



Photograph No. 4: - Histopathology/cytology report the cartilage appears to be benign. nuclear hyperchromatism and pleomorphism are evident At places the cells are small having stained nuclei is no evidence of psuedoepithelioid formation.

## DISCUSSION

Chondrosarcoma is a slow-growing cartilaginous tumor and is next to osteosarcoma in frequency. Lichtenstein and Jaffe in 1943 clearly established a chondrosarcoma as a distinct

entity separate from osteogenic sarcoma. It has a predilection for the flat bones, especially the shoulder and pelvic girdles, but can also affect the diaphyseal portion of long bones. Chondrosarcomas have an indolent natural history. Slow growing tumors show a greater degree of calcification, whereas highly malignant, rapidly growing tumors generally show little or no calcification. Most chondrosarcomas are resistant to standard sarcoma chemotherapy and surgical resection of primary or recurrent tumors is the mainstay of therapy. Low grade or "borderline" tumors can frequently be eradicated by *en bloc resection*, removing the surrounding normal muscles, especially when the tumors are small. Local resection is fraught with greater risk of recurrence and transformation to a more malignant tumor. It is wise to amputate at least one joint ahead of the lesion to prevent recurrence at the stump.

## RECOMMENDED READING

- 1 Dahlin, DC, Henderson ED: *Chondrosarcoma, a surgical and pathological Problem. J Bone Joint Surg.* 1965, 38A:1025
- 2 Lichtenstein L, Goldman RL: *Cartilage tumors in soft tissues, particularly in hand and foot. Cancer* 1964, 17:1203
- 3 Malawer MM et al: *Sarcomas of bone, in cancer: Principles and Practice of oncology, shied. VT Devita et al (eds) Philadelphia, Lippincott 1997, pp 1789-1852.*

## DRUG PROFILE

### RIMONABANT

**Clinical Pharmacology :** Rimonabant is a selective cannabinoid-1 receptor (CB1) antagonist that inhibits the pharmacological effects of cannabinoid agonists, both in vitro and in vivo.

**Mechanism of Action:** The endocannabinoid system is a physiological system present in brain and peripheral tissues (including adipocytes) that affects energy balance, glucose and lipid metabolism and body weight, and in neurons of the mesolimbic system modulates the intake of highly palatable, sweet or fatty foods. Following once daily doses of 20 mg to healthy subjects in the fasted state, maximum plasma concentrations of rimonabant are achieved in approximately 2 hours with steady state plasma levels achieved within 13 days. Steady state rimonabant exposures are 3.3 fold higher than those observed after the first dose. Population pharmacokinetic analysis demonstrated less fluctuation in peak to trough plasma concentration but no differences in steady state AUC as weight increases. As weight increases from 65 to 200 kg, C<sub>max</sub> is expected to decrease 24% and C<sub>trough</sub> is expected to increase by 5%. The in vitro human plasma protein binding of rimonabant is high (>99.9%) and non-storable over a wide concentration range. Rimonabant is metabolized by both CYP3A and amidohydrolase (predominantly hepatic) pathways in vitro. Circulating metabolites do not contribute to its pharmacologic activity. Rimonabant is mainly eliminated by hepatic metabolism and subsequent biliary excretion of metabolites. Only an approximate 3% of the dose of rimonabant is eliminated in the urine, while approximately 86% of the dose is excreted in the feces as unchanged drug and metabolites. In obese patients, the elimination half-life is longer (about 16 days) than in non-obese patients (about 9 days) due to a larger volume of distribution. Since rimonabant tablets contain lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take this medicine. Patients should be instructed not to increase the dose. Therapy with rimonabant should not be initiated in patients with uncontrolled serious psychiatric illness such as major depression. There are no adequate or well-controlled studies in pregnant women; drugs contraindicated during breast feeding.

**Drug Interactions:** Rimonabant is metabolized by both CYP3A and amidohydrolase (predominantly hepatic) pathways in vitro. Co-administration of CYP3A4 inhibitors will lead to increased exposure of rimonabant. Co-administration of CYP3A4 inducers is expected to reduce the exposure of rimonabant (e.g., ketoconazole, itraconazole, ritonavir, telithromycin, clarithromycin, nefazodone). Concomitant administration of CYP3A4 inducers (e.g., rifampicin, phenytoin, phenobarbital, carbamazepine, Co-administration of orlistat, ethanol or lorazepam has no significant effect on the plasma levels of rimonabant.

**Side effects:** The commonly reported side effects include nausea, upper respiratory tract infection, upset stomach, vomiting, insomnia, sleep disorders, nervousness, depression, irritability, dizziness, diarrhea, anxiety, itching (pruritus), excessive sweating (hyperhidrosis), muscle cramps or spasm, asthenia/fatigue, bruising, tendon pain and inflammation (tendonitis), memory loss, back pain, sciatica, hot flush, fall, influenza, joint sprain, gastroenteritis, mood alterations with depressive symptoms, insomnia, parasomnias, hypoesthesia and confusion. Uncommon side effects include lethargy, night sweats, panic symptoms, hiccups, anger, dysphoria, emotional disorder, sinusitis, and anorexia, stomach discomfort, dry mouth and rarely hallucinations.

**Dosage and Administration:** In adults, the recommended dose is 20 mg, to be taken daily in the morning, before breakfast. The treatment should be introduced with a mildly reduced calorie diet.