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Chemosis as a presenting symptom of systemic lupus erythematosus

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Abstract

We present a case of chemosis (conjunctival edema) as an early manifestation of severe systemic lupus erythematosus affecting multiple organs, including the central nervous system and the kidneys.

Keywords

Chemosis; neuro-psychiatric lupus; SLE

Case presentation

A 35-year-old woman with history of psoriasis was admitted because of suicidal thoughts. Three months prior to admission the patient started experiencing episodes of joint pain involving primarily the proximal interphalangeal (PIP) joints of the hands. The pain was associated with swelling of the joints and responded to ibuprofen. Three weeks prior to admission the patient developed swelling of her eyelids and conjunctivae, which was initially treated with antihistamines with minimal effect. Two weeks prior to admission she was given a 4-day course of corticosteroids with mild improvement of her symptoms. An outpatient evaluation was performed 11 days prior to admission which disclosed periorbital and conjunctival swelling (Figure 1), minimal tenderness over the PIP joints of both hands and a diffuse erythematous psoriasiform rash. The laboratory evaluation is shown in Tables 1 and 2. Over the next week, the patient developed increased anxiety, pressured speech, and expansive affect. She was admitted to the hospital shortly after she expressed suicidal thoughts.

On admission the patient was found to be afebrile; the blood pressure was 130/107 mmHg. She exhibited delusions of grandeur. There was no neck stiffness or tremor. General physical exam revealed decreased breath sounds on the right lung base, pain without synovitis of the PIP joints of both hands and a diffuse erythematous papular rash covering mainly the lower extremities but sparing the feet. Initial laboratory evaluation is shown in Tables 1 and 2. A radiogram of the chest is depicted in Figure 2. Soon after her admission the patient underwent a brain magnetic tomography, a lumbar puncture (Table 3) and a thoracentesis (Table 4).

Differential diagnosis

The patient presented with acute onset psychosis in the context of clinical and laboratory evidence of systemic lupus erythematosus (SLE). Lupus-associated psychosis is rare with 2–5% of SLE patients developing this complication, most often during the first year of disease onset.^{1,2} Although the clinical presentation of this patient was consistent with lupus psychosis, other conditions needed to be ruled out. In particular, because the patient received corticosteroids prior to this episode, steroid psychosis was entertained. Nevertheless, the onset of symptoms several days after the discontinuation of the corticosteroids and the low dose of prednisone used point against steroid-psychosis. Metabolic disorders such as hyperthyroidism and central nervous system infectious processes were excluded on the basis of lack of supporting clinical and laboratory findings from the blood and cerebrospinal fluid.

Ocular/peri-ocular edema in patients with SLE

Our patient developed prominent ocular signs which preceded the overt clinical picture of systemic lupus. The clinical and laboratory findings excluded other conditions such as severe allergic reaction, cavernous sinus thrombosis, increased intracranial pressure, and thyrotoxicosis that can cause severe ocular/periocular edema. Therefore we concluded that our patient had lupus-induced chemosis, a rather rare sign of SLE.³

Our patient presented with hypo-albuminemia (<2.8 g/dl) but no systemic signs of the nephrotic syndrome. Therefore, a possible cause could be the reduced osmotic pressure inside the vascular lumen of the conjunctival and/or periorbital capillaries. Nonetheless, this assumption finds little support from current evidence. To date, there is only one report of chemosis during established nephrotic syndrome⁴ in a pediatric patient.

The most plausible cause for these signs would be the inflammatory one. As early as 1990, Frith *et al.*⁵ reported in a case series of patients with SLE high incidence of deposition of immunoreactants in a linear pattern at the basement membrane zone in the bulbar conjunctiva. Later, Heiligenhaus *et al.*⁶ claimed that the rare epibulbar manifestations of SLE resulted from immune-complex-mediated reactions.

