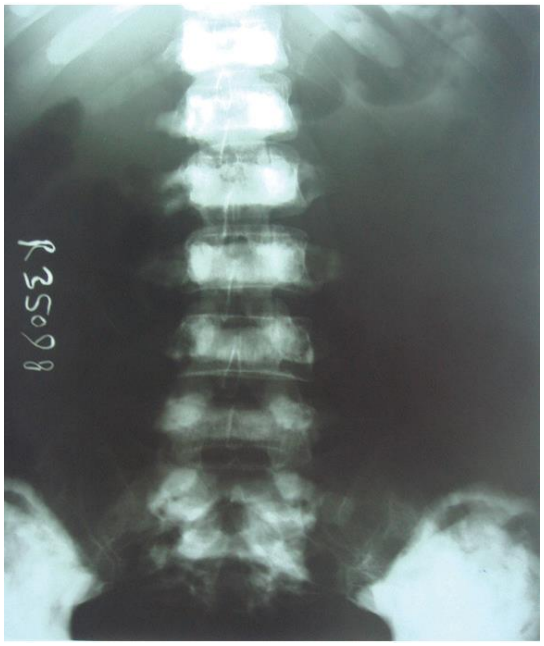

Fig. 7 Anteroposterior view lumbar spine showing sclerosis at all the levels and "bone-in-bone appearance.

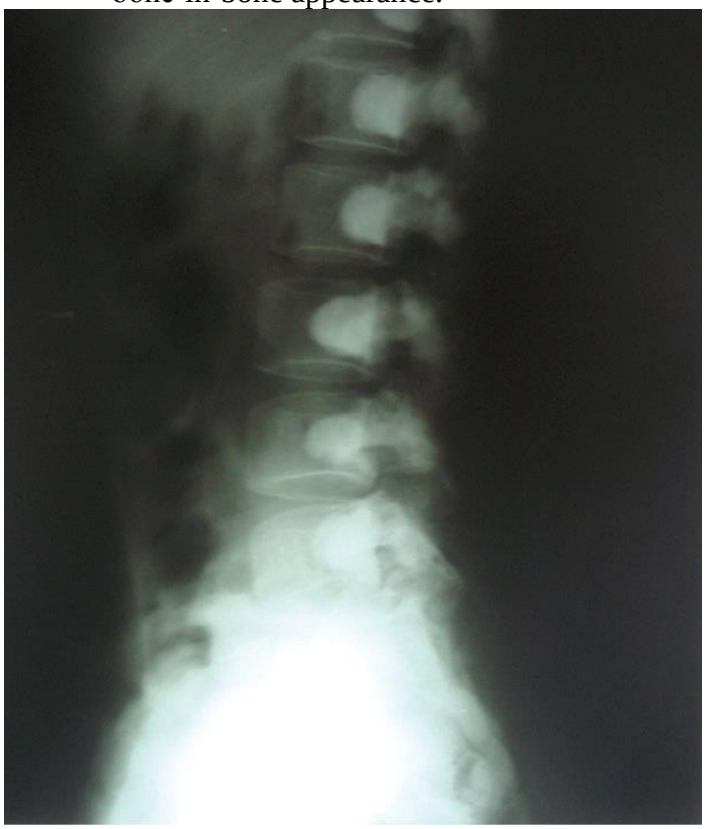

Fig. 8 "Lateral view of the lumbar spine showing "bone-within bone appearance."

