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Case report and review

Gold induced enterocolitis

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SUMMARY A case of gold associated enterocolitis is described. A review of all 27 previously reported cases revealed that the syndrome induced has common characteristics. The reaction occurs within three months of instituting gold therapy, is characterised by profuse diarrhoea and vomiting with abdominal pain, fever, and sometimes eosinophilia. Petechial changes are prominent on endoscopy and the endoscopic and histological features of the gut lesion do not resemble inflammatory bowel disease. The overall mortality is 26% but has decreased in recent years. There is no specific therapy but in severe cases diversional surgery may be justified.

Case history

Mrs B S was a 34 year old patient of Asian extraction who had lived in the UK for 29 years and was admitted with a three week history of diarrhoea. In 1980 she presented with symptoms typical of rheumatoid arthritis confirmed on serology. Treatment included a number of non-steroidal anti-inflammatory medications and choloroquine. In the summer of 1982, because of symptom deterioration, a decision was made to treat her with intramuscular sodium aurothiomalate. Twenty four hours after an initial dose of 10 mg she developed pruritis, sore eyes, a rash on the neck, and a sore throat. These symptoms settled after a few days and one week later she received a second dose of 10 mg, with no problems. A third dose of 50 mg was given after a further week and the following day she developed a fever, sore throat, vomiting, and diarrhoea. The diarrhoea progressively deteriorated over the next three weeks although her arthritis improved.

On admission she was dehydrated, shocked, had a temperature of 38°C and a pulse of 120. The serum potassium was low and there was a mild eosinophilia (800/cu mm). Stool examination for viruses, acid fast bacillae, parasites, yersinia as well as other common bacterial pathogens was negative. Barium meal and follow through showed a diffusely abnormal small bowel mucosa with loss of mucosal pattern and separation of loops. Colonoscopy revealed a total colitis with diffuse haemorrhage and inflammation but no mucus or pus. The endoscopic appearances did not resemble inflammatory bowel disease. Despite treatment with intravenous fluids, glucose and electrolyte solutions, prednisolone 60 mg daily and metronidazole she continued to deteriorate to the point of becoming moribund. It was decided to do a laporatomy. The findings at operation were of some thickening of the whole of the large bowel and lower few feet of the small bowel. The upper small bowel did not appear to be grossly abnormal. There were enlarged soft glands in the mesentery of the ileum and in the paracolic tissues. The transverse colon was opened and the mucosa appeared thickened and velvety. Biopsies were taken from this area. As the colon was the most severely inflammed part of the bowel it was decided to create a defunctioned loop ileostomy. Whilst this was being fashioned the opportunity was taken to obtain ileal biopsies. She made a good recovery from the operation with remission of her diarrhoea and surprisingly did not suffer extensive loss from her ileostomy, the effluent not exceeding 1·5 l/day.

The small intestine and colonic biopsies showed similar appearances. Initially there was surface ulceration and the lamina propria was oedematous containing a moderate degree of chronic inflammatory cells, amongst which plasma cells and eosinophils predominated. Some crypt absesses were also observed. There was no evidence of crypt distortion, mucus depletion, granuloma formation, vasculitis or amyloid deposition or tuberculosis.

