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Kummoona Jaw Lymphoma, Chemotherapy for Managements of Highly Malignant Tumor

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Abstract

Research in cancer and Kummoona jaw lymphoma was going on, and the aim was to correlate the aggressiveness of this tumor and therapeutic management.

Kummoona jaw lymphoma is a particular clinical-pathological tumor entity affecting children between the ages of 2-8 years; mean (5 years), twenty-nine cases were reported,17 males and 12 girls; we said only three children survived with a death rate of 93.3 %.

Tumors were developed in the odontogenic tissue in the cancellous bones of the child's jaws after the oncogenic virus (Herps-like virus) invasion. The illness duration was concise between 3-4 weeks.

This highly malignant tumor was characterized by rapid growth in the maxilla, mandible, or both, and sometimes 4 quadrants of the jaws were involved simultaneously. Metastasis to the brain and the abdomen were reported.

These tumors were associated with elevated temperature, anemias, and high ESR, and the patients passed through a series of debilitating conditions with early metastasis to the viscera and brain.

Electron microscopy (EM) showed lymphoblast cells as oval or round cells with a high nucleon-cytoplasmic ratio with invagination or cleft formation in the nuclear membrane. Chromatin clumps aggregated near the nuclear membrane, virus-like particles were seen in the nucleus and cytoplasm but not EBV of Burkitt's lymphoma but showed somewhat similar to herpes simplex viruses, mitochondria were homogenous, presence of RAR endoplasmic reticulum, collagen fibers observed and vacuoles contain lipid derbies.

This research aims to understand these types of tumors and correlate cancer's aggressiveness and therapeutic management.

Keywords: Kummoona. Jaw. Lymphoma. Chemotherapy

Introduction

Cancer is a dreadful and disastrous disease for humanity; most cases are expecting death, especially in pediatric cancer, which is more aggressive.

Kummoona Jaw lymphoma is one of the most aggressive cancer cases affecting children. Jaw lymphoma, a clinical-pathological entity, rare and highly malignant tumor, and lethal disease, sporadically scattered, affect children between the age 2-8 years and mean (5 years), 29 cases were reported they were 17 boys and 12 girls presented with the massive growth of the maxilla, mandible or both and even in both sides of the maxilla or mandible as 4 quadrants disease. **[2,4]**

It is very rapid growth, the duration of illness within 2-4 weeks associated with high temperature, and anemia with high ESR; the child looks toxic and very ill; it seems these children passed through a series of debilitating conditions affecting people of the low socioeconomic group.

The author reported two varieties of lymphoma; the first one, the primary located in the developing odontogenic tissue in the cancellous bone of the jaws affected by an oncogenic virus with early metastasis to viscera and cranium, and the prognosis was poor.

The second type, the primaries in the small intestine, affect young people between 2nd and 3rd decades who presented with pain in the abdomen, malabsorption, and obstruction; rarely metastasis to the jaws was reported, and the prognosis was acceptable4.h

Oncogenic viruses are a substantial cause of cancer, such as the EBV virus causing Burkitt's lymphoma and nasopharyngeal carcinoma herps-like virus causing Kummoona jaw lymphoma. Was found an association between herpetic papillomavirus with oral cancer. HIV and AIDS can cause leukoplakia as a precancerous white lesion and end with oral cancer. Also, Kaposi sarcoma is associated with HIV-infected cases. Human papillomavirus (HPV), particularly type 16, is a known risk factor and independent causative factor of oral cancer. HPV 18 is the same virus responsible for cervical cancer and is the most common sexually transmitted infection in the US.

Recent studies at Harvard Medical school found an association between advanced infection of periodontal diseases and the incidence of oral cancer, especially among people with a low socioeconomic

group with heavy smoking and alcohol. The microorganism causing periodontal disease is the Sreptomutant type.

Cancer might be associated with chronic hyperplastic candidiasis and syphilis in the second stage; spicey food like Chile induces precancerous status of sub-mucous fibrosis, and the squali of this disease is cancer.

There is a substantial cause of cancer by the effect of smoking with consumption of alcohol; hereditary and genetic and depleted uranium should not be excluded.