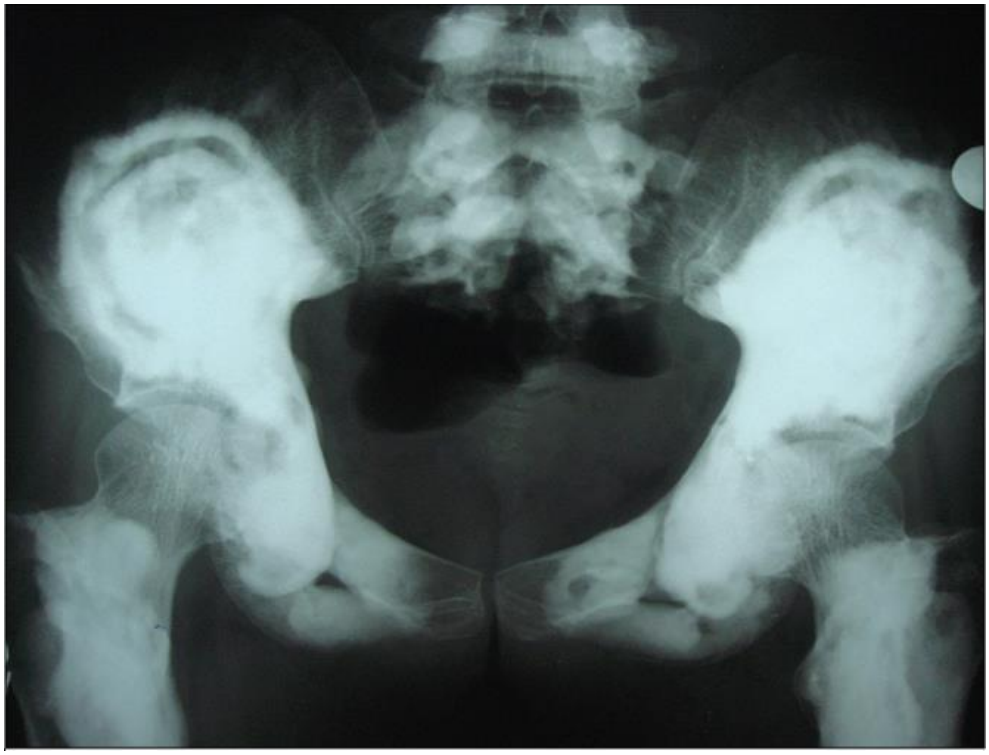

Fig. 9 Radiograph of the pelvis showed expanding osteosclerosis of the pelvic bone and the iliac wings

