University of Pittsburgh

Division of Laboratory Animal Resources

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MICROSCOPIC PATHOLOGY REPORT

Accession: JF 10-13 (JF 10-17A)*/PA 4859 **Date: 10-19-10**
Investigator/Dept: Dr. Joanne Flynn – MGB **Facility: RBL**
Photos: Gross DSCN 102 (4097-4130) Micro Img (192-198) **ID: M 81-09**
Species: Cynomolgus Breed: (*M. fasicularis*) **Age: Adult NOS Sex: Male**

***Note - This case was necropsied and assigned accession # JF 10-13, but also later redundantly assigned a JF 10-17A designation under which tissues were trimmed and slides were cut & labeled. These two numbers (JF 10-13 and JF 10-17A represent the same animal – M 81-09)**

Clinical History: This monkey had been low-dose infected with Mycobacterium *tuberculosis* approximately 4 weeks previously, with no scan lesions seen at 2 weeks PI. Only 3 suspect granulomas were noted on the terminal scan 3/3/10 along with some questionable enlargement of nodal structures in the carinal area.

Gross Findings: (see Gross Pathology report JF 10-13) **Gross Score: 9**

Microscopic Diagnosis (*JF 10-13/10-17A – see above **)

Slide #1
Tissue/location: RUL
(vial #10 – 7 pieces sub): (4 representative pieces)

Granulomas/granulomatous disease: None – Extensive atelectasis and a small focus of foreign body (aspiration) pneumonia is noted in one piece *(See Figure 1 with polarization)*

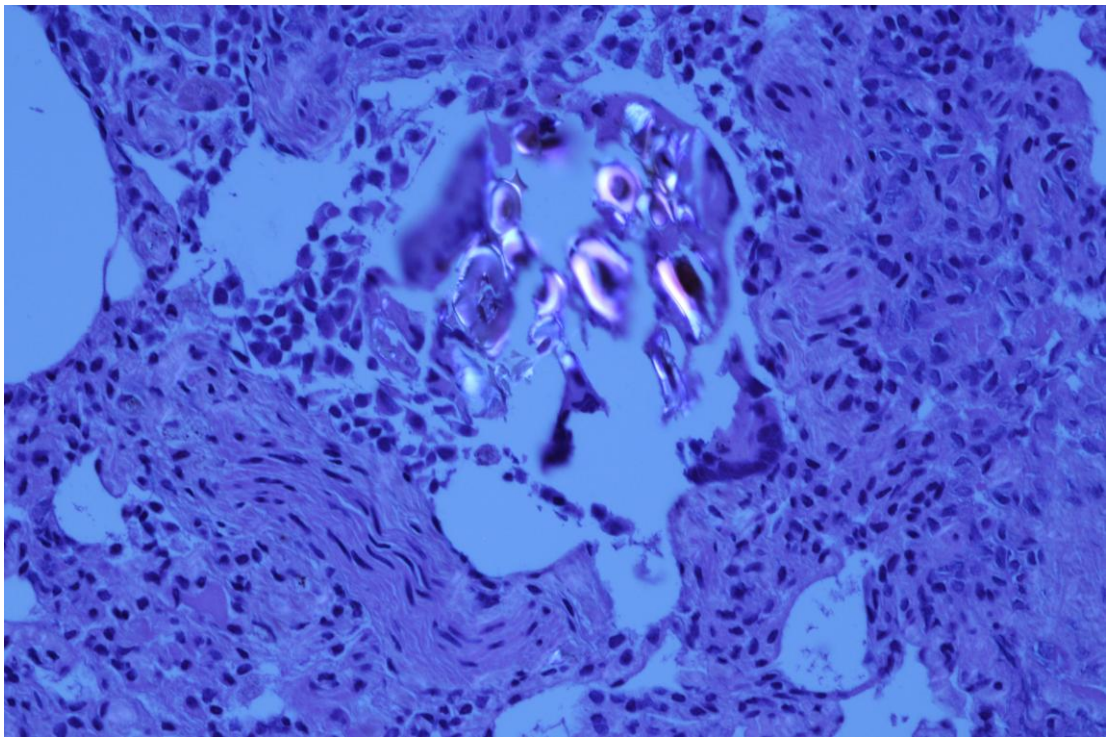

Figure 1 JF 10-13 (aka 17A) – 1 20X RUL – Focus of aspiration/FB pneumonia (with polarization demonstrating birefringence of gastrointestinal content)

