Med. J. Malaysia Vol XXX No. 2. Dec. 1975

Nasopharyngeal Carcinoma with Hypertrophic Pulmonary Osteoarthropathy

By: KENNETH CHIN (M.B.B.S.) and CHANG HAM LOONG (M.B.B.S.)
(Medical Unit II, General Hospital, Kuala Lumpur.)

INTRODUCTION

Hypertrophic osteoarthropathy or "Marie-Bamberger disease" was first described by Eugen von Bamberger in 1889 and then by Pierre Marie in 1890. It is a syndrome consisting of:

(a) non-pitting swelling of the tissues over the ends of long bones (this swelling is usually warm and tender to touch);

(b) clubbing of digits; and

(c) the radiographic appearance of periosteal new-bone formation beginning at the distal ends of long bones (Holling 1961).

Hypertrophic osteoarthropathy is most commonly seen in lung disorders such as carcinoma of the lung, bronchiectasis, chronic lung abscess, empyema and even in fibroma (Price Thomas and Drew 1953) and arteriovenous fistula (Adams, et al 1954). It is less commonly seen in extra pulmonary disorders such as liver cirrhosis (Pugh, 1954) leukaemia (Temple et al 1948) carcinoma of stomach (Singh, et al 1960) carcinoma of esophagus (Cayle et al 1962) myxoedema, polyposis and others. At the present time, bronchogenic carcinoma is considered to be the commonest cause of hypertrophic osteoarthropathy. According to Aufses and Aufses (1960) 0.73% of patients with bronchogenic carcinoma develop osteoarthropathy. However others quote an incidence of as high as 10% (Semple and McCluskie, 1955; Flavell 1956).

The gross pathologic process in osteoarthropathy is essentially one of proliferative subperiosteal osteitis surrounding the shaft of the bone. The long bones (tibia, fibula, radius, ulna, femur and humerus) are the bones primarily involved. However, in advanced cases, the clavicle, rib, scapula and vertebrae may be involved (Ray and Fischer, 1953).

There is proliferation of both the soft tissues and of bones. The periosteum is infiltrated by lymphocytes, plasma cells and leucocytes and as such becomes considerably thickened. Osteoid matrix is formed from the periosteum which develops into a layer of new bone. These changes can usually be demonstrated by X rays.

The new subperiosteal bone formation is from 1 to 5 mm thick in most instances and has a thin cortex surrounding the new cancellous bone. The new bone is soft and very vascular, and can be easily stripped from the old cortex.

Gall, Bennett and Bauer (1951) showed that the distal third of the long bones are involved initally, with progression toward the proximal portions of these bones. Later they found involvement of the shafts of the metacarpals and metatarsals. They also noted that the periosteal changes were greater on the dorsal and medial surfaces.

Various theories have been put forward to account for the association of a lesion in the thorax with a disorder of the limbs in hypertrophic pulmonary osteoarthropathy. These fall mainly into 2 broad categories: neurogenic and humoral. The neurogenic theory suggests that the syndrome is produced by a reflex mechanism with afferent impulses carried from the chest by the vagus producing increased blood flow to the affected regions. This theory has been supported by the observation that vagotomy may lead to prompt

regression of the limb swelling and the pain (Flavell 1956). Various pulmonary vascular shunts – arteriovenous (Hall 1959), venoarterial (Doyle 1959) – have been described in cases with clubbed fingers, and sometimes with osteoarthropathy, but the significance is not well understood.

CASE REPORT

A 45 year old chinese woman was seen in the General Hospital, Kuala Lumpur on 20/8/74 with the chief complaint of breathlessness on exertion for 1 week. She was apparently well till 1 year ago when she developed a vague pricking pain over both her knees which later spread to both her shins and ankles.

Subsequently both her ankles became swollen, red and were tender to touch. Two months later the distal parts of both the forearms became swollen, reddish and tender. Her finger tips then progressively became swollen and her nails beaked. There were no swelling of the toes. At about the same time she developed a low grade intermittent fever associated with occasional chills but no rigors or sweating. She was seen by several general practitioners with no improvement.