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Table 1 *Patient details*

Case no	Ref no and year	Age and sex	Time to onset of symptoms after first dose (weeks)	Dose to onset of symptoms (mg)	Gold preparation administered	Time from onset to outcome (weeks)	Race	Presenting disorder	Rheumatoid serology	Remission of RA	Eosinophilia
1	1 1929	30 F	8	5 injections	Krysolgan	2 D*	Jewish	SLE‡			
2	2 1935	47 F	?	240	Thioglucose	2 D	Unknown	PCP§			
3	3 1939	yng F	?	?	?	?	Unknown	SLE			
4	4 1939	33 F	?	5 injections	Na Thiosulphate	> 30 R†	Unknown	SLE			
5	5 1940	47 F	3	200	Na Thiosulphate	3 D	Caucasian	UA‖			
6	6 1961	53 F	?	74	Na Thiosulphate	R	Unknown	RA¶			
7	7 1972	56 F	8	?	Na Thiomalate	2 D	Caucasian	UA	−ve		
8	8 1973	24 F	5	250	Na Thiomalate	> 13 R	Jewish	RA	−ve	+	
9	8 1973	46 F	9	485	Na Thiomalate	> 5 D	Jewish	RA	+ve	+	
10	9 1976	50 M	?	200	Thiopropanolsulphate	20 R	Unknown	RA			+
11	10 1976	45 F	3	130	Na Thiomalate	6 D	Jewish	RA	+ve	+	+
12	11 1976	59 F	8	335	Na Thiomalate	> 4 R	Oriental	RA	+ve	+	
13	12 1979	41 F	?	485	Na Thiomalate	R	Caucasian	RA			
14	13 1979	25 F	4	200–250	Na Thiomalate	> 10 R	Caucasian	RA	−ve		
15	13 1979	77 F	?	290	Na Thiomalate	> 4 D	Caucasian	RA			
16	14 1980	64 F	150	2600P	Na Thiomalate	< 16 R	Unknown	RA	+ve	+	
17	14 1980	50 F	5	210	Na Thiomalate	8 R	Unknown	RA	+ve		+
18	15 1980	38 M	10	320	Na Thiomalate	8 R	Unknown	RA	+ve	+	
19	16 1981	50 F	8	205	Na Thiomalate	10 R	Caucasian	RA	−ve	+	+
20	17 1982	71 M	5	235	Thioglucose	13 R	Jewish	RA	−ve		
21	18 1982	59 F	8	410	Na Thiomalate	> 13 R	Unknown	RA	+ve	+	
22	19 1983	78 F	8	485	Thioglucose	12 R	Unknown	RA			
23	20 1983	58 M	4	130	Na Thiomalate	> 16 R	Unknown	RA	+ve		
24	21 1983	44 F	5	425	Thiopropanolsulphate	> 8 R	Unknown	RA	+ve		
25	22 1983	66 F	9	375	Na Thiomalate	> 8 R	Unknown	RA	+ve	+	
26	23 1983	69 F	4	Oral 168	Triethylphosphine	8 R	Unknown	RA	+ve	+	
27	24 1984	35 F	3	170	Na Thiomalate	2 R	Caucasian	RA	+ve	+	
Present case		34 F	3	70	Na Thiomalate	90 R	Asian	RA	+ve	+	+

*D=Died, †R=Recovered, ‡SLE=Systemic, lupus erythematosis, §PCP=Primary chronic, polyarthritis, ‖UA=Undefined arthritis, ¶RA=Rheumatoid arthritis, P This was the patients 2nd course of gold

Over the next 21 months she was colonoscoped at three monthly intervals. For the first year no major improvement occurred after which there was a steady return to macroscopic and microscopic normality. As her colitis gradually resolved her arthritis started to become more active again.

LITERATURE REVIEW

In the early 1920s gold was introduced for treatment of a number of diseases including rheumatoid arthritis and systemic lupus erythematosis. The first case of gold induced colitis was reported by O'Donovan in 1929 and since that time only a further 26 cases have been described in the world literature.[1-24] Twenty one of these have been reported since 1972, probably reflecting a combination of an increased awareness of the condition, after publication of a paper by Roe *et al* in that year, and a steady increase in the use of gold over the last two decades (Figure).

All the available data on the previously reported cases have been reviewed and is presented in Tables 1 and 2. As can be seen, the reaction is more common in women (6:1) and there is no particular age of predilection. Nineteen per cent of patients were Jewish and 41% experienced a remission of arthritic symptoms during their colitis.

Any part of the gastrointestinal tract can be involved and histological examination reveals non specific inflammatory changes, however, an early and transient eosinophilic infiltration may occur. Although overall mortality is 26% there have been no deaths in the 12 cases reported since 1979.

It is characteristic for the colitis to start relatively soon after initiation of gold therapy. All but one of the cases occured within 10 weeks of starting gold and had received less than 500 mg of the chosen preparation. Thus, the toxicity does not appear to be dose related but is more likely to be an hypersensitivity reaction. At least five different gold salts have been incriminated, with the implication that it is the gold rather than any other moiety that is responsible for the reaction.

A wide variety of therapies have been used (Table 2) with no regime appearing to be particularly effective. Twenty two patients have been reported since the introduction of corticosteroids in the 1950s. Of these, 13 patients including all those who died, were treated in this way. The deaths may have been a reflection of the severity of the enterocolitis rather than a deleterious effect of therapy, however, in general treatment with steroids seems to have had little benefit.