Slide #2
Tissue/location: RUL
(vial #10 – 7 pieces sub): (3 representative pieces)

Granulomas/granulomatous disease: None

Slide #3
Tissue/location: RLL
(vial #8 – 11 pieces sub): (4 representative pieces)

Granulomas/granulomatous disease: None

Slide #4
Tissue/location: RLL
(vial #8 – 11 pieces sub): (4 representative pieces)

Granulomas/granulomatous disease: A focal, large area of caseation necrosis extending from alveolus to alveolus, with little evidence of associated epithelioid cellularity and minimal amounts of a scant peripheral lymphocytic infiltrate is noted in one of the pieces *(See Figures 2&3)*

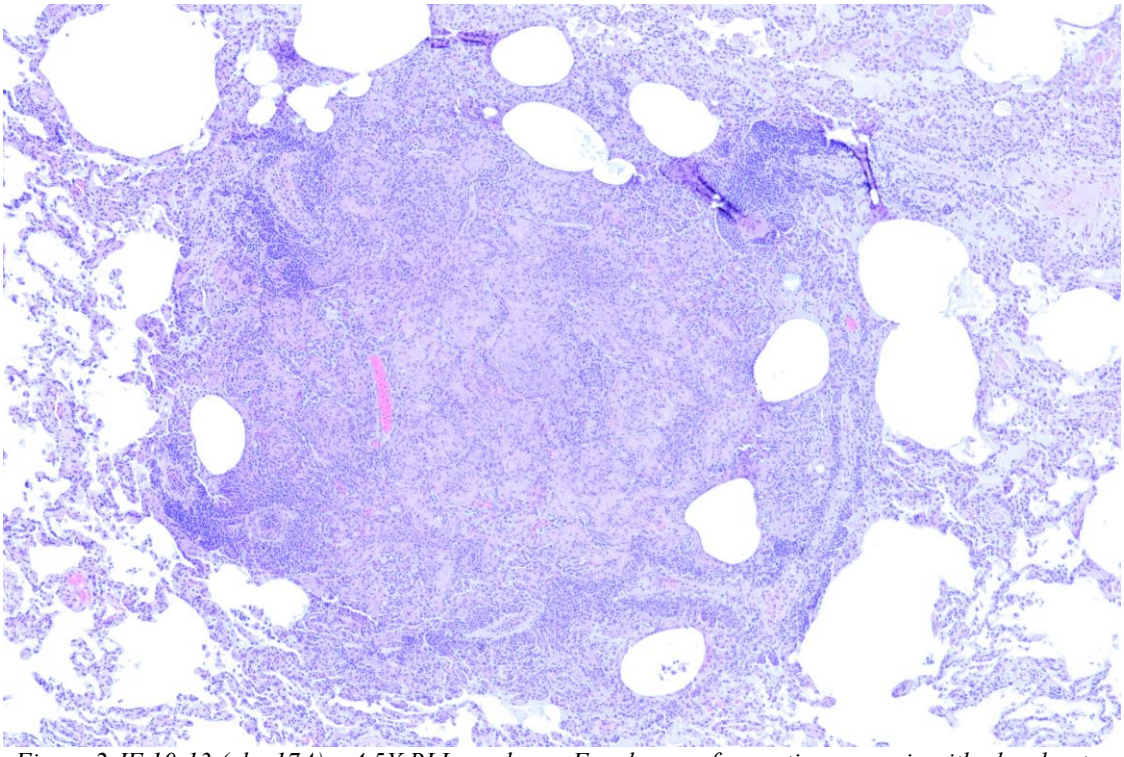

Figure 2 JF 10-13 (aka 17A) – 4 5X RLL random – Focal area of caseation necrosis with alveolus-to-alveolus spread and without significant epithelioid cell response (note marginal peripheral L-P infiltrate)

