

Original Research Article


Diagnostic usefulness of triple biopsies (Skin, Muscle and Nerve) in clinically suspected cases of vasculitis in a tertiary care hospital in Gujarat

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Abstract

Introduction: The term vasculitis refers to a heterogeneous group of diseases, all characterized by inflammation and destruction of blood vessel walls leading to ischemic, thrombotic, and hemorrhagic damage to tissues of central and peripheral nervous system. The main indication for triple biopsy (skin, muscle and nerve) is to rule out peripheral vasculitis neuropathy. However, the drawback is that any systemic inflammatory process may show changes in a skin biopsy and hence these changes need to be interpreted with caution. The aim of this study is to establish the diagnostic yield and the usefulness of the triple biopsies in clinically suspected cases of vasculitis.

Material and Methods: The present study was conducted in the Department of General Pathology, SBKS MI & RC, Vadodara over a period of one year (1/1/2022 to 31/12/2022). All the clinically suspected cases of vasculitis received at OPD were included in the study. Any case with either muscle, nerve or skin biopsy reported as inadequate were excluded from the study.

Results: On evaluation the usefulness of triple biopsies for vasculitis, we found a very low diagnostic yield with only 3.3% of peripheral nerve biopsy and 0.8% of muscle and nerve biopsy showed definite vasculitis. In case of suspected peripheral/systemic vasculitic neuropathy, nerve biopsy was sufficient in the majority of case and has the diagnostic armamentarium for the evaluation of vasculitis.

Conclusion: In conclusion, nerve biopsies provide the best yield for the diagnosis of vasculitis, as opposed to muscle and skin biopsies. The role of triple biopsies as a routine protocol for the evaluation of vasculitis is questionable.

Key words

Triple biopsies, Vasculitis, Skin biopsy, Muscle biopsy, Nerve biopsy.

Introduction

The term vasculitis refers to a heterogeneous group of diseases, all characterized by inflammation and destruction of blood vessel walls leading to ischemic, thrombotic, and hemorrhagic damage to tissues of central and peripheral nervous system. The main indication for triple biopsy (skin, muscle and nerve) is to rule out peripheral vasculitis neuropathy [1]. Peripheral neuropathy occurs in 60 to 70% of some systemic vasculitic syndromes [1]. Although sural nerve biopsy is a standard method of diagnosing vasculitic neuropathy [1, 2], the procedure yields unequivocal evidence of vasculitis in only 20% of patients biopsied for this indication [1]. As 40-50% of cases with polyarteritis nodosa show evidence of vasculitis on a muscle biopsy, the role of combined nerve and muscle biopsy through a single incision in the lower leg has emerged as an alternative for diagnosis of vasculitis [1-3]. Limited data is available on the role of skin biopsy in the evaluation of vasculitis. However in the case of small vessel vasculitis a skin biopsy often yields a positive result [4]. Triple biopsy included a skin biopsy from the site of nerve biopsy are preferred by some clinician in order to increase the diagnostic yield, particularly as immunofluorescence on skin is not technically difficult [4]. However, the drawback is that any systemic inflammatory process may show changes in a skin biopsy and hence these changes need to be interpreted with caution. The aim of this study is to establish the diagnostic yield and the usefulness of the triple biopsies in clinically suspected cases of vasculitis.

Materials and methods

The present study was conducted in the Department of Pathology, S.B.K.S. MI & RC,

Vadodara, over a period of one year (1/1/2022 to 31/12/2022). All the clinically suspected cases of vasculitis received at OPD were included in the study.

The clinical information, laboratory investigation and histopathological data of skin, nerve and muscle biopsies performed on clinically suspected cases of vasculitis were retrieved from clinical and pathology workstation during the period from 1st January 2022 to 31st December 2022. We received skin, segment of nerve and piece of muscle in different pre-labelled bottles containing neutral buffered formalin along with the requisition form. For nerve and muscle biopsy, cross and longitudinal sections were preferred for the histopathological examination. The ellipse of skin was submitted in toto. H&E stained sections were then examined microscopically. The cases were categorized in 5 entities. (1) with evidence of definite vasculitis, (2) probable vasculitis, (3) Moderate perivascular inflammation, (4) Mild perivascular inflammation, (5) Negative for vasculitis/perivascular inflammation. Perivascular inflammation seen without any other changes was not a criterion for vasculitis. We included due to predominant finding in majority of the cases. We noted this as a separate category to ascertain the prevalence of inflammation in these biopsies. A total of 120 biopsies were received during the period of one year (1st January 2022 to 31st December 2022). Any case with either muscle, nerve or skin biopsy reported as inadequate were excluded from the study.