For a better understanding of jaw lymphoma and therapeutic management, we did our classification of the Jaw Lymphoma disease:

Stage I tumors involve one quadrant of in the maxilla or the mandible

Stage II tumors involve both jaws upper and lower jaw, either by 2 or 4 quadrants

Stage III Jaw tumor extended to the brain.

Stage IV Jaw tumors involve the jaw with visceral metastasis.

This study aims to share our findings with other colloquies knowledge and experience for managing this lethal disease as an urgent case.

Material, Methods, and Results:

These studies include 29 cases of jaw lymphoma,17 males and 12 girls, their ages between 2-8 years mean (5 years), presented with massive growth of the maxilla, mandible, or both; each case with jaw lymphoma showed the general condition of protestation, toxicity, anemias, the elevation of body temperatures with higher and high mortality rates 93.3 % due to quick metabolic derangements and renal function impairments or CNS involvements and three patients survived on the long run follow up., [**Figure 5A,B,C, Figure 6 A,B]**

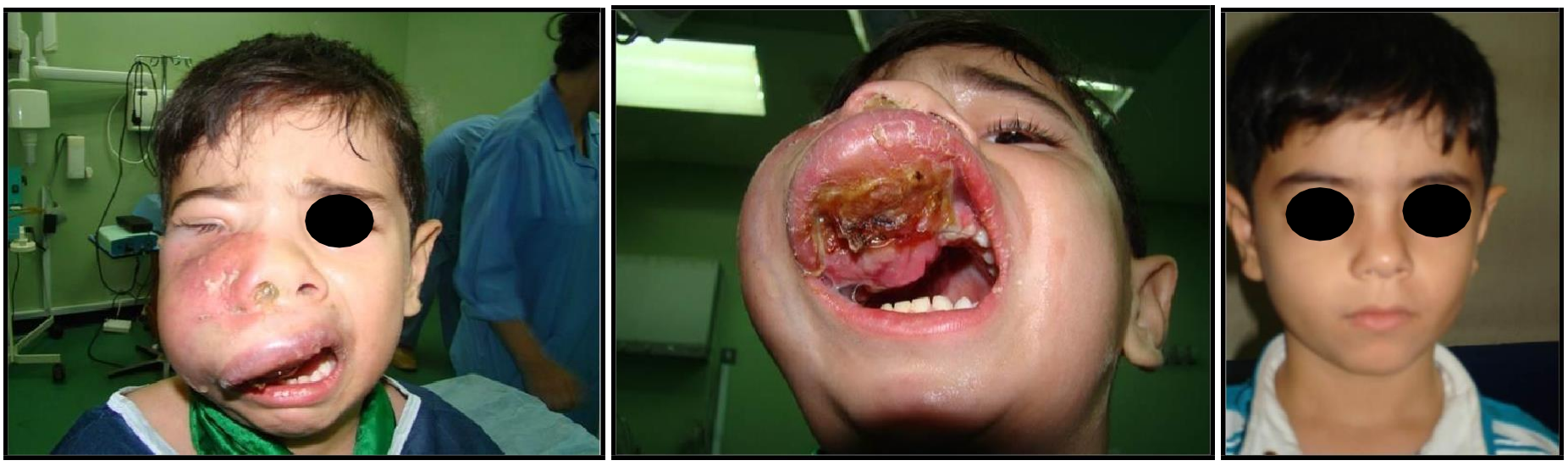


Figure 5: A, Extensive jaw lymphoma effecting the right side of the face, history of 4 weeks in a child of 3 years of age.

B-Intra oral view of tumor involving the right maxilla.

C-3 years of post-chemotherapy showing excellent results.

Figure 6: A jaw lymphoma of the left side of the face and orbit effecting 3 years female.

B- Post operative photo showing good response of the face to treatment.

The radiologic examination included a chest X-ray to rule out lung metastasis and mediastinal involvement.CAT scans of the abdomen were performed to evaluate the disease's extension and exclude the participation of retro peritoneum and Para-aortic lymph and mesenteric lymph nodes, kidneys, ovaries, and other organs. Radioactive isotopes such as 99Tc were used to detect skeletal metastasis as part of the investigations to be carried out. [**Figure 4**.]