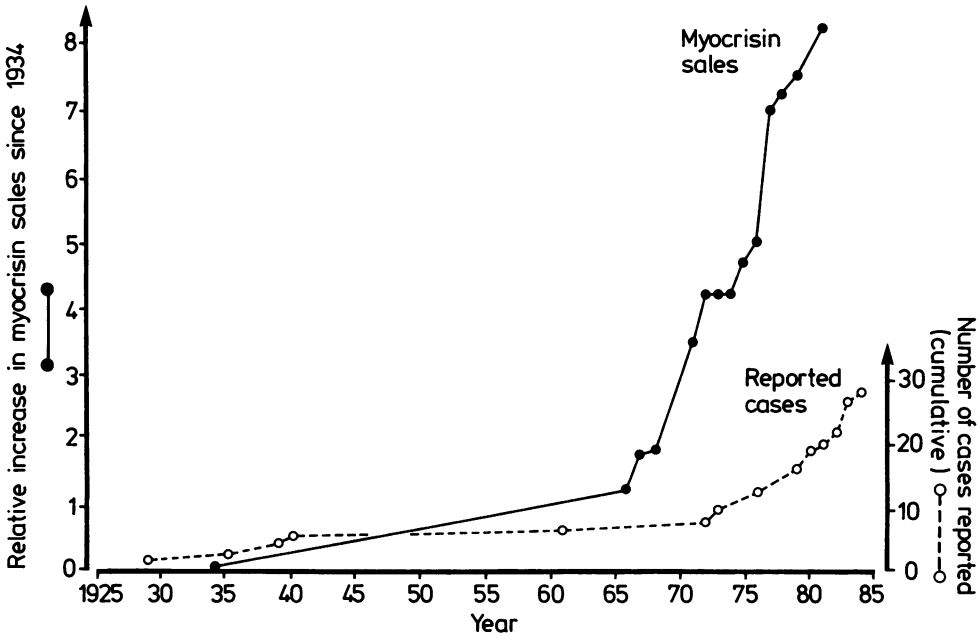

Figure *A graph relating Myocrisin sales expressed as a proportion of the 1966 sales figure and the cumulative number of cases of gold entercolitis with time.*

Table 2 *Patient details*

Case no	Time from onset to outcome (weeks)		Treatment					
			Steroids	*Antibiotics*	*TPN*	*Surgery*	*Antidiarrhoeal agents*	*Other agents*
1	2	D*						
2	2	D						
3	?							
4	>30	R†						
5	3	D						Salicylate, liver extract, vits, calcium
6		R	+	+				ACTH
7	2	D	+				Lomotil, opiates	Meprobamate
8	>13	R						BAL (Dimercaprol)
9	>5	D	+	+			Opiates	
10	20	R						
11	6	D	+	+	+		Opiates, atropine	Amphotericin, BAL
12	>4	R	+					
13		R						
14	>10	R	+	+	+		Lomotil	Milk free diet, BAL, vit K, ACTH, ISG‡
15	>4	D	+				Antidiarrhoeal agents	Antispasmodics
16	<16	R				+		
17	8	R	+	+	+			
18	8	R						K+ supplements
19	10	R			+		Metamucil, Lomotil	Sodium cromoglycate
20	13	R	+		+			
21	>13	R	+	+	+	+		
22	12	R	+	+			Lomotil, opiates, Loperamide	Lactose free diet, cholestyramine Mepacrine
23	>16	R	+					Sulphasalazine
24	>8	R						Sodium cromogycate
25	>8	R						Aluminium hydroxide
26	8	R	+	+	+		Retardin	
27	2	R						
Present case	90	R	+	+		+	Lomotil, Loperamide, opiates	Dioralyte, Complan, vit supplements

* Died, † Recovered, ‡ Immune serum globulin

Discussion

The case described here closely resembles the features of those reported in the literature. As this reaction is relatively rare, mild cases may well be overlooked and even in more severe cases, there may be a reluctance to confidently diagnose this condition and rule out other possibilities such as inflammatory bowel disease. It is suggested that if stool cultures are negative, the diagnosis should be suspected in the presence of an eosinophilia and endoscopic appearances characterised by petichial changes with no mucus or pus. Steroids had no beneficial effect on our patient and this may be another useful clinical feature. The role of surgery is questionable but in our moribund patient there was a dramatic improvement after a diversionary procedure and it would seem reasonable to consider this option in a patient who fails to respond to other supportive measures.