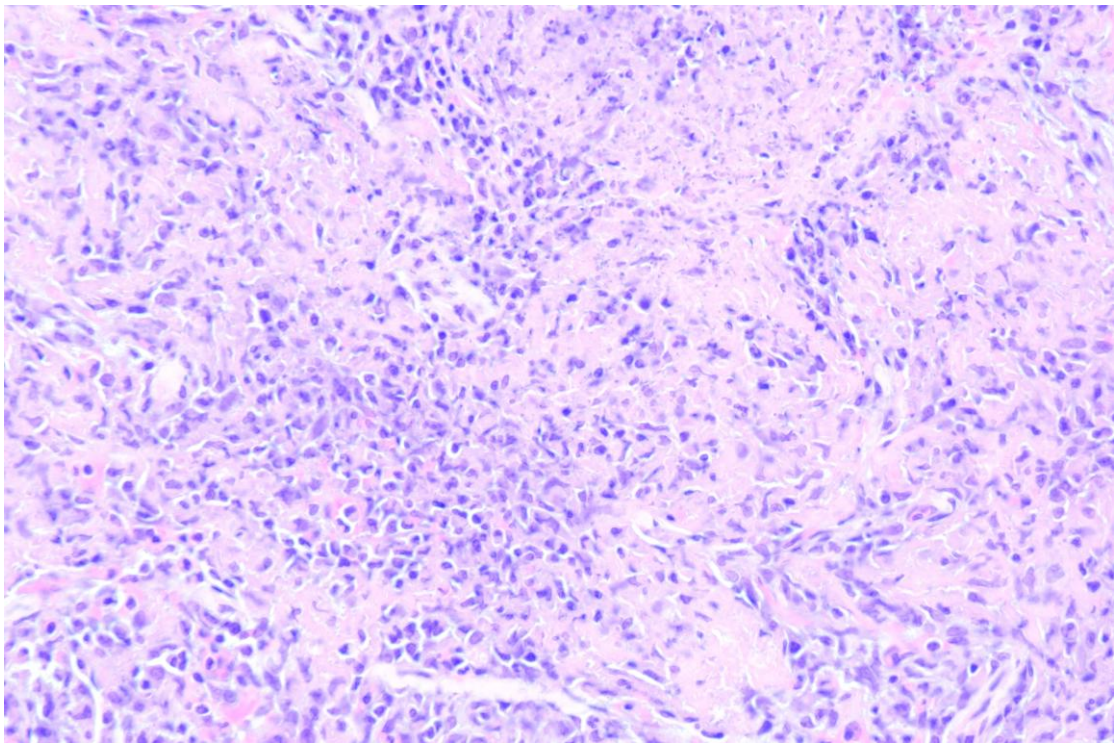

Figure 3 JF 10-13 (aka 17A) – 4 20X (Higher power from above) RLL random – Focal area of caseation necrosis with alveolus-to-alveolus spread and without significant epithelioid cell response

Slide #5
Tissue/location: RLL granl A, RLL granl C
(vial #s 6&7 -1 piece sub each): (granl A – larger piece, granl C, smaller piece)

Granulomas/granulomatous disease: RLL granls A&C – None - Unfortunately, neither granuloma was present on the slide, all that was noted were two small pieces of lung parenchyma. Whether it was missed in sectioning or simply not submitted when sampling is not clear.