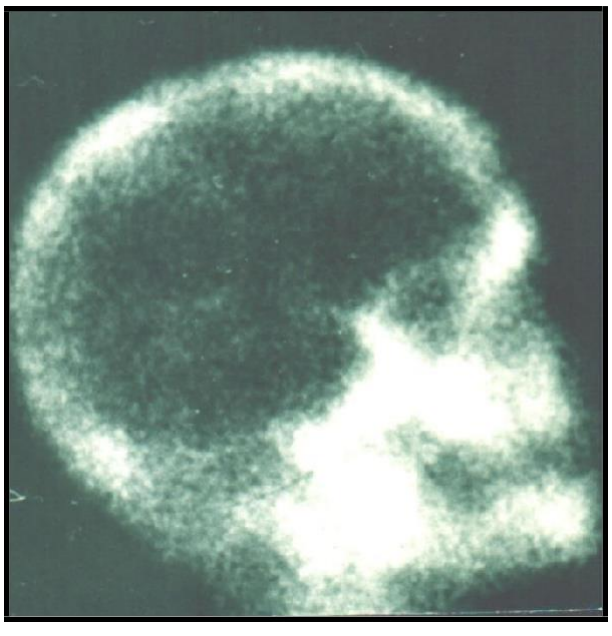
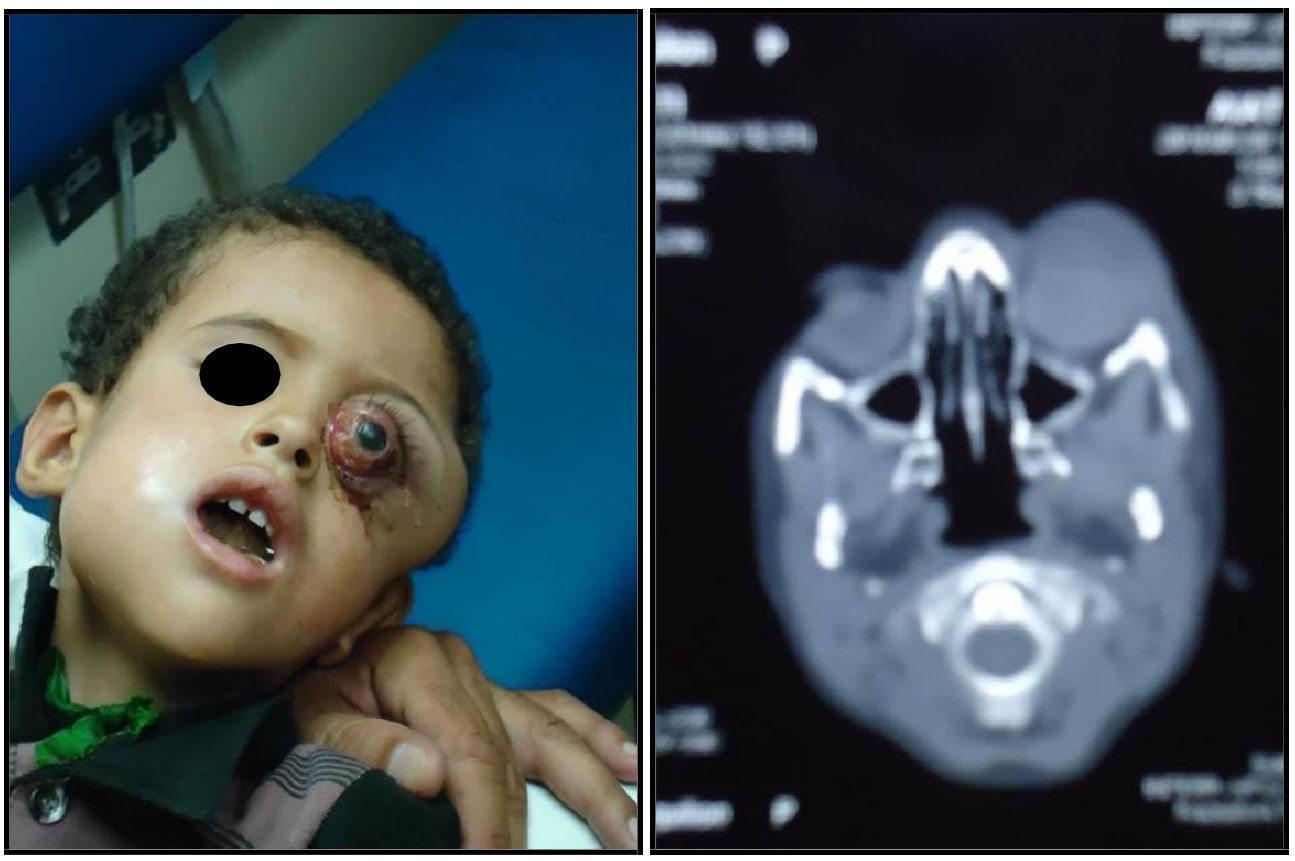


