

Multifocal Nodular Cutaneous Xanthogranulomatosis in A Goose (*Anser anser*) with Hypercholesterolaemia and Hypertriglyceridaemia

DG Black BVSc

SR Raidal BVSc, PhD, FACVSc (Avian Health)

Moama Veterinary Clinic, 61 Meninya Street, Moama NSW 2731 (Black)

School of Agricultural & Veterinary Sciences, Charles Sturt University, Locked Bag 588, Wagga Wagga NSW 2678 (Raidal)

Abstract

This paper describes the clinical case of multiple nodular cutaneous xanthogranulomata located at the right beak commissure and the submandibular space of a 5 year-old female goose. The masses were surgically excised and submitted for histopathological examination. A blood sample taken at the same time as this surgery revealed hypercholesterolaemia and hypertriglyceridaemia. A blood sample taken from a second goose housed with and fed the same diet as the affected goose revealed normal cholesterol and triglyceride levels. Dietary modification and other measures were instigated in an attempt to reduce the triglyceride levels in the affected goose and hopefully prevent the recurrence of the cutaneous xanthogranulomata. These measures resulted in a significant decrease in the levels of cholesterol and triglycerides in the goose. Xanthomatous lesions in association with high blood cholesterol and triglyceride levels have been rarely reported.^{1,2,3,4} A very similar case to the one reported here was reported by Jaensch and others.^{1,2} This second case in a goose suggests that the syndrome of persistent hypercholesterolaemia and hypertriglyceridaemia and resultant cutaneous xanthogranulomata may not be an isolated incident and avian veterinarians should be watchful for this clinical picture in geese.

Introduction

In birds, the liver is the principal site of lipid synthesis. In many species of birds, fatty acids, and not glucose, provide the main energy source and the avian liver has a very high capacity for lipogenesis.⁵ Elevated blood cholesterol levels in birds can be associated with high fat dietary intake, hypothyroidism, liver disease, egg-laying, starvation and diabetes mellitus.⁶

Hypertriglyceridaemia in birds is not as commonly reported but can occur in conjunction with egg peritonitis, copper deficiency, in response to oestrogen, cholestasis and familial or idiopathic causes.^{1,2,3,4,6} Persistent hypertriglyceridaemia has been reported to result in xanthoma formation in cats and other species.⁷ However, the association of persistent hypercholesterolaemia and hypertriglyceridaemia as a cause of xanthomatous masses in birds has been less frequently reported.⁸ There has also been a report of xanthomatosis occurring in commercial chickens attributed to lipid-soluble toxic hydrocarbons in the diet.⁹ Some xanthomatous lesions can occur in response to local stimuli such as inflammation, haemorrhage or neoplasia such as the xanthomatous nodular lesions reported by Raidal et al.¹⁰

associated with neoplastic airsac epithelium in cockatoos.

There has been recent discussion regarding the classification of xanthomatous lesions in birds, specifically in relation to the differentiation between the terms xanthoma, xanthomatosis and xanthogranulomatosis.¹¹ The lesions in this case are therefore consistent with a diagnosis of multifocal cutaneous xanthogranulomatosis.

Case Report

“Lou Lou”, an 8.9kg, 5 & 1/2-year-old female goose with a previous history of mild upper respiratory infections and aggression presented on 23/11/2006 with two xanthomatous, non-painful, semi-pedunculated masses about 1 cm diameter on the right side of her face near the commissure of the bill and on the right side of her upper neck as well as thickened pendulous skin in her submandibular region with a similar 1 cm diameter xanthomatous mass on the cranial pole of this pendulous area. (Fig. 1). It was noted that she was significantly overweight with excessive subcutaneous and intra-abdominal fat deposits. From a very early age her diet consisted of grain (organic wheat) as well as daily bread, vegetables, greens and ad libitum access to grass and weeds via free range grazing.



Figure 1: “Lou Lou” - Initial presenting appearance of right side of the face showing submandibular swelling and one of the xanthomatous masses.

In view of the difficulty that the owners have in transporting Lou Lou to the clinic it was decided to take a blood sample to analyse her haematology and biochemistry profile and investigate cholesterol and triglyceride levels on the same day of surgical excision of the xanthomatous masses.