In 1982 Smith *et al.*⁷ reported the first cases of periorbital edema and Shu *et al.*⁸ followed in 1992 reporting the first case of isolated chemosis, both related to SLE. It was clear at that time that it was not due to systemic edema but was considered a local inflammatory feature of the SLE. Norden *et al.*⁹ reported another case of bilateral orbital edema associated with SLE and confirmed the local inflammatory response of the conjunctiva. In 1996, Jarek *et al.*¹⁰ reported three more cases of conjunctival edema during SLE flares and confirmed the absence of systemic causes of edema, such as hypoalbuminemia, as the cause of its appearance. After that, the aforementioned association has been reported in other two occasions.^{11,12}

In conclusion, it appears that local inflammation of ocular structures can result in conjunctival edema, as was the case with our patient.

Diagnosis

Systemic lupus erythematosus affecting the central nervous system (CNS) and kidneys and prominent ocular inflammation.

Treatment course

The patient received 1000 mg of methylprednisolone intravenously each day for 3 days. Thereafter, she was maintained on methylprednisolone 60 mg intravenously per day. The suicidal thoughts, pressured speech and expansive affect improved significantly over the next ten days. The ocular symptoms and signs improved as well. The creatinine normalized after a week and the urine sediment improved significantly over the next weeks. Mycophenolate mofetil 2000 mg daily in divided doses was started as a steroid sparing agent/immunomodulator. Four weeks after the admission, the patient still had residual psychiatric symptoms despite being on 60 mg daily of oral prednisone. It was considered that mycophenolate mofetil was not effective and it was discontinued. Monthly intravenous cyclophosphamide was initiated. The patient had complete resolution of her symptoms and normalization of her laboratory values (Table 1) after two infusions of cyclophosphamide. Fertility concerns led to the discontinuation of cyclophosphamide after the third infusion and reintroduction of mycophenolate mofetil. The patient remained in clinical remission 1 year after the initial episode.

Treatment of psychiatric manifestations of SLE

The American College of Rheumatology recognizes 11 different syndromes of neuro-psychiatric lupus, one of which is psychosis. Most patients with lupus psychosis (61%) develop this complication soon after the onset of SLE. Contrary to other autoimmune diseases that affect the brain, such as multiple sclerosis and central nervous system vasculitis, that are isolated to the CNS, lupus psychosis is accompanied by symptoms and signs of systemic inflammation.²

The underlying pathologic process of neuro-psychiatric lupus is unclear. As in the case of our patient, there is little evidence of direct cell infiltration of the brain. Evidence of increased globulin in the cerebrospinal fluid (CSF) as well as presence of oligoclonal immunoglobulins point to the fact that humoral factors may be involved in the pathophysiology of neuro-psychiatric lupus. In fact it has been hypothesized that anti-neuronal antibodies that are found in the CSF of patients with SLE directly damage neurons. Furthermore, animal studies have shown that autoantibodies that bind the *N*-methyl *D*-aspartate (NMDA) receptor lead to cognitive impairment in the animals.^{13,14} Evidence though, that autoantibodies directly damage or impair human neurons is still lacking. Besides autoantibodies, toxic products of the abnormal immune response in SLE may account for the neuro-psychiatric manifestations. For example, interferon-gamma, which is produced by activated T cells leads to increased catabolism of *L*-tryptophan and production of quinolinic acid by activated macrophages.¹⁵ Quinolinic acid is neurotoxic and has been found to be elevated in the CSF of patients with neuropsychiatric lupus,¹⁶ thus linking the deregulated immune response in SLE to neurological dysfunction.

The rarity of this manifestation of lupus has precluded the conduction of large well-controlled clinical trials on the treatment of neuro-psychiatric lupus and in particular psychosis. As most patients with lupus psychosis present with multi-system disease, the initial treatment consists of high dose corticosteroids. The usefulness of cytotoxic drugs in the management of patients with lupus psychosis is unclear. There is only one randomized trial to date that compared cyclophosphamide and corticosteroids to corticosteroids alone in the management of primarily neurological manifestations of lupus.¹⁷ Despite the low number of patients included and the heterogeneity of the groups, the cyclophosphamide group had significantly better response and adherence to treatment than the corticosteroid only group. It has to be pointed out that patients with psychotic only features were not included in this study. Other modalities that have been used anecdotally or in small trials are

plasmapheresis, azathioprine,² intravenous gamma globulin,¹⁸ and intrathecal methotrexate and dexamethasone.¹⁹ Finally, the prognosis of patients with lupus psychosis varies but as many as one third of these patients relapse within a year after the initial psychotic episode.²

