



The First Case Report of Schnitzler Syndrome Presenting with Eye Pain

Richard R. Sadig, D. Wakefield & CL. Fraser

To cite this article: Richard R. Sadig, D. Wakefield & CL. Fraser (2019): The First Case Report of Schnitzler Syndrome Presenting with Eye Pain, Ocular Immunology and Inflammation, DOI: [10.1080/09273948.2018.1563704](https://doi.org/10.1080/09273948.2018.1563704)

To link to this article: <https://doi.org/10.1080/09273948.2018.1563704>



Published online: 22 Feb 2019.



Submit your article to this journal [↗](#)



Article views: 3



View Crossmark data [↗](#)



LETTER TO THE EDITOR

The First Case Report of Schnitzler Syndrome Presenting with Eye Pain

Richard R. Sadig, MBBS, B Pharm (hons)¹, D. Wakefield, MBBS (Hons 1) MD DSc FRACP FRCPA FFSc², and CL. Fraser, MBBS, MMed, FRANZCO³

¹St George and Sutherland Clinical School, Faculty of Medicine, University of New South Wales, Kogarah, NSW, Australia, ²Faculty of Medicine, University of New South Wales, NSW Health Pathology, Sutherland Centre of Immunology, The Sutherland Hospital, The Kingsway, Caringbah, NSW, Australia, and ³Save Sight Institute, University of Sydney, Sydney, NSW, Australia

ABSTRACT

Schnitzler syndrome is a rare, auto inflammatory condition known to manifest with bone pain, urticarial rash, fevers, relapsing arthralgia, and fatigue. In this case report, we describe a patient who was diagnosed with Schnitzler Syndrome that had initially presented with a unilateral pressure-type headache with a sensation of a 'dagger' stabbing into the back of the eye. He also had an associated ipsilateral redness of the conjunctiva, eyelid swelling, subtle optic disc elevations bilaterally and facial flushing - but with no visual acuity, pupillary, or lacrimal changes. Anterior segment, funduscopy, intraocular pressures and extraocular muscle movements were otherwise normal.

Keywords: Autonomic cephalgia, disc elevation, eye pain, injected conjunctivae, ophthalmology, Schnitzler

Schnitzler Syndrome is a rare auto-inflammatory condition of unknown etiology diagnosed by the presence of two major criteria – a chronic urticarial rash and a monoclonal IgM or IgG profile – in addition to the presence of two minor criteria: a recurrent fever, abnormal bone remodeling (via scintigraphy, MRI/or elevated alkaline phosphatase), a neutrophilic dermal infiltrate on biopsy, or evidence of leucocytosis ($>10000 \mu\text{l}$ or CRP changes $>30 \text{ mg/L}$). The presence of three of the minor criteria can be used to make the diagnosis according to the Strasbourg Criteria (Table 1).^{1,2}

Most of the 281 reported cases of Schnitzler syndrome published worldwide describe associated symptoms of Schnitzler syndrome such as bone pain, urticarial rash, fevers, relapsing arthralgia and fatigue.^{1,3,4}

In this case report, we present a 61-year-old Caucasian man who presented to private practice (Sydney Ophthalmic Specialists) with a right-sided ocular pain on the background of surgery for prostate cancer.

His past medical history was significant for having had prostate cancer for which he underwent surgery 2 months after the onset of the rash. He was otherwise fit and well and not on any regular medications. There was a past ocular history of having had a gunpowder injury to the right eye as a child. He denied any preceding overseas travels or any animal exposure or tick bites.

Two years earlier he developed a pruritic urticarial rash on his back, which progressively worsened to cover his back and arms. In the months prior to presentation he had the onset of a right-sided pressure-type headache with a sensation of a 'dagger' stabbing into the back of the eye. His face felt flushed from the corner of his mouth all the way up to his forehead (V1/V2 distribution). This progressed over a few hours with increasing ache behind the right eye. Within 12–24 h of the onset of the eye pain, the rash on his arms and body became significantly worse. When the rash worsened, the stabbing pain in the eye typically was also at its worst and his temperature was elevated to 40°C . There was associated redness of

Received 17 April 2018; revised 19 December 2018; accepted 21 December 2018

Correspondence: Richard Sadig, St George and Sutherland Clinical School, Faculty of Medicine, University of New South Wales, Clinical Sciences (WR Pitney) Building, Short Street, St George Hospital, Kogarah, NSW. E-mail: richard.sadig1@my.nd.edu.au

TABLE 1. A table of differential diagnoses for this presentation.^{2,5}

Differential Diagnoses	
Autonomic Cephalgia	Cryoglobulinemia
Polyneuropathy Organomegaly	Waldenström's
Endocrinopathy Monoclonal protein	macroglobulinemia
Skin changes (POEMS)	
Chronic idiopathic urticaria	Muckle-Wells
	syndrome
Still Disease (Adult onset)	Paraneoplastic
	phenomena
Urticarial vasculitis	

the conjunctiva, the lids were swollen and there was a feeling of fullness in his ears. There were no pupil changes and there was no lacrimation. As the rash and pain subsided, his face and eyes looked slightly yellow in color. Over this period he reported to have lost 20 kg in weight. There were no abnormalities found on endoscopy, colonoscopy, or chest/abdominal/pelvis CT scan.

