

THAMES AUDIT MEETING 28/10/2009
LABORATORY INVESTIGATION OF SUSPECTED MULTIPLE MYELOMA
AND PLASMA CELL DISORDERS.

SUMMARY OF RESPONSES ON QUESTIONNAIRE

1. There was a good response to the questionnaire with 34 respondents.
2. The investigations are performed mainly in Biochemistry (30 out of 34).
3. Most laboratories use serum electrophoresis for detection.
4. The majority of labs do not reflex test electrophoresis.
5. Most labs use scanning densitometry for quantitation and immunofixation for typing of serum and urine.
6. If only heavy or light chains are seen the majority of labs refer the samples to PRU.
7. Labs measure and report non-idiotypic immunoglobulins but do not report the immunoglobulins of the monoclonal heavy chains.
8. Not all labs receive urine for free light chains even when it is requested.
9. Most labs measure urine protein with Pyrogallol red.
10. A variety of ways are used to contact the requester when a monoclonal band is found.
11. Most laboratories offer serum free light chains but most refer samples to other labs.
12. All labs take part in the UKNEQAS scheme for monoclonal proteins and specific proteins.

DISCUSSION ON AUDIT QUESTIONNAIRE PRESENTATION

1. Question? Do you measure non-isotypic immunoglobulin from a different class? If IgG band would you report the IgG level? Some labs would not if < 5g/L, other if less than 10g/L
2. Use of serum free light chains. There is a list from Leukaemia 23: 215-224 that indicates the recommended uses of free light chains:
 - a. Serum FLC in combination with serum protein electrophoresis and immunofixation yields high sensitivity for screening for multiple myeloma.
 - b. Major prognostic value in virtually all plasma cell disorders
 - c. Quantitative monitoring of patients with oligosecretory plasma cell disorders, including AL.
 - d. FLC is required for documenting stringent complete response according to the International Response Criteria.
3. The technical limitations of the assay that make its serial use potentially problematic are
 - a. Lot to lot variation
 - b. Assay imprecision
 - c. Do not always dilute in a linear fashion

4. In patients with measurable intact serum immunoglobulins or measurable urinary whole paraproteins the only use advocated for serum FLC is in initial diagnosis and documentation of stringent complete response.
5. It was pointed out that the use of the Freelite assay is being sold by Binding Site to clinicians rather than laboratory scientists. Will use of FLC rise when the price comes down when the patent expires?

REVIEW OF DETECTION AND REFERRAL OF PPQ AT NORTH MIDDLESEX.

SUMMARY

1. All laboratories that practice discretionary SPE requesting need to have in place a robust protocol for transmission of the results. Paper and electronic reports are not always acted on.
2. An agreed protocol needs to be in place for the further management of patients with newly identified paraproteins between Biochemistry and Haematology.
3. Clear guidance needs to be given out to GPs. A standard letter is ideal.
4. National bodies such as the British Society of Haematology, UK Myeloma forum, International Myeloma forum and RCGP should be involved with this.
5. Should we only be doing discretionary testing?

DISCUSSION ON THE PRESENTATION

1. Limited data was presented regarding clinical usefulness of this approach.
2. Does prompt diagnosis reduce morbidity with the disease?
3. There are ethical concerns when tests are reflexed but patients consent to find out what is wrong with them.
6. There are financial implications to the lab if they initiate tests.

DISCUSSION FROM CONSULTANT HAEMATOLOGIST

1. Need a prompt from the lab to Haematology so can refer patients early.
2. When histology of lymph nodes are carried out a copy of the report is sent to the requesting clinician and to Haematology. There is a need for a similar alert system with paraprotein bands.
3. Median time from detection the band to the patient being seen in clinic is 11 weeks but there is a large range.
4. The clinician feels adding on SPE is clinically worth while. The registrar chases up patients who are not referred by the GP.
5. Clinical point of view is that when a test is requested the requesting clinician has responsibility to look at the results.
6. It is difficult to assess the usefulness of low level paraprotein but there could be significant BJP in urine. Refer all to clinicians.

- In MGUS clinicians use G, M or A greater than 10g/L to decide if a bone marrow biopsy is required. Amyloid also needs to be considered.
7. Haematologists contact the GP direct if the band is 30-40 g/L.