In conclusion, we present a case of severe lupus with involvement of multiple organs including the CNS, kidneys, serosal membranes, joints and skin. In addition this patient had, early on, prominent eye manifestations that could be attributed to ocular/periocular inflammation and/or edema due to hypoalbuminemia. Despite the initial success of high doses of corticosteroids, intravenous cyclophosphamide was needed in order to achieve full remission. Ocular/periocular manifestations can be an early albeit rare manifestation of severe SLE, and therefore a valuable clue to early diagnosis and prompt therapeutic intervention that may avert irreversible organ damage.

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Figure 1.
Conjunctival (chemosis), peri-orbital and eyelid edema.

Figure 2.
Chest X-ray depicting bilateral pleural effusions.

Table 1

Results of blood tests

Test (units)	Values			Normal range
	11 days prior to admission	On admission	10 weeks after admission	
Hematocrit (%)	30.9	35	34.1	36–48
Hemoglobin (g/dl)	10.3	12	11.3	12.0–16.0
White blood cells (cells/ μ l)	6200	7000	7300	4000–11,000
Differential (%)				
Neutrophils	73.4	81	87.9	50–70
Bands	0	1	–	0
Lymphocytes	20.9	15	7.8	18–42
Eosinophils	0.7	0	0.3	0–4
Monocytes	4.5	3	4.1	2–11
Basophils	0.4	0	0	0–2
Platelets	–	–	–	150,000–400,000
Erythrocyte sedimentation rate (mm/h)	58	–	35	0–20
c-Reactive protein (mg/l)	4.9	2.3	–	0–5
Albumin (g/dl)	–	2.3	4.1	–
Urea nitrogen (mg/dl)	–	54	23	6–20
Creatinine (mg/dl)	–	2.4	1.2	0.4–1.1
Complement C3 (mg/dl)	17	<15	100	90–180
Complement C4 (mg/dl)	4	3	43	10–40
Antinuclear antibody (titer)	1: 640	–	–	<1: 80
Anti-dsDNA antibody (titer)	1: 1280	–	Negative	Negative
Sm antibody (units)	3.9	–	–	<1
RNP antibody (units)	2.4	–	–	<1
SSA/SSB antibodies (units)	<1	–	–	<1
Ribosomal P antibody (units)	<1	–	–	<1
IgG Anticardiolipin antibodies (units)	17	–	–	0–15
TSH (μ IU/ml)	–	1.6	–	0.27–4.2
Thyroid stimulating immunoglobulin	–	–	100%	<125% of baseline

Table 2

Results of urinalysis

Test (units)	Results			Normal range
	11 days prior to admission	On admission	10 weeks post admission	
Red blood cells (cells/hpf)	3	2	0	0–2
White blood cells (cells/hpf)	11	11	0	0–6
Blood	Trace	Small	Negative	Negative
Protein/creatinine ratio	–	0.9	0.1	<0.1
Microscopy	Numerous granular and hyaline casts; few cellular casts	Numerous granular and hyaline casts	–	–

Table 3

Results of cerebrospinal fluid analysis

Test (units)	Values	
	On admission	Normal values
Red cells (cell/ μ l)	2	–
White cells (cells/ μ l)	125	–
Differential		
Neutrophils (%)	12	–
Lymphocytes (%)	80	–
Monocytes (%)	8	–
Total protein (mg/dl)	81	15–45
Glucose	81	–

Table 4

Results of pleural fluid analysis

Test (units)	On admission
Red cells (cell/ μ l)	775
White cells (cells/ μ l)	125
Differential	
Neutrophils (%)	1
Lymphocytes	9
Monocytes	3
Mesothelial	2
Macrophages	83
Nucleated red cells	1
Atypical lymphocytes	1
Total protein (g/dl)	2.0
Glucose (mg/dl)	148