One week before admission she developed breathlessness of mild exertion. There was no cough or hemoptysis; no paroxysmal nocturnal dyspnea or chest pain. Her effort tolerance was about 100 yards on a flat ground and one flight of stairs. She neither smokes cigarettes nor drinks alcohol. She lost about 10 lbs. over the past 1 year. There was no history of rash over the face or body; no history of tinnitus, epistaxis or blocked nose.

Five years ago, she had nasal obstruction, epistaxis and tinnitus. Biopsy of her post nasal space showed a poorly differentiated infiltrating squamous cell carcinoma. She was given a course of radiotherapy to the nasopharynx and she had no complaints for 4 years after that.

On examination she was febrile (100°F), thin and anaemic. There were gross clubbing of all the fingers but no clubbing of toes. There was no rash on the face or the body. No jaundice was seen.

The distal third of both forearms were warm, swollen, reddish and very tender with mild limitation of movement of both wrist joints. Similarly the distal third of both legs were swollen, warm and tender with slight limitation of movement of both ankle joints. Both the knee joints were warm and swollen and a mild effusion was present in each joint.

A massive left pleural effusion was detected in the lungs while there was no abnormality detected in the cardiovascular system. There was hepatosplenomegaly: the liver being enlarged to 5 cm below the costal margin, smooth, firm, non tender and nonpulsatile. The spleen was enlarged to 3 cm below the costal margin, smooth, firm, and non-tender. There were no cervical or axillary lymph nodes palpable but the inguinal nodes were bilaterally enlarged, firm and nontender.

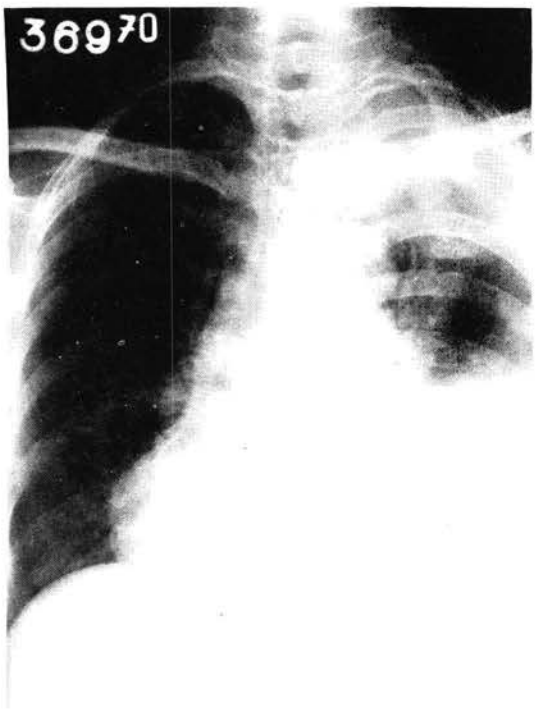
No neurological deficit was detected. There was no tenderness along the vertebral column. Vaginal examination was normal. Postnasal space examination showed an area of necrotic tissue over the roof of the post nasal space – especially on the left side. No growth was seen.

INVESTIGATIONS

The results of the investigations were as follows:-

(A) BLOOD:	Haemoglobin	–	6.0 gm/100 ml
	TWBC	–	10300 cells/cu. mm.
	Neutroplils	–	92%
	Lymphocyte	–	6%
	Monocyte	–	2%
	Platelet count	–	150,000 cells/cu. mm.
	ESR	–	125 mm/HR
	Full Blood Picture	–	showed an macrocytic and iron deficiency anaemia

	Bone Marrow puncture	–	Iron deficiency anaemia
	L.E. cells	–	negative (3X)
	Rheumatoid factor	–	negative
	Australian antigen	–	negative
(B)	RADIOLOGY Chest x ray	–	showed a massive left pleural effusion with multiple secondaries in both lungs; especially in the left upper zone as shown in Figures *1a, 1b* and 1c.
	x ray of distal 1/3 of both forearms	–	showed periosteal thickening in both the distal 1/3 of the ulna and radius consistent with hypertrophic osteoarthropathy as shown in figures 2a and 2b.
	x ray of distal 1/3 of both legs	–	showed periosteal thickening of both tibia as shown in Figure 3.
	x ray of both knee joints	–	showed a mild effusion.
	skeletal survey	–	showed no secondaries in the skeletal system.
	liver scan	–	showed an enlarged liver with irregular pick up areas. There was moderate splenomegaly. A querry of liver cirrhosis was made.