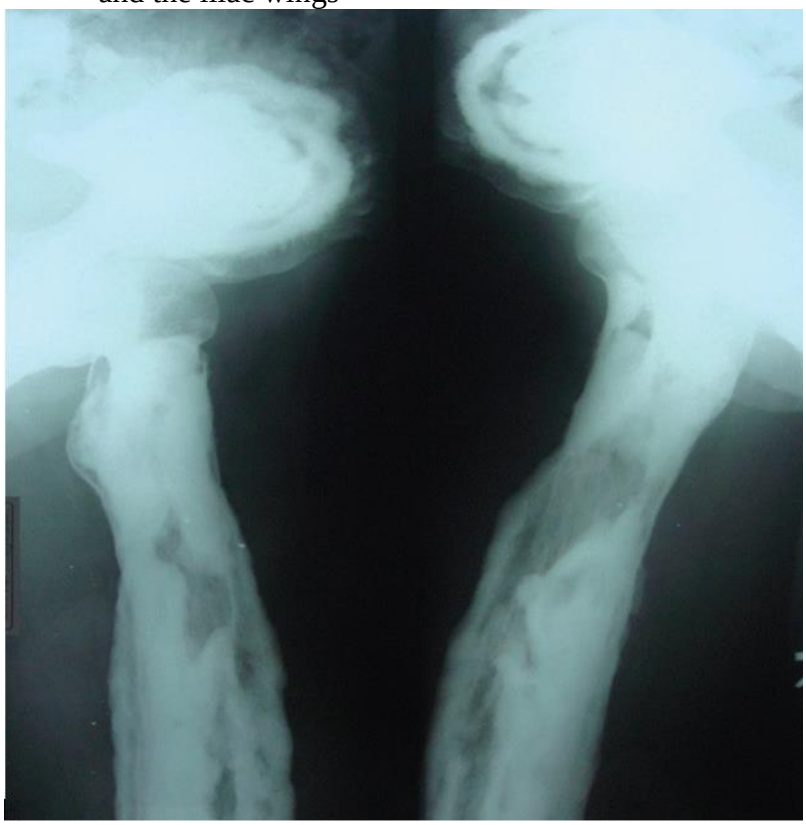

Fig. 10 髖關節呈 generalised sclerosis 的 pelvic rami 和 femur bone

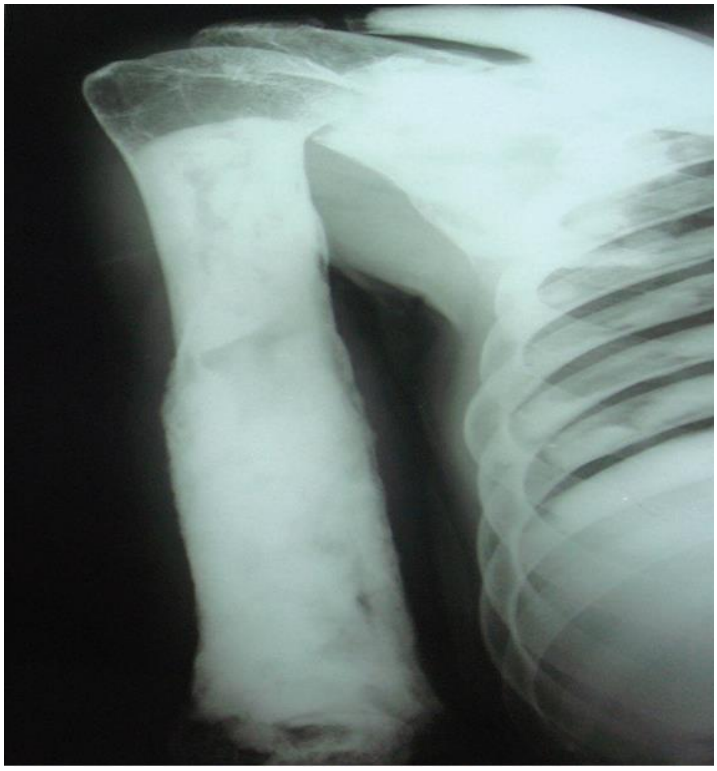

Fig. 11 緻密的硬化的肱骨(humerus)和肩胛骨 (scapula) “funnel-like appearance”的肱骨

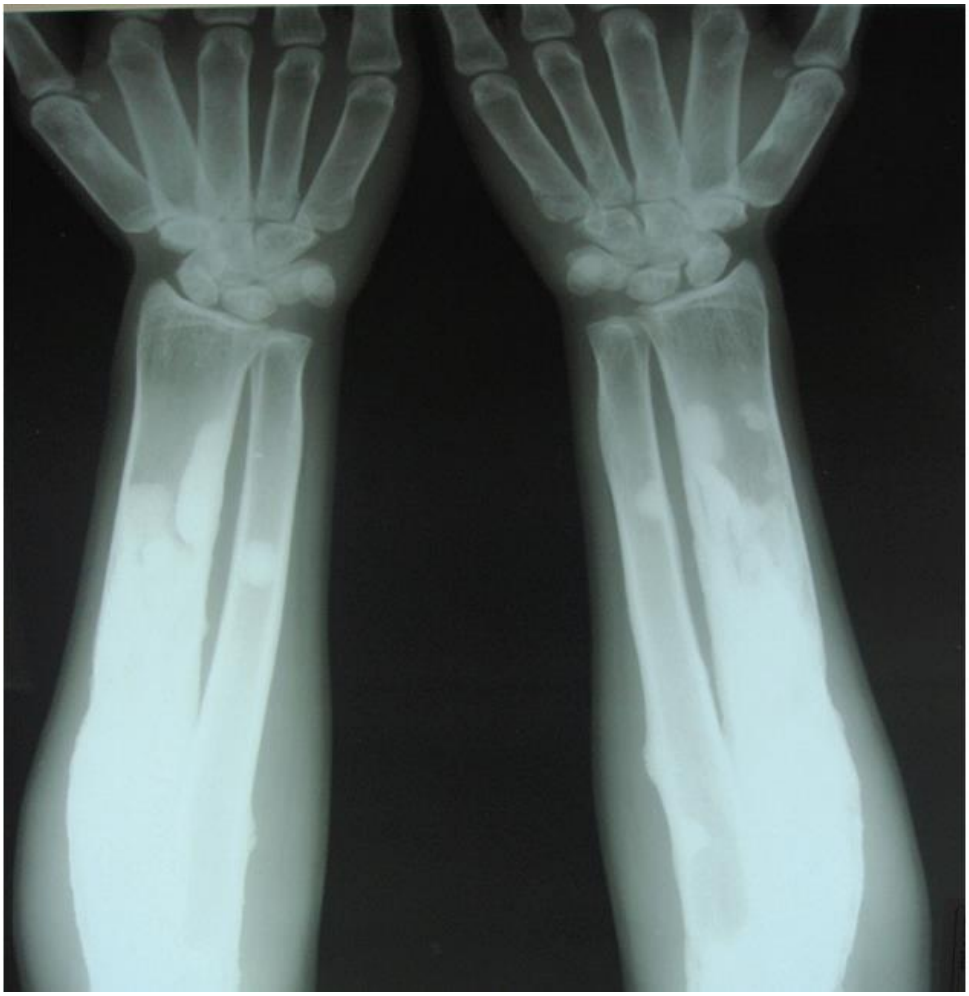

Fig. 12 AP view radius and ulna showing increased radiodensity in all the bones, smoothening of the bone surfaces, and cylindrical appearance of the metacarpals

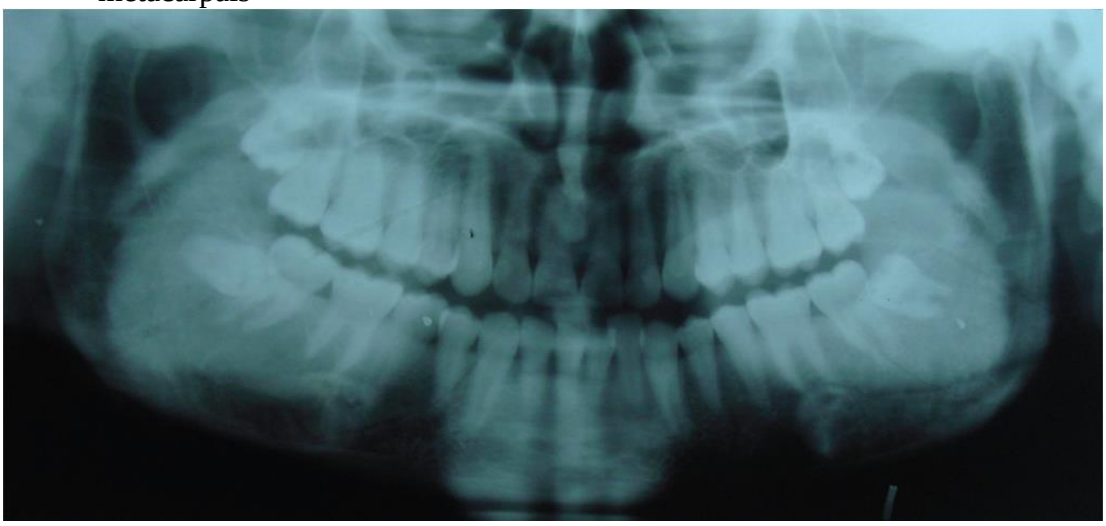

Fig. 13 Panoramic radiograph of the patient's brother

(7) Hematologic investigations: Hb、white blood、platelet count 均正常；Peripheral smear showed normocytic and Normochromic anemia. Red cell indices and iron profile were normal.腎功能和血清電解質在正常範圍內，肝功能檢查均正常。

(8) Final diagnosis : autosomal dominant osteopetrosis type II

(9) Treatment:

➀Supragingival, subgingival scaling, and root planning，每日兩次 0.2% chlorhexidine，局部塗氟

➁ Lower back pain:使用肌肉鬆弛劑