On examination his visual acuity was 20/20, N5 with full color vision in each eye. He was orthophoric with a full range of extraocular movements. Intraocular pressures were 19 mmHg. There was no ptosis and lid function was normal. The right lid skin appeared excoriated and thickened, as though he had been scratching. There was no anisocoria and no relative afferent pupillary defect. Cranial nerve examination was normal. Slit lamp examination showed slightly injected conjunctiva, particularly on the right side. The cornea and anterior segment was unremarkable. Fundoscopic examination showed some subtle disc elevation nasally bilaterally. The macula, vessels and retinal periphery were unremarkable. Automated visual fields were normal. He had a generalized urticarial rash without angioedema or dermatographia. There was no lymphadenopathy.

Blood tests revealed an elevated ESR (40 mm/hr), CRP (68.8 mg/L), white cell count ($15.1 \times 10^9/L$) and neutrophilia ($12.4 \times 10^9/L$). There was a monoclonal IgM lambda pattern on EPG. The rest of his blood count, liver and renal function tests were normal. Other markers of infection and inflammation were negative. PSA was normal. Biopsy of the skin lesions revealed urticarial changes without evidence of mastocytosis.

The patient was diagnosed with Schnitzler syndrome based on the Strasbourg Criteria of a neutrophilic urticarial rash with monoclonal IgM paraprotein, fever and weight loss. Many treatments are available to treat Schnitzler syndrome – however a trial of oral Prednisolone and subsequently Anakinra (an interleukin-1 receptor antagonist) was chosen in this patient to achieve good results. His headaches and ocular symptoms resolved with treatment of the Schnitzler syndrome concordantly.

DISCUSSION

The initial differential diagnosis of this patient was broad as the headaches were similar in nature to one of the autonomic cephalgias – which typically are associated with stabbing pain and autonomic features including redness, ptosis and ‘stuffiness’ in the ear. However, the duration of the pain and the association with fever and rash were not typical of a classic autonomic cephalgia. The rashes of autonomic cephalgias are typically present in the facial area spread over the trigeminal distribution of the face and can often coexist with autonomic dysfunction, such as temperature dysregulation and ocular changes.⁵

In this particular case report the urticarial rash spared the face which seemed atypical for an autonomic cephalgia. In addition, the patient was not on a regular medicines that would suggest an urticarial reaction secondary to drug induced urticaria. A paraneoplastic phenomena was considered given the recent diagnosis of prostate cancer and subtle disc changes with the rash seen in POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, myeloma protein and skin changes) – however no other features of organomegaly or endocrinopathy were present.

The presence of the IgM paraprotein led us to believe it might have been a Waldenström's, myeloma or lymphoma, however his other routine blood tests were not suggestive of any myeloproliferative disorder. In addition, this case was unique because it had features of urticaria, autonomic cephalgia, neuropathy and features of disc changes which are unusual in their combinations. The absence of hearing loss, amyloid deposition and familial pattern of inheritance were features against the diagnosis of Muckle-Wells syndrome.

CONCLUSION

We hypothesize that the ocular pain was primarily a manifestation of Schnitzler syndrome in the same fashion as the more typically associated bone pain and arthralgias.

PATIENT CONSENT

Patient has provided informed consent for details to be used in this case report. All personal details have de-identified.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

ORCID

Richard R. Sadig  <http://orcid.org/0000-0003-2267-7461>

REFERENCES

1. Simon A. Schnitzler's syndrome: diagnosis, treatment, and follow-up. *Allergy (Copenhagen)*. 2013;68:562–568.
2. Rowczenio DM, Pathak S, Arostegui JI, et al. Molecular genetic investigation, clinical features, and response to treatment in 21 patients with Schnitzler syndrome. *Blood*. 2018;131(9):974–981. doi:10.1182/blood-2017-10-810366.
3. de Koning HD. Schnitzler's syndrome: lessons from 281 cases. *Clin Transl Allergy*. 2014;4(1):41. doi:10.1186/2045-7022-4-41.
4. Lipsker D, Lenormand C. Management of Schnitzler's syndrome. *Expert Opin Orphan Drugs*. 2014;2(9):947–955. doi:10.1517/21678707.2014.939170.
5. Lambru G, Matharu MS. Trigeminal autonomic cephalalgias: A review of recent diagnostic, therapeutic and pathophysiological developments. *Ann Indian Acad Neurol*. 2012;15(Suppl 1):S51–S61. doi:10.4103/0972-2327.100007.