Rectal carcinoma presenting as massive metastatic involvement of foot bones

Although the overall incidence of metastatic involvement of bones in patients with malignant neoplasms is probably between 20 and 30%, metastatic lesions of the bones of the feet are extremely rare. So far as we are aware this is the first report of massive involvement of the foot by metastatic carcinoma.

Case report

A 79-year-old woman presented with a four-month history of pain on the medial side of the right foot. On examination the only abnormality was marked right hallux valgus and x-ray examination showed osteoporosis of the foot bones. Over the next eight months the pain in her foot worsened, with extreme pain on walking and increased swelling. Examination showed gross swelling of the dorsum, which was hot and pulsatile; mild hepato- megaly; a central abdominal mass; and a hard craggy mass felt per rectum. Radiographs now showed that the first, second, and third metatarsals and first cuneiform were eroded by neoplasm. Chest radiograph showed an enlarged heart but normal lungs. Erythrocyte sedimentation rate was 75 mm in first hour and alkaline phosphatase 256 IU/l (normal 20-95 IU/l).

A right below-knee amputation was performed. There was firm swelling over the medial and dorsomedial aspects of the foot with oedema of the subcutaneous tissue. The specimen was examined by removal of skin, soft tissues, and then the bones of the foot were sliced in the line of each toe, after disarticulating the tibia, fibula, calcaneus, and talus. The navicular, cuboid, all three cuneiforms, the major part of the first, second, and third metatarsals, and proximal parts of the fourth and fifth metatarsals showed replacement of normal architecture and expansion by variegated grey-white tumour with haemorrhagic foci. There was variable cortical destruction and extension of tumour into joint spaces and adjacent soft tissue (figure).

The extent of tumour and soft tissue involvement was clear on radiographs of the slices. In addition, the anterior surface of the calcaneum showed focal involvement with tumour, but the talus, tibia, fibula, and phalanges appeared to be unaffected. Microscopically, the affected bones were shown to be extensively infiltrated by acini of moderately well-differentiated, large, intestinal-type adenocarcinoma with areas of necrosis and new bone formation. After operation the patient suffered from persistent diarrhoea, the only local symptom of her rectal carcinoma. It was considered that local intervention would not improve the prognosis. She was therefore treated symptomatically and the diarrhoea eventually resolved. Her stump healed satisfactorily and she could walk comfortably in a frame. She died at home five months after the amputation.

Comment

Osseous metastases of the foot are rare. Only 17 histologically proved cases have been reported. In 14 of these cases only one foot bone was affected. Colson and Willcox, however, reported a case...
with metastases of the first metatarsal and proximal phalanx, while Bright and Wilkie\(^1\) reported involvement of the talus and four metatarsals by metastatic transitional cell carcinoma. Gall et al\(^2\) in their series included a case in which there was involvement of the calcaneum, fifth metatarsal, and fifth phalanx by metastatic squamous carcinoma. In our case 11 of the foot bones were partly or completely affected by metastatic carcinoma, this being the first report of such massive metastatic disease of the foot. Although foot pain is very common, this case shows that it may be a presenting sign of occult visceral carcinoma and an initial radiograph of the foot may not show evidence of metastatic carcinoma.

We are indebted to Mrs W Jones for secretarial help.

---

Increase of serum high-density lipoprotein in phenytoin users

An increase of serum high-density lipoprotein (HDL) cholesterol has been reported in association with regular alcohol intake\(^3\) and in men exposed to chlorinated hydrocarbon insecticides.\(^4\) These agents are known inducers of hepatic microsomes. Raised serum total cholesterol concentrations have been observed during treatment with phenobarbitone\(^5\) and phenytoin,\(^6\) also potent microsomal inducers. These findings suggest that hypertrophy of liver microsomes may stimulate the secretion of HDL and lead to higher serum HDL concentrations. To test this hypothesis we measured lipoprotein and apolipoprotein A concentrations in the serum of epileptic patients who were regular users of phenytoin.

Patients, methods, and results

Fasting serum was studied from 21 men and 7 women epileptic patients (mean \(\pm SD\) age 46 \(\pm 16\) years) and from 44 men and 49 women healthy controls (mean age 48 \(\pm 12\) years). The epileptic patients had used phenytoin regularly for 1 to 35 years in a daily dose of 200 to 300 mg and received no other medication. Alcoholics were excluded. Lipoproteins were separated from the serum by ultracentrifugation and the cholesterol and triglyceride contents were determined. Apolipoproteins A-I and A-II were measured from whole serum by radial immunodiffusion. The serum phenytoin concentration was assayed by routine laboratory method.

The table shows that the phenytoin users had higher mean HDL-cholesterol concentration than the controls. In 12 patients (43\%) HDL-cholesterol concentrations were above the upper limit of normal (determined as the mean \(\pm 2SD\) of control values). The highest concentrations were found in the patients who had serum phenytoin concentrations within the recommended therapeutic range (40-80 \(\mu\)mol/l). Thus, in these men the mean (\(\pm SD\)) HDL-cholesterol was 1.87 \(\pm 0.43\) mmol/l (72 \(\pm 16\) mg/100 ml) compared with 1.51 \(\pm 0.28\) mmol/l (58 \(\pm 22\) mg/100 ml) in men with suboptimal serum phenytoin concentrations.

The mean serum apolipoprotein A-I concentrations were also appreciably higher in phenytoin users compared with controls. Highest A-I values were again found in the patients who had serum phenytoin concentrations at therapeutic levels (mean (\(\pm SD\)) A-I 2.05 \(\pm 0.28\) g/l vs 1.77 \(\pm 0.30\) g/l in the "low" phenytoin group, \(P<0.05\)). HDL-cholesterol and apolipoprotein A-I concentrations showed a significant correlation \((r=0.77, P<0.001)\). The apolipoprotein A-II concentration of phenytoin users was not significantly different from that of controls.

Serum total cholesterol and triglyceride concentrations were similar in phenytoin users and controls. The male phenytoin users, however, showed a higher prevalence of hypertriglyceridaemia than the male controls. Thus, 35\% of the phenytoin users had a serum triglyceride >2.0 mmol/l (>177 mg/100 ml) compared with only 18\% of male controls.

Comment

These results support, but do not prove, our hypothesis because we do not know whether the phenytoin users had hypertriglyceridaemia or whether hepatic secretion of nascent HDL particles was increased. In fact, the site and mechanism of serum HDL synthesis in the liver are not known. It is thought that smooth endoplasmic reticulum is the site of synthesis and assembly of the secretory lipoproteins in the liver.

This study is one of a growing body of evidence in support of a negative association between serum HDL concentration and coronary heart disease. Epileptic patients, because they take phenytoin for many years, may therefore be protected from heart disease. Though we are not aware of any reports of this, a brief letter recently published in this journal noted an unusually low incidence of myocardial infarction in epileptic patients. This work was confirmed, agrees with our results and is an example of this possible beneficial side effect of a drug. It might also be a new approach to the prevention of coronary heart disease.

This work was supported by grants from the Finnish Medical Research Council (Academy of Finland) and the Sigrid Juselius Foundation, Helsinki.

---