Lou Lou was given 0.8mls of Ketamine (100mg/ml) and 0.65mls of Diazepam (5mg/ml) intravenously via the cutaneous ulnar vein, then intubated and maintained via Isoflurane gaseous anaesthesia. All cutaneous masses were surgically excised as well as resection of the

major portion of the abnormal submandibular skin. The skin was sutured with absorbable monofilament glyconate suture material (3/0 Monosyn, BRAUN, Aesculap) and the lesions placed in formal saline for histopathological examination. Blood was taken via the jugular vein for haematological and biochemical (including cholesterol and triglyceride) analyses. Lou Lou made an uneventful recovery and was sent home with oral meloxicam (0.2 mg/kg BID) and amoxicillin-clavulanic acid (50 mg/kg BID) treatment.

Lou Lou's blood results were as follows:

Table 1 Haematology and biochemistry parameters measured 23/11/2006

Test	Result	Normal Range
Biochemistry		
CK	97 U/L	
Glucose	7.6 mM	6.5-12 mM
AST	28 U/L	25-150 U/L
Uric Acid	0.6 mM	0.3-0.9 mM
Cholesterol	7.8 mM	3.2-6.2 mM
Triglycerides	44.1 mM	1.7-2.9 mM
Haematology		
Haematocrit	0.40	0.33-0.48
Plasma Protein	88 g/l	40-55 g/l
WBC (estimated)	10.0 x 10 ⁹ /l	

The sample was very lipaemic with no chylomicron layer and the lipid stayed in solution indicating that the fat present was very low density lipoproteins. Lipaemia becomes apparent when the triglyceride levels reach about 3.5mmol/l.

Histological examination of several sections of the biopsied tissue revealed well-vascularised, loosely encapsulated proliferative cellular nodules separated by thin fibro-vascular septae. Larger masses contained central areas of necrosis. The predominant cell type, particularly at the outer margins of each nodule were relatively well-differentiated foamy histiocytes with abundant cytoplasm containing variable degrees of micro- to macrovesicular intracytoplasmic vacuoles. The size of these vacuoles increased further deep into the nodules where there was often a line of demarcation towards the necrotic centre of the larger masses as cells became degenerate. In such areas there were cells with abundant acicular clefts consistent with cholesterol accumulation. There were coalescing areas of cellular degeneration forming lakes of amorphous pink material most likely rich in lipid and similar areas containing dystrophic calcification. Mitotic figures were rare and when present were in the reactive cell population. Mild to moderate multifocal lymphocytic and or heterophilic inflammatory cellular infiltrations without germinal centres were also present (Figures 2, 3, 4 and 5)

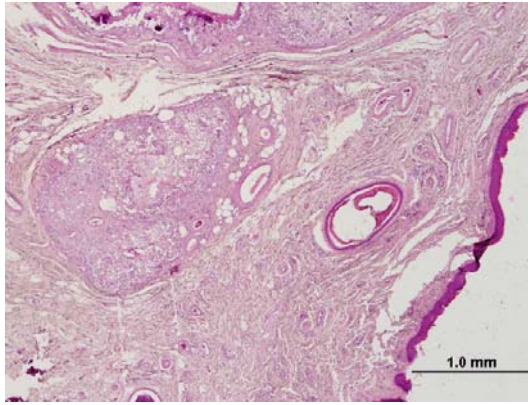


Fig. 2 A subcutaneous xanthogranulomatous nodule showing vascularisation at the margin of the nodule. There is one feather follicle to the right of the section

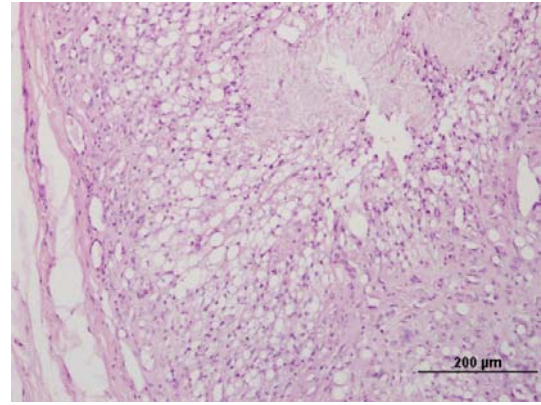


Fig. 3 Vacuolated histiocytes and a developing zone of cholesterol clefts (upper right) where cells have degenerated.