Slide #6
Tissue/location: RLL granl 1, RLL granl 2, RLL granl 3
(vial #s 3, 4 & 5 – 1 piece sub each): (granl 1 – 1 small piece, granl 2 – 1 large piece, granl 3 – 1 medium piece)

Granulomas/granulomatous disease: None

RLL granl 1: Minimally present focal area of unorganized caseation underlying a region of dense pleural thickening and fibrosis

RLL granl 2: Similar to RLL granl 1 – A somewhat larger area of unorganized & minimally cellular caseation necrosis is noted underlying what appears to be a pleural margin with associated dense thickening & sclerosis *(See Figure 4)*

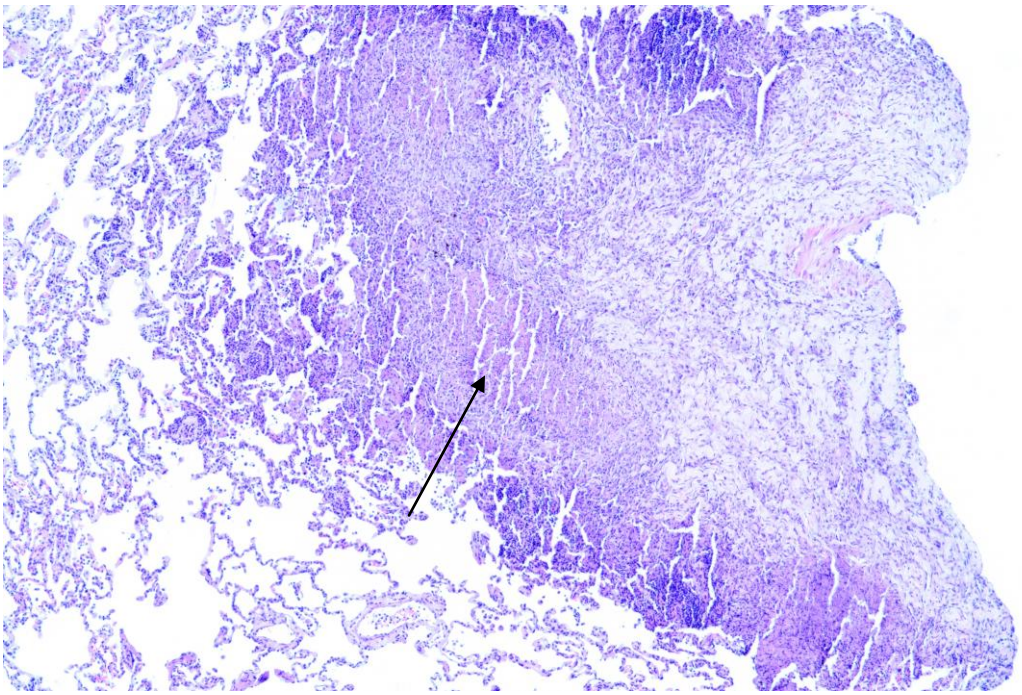

Figure 4 JF 10-13 (aka 17A) – 6 5X RLL granl 2 Area of unorganized caseum (arrow) underlying a thickened, dense pleural surface

RLL granl 3: None – a focal area of type II pneumocyte hypertrophy without associated inflammation is present (lesion apparently missed in section or submission)

Slide #7
Tissue/location: Accessory
(vial #11 – 2 pieces sub): (2 rep pieces)

Granulomas/granulomatous disease: None

Slide #8
Tissue/location: LML
(vial #14 – 2 pieces sub): (2 representative pieces)

Granulomas/granulomatous disease: None – In one piece, there is incidental pleural thickening and associated areas of differential alveolar inflation (including mild areas of hyperinflation) - but non granulomatous disease is observed

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Slide #9
Tissue/location: LUL
(vial #13 – 4 pieces sub): (3 representative pieces)

Granulomas/granulomatous disease: None

Slide #10
Tissue/location: LLL
(vial #15 – 5 pieces sub): (4 representative pieces)

Granulomas/granulomatous disease: None – Focally extensive areas of atelectasis, some with associated alveolar edema are noted.