Pathological selection criteria [3]

Nerve biopsies were classified as showing definite or probable vasculitis. Definite vasculitis was diagnosed if endoneurial or epineurial

vessels showed evidence of vessel wall infarction in association with perivascular or transmural infiltration by inflammatory cells. Vessel wall infarction was diagnosed if there was evidence of destruction and disorganisation of the muscularis by fibrinoid necrosis, disruption of the endothelium or internal elastic lamina, thrombosis of the lumen or hemorrhage in to the wall of the vessel. Probable vasculitis was diagnosed if there was transmural or perivascular inflammation not accompanied by vessel wall infarction but associated with at least one of the following: fibrous scarring/intimal proliferation, chronic organized thrombosis (with/without recanalization), hemosiderin deposits, prominent Wallerian degeneration or asymmetric nerve fiber loss. In muscle biopsy specimens, similar diagnostic criteria for definite vasculitis were applied. Probable vasculitis was diagnosed where transmural inflammation was not accompanied by fibrinoid necrosis of the vessel wall or any of

the other vascular changes described above as representing evidence of definite vasculitis. In muscle, transmural inflammation alone without the additional features which were applied to nerve biopsies was sufficient to diagnose probable vasculitis.

Results and Discussion

The present study was conducted to establish the diagnostic yield and the usefulness of the triple biopsies in clinically suspected cases of vasculitis. The demographic details of the patients were analyzed and following results were concluded.

Age and sex ratio

The age of patients who had a triple biopsy ranged from 9 to 84 years. The mean age was 52 years with male to female ratio was 1.7:1 (Figure – 1, 2).

Figure - 1: Age wise distribution of patients who submitted triple biopsy (N=120).

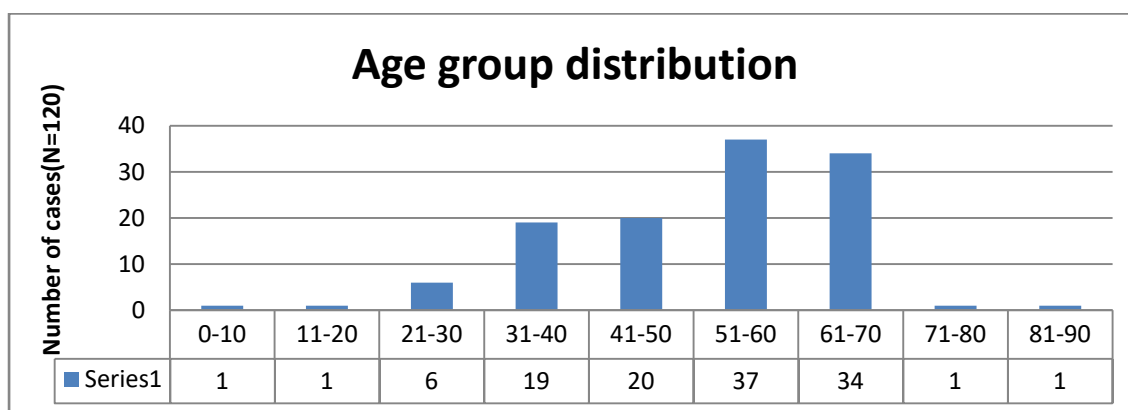


Figure - 2: Gender distribution of clinically suspected vasculitis on which triple biopsy had been performed.