Figure 4: Skeletal scanning with radioactive isotopes of Tc99showing high uptake of isotopes in hot area in the maxilla and mandible

Anatomical sites for a location for primaries and metastasis of 29 children were affected by jaw lymphoma, the maxilla was involved in 18 cases, the mandible in 8 instances, the thyroid in 2 patients, the testis in 2 points, the abdomen and viscera in 12 cases and 4 cases showed later visceral metastasis, the orbit was involved in 8 cases, and one patient showed axillaries lymph node deposit.

The orbit was involved due to the extension of the tumor from the maxillary and ethmoid air cells giving the features of ptosis, proptosis, and paralysis of recti muscles with the fixed pupil. [**Figure 7 A, B]**



The CNS was involved as a result of the extension of the tumors through the superior orbital fissure, and optic foramen features paralysis of cranial nerves as ocular paralysis or facial palsy, the abdomen involved as a result of mesenteric lymph nodes and Para-aortic lymph nodes and featured as distension of the abdomen due to ascetics.

The serological studies revealed EBV serology characterized by increased antibody titer to Epstein Barr Nuclear Antigen (EBNA), early antigen (EA), and virus capsid antigen (VCA); in some other cases, the profile was relatively high anti-VCA titer with the Epstein Barr Virus EBV associated Burkitt lymphoma, but the presence of low anti-EA and negative anti EBNA titer did not allow a definite conclusion to be made.

There is no indication or proof of the association of jaw lymphoma with EBV; it seems some profile can be found in EBV genome-positive cases.

Differential diagnosis of jaw lymphoma should be differentiated from other tumors of childhood, including Wilms tumor, neuroblastoma, or malignant giant cell tumor, and peripheral neuroectodermal tumor.

The bone marrow should be differentiated from B and precursor and myeloid leukemia B cell lymphoma; the primary differential diagnosis is diffuse large B cell lymphoma.

Post-mortems studies:

Post-mortem and gross anatomy examination showed extensive masses involving the terminal ileum and Para-aortic and mesenteric lymph nodes.

Jaw tumors featured an extensive growth of soft friable tissue with bleeding spots on the mucosa with the destruction of the alveolar

bones and floating teeth. From our series of 29 cases, only three patients survived and turned out to be among the long-term survivors with Stages I and II, while subjects with Stage III or IV were passed due to the advance and spread of the disease.

The therapeutic management of jaw lymphoma (JL) differed from that of Burkitt lymphoma (BL). This tumor has been treated with a few courses of cyclophosphamide 40 mg/m2, while jaw lymphoma cases were treated by a complicated therapeutic regimen based on NCI recommendations; the NCI recommendations were also used to manage the disease.

The therapy uses an intravenous combination of vincristine 1.5mg/m2, Adriamycin 50mg/m2, cyclophosphamide 1000mg/m2, methotrexate 10mg/m2 and prednisolone 50mg/m2 in 8 doses, and the duration of the therapeutic managements was 24 weeks.

Follow-up of the cases included CSF and bone marrow investigations to exclude acute lymphoblastic leukemia, serum creatinine, complete blood picture profile, serum electrolyte, body temperature, sonography, chest X-ray to rule out lung metastasis and mediastinal involvement, and pyelography to exclude impairment of renal function and Pet Scan been used nowadays for detection of metastasis.