Gold associated enterocolitis should probably be placed high on the list of possible differential diagnoses in a patient with acute diarrhoea, who has received gold in the past three months. Even mild diarrhoea should be treated with suspicion and if no specific cause can be found discontinuation of therapy should be seriously considered.

We are grateful to May & Baker Ltd for supplying us with sales information on Myocrisin.

References

1 O'Donovan WJ. Gold induced diarrhoea. *Br J Dermatol* 1929; **41:** 17.
2 Goldhammer S. A fatal case of Solganol poisoning. *Med Klin* 1935; **31:** 645–7.
3 MD, Connecticut. Gold injections and colitis. [Letter]. *JAMA* 1939; **112:** 1624.

4 Perry MW. Gold injections and colitis. [Letter]. *JAMA* 1939; **113:** 965.
5 Anderson NL, Palmer WL. The danger of gold salt therapy. *JAMA* 1940; **115:** 1627–30.
6 Kandrac M, Pav J, Pechova I. Successful steroid therapy of severe enteritis caused by gold therapy. *Cas Lek Cesk* 1961; **100:** 361–7.
7 Roe M, Sears AD, Arndt JH. Gold reaction panenteritis. *Radiology* 1972; **104:** 59–60.
8 Kaplinsky N, Pras M, Frankl O. Severe enterocolitis complicating chrysotherapy. *Ann Rheum Dis* 1973; **32:** 574–7.
9 Siegman-Igra Y, Yaron M, Siletzki M, Schujman E, Gilat T. Colitis and death following gold therapy. *Rheum Rehabil* 1976; **15:** 245–7.
10 Stein AB, Urowitz MB. Gold induced enterocolitis. Case report and literature review. *J Rheumatol* 1976; **3:** 21–6.
11 Gerster GC, De Kalbermatten A, De Peyer R, Tousaint M, Carrel J. Reactions toxiques aux sels d'or avec enterocolite grave chez un homme atteint d'une Polyarthrite Rhumatoide. *Schweiz Med Wochenschr* 1976; **106:** 1606–8.
12 Szpak MW, Johnson RC, Brady CE, Boswell RN. Gold induced enterocolitis [Abstract]. *Gastroenterology* 1979; **76:** 1257.
13 Sckolnick BR, Katz LA, Kozower M. Life-threatening enterocolitis after gold salt therapy. *J Clin Gastroenterol* 1979; **1:** 145–8.
14 Fam AG, Paton TW, Shamess CJ, Lewis AJ. Fulminant colitis complicating gold therapy. *J Rheumatol* 1980; **7:** 479–85.
15 Huston GJ, Gold colitis, therapy and confirmation of mucosal recovery by measurement of rectal potential difference. *Postgrad Med J* 1980; **56:** 875–6.
16 Martin DM, Goldman JA, Gilliam J, Nasrallah SM, Gold induced eosinophilic enterocolitis: response to oral Cromolyn Sodium. *Gastroenterology* 1981; **80:** 1567–70.
17 Sukenik S, Hirsch M, Yanai-Inbar I, Krawiec J, Freund B, Horowitz Y. Enterocolitis complicating crysotherapy. *Isr J Med Sci* 1982; **18:** 1040–3.
18 Eaves R, Hansky J, Wallis P. Gold induced entercolitis: case report and a review of the literature. *Aust NZ J Med* 1982; **12:** 617–20.
19 Nagler J, Paget SA. Nonexudative diarrhoea after gold salt therapy: case report and review of literature. *Am J Gastroenterol* 1983; **78:** 12–14.
20 Reinhart WH, Kappeler M, Halter F. Severe pseudomembranous and ulcerative colitis during gold therapy. *Endoscopy* 1983; **15:** 70–2.
21 Manigand G, Dumont D, Faux N *et al.* Colite aiguë au cours des traitements pars sels d'or. *Presse Med* 1983; **12:** 2112–3.
22 White RF, Major GAC. Gold colitis. *Med J Aust* 1983; **1:** 174–5.
23 Jarner D, Nielsen AM. Auranofin (SK&F 39162) induced entercolitis in rheumatoid arthritis. *Scand J Rheumatol* 1983; **12:** 254–6.
24 Wright A, Benfield GFA, Felix-Davis D. Ischaemic colitis and immune complexes during gold therapy for rheumatoid arthritis. *Ann Rheum Dis* 1984; **43:** 495–7.