(10) f/u (6 months):病人沒有顯示骨折和骨髓炎影響任何骨頭，沒有任何跡象顱神經牽連，無齲齒和膿腫。

Discussion:

ADO type II:

(1) 77.8%患者有 ClCN7 mutation (Del Fattore et al.)
(2) Most common form of osteopetrosis (1 in 20,000 births.)
(3) Onset: late childhood or adolescence
(4) Gender incidence : male: 55% female:45% (Del Fattore et al.)
Male >female (Waguespack et al.)
(5) Most individuals diagnosed :have an affected parent
(6) Extremely heterogeneous course ranging from an asymptomatic to a severe phenotype
(7) Clinical manifestations: ➀ Main:long-bone fractures
➁ Other : Hip osteoarthritis, scoliosis, andosteomyelitis, particularly affecting the mandible.
➂ Rare: Cranial nerve compression
➃ 40% :diffuse pain(Del Fattore et al)
➄ Fracture: 20%≤3 bones ；10%4–10 bones；15%>10 bones
(8) 最常見的臨床特徵為骨折:

1. 佔了報告中的 84% (Waguespack et al)
2. Femur and ribs being the most common (76%)(B´enichou et al)
3. 62%骨折率(femur most common)(El-Tawil AndStoker)
4. 67%的骨折最常見於闌尾骨架(Bollerslev and Andersen Jr.)