Ct scans of the abdomen were performed to evaluate the extension of the disease of the retroperitoneal and Para-aortic lymph nodes, liver, kidneys, ovaries, and other organs, and radioactive isotopes of Tc99 were used for detection of any skeletal deposit. **Figure 4**.

Study and analysis for EBV some other investigations were performed including print cytology and immunohistochemistry from LCACD45 and IMHC staining showing cells positive for myeloperoxidase (MPO) in (JL) besides serological studies for detection of EA, VCA, EBNA and antibody titer of EBV antigen was performed.

Cytological, light microscope, for (H&E), ground section, and electron microscope:

These investigations were carried out for a better understanding of the cytological behavior of jaw lymphoma.

Imprint cytology:

A quick technique by Gamesa stain for diagnosis of jaw lymphoma usually showed lymphoblastic cells darkly stained due to high ribonucleic acid content and cytoplasmic vacuoles due to high lipid content.

Light microscope (H&E):

Shows lymphoma with a starry sky pattern of uniform lymphoid cells exhibiting intense cytoplasmic pyronin philia. **Figure 1**.

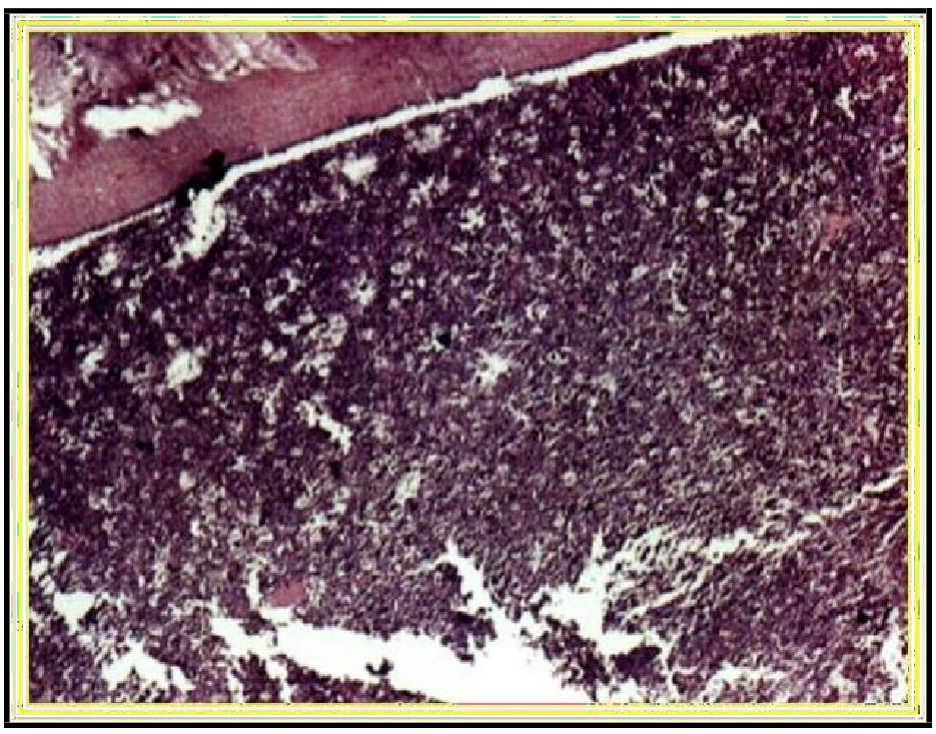


Figure 1: Light microscope of lymphoblastic jaw lymphoma, with darkly staining with stary sky appearance from section of tooth (H&E)

Ground sections, plastic section technique:

showed lymphoblastic lymphoma, the cytoplasm of the cells was darkly stained due to high ribonucleic acid content, with the cytoplasm rim tiny vacuoles visibly belonging to the fat droplets seen with fat stain in frozen sections, apoptotic changes of lymphoblastic cells also seen., **Figure 2**.

