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Case report/Kazuistyka

Bilateral orbital lymphoma: A diagnostic odyssey through surreal clinical and imaging features plus therapeutic implications

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ABSTRACT

The paper aim was to present a case of bilateral, advanced, orbital lymphoma diagnosed in a middle aged man who was admitted in a clinical condition which almost defied reality. The entire orbito-facial region was replaced by massive ulcero-necrotic masses which completely distorted the normal anatomy, giving an alien-like resemblance of an otherwise ordinary man. The patient was submitted to several imaging examinations (head and whole body computer tomography, head MRI, laterocervical ultrasound and elastography) and surgical biopsy. The final diagnosis was stage IVB diffuse large B-cell lymphoma (DLBCL). Currently the patient is undergoing chemotherapy with astonishing response (clinically visible tumoral shrinkage).

The differential diagnosis of orbital masses may be extensive, starting from inflammatory conditions, such as cellulitis, pseudotumor, sarcoidosis and finishing with metastases from lung, renal or breast cancers. However, considering the substantial tumor volume in this case and imaging aspects, lymphomatous origin was the first diagnostic verified and ultimately confirmed.

The peculiarities of the case do not reside in the final diagnosis, for DLBCL is the most common form of non-Hodgkin lymphoma in middle aged men, but its debut or spread to orbits is rare, usually unilateral and diagnosed in less advanced stage.

Case report

A 52-years-old man was referred to the Emergency Unit (ER) in a clinical condition which almost defied reality. The entire orbito-facial region was replaced by massive ulcero-necrotic tumors, which completely distorted the normal anatomy, giving an *alien-like* resemblance of an otherwise ordinary man (Fig. 1). Another disturbing feature was the persistent hemorrhage from what used to be the eye slits.

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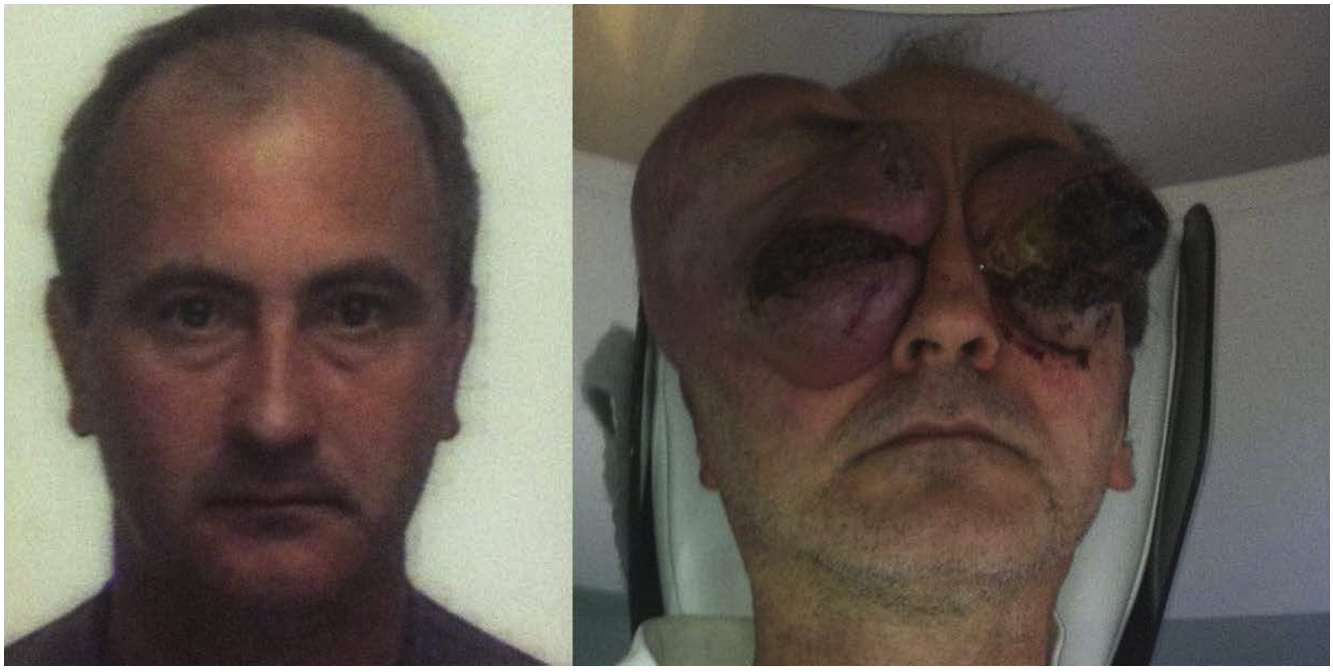