Slide #11
Tissue/location: R. Cranial HLN, L. Cranial HLN
(vial #s (&12 – 1 piece sub each): (R. Cranial HLN – larger piece, L. Cranial HLN – smaller piece)

Granulomas/granulomatous disease: None is noted in either node

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Slide #12
Tissue/location: R. Carinal LN with granl
(vial #17 – 1 piece sub): (1 representative piece)

Granulomas/granulomatous disease: Two caseous granulomas without sharp margination and extension into adjacent nodal parenchyma are noted. Both are characterized by only modest associated surrounding epithelioid cellularity and both also contain abundant degenerative neutrophilic infiltration centrally. *(See Figures 5&6)*. Perinodal fat and fascia has dense bands of fibrosis present within.

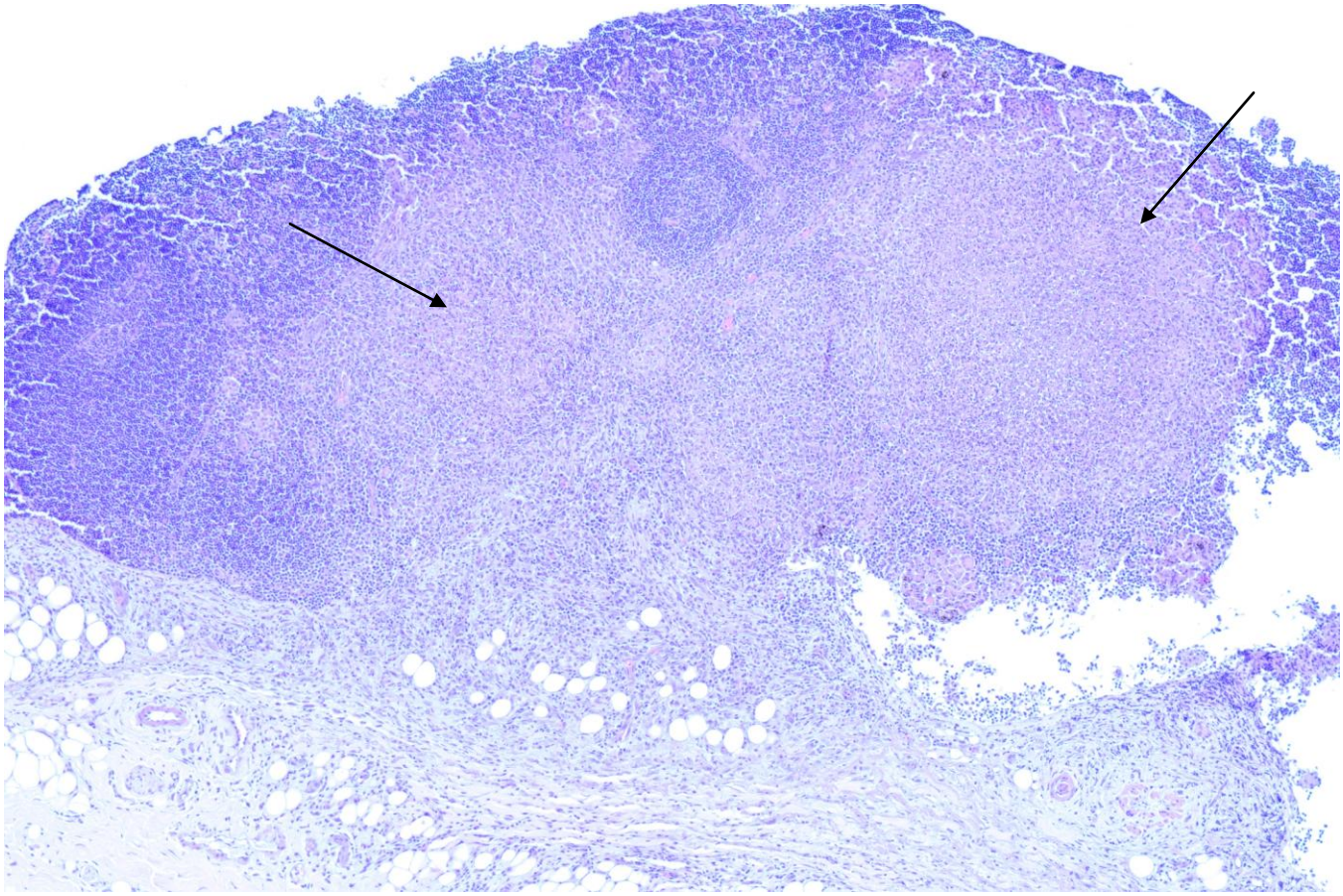

Figure 5 JF 10-13 (aka 17A) – 12 5X R. Carinal LN w granl – Two focal but not circumscribed areas of caseation necrosis (arrows) with modest peripheral epithelioid cellularity, abundant central degenerative neutrophils and infiltration into adjacent nodal parenchyma