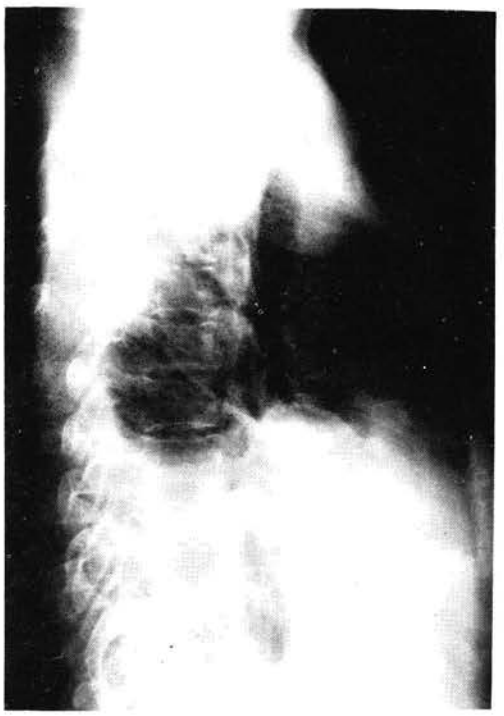


FIGURE 1A *FIGURE 1B*

Chest X-rays (PA View and Lateral View) showing massive left pleural effusion and multiple secondaries in the lungs.

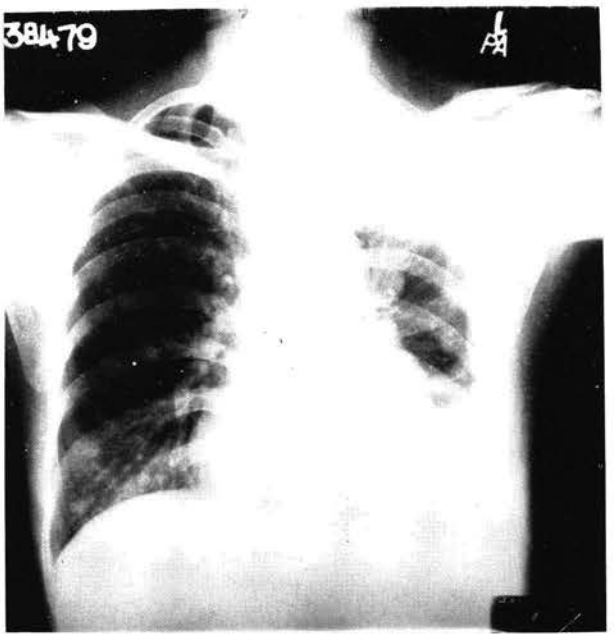


FIGURE 1C

Chest X-ray of same patient after pleural tap.

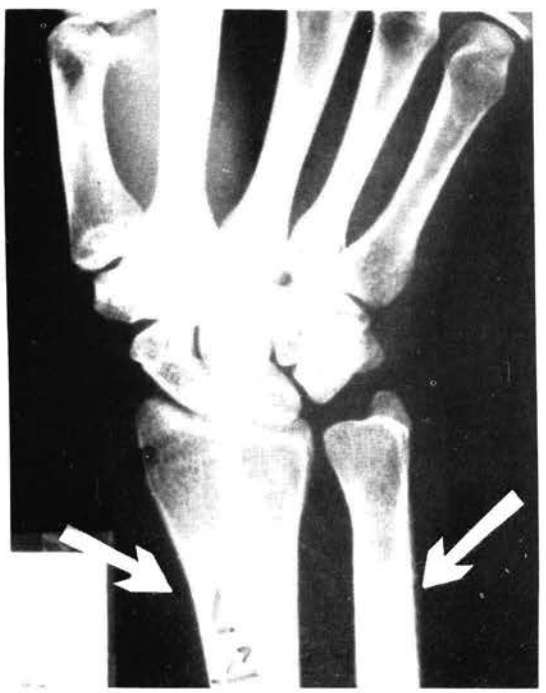


FIGURE 2A

X-ray of left forearm showing periosteal thickening.