Fig. 1 – A 52-year-old man – normal appearance as opposed to clinical presentation at the moment of admittance

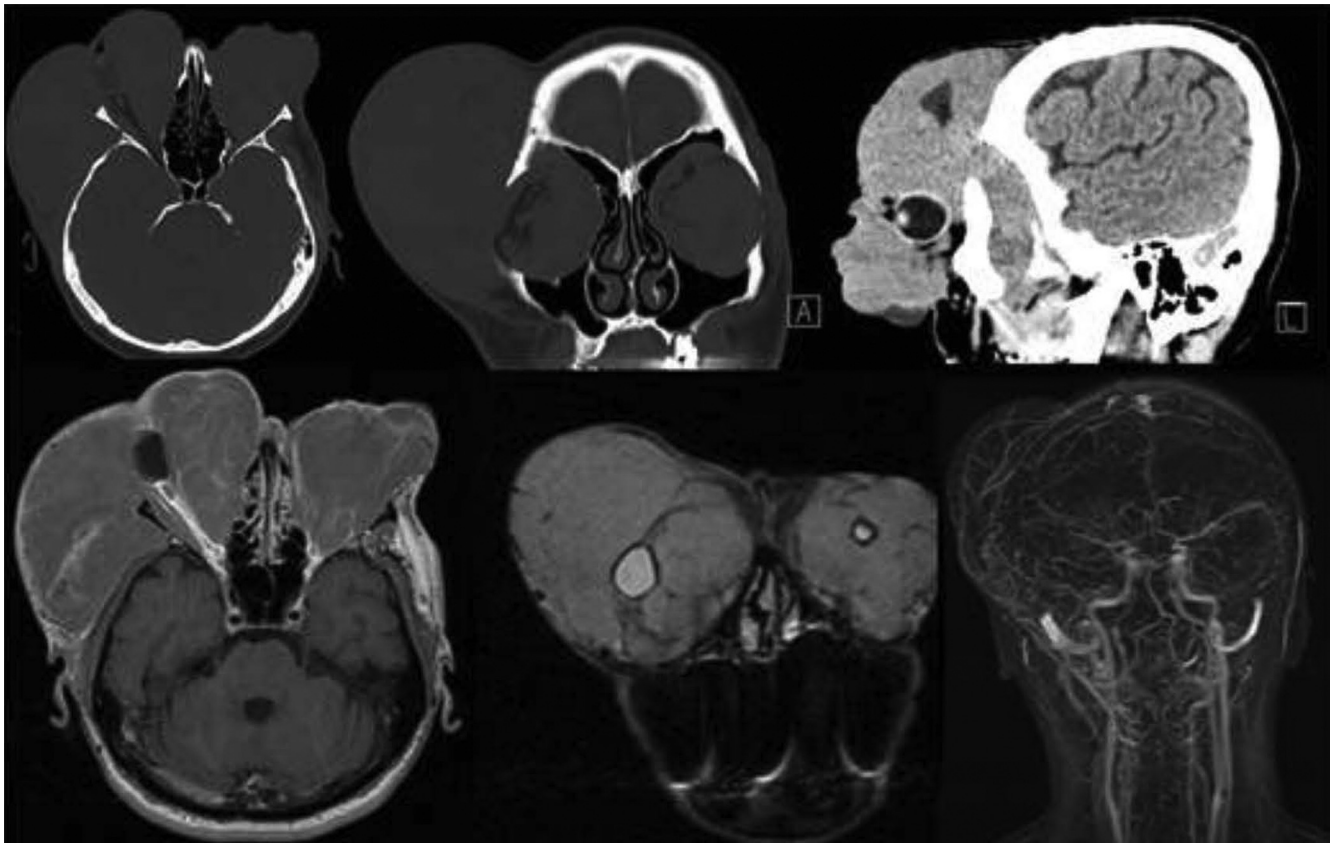

Fig. 2 – Computer tomography images (first row) and MRI sections (second row) displaying large, solid, enhancing orbital and periorbital masses. The eyeballs and optic nerves appeared totally engulfed and compressed by these large masses. No bone erosions and no endocranial extension were noted