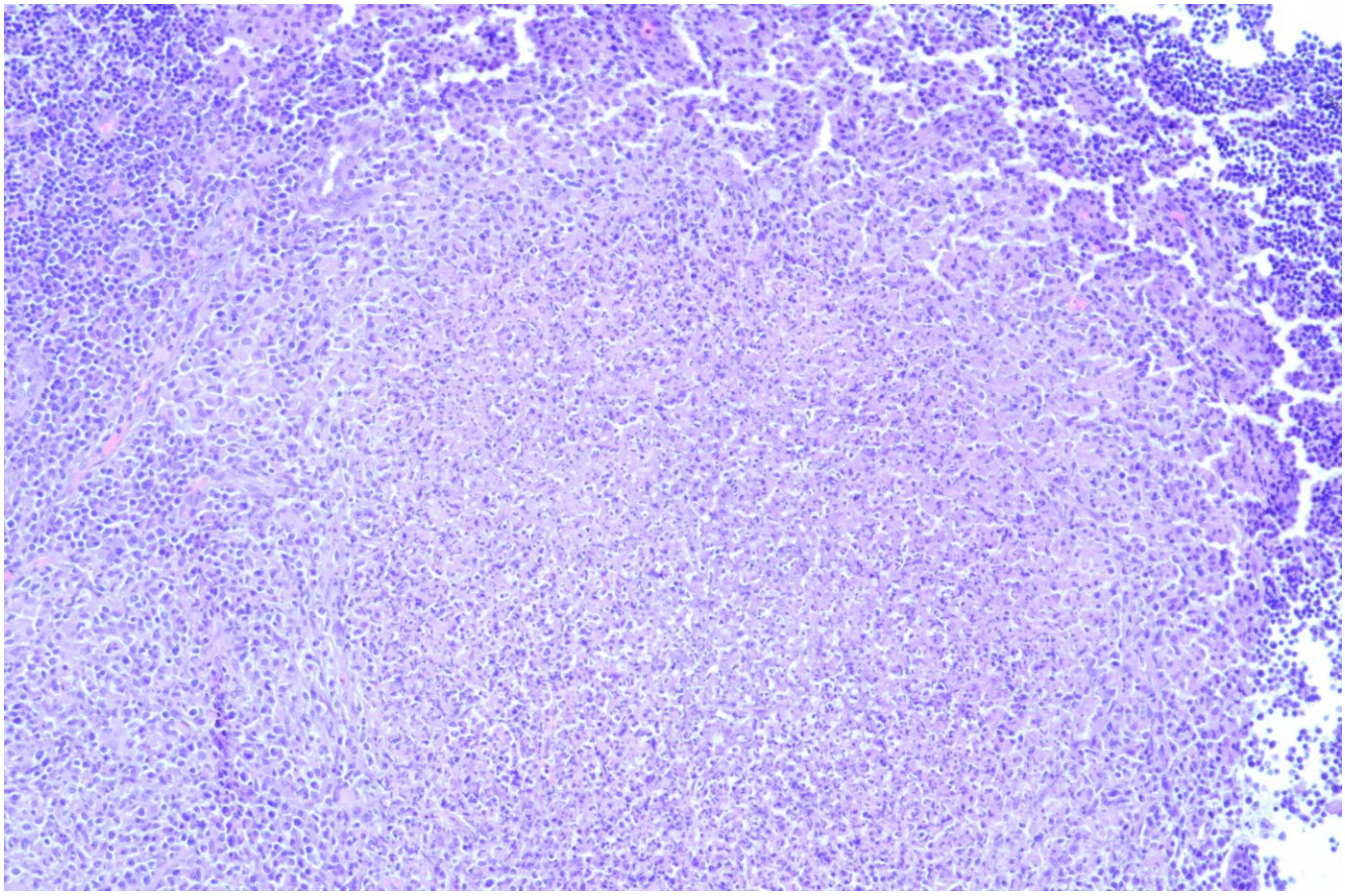

Figure 6 JF 10-13 (aka 17A) – 12 10X R. Carinal LN w granl –Focal but not well circumscribed area of caseation necrosis with modest peripheral epithelioid cellularity, abundant central degenerative neutrophils and infiltration into adjacent nodal parenchyma

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Slide #13
Tissue/location: R&L Axillary LNs
(vial #2 – 2 pieces sub): (2 representative pieces)

Granulomas/granulomatous disease: None

Slide #14
Tissue/location: L&R Inguinal LNs
(vial #1 – 2 pieces sub): (2 representative pieces)

Granulomas/granulomatous disease: None – Sinus histiocytosis & a mild degree of erythrophagocytosis are noted in some areas

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Slide #15
Tissue/location: Liver
(vial #20 – 2 pieces sub): (1 representative piece)

Granulomas/granulomatous disease: None

Slide #16
Tissue/location: Spleen
(vial #19 – 4 pieces sub): (1 representative piece)

Granulomas/granulomatous disease: None

Slide #17
Tissue/location: Paraesophageal LN
(vial #16(?) – 1 piece sub): (1 representative piece)

Granulomas/granulomatous disease: None – Focally extensive areas of sinus histiocytosis are noted, but do not represent granulomatous inflammation *(See Figure 7)*