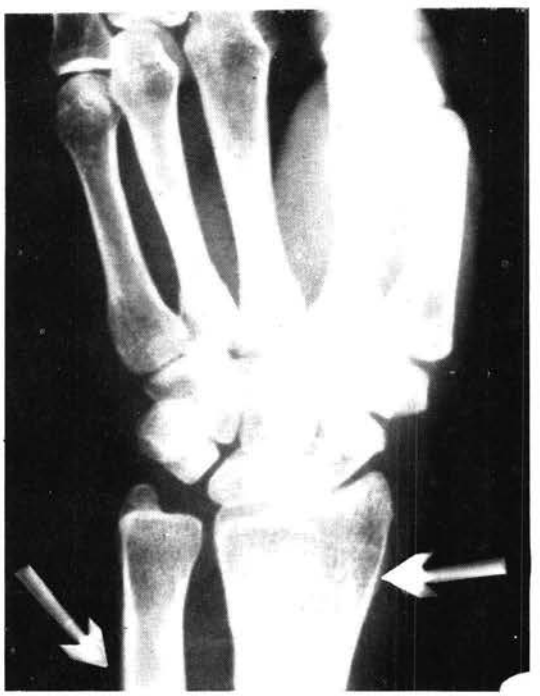


FIGURE 2B

X-ray of right forearm showing periosteal thickening.

(C) PLUERAL TAP

A pleural tap was done and 1200 ml of blood stained pleural fluid was obtained. The pleural fluid contained protein of 2.9/100 ml. No malignant cells were seen but there were many lymphocytes. Culture of the pleural fluid was negative.

(D) BIOPSY OF NASOPHARYNX

No malignant cells seen.

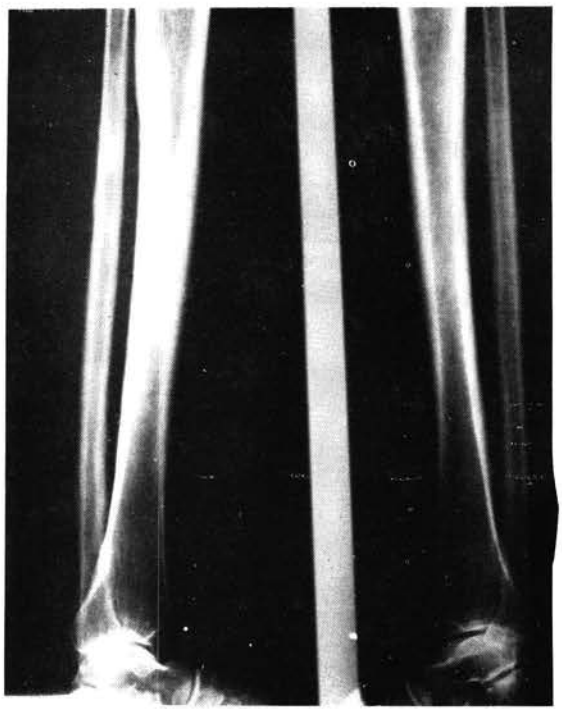


FIGURE 3
X-ray of left and right tibia and fibula showing mild periosteal thickening.

MANAGEMENT

The patient's pain was alleviated with analgesics such as paracetamol and dihydrocodeine while the fever was controlled with paracetamol. Cyclophosphamide (Endoxan) 200 mg was introduced into the pleural space after the pleural tap and subsequently the patient was given 200 mg cyclophosphamide intravenously on alternate days for 5 weeks. This was followed by a course of palliative deep x ray therapy to the left lung over a period of 6 weeks.

PROGRESS

The patient improved symptomatically after the pleural tap, the course of analgesics, cytotoxic drug and deep x ray therapy. She was no longer breathless; the fever settled, the swellings at the distal ends of her extremeties subsided and were nontender. However there was only partial diminution of the secondaries in the lungs.