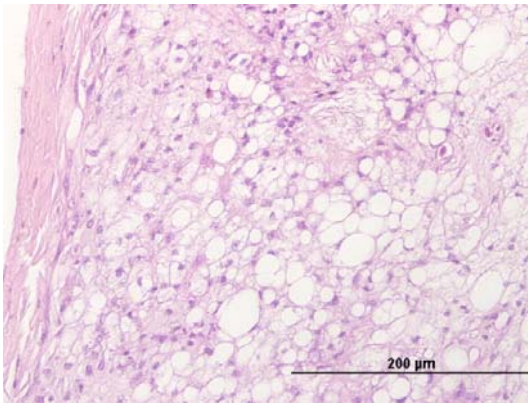


Fig. 4 Vacuolated cells and individual cells with cholesterol clefts.

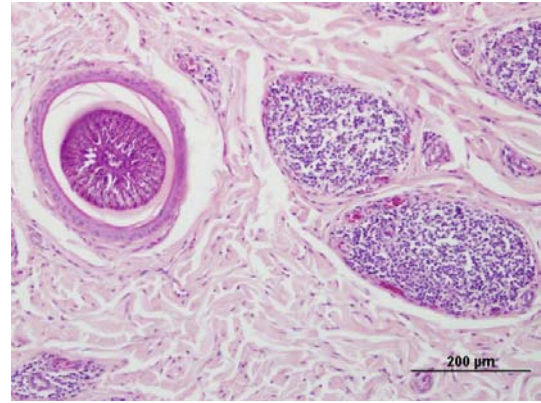


Fig. 5 Two lymphocytic nodules next to a normal feather follicle. There appears to be a mild perivascular lymphocytic infiltration that in this area has expanded out into 2 relatively large lymphohistiocytic nodules. It is not clear if this is a precursor to the larger xanthogranulomata or an inflammatory reaction.

The main lesion is composed of large vacuolated histiocytic cells with cholesterol clefts. The histopathology appeared almost identical to the case reported by Jaensch et al.^{1,2}, however in this case there was more of a multifocal nodular lymphohistiocytic infiltration. The conclusion in that case was that the lesions were consistent with a diagnosis of multiple papilliform, xanthomatous, cutaneous neoplasia. However, given the proposal put forward by Monks et al¹¹, to use the term xanthogranulomatosis to describe avian lesions in which intracytoplasmic lipid vacuoles are seen within macrophages, it is reasonable to classify the lesions in this case as multifocal cutaneous xanthogranulomata.

Despite the fact that Lou Lou had been examined and found not to have a phallus, DNA sex determination was also performed on blood taken from Lou Lou at the time of the surgery and this confirmed that she was female.

A blood sample was also taken from the only other goose housed with Lou Lou. This goose was a male (“Sam”) and was slightly overweight (7.65kgs) and being offered exactly the same diet as Lou Lou. His blood results were as follows:

Table 2 *Haematology and biochemistry parameters measured 12/12/2006 – Sam*

Test	Result	Normal Range
Biochemistry		
Glucose	14.2 mM	6.5-15 mM
AST	54 U/L	25-150 U/L
Uric Acid	0.3 mM	0.3-0.9 mM
Calcium	2.15 mM	
Cholesterol	4.2 mM	3.2-6.2 mM
Triglycerides	2.43 mM	1.7-2.9 mM
Haematology		
Haematocrit	0.50	0.33-0.48
Plasma Protein	58 g/l	40-55 g/l

The sample showed no lipaemia.

On confirmation of the high cholesterol and triglyceride levels in the blood it was advised that Lou Lou be put onto a reduced amount of fat and carbohydrate in her diet. Her intake of grain and bread was stopped and she was started on a restricted amount of layer pellets of moderate energy content. She was offered more vegetables and had ad libitum access to grazing. Her level of exercise was higher than that of her earlier life but was not increased significantly since the blood sample was taken.