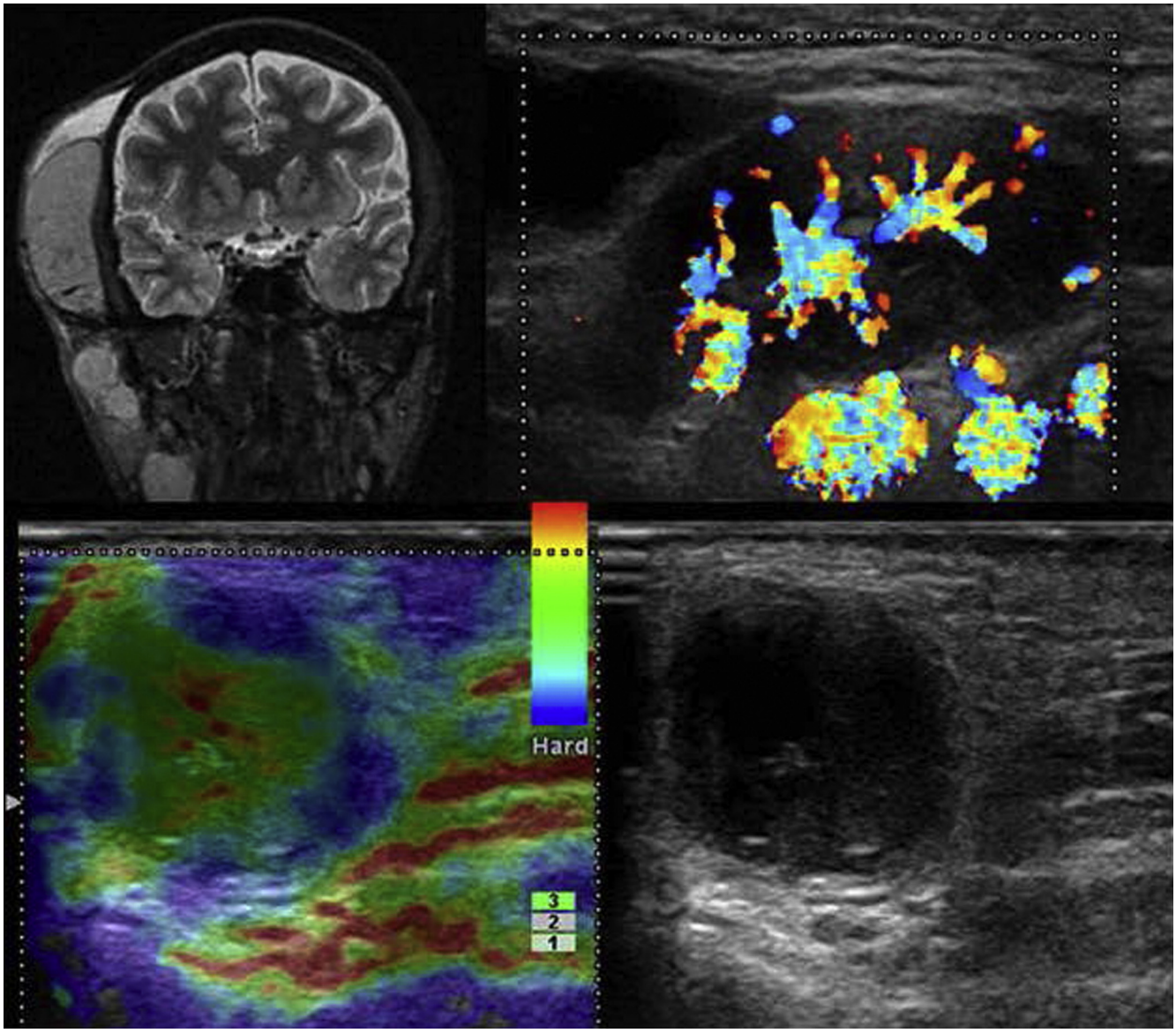

Fig. 3 – Right laterocervical neoplastic adenopathies: MRI, Color Doppler and USE appearance (note the mixt elasticity pattern within afflicted lymphnodes: soft cores with stiff periphery)

The patient stated that his eyes started swelling 4 months prior to presentation and although he had lost completely his visual function during this interval, he chose to remain home, assisted by relatives and motivating the lack of financial means and medical insurance. He was brought to ER unit only when the orbital hemorrhage could not be autonomously resolved.

The head CT and MRI revealed that the entire periorbitar space and both orbits were occupied by large, moderately enhancing masses with relatively homogeneous aspect, with the exception of a few necrotic, abscess-like middle areas. The eyeballs and optic nerves appeared totally engulfed and compressed by these large masses, but with no sign of infiltration. No bone ersosions or endocranial extension was noted (Fig. 2). However several bilateral laterocervical pathologic lymphnodes were detected.

The laterocervical adenopathies were further studied using conventional ultrasound (gray scale and Doppler mode) and free-hand elastography (USE). All analyzed features were consistent with malignancy: round shape, hypoechoic structure, no echogenic hillum, necrotic areas included, more than three vascular pedicles per lymphnode. Elastography (Hitachi 8500 EUB machine) revealed a rigid aspect in the periphery of affected lymphnodes with soft cores corresponding to necrotic areas (Fig. 3).

Body CT showed homogeneous hepatosplenomegaly and few retroperitoneal adenopathies. No pathologic lymphnodes or masses were noted within the thorax.

The patient was sent initially to an oral-maxilofacial surgery service for haemostasis and wound specialized treatment. A biopsy was performed from the periorbitar swellings.