(9) 視覺障礙和牽涉中樞神經系統是罕見的:19 %的患者有嚴重視力喪失(Waguespack et al)；5%的患者有視力喪失(B´enichou et al)

	This case	ADO type II
Gene	Unclear	Parent
Gender	Female	Male > Female
Fracture	no history of fractures reported in any of the bones	62%-84% fracture
Visual loss	no signs of visual loss and central nervous system involvement	5% (B´enichou et al) 19%(Waguespack et al)
Osteomyelitis	No signs and symptoms of osteomyelitis	11% (B´enichou et al) 13% affecting either the maxilla and or mandible (Waguespack et al)
Other clinical manifestations	Early periodontitis with generalized gingival inflammation, shallow pockets, and gingival recession	disturbance of tooth eruption, hypodontia, malformed teeth, multiple caries, enamel dysplasia, abnormal pulp chambers, and hypercementosis
Radiographs	1. Generalised increase in the bone density 2. Lack of distinct lamina dura, and absence of normal trabecular pattern involving both jaws, obliteration of the inferior alveolar nerve canal, cotton wool 3. Appearance on the right side of the mandible, and bilateral hypoplasia of the maxillary sinus.	1. A generalized increase in radio density of the maxilla and mandible 2. Abnormal trabecular pattern and diminished marrow spaces, constriction of the inferior alveolar nerve canal, and dental pulp canal as well as thickening of the lamina dura 3. Maxillary sinuses also appear hypoplastic
	Our patient had hallmark diffuse sclerosis, affecting the skull, spine, pelvis, and appendicular bones; bone modelling defects at the metaphyses of long bones, such as funnel-like appearance ("Erlenmeyer-flask" deformity), and characteristic lucent bands; **"bone-within-bone"** appearance in the vertebrae	1. Osteosclerosis of the spine predominates, with a "sandwich vertebra" appearance. 2. Most individuals have a **"bone-within-bone"** appearance primarily in the iliac wings, but also in other bones. 3. Transverse bands of sclerosis, perpendicular to the main axis, are often observed in long bones. 4. Increase in the skull base density can also be seen
Differential diagnosis		Sclerosing bone dysplasias, such as pycnodysostosis,

		craniometaphyseal dysplasia, diaphyseal dysplasia, melorheostosis, osteopoikilosis, and osteopathiastriata. Fluoride poisoning and secondary hyperparathyroidism from renal osteodystrophy also may produce a diffuse osteosclerosis
Hematological system	Our patient hemoglobin was 10.8 g/dL, and white blood cell count and platelet count were in the normal range. Peripheral smear showed normocytic normochromic anemia. Other investigations, that is, renal function test, liver function test, ESR, serumcalcium, and serumphosphorus,were also within the normal limit	Bone marrow function in benign osteopetrosis is not compromised, and the hematological findings are often normal

(10) 骨折和關節炎是常見的，可由經驗豐富的骨科治療外科醫生治療，但由於骨骼的脆性，會相對頻繁發生的繼發性併發症例如延遲癒合或不癒合骨折，骨髓炎。例行的維持口腔清潔可預防骨髓炎，而因為會有明顯的感染風險，biopsy 必須避免，目前，還沒有有效的治療骨症存在。如果發生骨髓炎，必須考慮手術，因為抗生素不會達到損害區域。

Conclusion

良性骨硬化症是一種罕見的疾病，可能臨床無症狀.適當的臨床和影像學的調查是不可少的準確的診斷。牙科問題，像牙齒 delayed tooth, eruption, ankylosis, abscesses, cysts, and fistulas 是常見的在良性骨硬化症患者。因為骨密度增加閉塞的下牙槽神經管和牙髓管和硬腦膜層增厚，這種情況經常出現在牙科 X 光片。由於高感染風險和增加易感性在頜骨骨折患者中，他們應該得到更多的重視和預防。