In consultation with a homeopathic veterinarian, Lou Lou’s owners also gave her the following homeopathic remedies:

1. Thuja 30 C once/week x 6 weeks - apparently this is commonly used for benign growths (especially papillomas) and malignant masses and was used in this case to help prevent re-occurrence after surgery.
2. Nux Vomica LM once /day x 1 month – was used to reduce aggression as Lou Lou became quite aggressive and demanding towards her owners and other waterfowl after her grain access was denied. Nux vomica apparently also has a strong action on liver

metabolism and so was used for this purpose given the likelihood of hepatopathy secondary to fat infiltration in this case.

3. Sepia 200 twice/week x 2 weeks – was used to attempt to ameliorate certain behaviours she exhibited such as over-protectiveness and possessiveness of ducklings and a hysterical and highly strung moody nature. During the night, if the ducklings she obsessively protected made any noise, Lou Lou would begin shrieking.
4. One 500 mg fish oil cap/day and 1 teaspoon psyllium husk/day – to attempt to reduce her hypertriglyceridaemia.

It is unknown to what the level the homeopathic measures contributed to the resolution of this case.

On 10/5/2007, approximately 6 months since the surgical excision of the masses, the changes in diet and exercise and the instigation of the homeopathic measures, Lou Lou again presented to the clinic for further examination and repeat blood sampling. At this examination she weighed 7.85kgs, a loss of about 1kg. Her blood results at this time were as follows:

Table 3 *Haematology and biochemistry parameters measured 10/05/2007 – Lou Lou*

Test	Result	Normal Range
Biochemistry		
Bicarbonate	24 mM	
Total protein	42 g/l	
Albumin	16 g/l	
Globulin	26 g/l	
Calcium	2.72 mM	
Phosphate	1.47 mM	
Amylase	2707 U/L	
CK	212 U/L	
Glucose	11.3 mM	6.5-12 mM
AST	14 U/L	25-150 U/L
Uric Acid	0.8 mM	0.3-0.9 mM
Cholesterol	2.5 mM	3.2-6.2 mM
Triglycerides	3.05 mM	1.7-2.9 mM
Haematology		
Haematocrit	0.38	0.33-0.48
Plasma Protein	48 g/l	40-55 g/l
WBC (estimated)	3.8 x 10 ⁹ /l	

The sample showed no lipaemia.

At the time of this examination there were no further xanthomatous nodular masses anywhere on the body surface but the submandibular region remained slightly pendulous. (Figs. 6, 7 & 8). Because of ongoing problems with aggression and constant harassment of her owners associated with food and feeding, after reviewing the blood results, Lou Lou was allowed a slightly greater amount of pellets and some access to a small amount of mixed grain in her diet. At the time of writing this paper (2 months after this increase in food access and 7 months after her surgery), Lou Lou still remains free of any further skin masses and her temperament has improved significantly.



Fig. 6 Lou Lou 6 months after surgery – note residual pendulous submandibular region and lack of xanthomatous masses



Fig. 7 Lou Lou 6 months after surgery



Fig. 8 Lou Lou 6 months after surgery

Discussion

Although the histopathological appearance of the lesions in this case very closely resemble those previously reported by Jaensch et al.^{1,2}, there were fewer of the nodular masses, they were all restricted to the head and neck regions and no masses were found on the feet. It is postulated that Lou Lou may have been at an earlier stage than the case reported by Jaensch et al.^{1,2} and, given time and no control measures, Lou Lou may have developed more widespread lesions.

The other noteworthy and interesting difference in this case was the response to therapeutic and dietary measures. In the case reported by Jaensch et al.^{1,2}, the number and location of the masses meant that complete surgical excision was not possible and a combination of surgery and chemotherapy was attempted. The remaining lesions in that case failed to regress and further lesions developed despite treatment. In the case reported here, there was a significant response to treatment. Surgical excision followed by dietary modification and various homeopathic treatments not only prevented a reappearance of further nodular xanthomatous masses but also significantly reduced the levels of cholesterol and triglycerides in the blood.