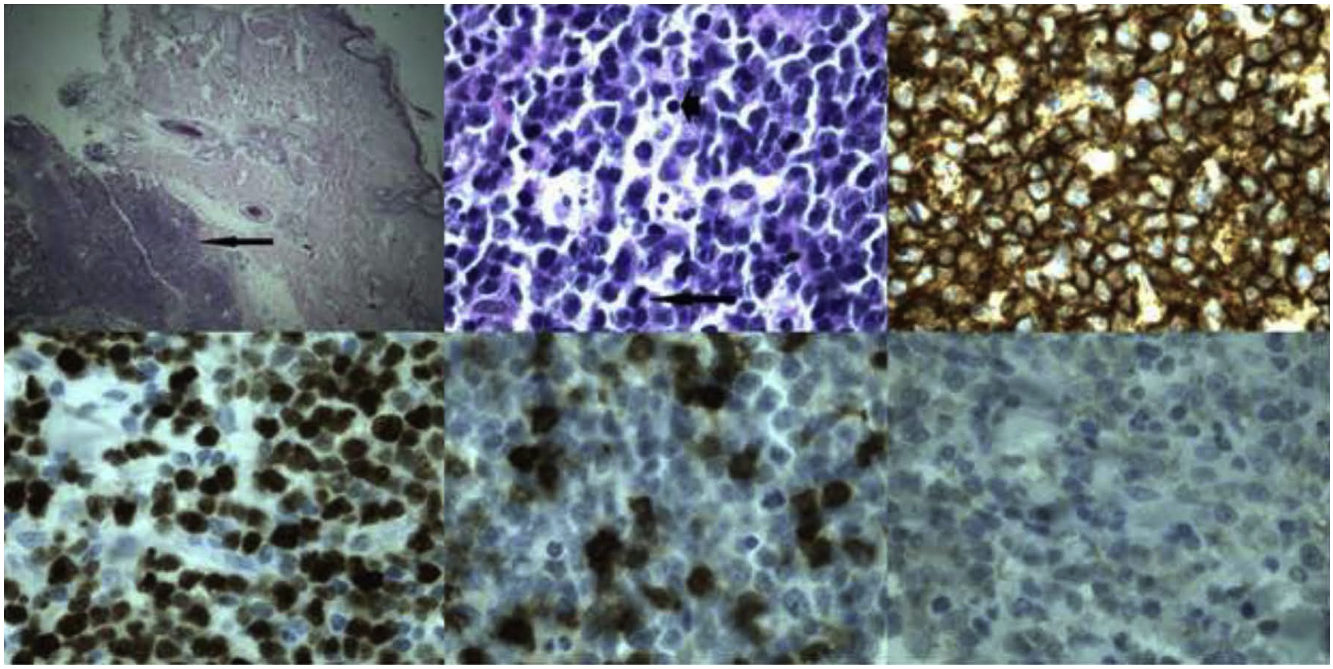

Fig. 4 – The pathology report indicated a large B cell diffuse lymphoma (from right to left large cell lymphomatous infiltrate, with numerous mitoses, intense positive staining for CD20 and Ki67, negative staining for CD10 and CD5)

The pathology report concluded that the microscopic aspect and the immunohistochemistry tests correspond most likely to a large B cell diffuse lymphoma (DLBCL) not otherwise specified: large cell lymphomatous infiltrate, with numerous mitoses, LCA positive staining, intense positive staining for CD20 and Ki67, negative staining for CD10 and CD5 (Fig. 4). Further laboratory tests excluded a HIV, Epstein–Barr or Chlamidia trachomatis infection. A bone marrow aspiration was performed revealing lymphomatous neoplastic cells.

The patient was also submitted to a lumbar punction to check for lymphomatous cells within the spinal fluid. CSF proved to be negative for malignant cells. However the patient was given Methotrexate and Cytosar as intratechal prophilaxis treatment. Oncologic therapy also included Rituximab and CHOP. After 4 chemotherapy cycles, the clinical outcome seemed optimistic since there was clinical proof of tumor shrinkage (Fig. 5) and biological tests were still within tolerable limits. Unfortunately, in spite of psychiatric and psychological assistance, the patient and his relatives refused any form of treatment after the 4th chemotherapy cycle and went home. No further data about his status have come yet to our knowledge.

Discussion

Orbital lymphoma and lymphoma of the orbital adnexae are relatively rare lymphomas, representing less than 2% of all lymphomas and have most likely a B cell lineage rather than T or NK cell origin [1, 2].

True primary orbital lymphomas are very rare (less than 0.1% of all lymphomas), usually unilateral, low grade or indolent and derive from mucosa associated lymphoid tissue (MALT). Their outcome is often favorable and diseases may be locally controlled with radiotheraphy [1–4].

Secondary orbital lymphomas are sensibly more frequent (4.7%) and represent an extension of an aggressive systemic disease, usually DLBCL. They also tend to develop unilaterally and are treated using a combination of chemo-, immune- and radiotherapy [2–5].