DISCUSSION

It is of interest to note that the patient developed nasopharyhgeal carcinoma in 1970 and after a course of radiotherapy, she had no complaints for about 4 years until she began to develop symptoms from the hypertrophic pulmonary osteoarthropathy and subsequently symptoms from the secondaries in the lungs. Besides involvement of the distal 1/3 of both the forearms and legs, there were effusion in both her knee joints. The joints are usually less commonly involved and histologically they show thickening of periarticular tissues and erosion of the cartilage may also be present.

Hypertrophic pulmonary osteoarthropathy associated with metastases in the lungs is rarely encountered as in this patient. In a review of world literature by Yacoub et al (1967) he noted only 41 cases. Of the 41 cases reported, only 9 of the cases are attributed to nasopharyngeal carcinoma. Recently, another case of nasopharyngeal carcinoma with hypertrophic pulmonary osteoarthropathy has been reported in Singapore (Toh 1968).

The following table shows the reported cases of nasopharyngeal carcinoma with hypertrophic pulmonary osteoarthropathy.

	Author	Year	Age	Sex	Tumour
1.	Schlagenhaufer	1904	21	F	Carcinoma of nasopharynx
2.	Compere et al	1935	50	M	Carcinoma of nasopharynx
3.	Martin	1939	19	M	Transitional cell carcinoma of nasopharynx
4.	Martin	1939	15	M	Transitional cell carcinoma of nasopharynx
5.	Diner	1962	17	M	Lymphoepithelioma nasopharynx
6.	Papavasiliou	1963	22	M	" "
7.	Papavasiliou	1963	23	M	Epidermoid carcinoma of nasopharynx
8.	Papavasiliou	1963	25	M	Lymphoephithelioma of nasopharynx
9.	Jaffee	1964	27	F	Undifferentrated carcinoma nasopharynx
10.	Toh	1968	40	M	Nasopharyneal carcinoma

ACKNOWLEDGEMENT

We would like to thank Datuk (DR) R.P. Pillay and Dr. J.S. Eapen for their advice and their permission to publish this paper. We would also like to thank Dr. S.T. Kew for his encouragement; Dr. Murkherjee for his excellent interpretation of the X rays and Mr. Charlie Abraham for his fine photography.

REFERENCES

ADAMS W.E., THORNTHON. T.F.,and ERCHELBERGER L., (1954) Arch. Surg. 49, 51.

AUFSES, A.H. and AUFSES, B.H. (1960) Dis. chest 38, 399

DINER W.C. (1962) J. Amer, Med. Ass. 181, 555

FLAVELL, G.C. (1956) Lancet 2, 260

GALL E.A., BENNETT, G.A., and BAVER, W. (1951) Amer. J. Path 27, 349

GIBBS, D.D. SCHILLER, K.F.R. and STOVIN, P.G.E.I. (1960) Lancet 1, 623

HOLLING, H.E., BRODEY R.S. and BOLAND, H.C. (1961) Lancet 2, 1269

JAFFEE I.S. (1964) Arch. Otolaryny 80, 450

PAPAVASILIOU, C.G. (1963) Brit. J. Radiol, 36, 680

PRICE THOMAS, C and DREW C.E. (1953) Thorax 8, 180

RAY, E.S. AND FISCHER, H.P. Jr. (1953) Ann. Int. Med. 38 239

SEMPLE J. and MCLUSKIE, R.A. (1955) Brit. Med. J. 1, 754

SINGH G. JOLLY, S.S. and BANSALL, B.B. (1960) Brit Med. J. 2, 581

TEMPLE H.L. AND JASPIN, G. (1948) Amer. J. Roentgenol 60, 232

TOH, B.H. (1968) Sing. Med. Journ. 2, 103

YACOUB M.H. (1965) Brit. J. Disc. Chest 59, 28

YACOUB M.H. (1965b) Thorax 20., 537

YACOUB M.H. and SIMON G. (1966) Brit. J. Disc. Chest, 60, 81.