Because Lou Lou was clinically normal and had no abnormal haematological and serum biochemistry results, the cause of her persistent fasting hypercholesterolaemia and hypertriglyceridaemia was unlikely to be due to an underlying infectious or hepatic disease. Based on the response to dietary modification and homeopathic treatments, it is most likely that the cause of Lou Lou's fasting hypercholesterolaemia and hypertriglyceridaemia may have simply been due to a long term access to a high fat, high energy diet. Obviously not all geese exposed to high fat diets will develop persistent fasting hypercholesterolaemia and hypertriglyceridaemia. Even in this limited trial, two geese exposed to the same diet had significantly different blood cholesterol and triglyceride levels – one markedly elevated and the other within normal ranges. In view of the fact that Lou Lou had never laid an egg and there had been no investigation of thyroid function, it is possible that there may have been some hormonal influence on her cholesterol and triglyceride levels. This could explain the difference between the responses of the two geese in this case after exposure to the same diet. Alternatively, there may be an underlying familial or idiopathic metabolic defect of lipid metabolism as a cause of Lou Lou's abnormally high cholesterol and triglyceride levels.

Although not proven here, it is postulated that persistent hypercholesterolaemia and hypertriglyceridaemia was the cause of the cutaneous xanthogranulomata in this case and in the Jaensch et al case and it is interesting that both of these cases involve geese. It is possible that some geese may develop xanthogranulomatosis if exposed to high blood cholesterol and triglyceride levels for a long enough period of time, regardless of the cause of those high blood levels. It is recommended that a full blood biochemical investigation (including cholesterol and triglyceride levels) be performed on any bird presenting with multiple xanthomatous masses.

References

1. Jaensch SM, Butler R, O'Hara A, Raidal SR and Wyatt K (2002). Atypical multiple, papilliform, xanthomatous, cutaneous neoplasia in a goose (*Anser anser*). *Aust Vet J.* **80**: 277-280.
2. Jaensch S and Raidal S (2001). Orlando: The lumpy, bumpy goose (Atypical multiple, papilliform, xanthomatous, cutaneous neoplasia in a goose (*Anser anser*)). *Proc Annual Conf Assoc Avian Vet – Aust Comm, Hobart.* pp 53-56
3. Tu-Fa Lien, Rong-Chi R Chou, Shih-Yi Chen, Yih-Ing Jeng and Der-Fang Jan (1999). Lipid metabolism of Tsaiya ducks: plasma and liver related traits under ad libitum and fasting. *J Sci Food Agric.* **79**:1413-1416
4. Kaya A, Altiner A and Özpınar A (2006). Effect of Copper Deficiency on Blood Lipid Profile and Haematological Parameters in Broilers. *Journal of Veterinary Medicine Series A.* **53**:399–404
5. Du M and Ahn D U, Dietary Conjugated Linoleic Acid (CLA) Effects Lipid Metabolism in Broiler Chicks. *Iowa State University Animal Industry Report 2004, A.S. Leaflet R1934.* URL: <http://www.ans.iastate.edu/report/air/2004pdf/AS1934.pdf>
6. Kudzma DJ, St. Claire F, DeLallo L and Friedberg SJ (1975). Mechanism of avian estrogen-induced hypertriglyceridemia: evidence for overproduction of triglyceride. *Journal of Lipid Research.* **16**: 23-133
7. Johnstone AC, Jones BR, Thompson JC and Hancock WS (1990). The pathology of an inherited hyperlipoproteinaemia in cats. *Journal Comp Path.* **102**: 125-137
8. Hoekstra KA, Nichols CR, Garnett ME, Godin DV and Cheng KM (1998). Dietary cholesterol-induced xanthomas in atherosclerosis-susceptible Japanese quail (*Coturnix japonica*). *J Comp Pathol.* **119**: 419-427
9. Sanger VL and Lagace A (1996). Avian Xanthomatosis. Etiology and Pathogenesis, *Avian Diseases.* **10**: 103-111
10. Raidal S.R. Butler R., Monks D. and Shearer PL (2006). Airsac cystadenocarcinomas in cockatoos. *Australian Veterinary Journal.* **84**:213-216.
11. Monks DJ, Zsivanovits HP, Cooper JE and Forbes NA (2006). Successful Treatment of Tracheal Xanthogranulomatosis in a Red-Tailed Hawk (*Buteo jamaicensis*) by Tracheal Resection and Anastomosis. *Journal of Avian Medicine and Surgery.* **20**: 247-252