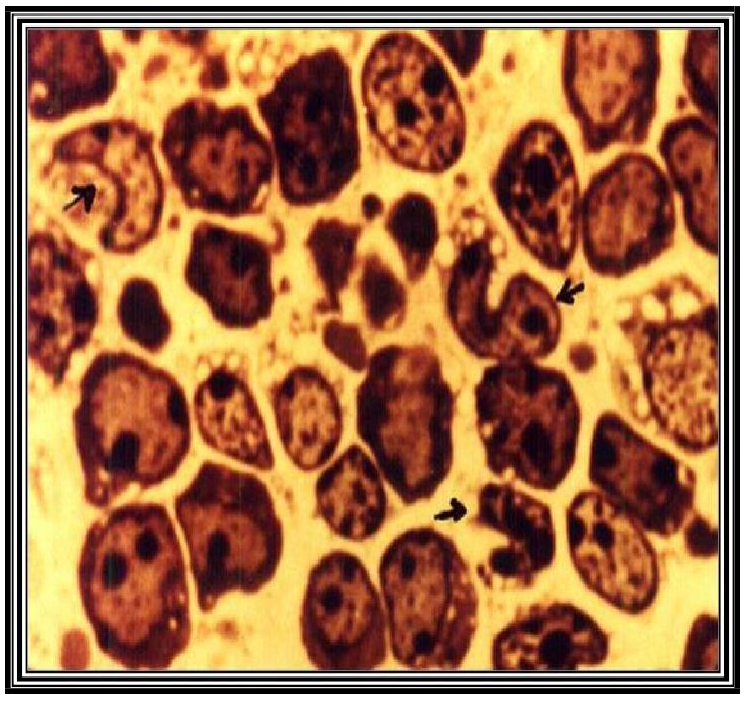


Figure 2: Ground section of plastic showing lymphoblastic lymphoma darkly stained due to high content of ribonucleic acid with apoptosis changes of the cells.

Electron Microscopy Study:

The general feature of jaw lymphoma is oval, round, or elongated cells with high nucleon-cytoplasmic ratio with invagination or aperture in the nuclear membrane and chromatin clamps around the nuclear membrane, and mitochondria not well developed, and some show marked swelling also, cytoplasmic processes observed as a sign of apoptosis, the virus-like structure was noticed in the nucleus and cytoplasm, some cell showed double nuclei or crest or convoluted shape, vacuoles also seen due to high content of lipid and debris, a massive amount of collagen fibers was seen, rough endoplasmic reticulum was partially dilated, some losing ribosomes, virus particles has a distinct body and were not EBV rather similar to herpes simplex virus., **Figure 3. A,B**