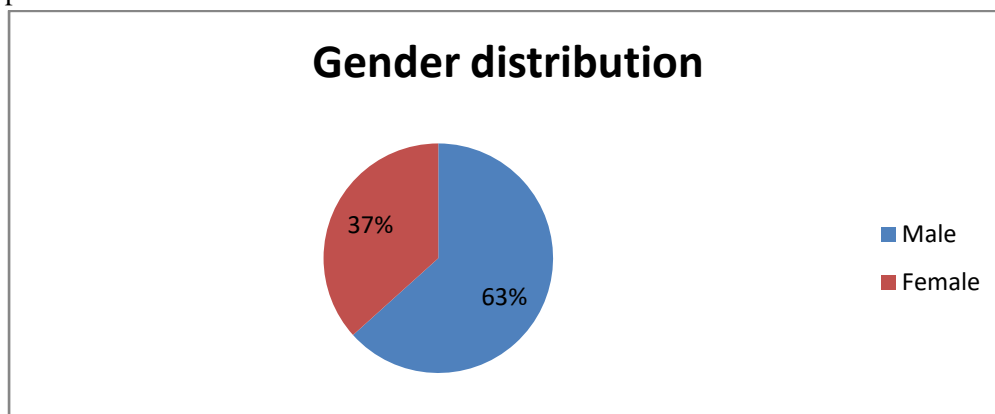


Table - 1: Diagnosis on triple biopsy (N=120).

1. Definite vasculitis (n=4)	
Nerve	4
Muscle	1
Skin	0
Muscle and nerve	1
Muscle, nerve and skin	0
2. Probable vasculitis (n=10)	
Nerve	10
Muscle	0
Skin	0
3. Moderate perivascular inflammation (n=3)	
Nerve	1
Muscle	0
Skin	2
4. Mild perivascular inflammation (n=16)	
Nerve	1
Muscle	3
Skin	11
Skin and Muscle	1
5. Negative for vasculitis or perivascular inflammation (n=82)	
Total number of cases	
	120

Table - 2: Details of definite vasculitic cases.

Sr. no.	Age	Sex	ANA	Histopathological findings		
				Nerve	Muscle	Skin
1	52	M	2+	Granulomatous Vasculitis	Granulomatous Vasculitis	Moderate perivascular inflammation
2	62	M	Neg.	Chronic vasculitis	Mild perivascular inflammation	NO
3	25	M	Neg.	Definite vasculitis (Churg Strauss is a possibility)	Dermatomyositis	Mild perivascular Inflammation
4	60	F	3+ (homogenous)	Chronic vasculitis	Mild perivascular inflammation	NO
Definite Vasculitis				4/4	1/4	0/4

M=Male, F: Female, N=Normal, NO: No evidence of vasculitis or perivascular inflammation.

Table - 3: Overall usefulness of triple biopsy.

Biopsy	Definite vasculitis	Probable vasculitis
Nerve biopsy	3.33%	8.3%
Combined nerve and muscle biopsy	0.8%	0%
Triple skin, nerve and muscle biopsy	0%	0%

As per **Table – 1**, about the diagnosis on triple biopsy showed that definite vasculitis was seen in 4 cases out of 120 cases. Total 10 cases showed probable vasculitis, 3 cases showed moderate perivascular inflammation and 16 cases showed mild perivascular inflammation. Rest all 82 cases were negative for vasculitis or perivascular inflammation.

On evaluation the usefulness of triple biopsies for vasculitis, we found a very low diagnostic yield with only 3.3% of peripheral nerve biopsy and 0.8% of muscle and nerve biopsy shows definite vasculitis (**Table - 3**). Of this triple biopsy it was this nerve biopsy that yielded the highest incidence of vasculitis with all 4 cases diagnosed definite vasculitis showing changes of vasculitis. On the other hand only 1 out of 4 cases showed in muscle (**Table - 2**). None of the skin biopsies showed evidence of vasculitis. We noted that majority of a skin biopsies were superficial and did not include the subcutis. This input explains the low diagnostic yield of the skin biopsy.

Recommendations

- In case of suspected peripheral/ systemic vasculitic neuropathy, nerve biopsy is sufficient in the majority of case and has the diagnostic armamentarium for the evaluation of vasculitis.
- It's better to avoid skin biopsy as routine protocol for any suspected case of vasculitis, unless there are definite systemic, clinical and serological features suggestive of small vessel

vasculitis. In such cases a skin biopsy must include the subcutis.

Conclusion

In conclusion, nerve biopsies provide the best yield for the diagnosis of vasculitis, as opposed to muscle and skin biopsies. The role of triple biopsies as a routine protocol for the evaluation of vasculitis is questionable.

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