DISCUSSION FROM MEETING ATTENDEES

1. North Middlesex say the cost is £2-17 per electrophoresis. It was queried that this was quite low and was this just the price of the raw materials. £20 needs to be added for the cost of immunofixation.
2. When the lab at Royal London picks up a myeloma they contact the GP asking them to refer under 2 week cancer wait. None got near to this and can be as long as 24 weeks so has the laboratory report been read? Some Clear guidance is needed for GPs as some refer straight away, some sit on the report.
1. It is important to agree paraprotein guidelines/ protocol with Haematology. There needs to be readily available contacts to ensure these patients can easily be referred. The joint policy needs to state who is responsible for contacting the requesting clinician and what further action is needed.
2. East Sussex has a good letter which is sent out with all newly diagnosed paraproteins
3. At Addenbrookes GPs refer too many small bands to Haematology. They have a coded comment to say do not refer IgG less than 15g/L or IgA/IgM less than 10 g/l. The clinicians present felt it is dangerous for the lab to make these decisions without seeing the patient as other factors such as viscosity, Stage 3 CKD could be involved. It is not down to the lab to decide if MGUS or MM from SEP/IF picture.

A DELAY IN THE DIAGNOSIS OF HAEMATOLOGICAL MALIGNANCIES **DR JENNIE TRELEAVEN**

SUMMARY

1. It is not always possible to diagnose a malignancy early.
2. If a disease is diagnosed and treatment started early the prognosis may not be altered but may reduce pain and suffering.
3. General public perception is that early diagnosis improves outcome.
4. GPs need to look for symptoms that trigger the possibility of malignancy as well as persistent symptoms.

DISCUSSION

1. If claim is the payout related to the survival risk? Not always
2. Is there a lot of litigation? Not many from each hospital. Try to sort them out by the Ombudsman, not court. It needs to be settled before going to court, with 1-2 weeks of evidence. Certain money is paid for length of delay and symptoms. The lymphoma case was given £25,000. People need to be more aware of potential litigation.

3. Do you get loaded for insurance? This depends, if only seen once a year by doctor this is usually alright if insurance company is aware of it. In CLL look at prognostic indicators. In leukaemics with transplants can get life insurance after 5 years.
4. CCa in lymphoma patient was 2.94 mmol/L and Hb low. All labs should follow up hypercalcaemia. The right tests were done but the results were not acted on. The GP was sent a copy which was filed.

**HISTOPATHOLOGY OF MULTIPLE MYELOMA AND PLASMA CELL
DYSPLASIAS**
DR MYONA. NORTH MIDDLESEX HOSPITAL

SUMMARY

There are WHO criteria for investigation of plasma cell neoplasms.

The diagnostic samples used are

1. Bone marrow trephine biopsy
2. Soft tissue or renal biopsies
3. Femoral head
4. Lymph nodes
5. Colonic biopsy for amyloid and FLC secretors.

Genetics are also useful on bone marrow biopsies. In MGUS there is a deletion in chromosome 13 and an abnormal chromosome 13. 13q⁻ predicts transformation from MGUS to MM. In MM there is a translocation on 14q32.

DISCUSSION

Are bone marrows done in all patients? No. They are done for specific types of treatment. Different features, abnormal cytogenetics are risk stratified for treatment in next 5-10 years.

DISCUSSION AT STANDARD SETTING

1. REFLEX TESTING

There are no national guidelines from the British Haematological Society or UK Myeloma Forum. This is left to local labs who may reflex on the basis of a raised globulin. Some labs have a huge workload without reflex testing.

It may be useful to assess the clinical information and source of the request before adding on electrophoresis.

If patients have a raised creatinine, calcium and raised globulin are going to be investigated anyway

Added on tests need to be funded from a budget.

2. CZE

Is CZE a better screening method than gel electrophoresis? CZE has the advantage of automation, throughput and speed. CZE by Sebia has software which replicates the gel method. There are sometimes bands seen on gels as they are more sensitive that are not seen on CZE. Sometimes the physical properties of bands in CZE mean they get stuck or washed away. IgM bands need treatment with mercaptoethanol for CZE. Each lab needs to compare them with their workload to decide which is best.

3. IS EARLY DETECTION A BENEFIT?

Early detection may be a benefit by reducing bone fractures and renal impairment. East Kent find a lot of myelomas in patients with acute renal failure. The Royal London has a high pick up rate in the renal department, followed by the Dental Hospital and Rheumatology.

In MGUS 3% of patients go on to have a myeloma. If symptomatic it is useful to have early detection and treatment

4. FOLLOW UP OF ABNORMALITY

We have a duty to follow up abnormalities. The minimum is to alert. Should the Biochemistry lab, Haematology or requesting physician follow up? As professionals we have a duty to follow up an abnormality in a globulin.