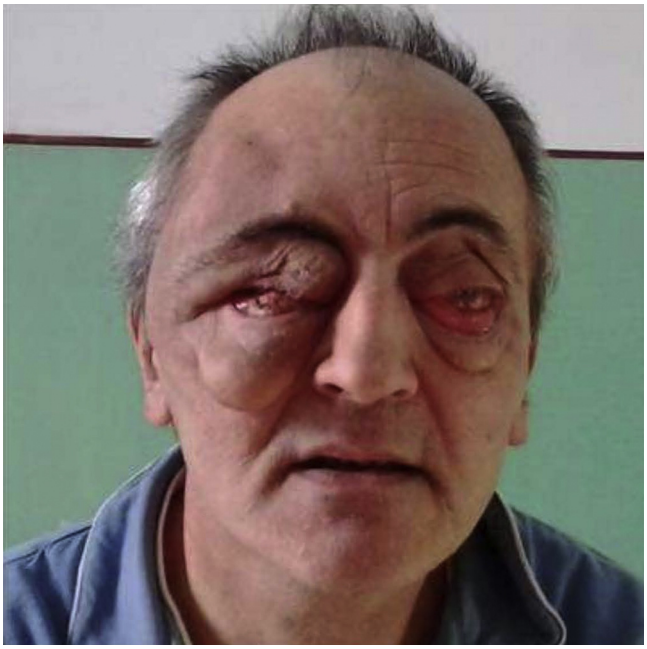

Fig. 5 – Post 4th cycle of R-CHOP chemotherapy: clinical proof of tumoral shrinkage

Imaging studies are critical in delineating the extent of orbital involvement. On CT and MRI orbital lymphoma appears as a rather circumscribed mass, with homogeneous structure, moderately enhancing post intravenous contrast, molding to the eyeball, optic nerve and facial bones [3]. Appreciating endocranial extension, especially the meninges is essential for further therapy management which may include high Methotrexate doses if central nervous system is affected.

In our case the clinical presentation was striking due to bilateral orbital and periorbital involvement with large, facial distorting masses. We may speculate that the onset of lymphoma was possibly extranodal, within orbital or periorbital soft tissue and in the last few months the neglected disease becomes systemic with nodal, visceral and bone marrow involvement. From an imaging point of view, sectional imaging features were quite similar with those described in literature [3]. The novelty resides in ultrasound elastography revealing a combined elasticity pattern within afflicted lymphnodes: soft cores with stiff periphery.

Presentation of DLBCL can be quite heterogeneous when it comes to biological, morphological and genetical factors. 70% of DLBCL may be positive for BCL-6, 30–60% positive for CD 10 and 35–65% positive for MUM1/IRF4. Coexpression of MUM 1 and BCL-6 antigens may be found in 50% of diffuse non-Hodgkin lymphomas with large B cells. In our case, at the moment of diagnosis the Pathology Department could not perform tests for BCL 6 and IRF4/MUM 1 antigens. However due to a rather characteristic morphology in conjunction with positive staining for pan B lymphoma markers: CD 20 and CD 79a our pathologists indicated a most likely DLBCL NOS diagnosis. Other diagnostic possibilities would have been: non-Hodgkin plasmablastic lymphoma (which may have positive staining for CD 138 – again, not performed in our case) or with gray zone lymphoma (mixed B cell plus Burkitt features: positive staining for BCL-6 or t(14;18), positive staining BCL 2, ki 67 less than 95% of all tumoral cells). Nodular lymphocyte predominant Hodgkin's lymphoma (NLPHL) may be also considered if positive staining for CD 13 and CD 30. The anaplastic variant of DLBCL NOS may be easily superposable from a morphologic point of view with anaplastic T cell lymphoma which is intensely positive for CD 30 (ki-1). It is important to mention that most of those subentities of lymphomas benefit from the same therapeutical approach which is mainly based on staging and clinical presentation.

Among other malignant differential diagnosis we should also include melanoma (positive staining for S100 and HMN-45) and carcinoma which may present large, atypical cells with positive staining for cytokeratin.

Differential diagnostic at presentation could also have included non-malignant conditions such as a form of orbital and periorbital cellulitis [5], but the clearly neoplastic laterocervical and abdominal adenopathies shifted the diagnostic suspicion toward lymphoma from the first hours after admittance.

If the patient had been compliant to treatment, the oncologic team would have also included orbit radiation therapy. Unfortunately the patient will remain forever deprived of his visual function and overall prognosis is poor, with a 5 year survival rate, less than 30% even if the treatment would have been completely administered [6].

Authors' contributions/Wkład autorów

MMD – study design, data interpretation, manuscript preparation, literature search. AL – data collection and interpretation, manuscript preparation. LML, LU, BF – data collection and interpretation. SS – data interpretation, manuscript preparation.

Conflict of interest/Konflikt interesu

None declared.

Financial support/Finansowanie

None declared.

Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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