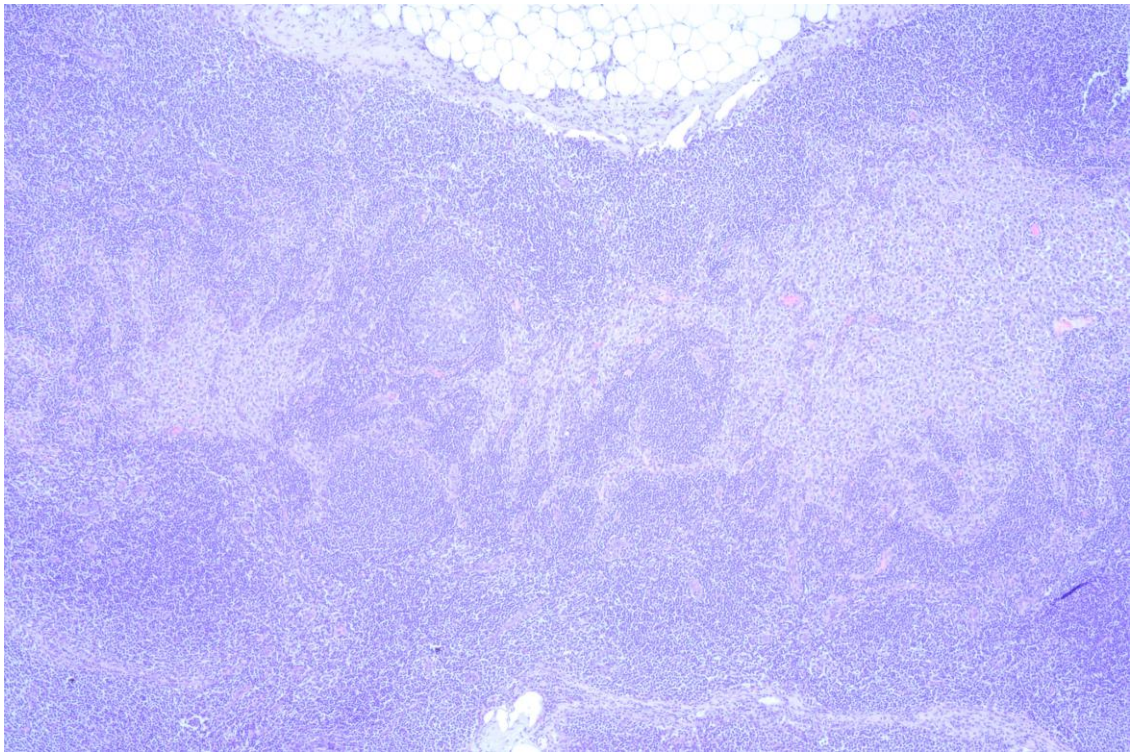

Figure 7 JF 10-13 (aka 17A) – 17 5X Paraesophageal LN – Focally extensive areas of sinus histiocytosis without associated evidence of granulomatous inflammation

Slide #18
Tissue/location: LMS bronchus LN
(vial #18 – 1 piece sub): (1 representative piece)

Granulomas/granulomatous disease: None – only perinodal fat and fascia are noted on the slide

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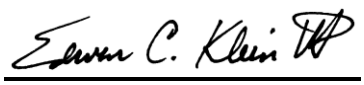
Final/Summary Comments: The microscopic findings in this case are generally consistent with the gross and representative of early disease without substantial evidence of immunological containment. Most granulomas present consisted of accumulations of caseously necrotic debris – in some lesions (especially the R. Carinal LN), associated with an abundant central neutrophilic infiltrate. Generally, epithelioid/macrophage cellularity was modest. Some of the foci of harvested RLL granulomas appeared pleural based and the adjacent overlying lung margin was prominently thickened and sclerotic. Unfortunately as has been seen in other cases, a number of the designated granulomas submitted were not noted in section – either missed in the block cutting process or subject to minimal tissue presence in the submission sample. It is of interest that the largest focus of granulomatous inflammation was seen in one of the RLL random pieces, in which a focally extensive area of caseous necrosis appeared to extend from alveolus to alveolus, with only minimal directly associated inflammatory cellularity – although a scant lymphoplasmacytic infiltrate was noted surrounding it. A small confounding focus of FB/gastric aspiration was noted in the RUL.

The pathogenesis of the massive pleural adhesive process in the left lung was not determined, although it is thought to be unrelated to the tuberculous infection present and probably related to a prior pleuropneumonia of undetermined etiology.

In synopsis, multiple foci of poorly organized caseous necrosis were noted in the right lower lobe and right carinal lymph node, without significant evidence of typical tuberculosis granuloma architecture formation (i.e. modest macrophage/epithelioid and associated peripheral lymphoplasmacytic infiltrates). However; in some of the lesions (especially the R. Carinal node – a prominent degenerative neutrophilic infiltrate was seen). All-in-all, the tuberculous lesions were not of unexpected appearance (either grossly or microscopically) for a 4 week post infection animal, although a number of confounding processes of both known (i.e. aspiration) and unknown (i.e. residual pleural-to-body wall adhesions) were also present.



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Date Reported: 10/19/10
Report prepared/reviewed by: eck