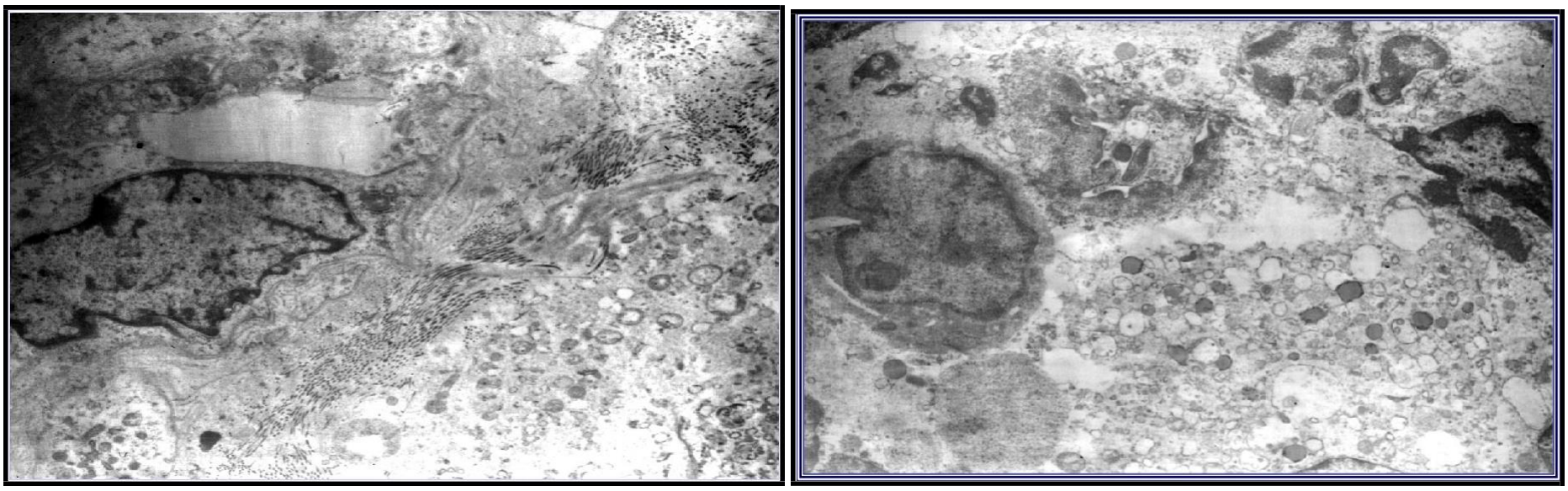


Figure 3: A,EM of jaw lymphoma showing the cell became convoluted appearance with chromatin particles scattered in the nucleus due to apoptosis, mitochnderia was underdeveloped and homogenous with collagen fibers and oncogenic virus scattered which is not EBV but similar to herpes simplex virus B,EM of jaw lymphoma showing the typical appearance of round cell with invagenation in the nucleus membrane and chromatin clumps near the nuclear membrane, mitochondria homogenous and virus particles scattered in both the cytoplasm and nucleus, vacuoles seen and collagen fibers.

Discussion

Current cancer research on jaw lymphoma focuses on understanding this tumor's cellular changes and the correlation between response to treatment and apoptosis. Apoptosis or programmed cell death is an active process of self-destruction that require the activation of a genetic program that may lead to changes in cell morphology, DNA fragmentation, and protein cross-linking, and defect in apoptosis mechanisms could lead to tumor formation.

The drug manufacturer concentrates nowadays on drug induces apoptosis. **[1,3]**

Another classification of lymphoma and jaw lymphoma is a modified classification of the disease, stage I (early disease), the tumor found only in one side of one jaw, upper or lower jaw in the premolar-molar area or cancer in lymph node and surrounding area, stage II (locally advanced disease), the tumor was found in both sides of the mandible and maxilla or more nodes region in one side of the diaphragm. Stage III (progressive disease) tumors involve the viscera, or lymphoma cancer involves lymph nodes above and under the diaphragm. Stage IV (comprehensive spread disease) cancer involves the CNS (central

nervous system), bone marrow, and reticular-endothelial system; in lymphoma, cancer is found in several parts of one or more organs of tissue lymph nodes or liver, blood, and bone marrow. **[9,10]**

From our studies by serological, ground sections, and electron microscopy (EM), there is no evidence of jaw lymphoma associated with EBV. Observation of the viruses seen by EM was not EBV but somewhat similar to herpes simplex virus, although the light microscope by H&E showed the appearance of Burkitt lymphoma, and even the response to treatment was quite different. **[5,6,7,8]**

Current therapeutic cancer research focuses on understanding the response and resistance to treatment and apoptosis. Cancer treatment not only on cellular damages as achieved by chemotherapy and DXT but also on the ability of the cell to respond to damages by inducing apoptotic changes and mutation in the apoptotic pathway to end with resistance to chemotherapy drugs and radiation. **[1,2,3]**

Mitochondria and cell surface receptors mediate the pathway for apoptosis, and the BcL2 family protein mediates this pathway. The caspase cascade performs the final excursion of cell death, triggered by the release of cytochrome C from mitochondria. **[1]**

Most of the activity in developing apoptosis drugs nowadays is concentrated on apoptosis-inducer drugs for treating malignancy. The recent advances in chemotherapy have seen the application of Gemzar (Gemcitabine), this drug had the ability to interfere with the growth and spread of cancer cells by inducing apoptosis and anti-metabolite; this drug has been used in combination with Carboplatin, which is a specific chemotherapy drug for pancreatic Adenocarcinoma even in advance cases of the fourth stage of pancreatic carcinoma. **[1,2,3]**

The future of chemotherapy and advances in radiotherapy might be auspicious for controlling the spread of cancer, including jaw lymphoma.

Conclusion

Kummoona jaw lymphoma is a clinically pathological entity highly aggressive tumor with early metastasis to the brain and viscera. Cancer was not caused by EBV but by herpes simplex-like viruses, and the management of these cases was more complicated by a combination of many chemotherapy drugs with a duration of administration of up to one year.

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